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Neurophysiology of visually-guided eye movements:

Critical review and alternative viewpoint

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ABSTRACT (241 words):

In this article, we perform a critical examination of assumptions which led to assimilate measurements of the movement of a rigid body in the physical world to parameters encoded within the brain activity. In many neurophysiological studies of goal-directed eye movements, equivalence has indeed been made between the kinematics of the eyes or of a targeted object and the associated neuronal processes. Such a way of proceeding brings up the reduction encountered in projective geometry when a multidimensional object is being projected onto a one-dimensional segment. The measurement of a movement indeed consists of generating a series of numerical values from which magnitudes such as amplitude, duration and their ratio (speed) are calculated. By contrast, movement generation consists of activating multiple parallel channels in the brain. Yet, for many years, kinematical parameters were supposed to be encoded in the brain activity, even though the neuronal image of most physical events is distributed both spatially and temporally. After explaining why the "neuronalization" of such parameters is questionable for elucidating the neural processes underlying the execution of saccadic and pursuit eye movements, we propose an alternative to the framework which dominated the last five decades. A viewpoint is presented where these processes follow principles which are defined by intrinsic properties of the brain (population coding, multiplicity of transmission delays, synchrony of firing, connectivity). We propose to reconsider the time course of saccadic and pursuit eye movements as the restoration of equilibria between neural populations which exert opposing motor tendencies.

"*Facts and theories are natural enemies. A theory may succeed for a time in domesticating some facts, but sooner or later inevitably the facts revert to their predatory ways. Theories deserve our sympathy, for they are indispensable in the development of science. They systematize, exposing relationship between facts that seemed unrelated; they establish a scale of values among facts, showing one to be more important than another; they enable us to extrapolate from the known to the unknown, to predict the results of experiments not yet performed; and they suggest which new experiments may be worth attempting. However, theories are dangerous too, for they often function as blinkers instead of spectacles. Misplaced confidence in a theory can effectively prevent us from seeing facts as they really are*" (Wilkie 1954)

VISUOMOTOR TRANSFORMATION AND ITS NUMERICAL PROCESSING

The procedures used to measure the movement of a rigid body (eyeball or object) influence the neurophysiological study of visuomotor transformation through notions which either distort the underlying neuronal processes or even have no substrate. To start with the simplest example, it is frequent to read that gaze direction (or the line of sight) is shifted from one point to another. Attributing point-like values (coordinates) to gaze and target inevitably leads to numerical differences, especially when the measurements are made with high resolution. However, numerical differences do not imply corresponding mismatches in the brain activity. Objects in the physical world are obviously not mathematical points and visual fixation does not involve a fovea composed of one single photoreceptor where all light beams would converge. Because of the divergence of anatomical projections, any object leads to the excitation of a large number of neurons. When we record their emission of action potentials, we discover that neurons (visual-only, visuomotor or motor) have a

spatially extended response field. This extent indicates that any object in the visual field or any saccade is associated with the excitation of a large set of cells (e.g., McIlwain 1976; Sparks et al. 1976). Moreover, in many visual and visuomotor regions of the cerebral cortex, as in the superior colliculus (SC), neurons are laid out such that neighboring cells respond to the stimulation of neighboring regions of the visual field, or fire a burst of action potentials during saccades to neighboring locations in the physical world. In spite of the divergent connectivity, retinotopy is preserved.

The consequence is that neighboring objects, or saccades toward their location, excite populations of neurons which overlap. This functional overlap is overlooked when the focus is made onto the numerical difference between the gaze and target directions, an error considered to be the command specifying the goal of gaze orientation. Indeed, the overlap could participate in movement triggering insofar as gaze may not be shifted as long as the visuo-oculomotor system remains within a mode where opposite commands counter-balance each other (Fig. 1). In some experimentally-induced pathological disorders (cerebellar: Guerrasio et al. 2010; Sato and Noda 1992; corticofrontal: Dias and Segraves 1999; collicular: Goffart et al. 2012) and even normal cases (Goffart et al. 2006), stable fixation is engaged even though gaze is not directed toward the target center but toward an offset location. No eye movement is triggered in spite of a numerical difference between gaze and target directions (non-zero error). Likewise, an altered balance between opposing commands can explain the offset of head direction with respect to a food target during a collicular or cerebellar lesion (Goffart and Pélisson 1998; Isa et al. 1992). The neural processes specifying the location where to look during fixation or where to direct the head may not specifically involve an “encoding” of spatial attributes (such as gaze, head or target directions and their difference) but a balance of activity between sets of neurons exerting

87 opposite directional tendencies (as documented in the cat brainstem by the group of
88 Yoshikazu Shinoda; e.g., Takahashi et al. 2005, 2007, 2010). From this viewpoint, changes of
89 gaze direction (during saccade and pursuit) do not result from reducing differences between
90 signals encoding kinematical parameters. The movement is the behavioral outcome of a
91 transition from an unbalanced state of activities to equilibrium of opposing tendencies
92 distributed in several regions of the brain. Thus, we can understand why alterations of
93 saccade velocity happen during functional perturbation of regions (SC: Sparks et al. 1990;
94 frontal eye field: Dias and Segraves 1999) which are classically considered as encoding the
95 location where to look (Dassonville et al. 1992; Hanes and Wurtz 2000; Sparks 1989, van
96 Horn et al. 2013).

97 **Figure 1 approximately here**

98 Contemporary techniques enable to measure eye movements with such high
99 temporal resolution that numerical estimates of instantaneous velocity and acceleration can
100 be calculated. Thus, we discover that up to some amplitude, a saccade exhibits a bell-shaped
101 velocity profile and that maximum velocity and duration increase with saccade amplitude
102 (Fuchs 1967; Westheimer 1954). Attempts were then made to study how the instantaneous
103 firing rate of neurons could account for the current velocity or acceleration of eye
104 movements. However, we must keep in mind the fact that while a saccade is the behavioral
105 outcome of flows of activity distributed within the brain (between the optic and extraocular
106 motor nerves) and unfolding from target onset time to saccade landing time, the velocity
107 profile is the outcome of a transformation performed over a shorter time interval within a
108 numerical line. Between the brain activity and the behavioral measurements, a kind of
109 geometrical projection is made between a multidimensional object and a one-dimensional

