

Synchronizing the tracking eye movements with the motion of a visual target: Basic neural processes

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28 Abstract

29 In primates, the appearance of an object moving in the peripheral visual field elicits an interceptive saccade that brings the target image onto the foveae. This foveation is then 30 31 maintained more or less efficiently by slow pursuit eye movements and subsequent catch-up 32 saccades. Sometimes, the tracking is such that the gaze direction looks spatiotemporally 33 locked onto the moving object. Such a spatial synchronism is guite spectacular when one considers that the target-related signals are transmitted to the motor neurons through multiple 34 35 parallel channels connecting separate neural populations with different conduction speeds and 36 delays. Because of the delays between the changes of retinal activity and the changes of extraocular muscle tension, the maintenance of the target image onto the fovea cannot be 37 38 driven by the current retinal signals as they correspond to past positions of the target. Yet, the 39 spatiotemporal coincidence observed during pursuit suggests that the oculomotor system is 40 driven by a command estimating continuously the current location of the target, i.e., where it is 41 here and now. This inference is also supported by experimental perturbation studies: when the 42 trajectory of an interceptive saccade is experimentally perturbed, a correction saccade is 43 produced in flight or after a short delay, and brings the gaze next to the location where 44 unperturbed saccades would have landed at about the same time, in the absence of visual 45 feedback. In this chapter, we explain how such correction can be supported by previous visual 46 signals without assuming "predictive" signals encoding future target locations. We also 47 describe the basic neural processes which gradually yield the synchronization of eye 48 movements with the target motion. When the process fails, the gaze is driven by signals related 49 to past locations of the target, not by estimates to its upcoming locations, and a catch-up is 50 made to reinitiate the synchronization.

51 Keywords

52 Tracking, saccade, pursuit, foveation, neurophysiology, synchronization, prediction

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54 Over the course of their phylogenetic and ontogenetic evolution, the animals were 55 faced with the need to manage an environment which is not composed of static objects. In 56 their world (Umwelt), the significant events occur most often when something moves (whether 57 it is animal or not, predator, prey, congeners, or other) or when themselves, they move. In front 58 of this dynamism, the animals exhibit the ability to pursue and catch a prey, to avoid a predator, 59 in flight for some of them. How are such performances, spatiotemporally accurate, possible? 60 Should we believe that the functioning of the brain sets general frames (such as space and 61 time) and principles similar to those used by the Newtonian mechanics for describing the 62 motion of a rigid body? In this chapter, we will explain how the neurophysiology of eye 63 movements made toward a moving visual target addresses these fundamental questions. A 64 new line of investigation is proposed to identify the neurophysiological processes which 65 underlie the ability to produce a visuomotor behavior which is accurate both spatially and 66 temporally.

1. SPATIOTEMPORAL "DILUTION" OF VISUAL SIGNALS IN THE BRAIN.

68 Most visually guided actions consist of localizing and aiming at selected objects in the 69 external world while avoiding obstacles, and grasping them once their location becomes within 70 reach. They involve a multitude of saccades whereby the gaze is oriented toward selected 71 parts of the external world. By bringing the object within the central visual field, each saccade 72 leads to a situation where the target excites a larger population of neurons. In the visual areas 73 of the cerebral cortex and in the superior colliculus (SC), more neurons are indeed sensitive 74 to stimuli located within the central visual field (McIlwain, 1976). If the target is static, the 75 primary saccade is often completed by a small secondary saccade (also called correction 76 saccade). If the target is moving, the interceptive saccade is followed by a slow movement of 77 the eyes and later by a small catch-up saccade. We will avoid considering this sequence of 78 eye movements as the signature of a purposive process whereby a desired future state would 79 drive the evolution of the current state. Instead, we will try to view it as an inevitable process 80 unfolding in the inhomogeneous structure of the visuomotor system, through parallel streams 81 of activity constrained by the brain connectivity.

From the excitation of ganglion cells in the retina to the recruitment of motor neurons (MNs) in the reticular formation and the contraction of extraocular muscles, multiple trains of action potentials are conveyed by parallel channels connecting, with different conduction speeds, assemblies of diverse types of neuronscharacterized by different response times (Nowak and Bullier, 1997; Pellionisz and Llinas, 1982; Schmolesky et al., 1998). The generation of saccadic and slow eye movements indeed involves streams of activity which, on 88 their way from the optic nerve toward the oculomotor nerves, mobilize several populations of 89 neurons in the thalamus, the cerebral cortex, the basal ganglia, the cerebellum, and the 90 reticular formation (Büttner-Ennever, 2005; Krauzlis, 2004; Lynch, 2009; Moschovakis et al., 91 1996; Wurtz and Goldberg, 1989). Thus, the activity yielded by the projection of a small static 92 spot of light on the retinal surface, spatially delimited, spreads out and becomes largely distributed (spatially and temporally) in the brain networks before converging onto the groups 93 94 of premotor andMNs, and causing the contraction of two pairs of six extraocular muscles 95 (Goffart, 2017).

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< Figure 1 approximately here >

97 Beyond the apparent entropy exhibited by this spatiotemporal "dilution" of afferent 98 signals within the cerebral medium, the massive interconnectedness of neural populations 99 actually facilitates the persistence of visual activity for a duration which largely exceeds the 100 actual duration of even a brief spot of light in the external world. Unlike the artificial light which 101 turns off immediately after an electric switch is pressed, the visual activity persists and 102 continues its diffusion within the brain networks. Fig. 1 shows examples of saccades aimed at 103 a target LED that was flashed for a short duration (50 ms) in the peripheral visual field of two 104 macaque monkeys (Be and E). From the onset of the target to the beginning of the saccade 105 toward its location, the saccade latency is the time interval for localized changes in retinal 106 activity to be transmitted to the muscle fibers and initiate their contraction. The contraction lasts 107 for a duration which is sufficient to rotate the eves and accurately direct the foveae toward the 108 target with a time course which does not slow down with longer latencies. Regardless of its 109 onset time, the saccade indeed consists of a sudden increase in angular velocity (acceleration) 110 followed by a decline (deceleration). The persistence of the target-related activity is nicely 111 appreciated when the intensity of visual signals is reduced. Indeed, the use of LEDs allows 112 testing the influence of target energy (Barnes, 1995), and discovering that low-intensity targets 113 lead to saccades which are not characterized by a slower rise in eye velocity and a longer 114 deceleration; it is their onset which is actually delayed (the latency increases). The variability 115 of latencies also increases when the target contrast is reduced (see gray traces in Fig. 1). 116 Interestingly, the latency of the first spike of the response of neurons in the primary visual 117 cortex is also variable and can be correlated with the saccade latency (Lee et al., 2010). Of 118 course, this attractive influence of such a dim spot of light has been amplified by the fact that 119 the monkey learned that it was a signal whose foveation led to a reward. This artificial 120 association would have hardly been observed in the wilds; such a transient stimulus would 121 have likely been unnoticed. Beyond the rigorous description of a behavioral response, the point 122 that we want to address here concerns the identification of the propagation of signals within the cerebral medium (see also Van Rullen et al., 2005) for that specific case when an orienting
response is being elaborated and made toward a visual target.

125 2. SYNCHRONOUS POPULATION ACTIVITY AGAINST FUNCTIONAL126 ENTROPY

127 Considering that the action potentials are conducted along the axons of cells with fixed 128 speeds of propagation, the difference of saccade latencies illustrated in Fig. 1 can be explained 129 by changes in the excitability of neurons. One possible mechanism is that the number of 130 ganglion cells, which, in the retina, are simultaneously excited, is larger with a high-contrast 131 stimulus than with a low-contrast one. This synchronous activation would then facilitate the 132 recruitment of postsynaptic neurons in the thalamus or in the SC, then in the visual cortex, etc. 133 The same principle could be involved in reducing the delay of propagating signals between the 134 relays interposed between the retina and the MNs: simultaneous excitatory signals from an 135 assembly of neurons are more efficient in exciting their targeted cells than temporally scattered 136 input. Thus, the variability of saccade onsets would depend upon the synchronies of action 137 potentials which are transmitted to the next relay: weaker synchrony yielding scattered and 138 longer reaction times.