segment. Moreover, if the sampling of eye position did not systematically start from the same threshold or its rate was not constant from one measurement to the other, matched-amplitude saccades would erroneously exhibit different velocity profiles. And yet, when the time course of neurons' firing rate varies from one measurement to the other and differs from the time course of precisely measured saccades, we do not suspect a "neuronal sampling" problem. The notion of "noise" is put forward and considered as a biological phenomenon, as if the firing rate ought to precisely fit with the dimensionality of measurement. Variable discharges can result from the fact that eye movements are not the unique output that the activity of central neurons can influence: spikes can also be emitted as part of processes which do not lead to saccadic or pursuit eye movements. Neuroanatomical and electrophysiological studies indeed teach us that neurons do not form a homogeneous population: those which exhibit target- or eye movement-related activities are diverse and project to a multitude of regions in the brain (Moschovakis et al. 1996). Even though thermodynamic laws govern the cellular and molecular processes (Choquet and Triller 2013) and can account for the variability of neural discharges, the latter can also be caused by the measurement itself, i.e. by the fact that we map (like in projective geometry) a multidimensional physiological phenomenon (with time-overlapping processes) onto one single series of totally-ordered numerical values (i.e., eye position values ranked according to their time stamp). Mapping the change of neuronal activity to the velocity of the movement of a rigid body (eyeball or object) supposes a one-to-one correspondence between a time series of numerical values on the one hand, and the time course of multiple and parallel flows of activity within the visuomotor brain on the other hand. Supposing such a correspondence is a reduction which overlooks the fact that the brain activity corresponding to any situation (measured here and now) is not reducible to a point of coordinates (x,y,z,t).

134 Spatially and temporally distributed in the brain (e.g., Nowak and Bullier 1997; Schmolesky
135 et al. 1998), the activity does not change like the measured coordinates of a moving body.
136 For example, when we study the action potentials that saccade-related neurons in the
137 superior colliculus (SC) emit during saccades toward a moving target, we discover that the
138 population of active neurons does not change as fast as the target, that residual activity
139 related to recently travelled locations persists (Keller et al. 1996b; Goffart et al. 2017b). Also,
140 when we study saccades toward a transient moving target (Quinet and Goffart 2015a) or eye
141 movements pursuing a target which suddenly disappears (Mitrani and Dimitrov 1978), we
142 find many instances where gaze is directed toward locations where the target never went,
143 signaling the mass of neural activity that persists beyond the time when a physical event
144 ends.

145 Diverse kinematical parameters (position, velocity and acceleration errors) are
146 considered as signals "encoded" in the firing rate of neurons and the relationship between
147 their linear combination and the firing rate has been statistically tested over more or less
148 limited time intervals (e.g., Sun et al. 2017). The activity of single neurons in various brain
149 regions is then proposed to convey kinematical functions. Depending upon the location of
150 recorded neurons, such statistical procedures become questionable because they assume
151 that the signals (action potentials) are transmitted across a medium identical to the physical
152 medium (continuous, homogeneous and with orthogonal spatial and temporal attributes).
153 Techniques have indeed been developed to make continuous the firing rate and to study
154 linear correlations. However, the establishment of this continuity would be misleading if the
155 parameter critical in neural transmission were not the time course of action potentials but
156 the membrane potential and the timing (synchrony) of presynaptic action potentials

157 “bombarding” the recorded neuron. These action potentials are emitted by presynaptic
158 neurons distributed in several brain regions at times which are not necessarily synchronous.

159 When we consider for example the discharge of motor neurons which innervate the
160 extraocular muscles, the correlation between the saccade kinematics and the sequence of
161 action potentials can be interpreted relatively well because the latter cause the contraction
162 of extraocular muscle fibers which in turn, exert the torque responsible for the rotation of
163 the eyeball (e.g. Sylvestre and Cullen 1999). However, if we now turn to the premotor
164 neurons innervating the motor neurons, the interpretation is complicated by the fact that
165 several inputs converge onto the motor neurons. The motoneurons indeed receive input
166 from excitatory burst neurons located in the ipsilateral paramedian reticular formation
167 (Strassman et al. 1986a), from inhibitory burst neurons in the contralateral medullary
168 reticular formation (Strassman et al. 1986b) and from burst-tonic neurons located bilaterally
169 in the left and right nuclei prepositus hypoglossi and medial vestibular nuclei (Moschovakis
170 et al. 1996; Scudder et al. 2002; Sparks 2002). The discharges of these different groups of
171 neurons do not exhibit identical time courses. Consequently, since the input to the
172 motoneurons originate from neurons distributed across different origins, the correlation
173 between the firing rate and the saccade kinematics becomes weakened. We realize then
174 that the correlation inevitably becomes misleading when we study the firing rate of neurons
175 which innervate those premotor neurons, like those located in the SC (Sparks and Gandhi
176 2003) or the caudal fastigial nuclei (Kleine et al. 2003).

177 One possible way to “save” the correlation between the spiking discharge and the
178 kinematics would be to retrogradely track the origin of action potentials converging more or
179 less synchronously onto the recorded neurons. However, this analysis is complicated by the

fact that afferent signals are transmitted with diverse conduction speeds through axons of also diverse lengths. In other words, the firing of a premotor neuron can be driven by action potentials which are emitted at different times by presynaptic neurons located in different regions. Thus, the time interval during which we estimate the instantaneous velocity of a measured eye movement is the outcome of action potentials emitted during a different but also longer time interval. The picture is further complicated by the fact that the neural transmission depends on the location of synaptic contacts (de No 1938) onto the cell (soma and/or dendrites) whose intrinsic properties also influence the time course and pattern of spiking discharge (e.g., Bras et al. 1987; Durand 1989). Finally, a more macroscopic viewpoint reveals that the activity does not remain bounded but spreads toward neighboring cells as shown in the superior colliculus (Anderson et al. 1998; Sparks et al. 1976) and primary visual cortex (Muller et al. 2014). In summary, the interpretation of the correlation between the firing rate of central neurons and the kinematics of eye movement should be made while reminding these limitations.

For assessing the changes taking place within the brain activity while a target is moving across the visual field or while gaze captures and pursues it, there is no logical necessity to pair the firing rate with kinematical notions; it is simplicity and convenience which led to make this choice (Poincaré 1921). Moreover, as Pellionisz and Llinás (1982) explained, the classical usage of separate space and time coordinates may not be applicable in the case of describing the inner workings of the CNS (see also Buzsáki and Llinás 2017). When we say that target velocity is the stimulus driving pursuit eye movements, such a relation should be restricted to the sets of numerical values which belong to the same medium (the physical world) and for which the kinematics has proven its efficiency. This medium is different from the inner functioning of the brain. From the optic nerve to the

oculomotor nerves, the neural activity does not go through a medium which is neutral, homogeneous, isotropic, continuous and uniform. Imagining that a mathematical differentiation has been performed is questionable because neural activities are not reducible to points. The time series of measurements is a continuum which is not homeomorphic to the fundamentally parallel and distributed aspect of neurophysiological processes, at both the cellular and network levels.