139 Providing a direct support to this hypothesis is difficult with the contemporary 140 electrophysiological recording techniques. However, the analysis of the effects of electrically 141 exciting the same neural site in the SC of the macague monkey is very instructive for that 142 particular issue. The SC is a structure anatomically situated between the visual cortical areas 143 of the cerebral cortex and the premotor regions in the pontomedullary reticular formation 144 responsible for the generation of saccades (Hall and Moschovakis, 2004). In its deeper layers, 145 one finds cells which fire selectively prior to saccades within a limited range of directions and 146 amplitudes (Schiller and Koerner, 1971; Sparks et al., 1976; Wurtz and Goldberg, 1972). The 147 size and the extent of this movement field depend upon the location of the cell in the SC. In 148 the anterior region, the neurons emit a burst of action potentials during small saccades, 149 whereas neurons located more posteriorly fire during saccades of larger amplitude. Neurons 150 located in the medial border burst prior to upward obligue saccades, and those located on the 151 lateral border discharge before downward oblique saccades. Interestingly, when an electrical 152 microstimulation is applied to a particular site, a saccade is elicited with an amplitude and 153 direction which belong to the movement field of recorded neurons (Schiller and Stryker, 1972). While the amplitude and direction of evoked saccades depend upon the stimulated site 154 155 (Robinson, 1972), their latency depends upon the rate of stimulation pulses: the lower the rate, 156 the longer the latency (Katnani and Gandhi, 2012; Stanford et al., 1996). Fig. 2A illustrates this

157 effect. For frequencies ranging from 300 to 500 pulses per second (pps), the electrically evoked 158 saccades have identical velocity profiles (Fig. 2B) and thus, identical amplitude and direction 159 (identical amplitudes of their horizontal and vertical components). However, their latencies 160 increase when the stimulation frequency diminishes. When the frequency is reduced to 200 161 pps, the latency becomes more variable (Fig. 2C). The "synchronous recruitment" hypothesis 162 described at the beginning of this section can account for this phenomenon: increasing the 163 frequency of stimulation favors the synchrony of firing between the electrically excited neural 164 elements (cells and axons), and this facilitates the recruitment of targeted premotor cells, 165 shortening the latency of elicited saccades.

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< Figure 2 approximately here >

167 To our knowledge, Schiller (1970) was the first to consider the influence of the number 168 of neurons discharging in synchrony as an important determinant of saccade generation. And 169 this intuition leads us to another important point, i.e., that the rate of firing is not the sole 170 parameter by which the SC activity contributes to the generation of saccades; the number of 171 active neurons also matters. Indeed, when a subset of the active population of neurons is 172 inactivated by the local injection of a small volume of pharmacological agent, the velocity of 173 saccades is reduced (Lee et al., 1988) and their latency increased (Sparks et al., 1990) in a 174 correlated manner (Goffart et al., 2012). This influence of the number of active neurons can 175 likewise be demonstrated with the microstimulation technique by varying the current of 176 stimulation. When the frequency and duration of stimulation are maintained fixed, increasing 177 the current of stimulation reduces the latency of saccades (Fig. 2D; Katnani and Gandhi, 2012; 178 Stryker and Schiller, 1975). However, contrary to a transient visual target which leads to a 179 complete saccade long after its disappearance (Fig. 1), electrical microstimulation in the deep 180 SC evokes a saccade whose amplitude depends upon the stimulation duration. If the 181 stimulation is not sufficiently long, the evoked movement is truncated; the amplitude specified 182 by the locus of activity in the SC cannot be fully accomplished (Freedman et al., 1996; Stanford 183 et al., 1996). Sustained activity is an important aspect of the collicular involvement in 184 generating saccades toward the location encoded by the population of active neurons. The 185 maintenance of firing only concerns the activity generated during saccades and not the 186 complete activity which elapses from the target onset until the saccade end. Indeed, before 187 the emission of their saccade-related burst, numerous neurons exhibit a reduction or even a 188 pause of their firing after their visual response (Bell et al., 2006; Mays and Sparks, 1980). The 189 activity during saccades steers the gaze toward a location which is specified by the current 190 population of active neurons in the SC, whether the saccade is made toward static (Gandhi and Keller, 1999; Glimcher and Sparks, 1993) or moving targets (Fleuriet and Goffart, 2012;Goffart et al., 2017a; see below).

193 3. REDUCING THE LAG BETWEEN THE PAST AND THE PRESENT

194 The conduction delays between the firing of retinal ganglion cells and the burst 195 discharge of ocular MNs make impossible that the gaze is driven by the contemporary retinal 196 signals during its saccadic shifts. The problem becomes sharper when one considers the 197 generation of saccades toward a moving target. If the saccades were aimed at the locations 198 traveled by the target, they would always fall short and miss it with an error which would depend 199 upon the target speed and the time of saccade "landing." Yet, despite that the retinal signals 200 yielded by a moving target always correspond to its past locations, the interceptive saccades can be as accurate, though not as precise, as saccades toward a static target (e.g., Barmack, 201 202 1970; Cassanello et al., 2008; Fuchs, 1967; Keller and Johnsen, 1990; Robinson, 1965). Fig. 203 3 compares the landing errors between saccades made toward a static target (red symbols) 204 and saccades made toward a target moving with a constant speed of 21 degrees (deg)/s (blue) in the same region of the visual field (Fleuriet et al., 2011). After a step of 16 deg along the 205 206 vertical (Fig. 3A) or horizontal meridian (Fig. 3B), the target moved horizontally or vertically 207 (respectively), i.e., along the axis orthogonal to the step. In comparison to saccades toward 208 the static targets, the interceptive saccades can be accurate (overlap of error values), with a 209 tendency for more frequent undershoots (negative values of error). However, the guasi-210 absence of overshoots (positive values) whose size is larger than the errors of saccades 211 toward a static target indicates that the interceptive saccades are not aimed at a future location 212 of the target, contradicting the claim that "in [their] programming, target motion is used to 213 predict the future target position so as to assure a spatial lead of the gaze at the saccade end, 214 instead of attempting a precise capture of the target" (Klam et al., 2001). In fact, the idea that 215 the brain would predict the future location of a moving target, and, accordingly, that it would 216 issue a command corresponding to a kind of foresight (Berthoz, 2012; Optican and Pretegiani, 217 2017) lacks of any empirical evidence.

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< Figure 3 approximately here >