All these fundamental pitfalls do not lead the neurophysiology of movements to a dead end but toward the necessity of establishing more solid grounds. We are going to discuss the models which consider error signals as stimuli driving the execution of saccadic and pursuit eye movements.

POSITION ERROR AND THE FEEDBACK CONTROL OF SACCADE AMPLITUDE

The simplest solution that has been proposed to model saccade execution is a process which reduces the difference (negative feedback loop) between a desired position of the eyes (an estimate of the selected target location) and an estimate of their current position. If we assume the neural encoding of such spatial attributes (instead of a neural encoding of desired and actual works for example), they must be expressed in the same reference frame, for example relative to the trunk (Robinson 1975; Laurutis and Robinson 1986). In this framework, the motor error signal that results from their comparison feeds the premotor neurons which themselves fire at a rate proportional to the size of the error. As gaze moves toward the target, the error diminishes and the firing of premotor neurons declines until they cease firing and stop exciting the motoneurons (Robinson 1975). This

viewpoint was refined a few years later by replacing the encoding of position by an encoding of displacement (change in position; Jürgens et al. 1981). This displacement model was proposed as a possible alternative because electrophysiologists failed to find, in the visuomotor neuronal network, cells whose activity would signal the location of a target relative to the trunk. Instead, the large majority of encountered neurons ("visual" or "visuomotor") exhibit a response field which moves with the eyes; they emit action potentials whenever a stimulus appears within a bounded region of the visual field (retinotopically defined). The feedback signal has then been replaced by a signal encoding the eye displacement. Saccades would be driven by the same motor error signal; the only thing that has changed is the input (reference) and the signals updating the motor error.

The concept of negative feedback loop was well-accepted because it was a convenient and simple solution to a more fundamental question: the so-called "spatiotemporal transformation", i.e., how a locus of activity (in the retina or in the SC) is transformed into a duration of motor neuron activity (Moschovakis et al. 1996, 1998; Scudder et al. 1992; Sparks 2002). The solution was simple since it removed the need to search within the brain activity a process encoding the duration of saccades, as initially proposed in the chronometric hypothesis of Hans Kornhüber (1971). With the negative feedback control, there is no need for an internal chronometer; the saccade duration is a secondary by-product of the process reducing the mismatch between two spatial magnitudes (position or displacement) that some other processes would somehow estimate. The difference between the two proposed options ("position" versus "displacement" options; Sparks 1989; 1999) is that the feedback signals must be "zeroed" after the end of each saccade in the displacement model. Otherwise, the combination of residual eye movement-related signals with signals elicited by the appearance of another target would

250 lead to inaccurate saccades toward its location. A series of experiments were performed to
251 confront these two hypotheses and refute the “position” option (Nichols and Sparks 1995).
252 However, the question was reopened by following experiments (Keller et al. 1996a) until the
253 suggestion was made that the eye position feedback signals do not follow the same time
254 course as the physical eye position (Schlag et al. 1998). For the first time, a mismatch was
255 considered between on the one hand, the time course of eye position encoding, and on the
256 other hand, the time course of the physically measured eye position. Indeed, the neural
257 signals would precede saccade onset, change as the eyes move, though not as fast, and lag
258 the end of the saccade.

259 The feedback loop hypothesis is a conceptual framework which has been admittedly
260 useful to generate experiments, make new observations and interpret them. However, it
261 also seems to be irrefutable insofar as it assumes signals and processes which cannot be
262 negated if they do not exist. A first difficulty is brought up by the interpretation of saccade
263 inaccuracy during cerebellar dysfunction. This dysmetria has been considered as resulting
264 from an altered neural estimate of eye movement amplitude (Keller et al. 1983; Keller 1989;
265 Goffart et al. 1998; Goffart et al. 2004). Unfortunately, the origin of feedback signals carrying
266 eye movement-related information remains unknown. Proprioceptive signals from
267 extraocular muscles have been excluded because saccade accuracy is not altered after their
268 deafferentation (Guthrie et al. 1983; Lewis et al. 2001). The exclusion of extraocular
269 proprioception is also supported by the observation that saccades electrically-evoked (by
270 microstimulation in the fastigial nucleus or the pontine reticular formation) while a saccade
271 is being prepared toward a visual target are not subsequently corrected (Noda et al. 1991;
272 Sparks et al. 1987). Contrary to the cases where the microstimulation is applied in the frontal
273 eye field or the SC (Schiller and Sandell 1983; Sparks and Mays 1983), the visual saccade

274 misses the target by an error equal to the electrically-evoked displacement. If proprioceptive
275 signals were involved in the feedback control, gaze should aim at the target after the
276 perturbation.

277 Corollary discharge (efference copy or *sui generis* sensation) was the proposed
278 explanation. However, the problem is complicated by the fact the eye movement-related
279 signals from tonic neurons in the nucleus *prepositus hypoglossi* (NPH) and the medial
280 vestibular nucleus (MVN) can also be excluded since their lesion does not alter saccade
281 accuracy (Cannon and Robinson 1988; Kaneko 1997). If the estimate of gaze direction is not
282 fed by proprioceptive signals or by tonic signals which directly drive the motor neurons, the
283 question how it is built remains unanswered. On the basis of neuromimetic modeling, the
284 suggestion was made that the signals imagined in the models may not be explicitly conveyed
285 by separate groups of neurons that neurophysiologists ought to identify. They would
286 correspond to activities involving populations of neurons that are massively interconnected
287 and distributed over several neuronal territories (Robinson 1992). In other words, the signals
288 involved in the feedback control are not tractable by classical unit recording techniques. The
289 major question then becomes to discover the spatiotemporal architecture of the network.

290 While the feedback control hypothesis encountered these complications for
291 experimental testing, the chronometric hypothesis of Kornhüber (1971) was being revisited
292 by the group of Peter Thier (2011). Putting the emphasis on the temporal measurements of
293 saccades, this group suggested that the population response of Purkinje cells in the
294 cerebellum gives a precise temporal signature of the onset and offset of saccades.
295 Unfortunately, the population response was defined ad hoc: the onset and offset of the
296 population response were defined as the activity which is four times the mean baseline

activity. If different thresholds were used to quantify the timing of the population response, then the chronometric hypothesis would not be valid anymore. Moreover, the population was restricted to the subset of Purkinje cells which enhance their firing, ignoring those which have been shown to reduce their firing during saccades (Herzfeld et al. 2015; Soetedjo and Fuchs 2002; Suzuki and Keller, 1988). Finally, the duration of the population burst does not increase when the size of saccades is experimentally enhanced with a paradigm called saccade amplitude adaptation (Catz et al. 2008). This result could have been considered as a refutation of the chronometric hypothesis, but another ad hoc argument (fatigue) was added to maintain a viewpoint which assimilates learning to an "optimization of a representation of time" (Thier et al. 2000) rather than to the modification of flows of activity within the brain networks.

Negative feedback control has also been proposed for the guidance of eye movements toward a moving visual target. Two main processes would operate in parallel (more or less independently): one process reduces the mismatch between gaze and target directions (see above) while the other reduces the velocity difference (velocity error) between the eye and target movements. Before discussing this hypothesis, we are going to examine how the notion of target velocity (a notion which belongs to the language of kinematics) was introduced in the physiological sciences.

IS PURSUIT DRIVEN BY A TARGET VELOCITY NEURAL SIGNAL?

A little more than five decades ago, Rashbass (1961) designed a task where the eyes, instead of making a saccade to a target moving toward the foveal field, drift away from it. They move away but in the same direction as the target motion, though with a lower speed. This observation was taken as evidence for considering target velocity as a stimulus driving

320 the initiation of pursuit eye movements. In Rashbass' task, the target appears at a location
321 slightly eccentric in one visual hemi-field (e.g. to the left) and moves slowly toward the
322 foveal field (toward the right). Then, for a few tens of milliseconds, the eyes also move
323 slowly in the same direction as the target (but away from its physical location). To observe
324 this slow eye movement with no visible saccade, the target must start its motion from a
325 location whose eccentricity is approximately 0.15 to 0.2 times its speed. In most
326 experiments, the target moved with a constant speed less than 10°/s, requiring a target
327 motion onset from a 2 degrees eccentric location. Thus, the target center was located at the
328 boundary of the foveal field. Obviously, a target, even a very small spot of light does not
329 excite one single cell but many cells. In the SC for example, regardless of whether the target
330 is located in the peripheral or central visual field, a large population of neurons is recruited
331 and occupies a territory corresponding to several degrees of visual angle (Anderson et al.
332 1998; Goossens and van Opstal 2006; Hafed et al. 2008; Hafed and Krauzlis 2008;
333 Moschovakis et al. 2001; Sparks et al. 1976). A saccade is not launched toward the
334 centripetal target because the equilibrium which specifies gaze direction is not broken; the
335 visuo-saccadic oculomotor system is within a mode where opposite commands counter-
336 balance each other (see the first section).

337 By contrast, the drift of the eyes (in the same direction as the target motion) tells us
338 that initiating a slow eye movement involves another symmetry breaking. It results from an
339 imbalance between commands that tonic neurons in the left and right NPH/MVN exert upon
340 the motoneurons (McFarland and Fuchs 1992; Scudder et al. 1992). Their equilibrium (akin
341 to the one shown in Fig. 1) can be broken by an imbalance of excitation, for instance in their
342 visual input from the pretectum, i.e., an imbalance between the left and right nuclei of the
343 optic tract (NOT). Thus, in the Rashbass' paradigm, an imbalance between opposite

344 directional tendencies could drive the eyes in the same direction as the target. This
345 explanation is consistent with observations made after unilateral inactivation of NOT: the
346 monkey exhibits an irrepressible drift of the eyes toward the contralesional side (Inoue et al.
347 2000; our unpublished results). The fact that the drift occurs even in presence of a central
348 visual target (Fig. 2) indicates that the bilateral activity which in the SC maintains gaze
349 direction steady is not sufficient to counteract the drift caused by the imbalance of NOT
350 activity. After some time, a correction saccade is made back toward the central target; the
351 bilateral equilibrium supported by the fastigiocollicular activities (Goffart et al. 2012;
352 Guerrasio et al. 2010; Krauzlis et al. 2017) has been broken by the recruitment of saccade-
353 related cells.

354 **Figure 2 approximately here**

355 Such a slow drift does not happen during unilateral SC inactivation: the monkey is
356 able to maintain stable gaze. Its direction is offset with respect to the target with an angle
357 which is relatively constant even while the monkey is pursuing a moving target (Hafed et al.
358 2008). Despite the mismatch between gaze and target directions, the pursuit is preserved.
359 Comparable observations have been reported during caudal fastigial inactivation (Robinson
360 et al. 1997; see figures 1 in Bourrelly et al. 2018a, 2018b). Made in experimentally-induced
361 pathological conditions, these observations indicate that the target does not have to be
362 centered within the foveal field for being smoothly pursued. As a matter of fact, several
363 behavioral experiments in the normal subject have demonstrated this possibility (Fuchs
364 1967; Pola and Wyatt 1980; Robinson 1965; Segraves and Goldberg 1994; Winterson &
365 Steinman 1978). In summary, during the Rashbass' paradigm, a velocity signal is not the
366 unique explanation accounting for the observation that the eye moves away from the target.

The motion of the target image across the foveae yields an imbalance of activity between the left and right NOT (Gamlin 2006; Hoffman et al. 2009; Mustari and Fuchs 1990). Interestingly, the retinal motion declines while the eyes accelerate. What remains to be understood then is how the slow eye movement persists and increases to reach the same speed as the target, in spite of the reducing “velocity error”.

The idea that pursuit consists of matching the velocities of eye and target movements can be traced back to the studies of Rashbass (1961) and Robinson (1965). It pervades so much the contemporary sciences of eye movements that in most reviews, pursuit eye movements are considered as involving a negative feedback loop for reducing the difference between estimates of eye and target velocities complemented by a positive feedback loop for sustaining the movement when the velocity error is zeroed (e.g., Barnes 2006; Carpenter 1988; Fukushima et al. 2013; Lisberger et al. 1987; Leigh and Zee 2006; Robinson et al. 1986).