Electrophysiological recording studies teach us that any saccade made toward a static target is commanded by a population of neurons in the SC (Anderson et al., 1998; McIlwain, 1976, 1991; Sparks et al., 1976, 1990). Some cells discharge maximally before and during the movement, while others fire less. Those which burst the most vigorously are located at the center of the active population, surrounded by the others. Let's consider five hypothetical 224 neurons, A, B, C, D, and E; the neuron B firing maximally during a 10 deg rightward saccade, 225 the neuron A during a 8 deg rightward saccade, and C during a 12 deg rightward one. The 226 neurons D and E prefer slightly oblique rightward saccades: D when the 10 deg rightward 227 saccade has a 2 deg upward component, and E when it has a 2 deg downward component. 228 The activity of each neuron can be symbolized by a vector with two coordinates, each 229 corresponding respectively to the horizontal and vertical component of the saccade during 230 which it fires maximally: (8,0) for A, (10,0) for B, (12,0) for C, (10,2) for D, and (10, 2) for E. 231 According to the vector-averaging hypothesis (Pitts and McCulloch, 1947; Sparks et al., 1976, 232 1997), the direction and amplitude of the ensuing saccade is specified by the average activity 233 of the population of firing neurons. A 10 deg rightward saccade would involve our five neurons 234 A, B, C, D, and E. The discharge of neuron B would be the most vigorous, while A, C, D, and 235 E would fire less. Situated outside the active population, the other neurons (e.g., F: (10,6), G: 236 (10,-6), H: (10,4), and I: (10,-4)) would be silent. Let's consider now that an identical 10 deg 237 rightward saccade is made toward a target which moves downward, along a path parallel to 238 the vertical meridian. If the same vector-averaging principle steers the interceptive saccade, 239 then a larger population of active neurons should be observed in the SC. The moving target 240 indeed traveled locations in the upper visual field which correspond to vectors like (10,6) and 241 (10,4), involving the activity of neurons F and H. Thus, for generating exactly the same 242 horizontal saccade, the neurons (G and I) coding for the vectors (10,-6) and (10,-4) should also 243 fire, even though the target did not yet "reach" their response field. In other words, these 244 neurons should fire action potentials during interceptive saccades and not during identical 245 saccades made toward a static target. Their movement field should exhibit a shift of their 246 boundary in the direction opposite to the target motion direction. But the available evidence 247 argues against this scenario; the boundaries of the neurons' response field are not shifted in 248 the direction opposite to the direction of the target motion. Many neurons do not exhibit any 249 shift. Other neurons do, but the shift is in the same direction as the direction of the target 250 motion. In other words, the active population in the SC is dynamical and consists of a 251 continuum of neurons issuing commands ranging from vectors related to the past location of 252 the target to vectors related to its present location (Goffart et al., 2016, 2017a; Keller et al., 253 1996), amending the suggestion that the locus of activity in the SC would only encode the 254 location that the target occupied in the past, at the time of its appearance (Optican, 2009; 255 Optican and Pretegiani, 2017). Finally, the empirical data do not refute the vector-averaging 256 hypothesis because different weights can be attributed to the spikes that the saccade-related 257 neurons emit during the interceptive saccade.

4. CAPTURING A MOVING TARGET HERE AND NOW

259 The majority of behavioral studies show that in response to a moving target, the gaze 260 does not land on a location where it will be in the future. The world of living animals contains 261 too many uncertainties that they do not behave as if their prey, predator, or congeners were 262 moving along predetermined routes comparable to public transportation lines. The most 263 spectacular ability with which animals are endowed is to physically capture one to several 264 moving objects. By reducing both the delay between the detection and the reaction to a moving 265 object, and by maintaining it within the central visual field, the object becomes quasi-stable, 266 both spatially and temporally. Instead of considering processes which "predict" or "foresee" the 267 future location of moving target, we propose that tracking a moving target consists of 268 establishing spatial synchrony with it (see also Becker and Fuchs, 1985). The fact that 269 engineers found procedures and built machines which can point toward the future location of 270 an object does not necessarily imply that the same "computation" happens in the brain when 271 a moving target is being captured.

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< Figure 4 approximately here >