Yet, Raymond Dodge, one of the earliest scientists who analyzed the time course of eye movements, reported that "*since the pursuit movements invariably lag, they alone would give very erroneous data concerning the velocity of the object*" and that "*direct observation of an eye, following a uniformly moving object, discloses a relatively complex phenomenon, which apparently includes at least two distinct kinds of eye movements. A succession of rapid, jerk-like movements are separated by what appear to be longer regular movements of less velocity*"(Dodge 1903). He also indicated that "*even in slow movements of the object of regard, in which the twenty degrees was covered in about three seconds, the little jerks still persisted, though they were of extremely small amplitude. Since the velocity of the true pursuit movements constantly decreased with the velocity of the object of regard, it*

seems probable that we must regard the auxiliary jerks of the first type as constant accompaniments of the pursuit movements; and since they always appear in the direction of the pursuit, they indicate that the true pursuit movement tends to lag a little, and is supplemented from time to time by movements of the first type" (Dodge 1903).

The saltatory (not smooth) aspect of eye movements tracking a visual target has been notified in several other studies. Puckett & Steinman (1969) observed a mismatch between the velocity of pursuit eye movements and the constant velocity of a moving target whereas Steinman et al. (1969) documented that highly experienced subjects were unable to match eye to target velocity, even when they voluntarily tried to do so. Interestingly, neither subject was able to make slow eye movements faster than the target. A few years later, Kowler et al. (1978) observed that the pursuit eye movements could only match the target velocity after considerable practice. During almost daily practice for a month, the performance of one subject gradually and systematically rose to quasi-complete velocity matching. Whitteridge (1960) reported comparable observations by Stroud (1950).

In the monkey, Fuchs (1967a) reported that "*when first presented with a high velocity ramp, some monkeys also have difficulty attaining target speed. The response to the first presentation of a 30 deg/sec ramp is usually composed entirely of closely spaced […] saccades with no attempts to match target velocity. Only two target presentations later the monkey [Macaca Speciosa] already tries a velocity correction although the movement is still primarily saccadic. Finally, after a total of about forty presentations, the monkey has mobilized his smooth response so as to be able to track the target for a sustained period of time*." Another study reports that one of their animals (*Macaca Mulatta*) made mostly saccadic eye movements to the target motion and only occasional smooth pursuit (Neary et

al. 1987). However, after they employed "*a modified training procedure which required the monkey to accurately track a moving target and thus presumably pay close attention to its motion (the monkey had to keep its eye within an "electronic window" which moved along with the target, to obtain the reward), the monkey began to show vigorous smooth pursuit movements to the square-wave target motion"* (see also Neary 1986).

The evolution of oculomotor tracking with practice has recently been documented in a study testing a relatively large number of naive rhesus monkeys (*Macaca Mulatta*). In this study, Bourrelly et al. (2016) show how inexperienced monkeys track a visual target that moves with a constant speed along a horizontal path and how the time course of their tracking eye movements gradually evolves across several days of practice with barely any spatiotemporal constraints. Indeed, the "electronic window" around the moving target within which the monkey had to direct its gaze was very large (10–12° horizontally and 6–10° vertically). If a smaller window had been used, the monkeys would have failed to track the target and the trial would have been aborted. It is therefore not surprising that studies that used small electronic windows report faster pursuit eye movements. They were faster because the visual tracking was selected by experimental constraints to become so, smooth and devoid of saccades. In the study of Bourrelly et al. (2016), catch-up saccades were permitted, especially those which would aim at a future location of the target (because the electronic window extended beyond the current target location). However, these "predictive" saccades landing ahead of the moving target just did not happen; gaze direction lagged behind the target most of the time. With practice, more trials appeared during which gaze moved as if it were "attached" to the target. Initially, the monkeys did not exhibit such a smooth tracking; it was mostly saltatory, i.e., composed of catch-up saccades. From this initial state where the gaze tracked a past target location most of the time, the behavior

437 evolved with successive trials and daily sessions to a mode where gaze appeared more often
438 locked onto the current target location (Fig. 3).

439 While most studies viewed this improvement as a gain increase in the positive
440 feedback loop, to our knowledge, none of them explained what this gain change meant in
441 neurophysiological words. Recently, the proposal was made that the enhancement of
442 pursuit velocity could result from the recruitment of neurons in pursuit-related regions
443 targeted by the oculomotor cerebellum and/or from the acquisition of a saccade-contingent
444 burst by pursuit-related neurons (Bourrelly et al. 2018b; Goffart et al. 2017a). Finally,
445 although the target moved along the same horizontal path and the reward was always given
446 at the end of the trial, the monkeys did not make saccades directly toward the rewarded
447 location. Given the large extent of the electronic window, such saccades would not have
448 been punished either.

449 This oculomotor performance was "mathematically" simulated and reproduced using
450 dynamic neural field models (Quinton & Goffart, 2018). In such models, a population of
451 topologically organized units (themselves representing assemblies of neurons) drives the eye
452 movements, with delays and projections expanding the population of active units. By
453 altering the projections through a simple learning mechanism, the velocity of simulated
454 pursuit eye movements was progressively increased, making it possible to synchronize the
455 eye movement with the target motion; the number of catch-up saccades diminished as a
456 consequence.

457 **Figure 3 approximately here**

458 At this point, the idea that velocity error would be the signal that spontaneously
459 drives the pursuit eye movements becomes questionable since the ability to move the eyes

with the same velocity as the target appears to be the outcome of a learning (training) procedure (see also Botschko et al. 2018). Using a task that required the foveation of a small circular target in order to identify the orientation of striae contained inside (dynamic visual acuity), Barmack (1970a) trained a monkey to execute horizontal pursuit eye movements at velocities of up to a maximum of 140 deg/s. However, no information was given about the time taken to reach this performance. Human subjects are capable of executing pursuit eye movements of 90 deg/s but after a few saccades were made. Neil Barmack suggested that the discrepancy did not result from different amounts of practice, but from different testing conditions. Indeed, by requiring the identification of details within the target, the dynamic visual acuity task might provide a greater incentive to accurately pursue the target. However, the question then is whether the task consists of matching the eye velocity to target velocity or maintaining the target foveation by matching the eye position to the target position, or, for those who do not wish to plunge spatial notions within the brain, balancing opposing tendencies emitted in the left and right parts of the brainstem.

EYE AND TARGET POSITIONS DURING TRACKING

In the majority of cases, whenever a target moves in the peripheral visual field, the first eye movement is an interceptive saccade. Contrary to the claim that "*in [their] programming…, target motion is used to predict the future target position so as to assure a spatial lead of the gaze at the saccade end, instead of attempting a precise capture of the target*" (Klam et al. 2001; see also Berthoz 2012), most behavioral studies show that the saccades are such that they do not direct gaze toward a location where the target will be in the future. They direct gaze either toward its current location or toward a location lagging behind (Barmack 1970; Bourrelly et al. 2016, 2018a; Fleuriet et al., 2011; Fuchs 1967a,

483 1967b; Keller and Johnsen 1990; Robinson 1965). The saccades do not orient the foveae
484 toward a location where gaze would wait for the target (like the traveler waits for a bus) to
485 enter within the foveal field and initiate the pursuit.

486 The fact that saccades do not aim at the future but the current location of a moving
487 object is strongly suggested by results of experiments during which the interceptive saccade
488 is perturbed by the application of a brief electrical microstimulation in the deep SC (Fleuriet
489 and Goffart 2012). Under such circumstances, the electrically-induced change in eye position
490 is corrected in flight or after a short delay, and gaze is brought back to the location where
491 unperturbed saccades would have landed at about the same time. This observation is
492 primarily made when the stimulation is applied at sites which are not involved in the
493 generation of the interceptive saccade (i.e., at sites which evoke saccades with amplitude
494 and direction close to those of the interceptive saccade). Otherwise, the interpretation is
495 complicated by interactions between the electrically- and visually-evoked activities. When
496 the microstimulation is applied in the SC opposite to the visually excited one, after the
497 electrically-induced change in gaze direction, most correction saccades do not overshoot
498 along the motion path. They do not bring gaze toward a location where the target will be
499 later; they either fall short or land accurately on the location where unperturbed saccades
500 would have landed (see Figs. 2-4 in Fleuriet and Goffart 2012 and also Fig. 4 in Goffart et al.
501 2017a). In these experiments, the target was made invisible for a brief interval (150 or 300
502 ms) to avoid that visual signals guide the correction.

503 Two groups of signals can participate in the elaboration of the command that guides
504 the interceptive saccade toward a transiently invisible target, regardless of whether its
505 trajectory is perturbed or not: i) the target motion-related signals which precede the interval

of target invisibility but also ii) mnemonic signals that the target is expected to reappear and continue to move along the same path. Concerning the first group of signals, it is quite possible that after the moving target disappears, activity persists within the visuomotor channels. The massive interconnectedness of neural populations in the brain likely contributes to the persistence of activity for durations which largely exceed the actual duration of the physical event (e.g., Mays and Sparks 1980; Sommer and Wurtz 2000; Edelman and Goldberg 2001). Behavioral studies suggest that the persistence is influenced by signals related to the target motion direction. As we said earlier, pursuit eye movement persists in the same direction beyond the time and location where a moving target disappeared (e.g., Mitrani and Dimitrov, 1978). Likewise, a significant proportion of saccades made in response to a transient moving target land on positions situated beyond the location where the target disappeared (Quinet and Goffart, 2015). Thus, the correction saccades reported in the perturbation experiments of Fleuriet and Goffart (2012) could be guided by residual visual signals. Concerning the second group of signals, the target reappeared 150 or 300 ms after its disappearance, continuing its motion along the same path with the same velocity. There was no uncertainty that the target would reappear and keep moving along the same path. The monkeys never experienced trials where the target would start moving backward or change its direction during the interval of invisibility. Moreover, they were not trained to only make a saccade toward the transient moving target (like in Quinet & Goffart 2015); they were rewarded after they continued to track the re-appeared target, until the end of the trial. Hence, additional central factors contributed to the guidance of correction saccades. If the residual signals which persist after target disappearance merge with prelude signals related to its upcoming reappearance, then the interval during which the target is absent is “filled” in by the brain activity. Such an

530 interpolation would drive the activity of premotor neurons and guide the eye movement,
531 regardless of whether it is a saccade or a pursuit eye movement. Therefore, the command
532 which encodes *at best* the expected and current (here-and-now) location of the target and
533 guides the gaze direction when a target becomes invisible, could correspond to a merging of
534 signals related to the recent past with signals carrying an expectancy of reappearing (built
535 upon the past and repeated experience). If this explanation holds also for any moving target,
536 constantly visible or briefly invisible, then its neural image does not need to be reduced to
537 an internal model of its trajectory (a physical notion) (see also Quinton and Girau 2011 for
538 similar observations *in sillico*).

539 GENERAL CONCLUSION

540 For several decades, the eye movements have been used as a probe to understand
541 how neuronal networks in the brain process visual signals and how they endow foveated
542 animals with the ability to locate a stimulus, even when it is moving. Notions of kinematics
543 were used to "decode" the firing rate of neurons and to explain the neurophysiology
544 underlying the generation of tracking eye movements. The appropriateness of these notions
545 to a medium radically different from the physical world (the brain) was not questioned. Yet,
546 an alternative explanation is possible: the maintenance of target foveation could consist of
547 dynamically balancing opposing tendencies emitted in the left and right parts of the
548 brainstem, as proposed for the control of saccade trajectory (Bourrelly et al. 2018a; van
549 Gisbergen et al. 1981; Goffart et al. 2004) and fixation (Goffart et al. 2012; Guerrasio et al.
550 2010). Regarding the question how eye movements can reach the target speed, the
551 acceleration could involve a process of neuronal recruitment: increasing the firing and the
552 number of motion-related neurons moves the eyes faster while decreasing them reduces the

553 velocity. Thus, the central problem for understanding the neural control of pursuit eye
554 movement becomes to characterize the adjustment of the appropriate population size
555 through recruiting neurons and synchronizing their firing rate.

556 Saccadic eye movements can also be used as a probe to study this question. Within
557 the SC and downstream, a neuronal recruitment seems to be involved also in determining
558 the total saccadic eye displacement, as suggested by recording and modeling studies (Sparks
559 et al. 1976; Badler and Keller 2002) and by perturbation experiments using microstimulation
560 (Quinet and Goffart 2015b; Sparks et al. 1987), local pharmacological inactivation (Goffart
561 2017; Goffart et al. 2017c) or the trigeminal blink reflex (Gandhi and Bonadonna 2005;
562 Jagadisan and Gandhi 2017). The use of moving visual stimuli should enable to investigate
563 whether this recruitment consists of including more neurons in the SC and/or more
564 synchronized firing in the reticular formation. Indeed, in response to identical brief target
565 motions (identical durations and displacements), the saccades not only land on different
566 location depending upon whether the target accelerates or decelerates, but their amplitude
567 also increases linearly with time when the target accelerates (Quinet and Goffart 2015a).
568 Finally, instead of grounding the encoding of eye velocity or acceleration in the sole firing
569 rate of single neurons, we propose that the dynamics of eye movements reflects the
570 transition from an unbalanced state to equilibrium between opposing motor tendencies. In
571 any case, the neural processes underlying the generation of eye movements follow
572 principles which are primarily defined by the intrinsic properties of the brain network and its
573 diverse neurons rather than the physical laws of motion.

574 Such a research should not be restricted to primates, but extended to other species,
575 even to invertebrates such as *Mantis religiosa* (Rossel 1980; Yamawaki et al. 2011) and

perhaps *Daphnia magna* (Consi et al. 1987) in order to discover how biologically more rudimentary bilateral structures enable animals to dynamically adjust the orientation of their visual organ toward the location of an object, static or moving. The use of such animals guarantees that we do not fall under the anthropocentric "*illusion that the relations an animal has with the objects in its environment take place in the same space and the same time as those which bind us to the objects of our human world. This illusion is fed by the belief in the existence of a unique world in which all living beings would be embedded. It follows the general and long-lasting conviction that there must be one single space and time for all living beings*" (von Uexküll 1956).

Regarding the mathematical modeling, novel techniques combining spiking neuron networks (Paugam-Moisy and Bohte 2008; Kasap & van Opstal 2017) and dynamic neural fields (Amari 1977) should be developed or created in order to complement those which, during the last five decades, overlooked the neuronal complexity and the parallel and distributed nature of visuomotor flows, and considered behavioral parameters as encoded within their nodes rather than as their ultimate outcome. As Claude Bernard wrote, "*our ideas are merely intellectual instruments which allow us penetrating inside the phenomenon; they must be changed after having fulfilled their role, like one change a blunt scalpel blade which has served after enough time*" (Bernard 1865).

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894 **LEGENDS OF FIGURES**

895

896 Figure 1: Visual fixation as equilibrium. A saccade may not be launched if the visuo-
897 oculomotor system is within a mode where opposite commands (presumably issued by the
898 left and right superior colliculi) counter-balance each other. The initiation of a slow eye
899 movement could involve the same symmetry breaking though with different groups of
900 neurons (see text).

901 Figure 2: Nystagmus observed after injecting a small amount of muscimol (0.6µl) in the left
902 nucleus of the optic tract. The eye drifts horizontally toward the contralesional side until a
903 saccade is made toward the left. The unilateral suppression of NOT signals causes an
904 imbalance of visual input to the nucleus prepositus hypoglossi, which itself affects the
905 balance of tonic input onto the abducens motoneurons.

906 Figure 3: Typical oculomotor behavior of a monkey tracking a visual target moving
907 horizontally with a constant speed. The horizontal eye position is plotted as a function of
908 time after the target motion onset for three trials recorded during the first (left column:
909 Beginning) and last training sessions (right column: End). The time course of horizontal
910 target position is illustrated by the red line. The selected trials were recorded in five
911 monkeys (A, B, C, M, and G: from top to bottom, respectively) when the target moved in the
912 upper right quadrant with a constant speed (20 degrees/s). During the other randomly
913 interleaved trials, the target moved similarly, horizontally and away from the vertical
914 meridian, but in the lower right, the lower left or the upper left quadrant. Additional
915 methodological information can be found in Bourrelly et al. (2016).

Figure 1

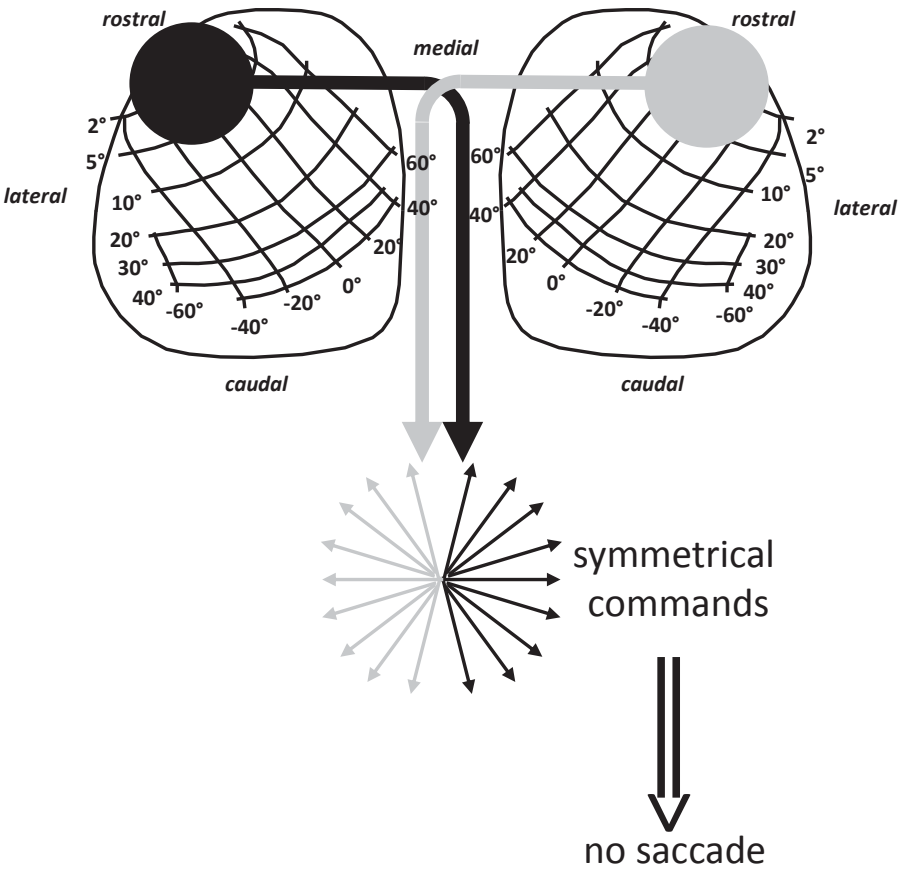

rostral
medial
rostral
2°
5°
lateral
10°
20°
30°
40°
-60°
-40°
-20°
0°
20°
40°
60°
60°
40°
20°
0°
-20°
-40°
-60°
40°
20°
30°
40°
2°
5°
10°
lateral
caudal
caudal
symmetrical
commands
no saccade

Figure 2

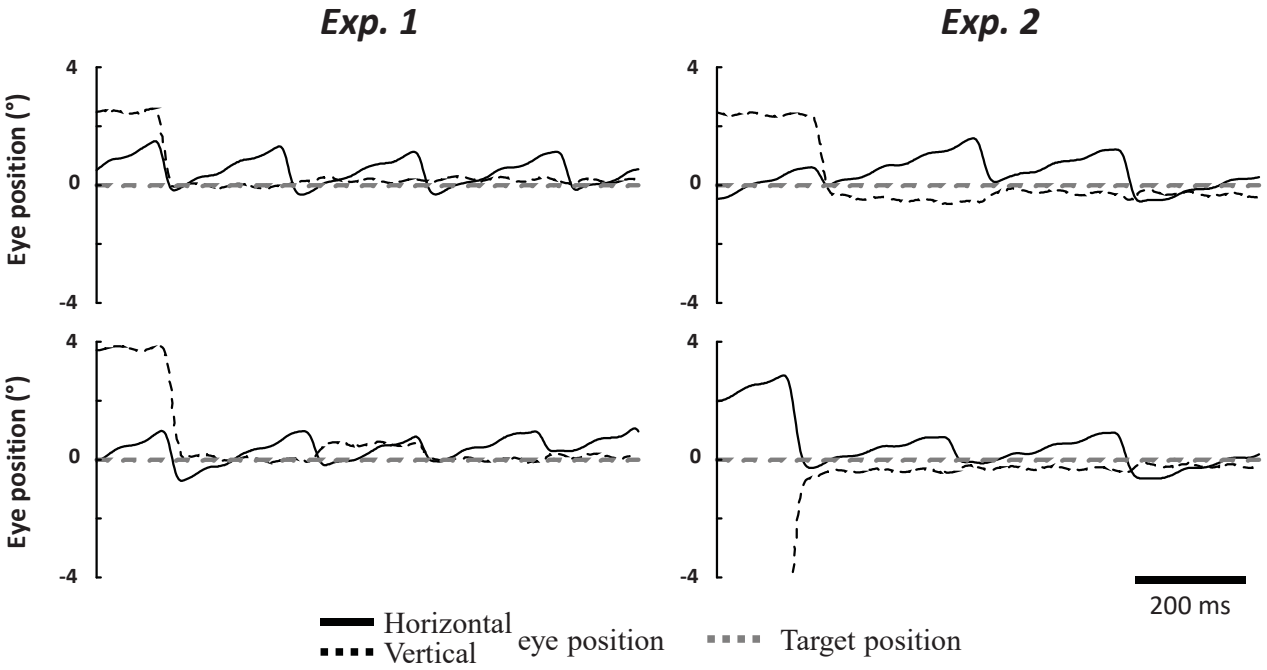
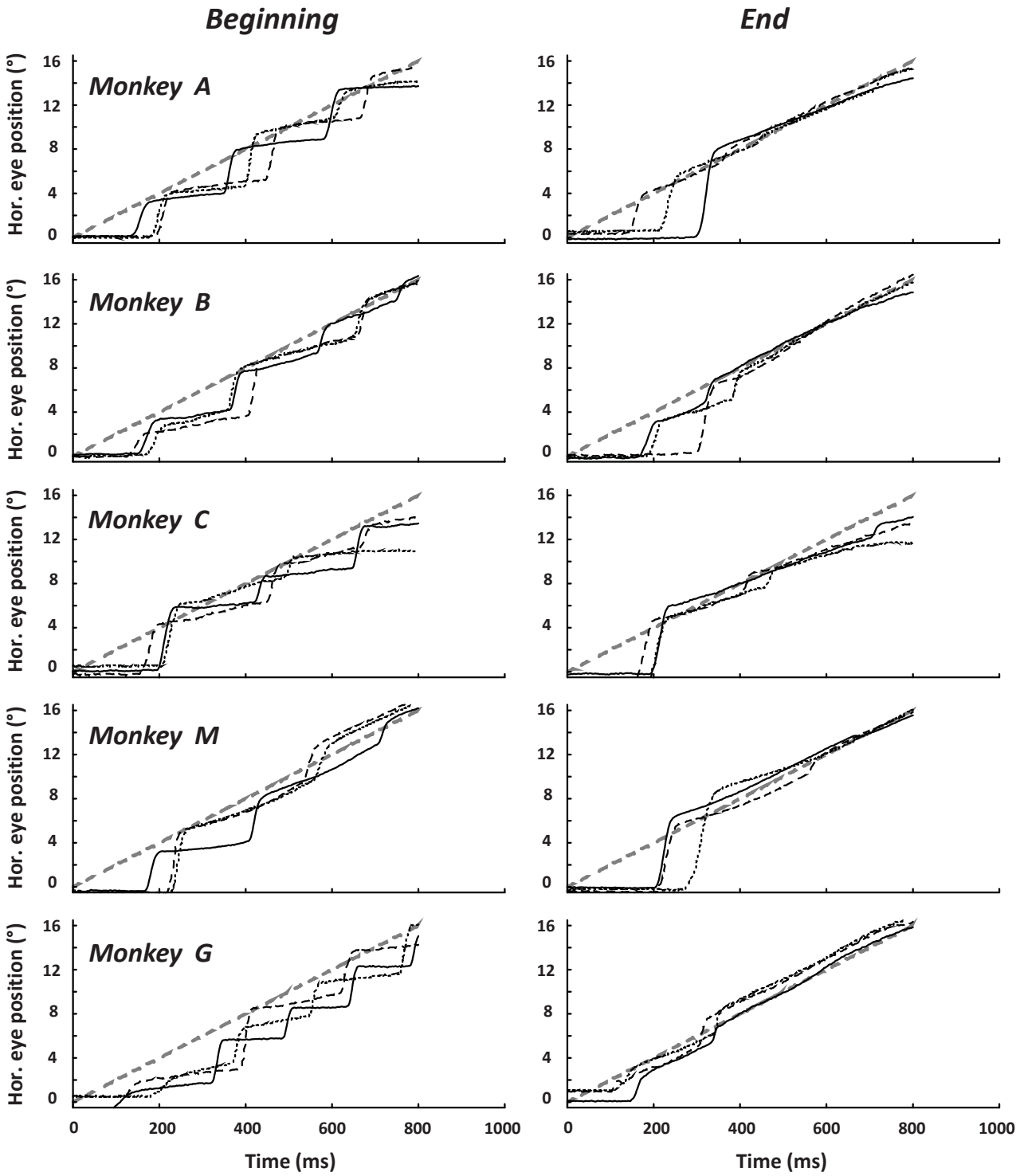

Exp. 1
Exp. 2
Eye position (°)
Eye position (°)
4
0
-4
200 ms
Horizontal
Vertical
eye position
Target position

Figure 3


Beginning
End
Monkey A
Monkey B
Monkey C
Monkey M
Monkey G
Hor. eye position (°)
0
4
8
12
16
0
200
400
600
800
1000
Time (ms)