273 This fact that the saccades do not target the future but the current location of a moving 274 object is strongly suggested by the results of experiments which tested the robustness of 275 interceptive saccades in the monkey (Fleuriet and Goffart, 2012). When a saccade toward a 276 moving target is perturbed by a brief microstimulation in the SC, the electrically induced change 277 in eye position is corrected in flight or after a short delay, bringing the direction of gaze toward 278 the location where unperturbed saccades would have landed at about the same time. In 279 particular, when the microstimulation is applied in a site which is not involved in the generation 280 of saccades with amplitude and direction close to those of interceptive saccades (when the 281 direction of the perturbation is opposite to the saccade direction), after the electrically induced 282 change in gaze direction, most correction saccades do not overshoot along the motion path. 283 They either fall short or "land" accurately on the moving target. Fig. 4 shows examples of such 284 corrections observed in one experiment (see Fleuriet and Goffart, 2012 for other examples). 285 The experiment was composed of trials which started with the fixation of a central target for a 286 variable interval (the latter is a methodological precaution for avoiding the generation of 287 premature saccades). At the end of the fixation interval, the central target was turned off and, 288 at the same time, a peripheral target appeared 12 deg along the vertical meridian (downward 289 or upward) and moved horizontally to the left or to the right with a constant velocity of 20 deg/s. 290 To avoid the use of visual signals in the guidance of corrections during the perturbed trials, the 291 target became invisible 150 ms after the onset of its motion and for an interval lasting 300 ms. 292 After this interval of target invisibility, the target reappeared moving in the same direction and 293 with the same velocity for 500 ms. The monkey's task was to make a saccade toward the target 294 and to pursue it until it reached its destination (trial end). In 50% of the trials, the interceptive 295 saccade was perturbed by an electrical microstimulation in the deep SC at the onset of the 296 blank interval (i.e., 150 ms after the target motion onset). For both unperturbed and perturbed 297 trials, a fruit juice reward was delivered to the monkey at the end of the trial. Interestingly, the 298 microstimulation evoked saccades whose amplitude and direction were influenced by the 299 target motion (compare the eye displacements indicated by the black arrows). When the target 300 moved in the upper right quadrant (Fig. 4B), the stimulation evoked a saccade with small 301 upward and rightward components. When the target moved in the upper left quadrant (Fig. 302 4A), the horizontal component almost disappeared. When it moved in the lower left quadrant 303 (Fig. 4C), both horizontal and vertical components were strongly reduced; the interceptive 304 saccade was delayed. These different perturbation vectors illustrate interactions between the 305 electrically-evoked and target-elicited activities. Their study should be informative because 306 they illustrate the dynamics (rise and decline) of target-related signals, as previously 307 documented with a static target (Nichols and Sparks, 1995, 1996; Schlag et al., 1998; Sparks 308 and Mays, 1983; Sparks et al., 1987). Following the perturbation, a correction saccade was 309 made that brought the gaze direction, not where the target will reappear (future location), but 310 toward a location close to those captured by unperturbed saccades.

311 Two groups of signals can participate in the elaboration of the command which guides 312 the interceptive saccade toward the transiently invisible target regardless of whether its 313 trajectory is perturbed or not: (1) the target motion-related signals that precede the blank 314 interval and (2) mnemonic signals that the target is expected to reappear and continue to move 315 along the same path. As explained in the first section, the massive interconnectedness of 316 neural populations in the brain facilitates the persistence of visual activity for duration which 317 largely exceeds the actual duration of an event in the external world. Thus, it is guite possible 318 that after the moving target disappears, the visual activity persists and continues its diffusion 319 within the brain networks. Presumably, the diffusion is not isotropic but biased by the target 320 motion direction. It has indeed been shown that the pursuit eye movement persists beyond the 321 time and location where a moving target has disappeared (e.g., Mitrani and Dimitrov, 1978). 322 The activity driving this persistent slow movement of the eyes is likely not restricted to the 323 ocular MNs; it must be driven by premotor neurons, which themselves could be driven by 324 persisting activity of visual neurons. Thus, the correction saccades observed after the 325 "spatiotemporal" perturbation induced by electrical microstimulation in the dSC (Fig. 4; Fleuriet 326 and Goffart, 2012) could well be driven by residual activity from the visual signals which 327 preceded the target disappearance. Later experiments testing saccades toward a transient 328 moving target showed indeed a large number of landing positions situated beyond the location 329 where the target disappeared. When the target moved at constant speed, the saccades landed 330 approximately where the target would be if it were still moving during the next 100 ms (see Fig. 331 8B, E, and H in Quinet and Goffart, 2015a). Therefore, the visual signals that persisted after 332 the target disappearance could contribute to guide the correction saccades reported in Fleuriet 333 and Goffart (2012) because the added delays did not exceed 100 ms (see our Fig. 4 and Figs. 334 6 and 7 in Fleuriet and Goffart, 2012). In addition, the target disappeared for a short interval 335 and reappeared 150 or 300 ms later, continuing its motion along the same path with the same 336 velocity. There was no uncertainty about whether the target would reappear and keep moving 337 along the same path. The monkeys never experienced cases where the target would start 338 moving backward or change its direction during the interval of invisibility.

339 Moreover, the monkeys were not tested to only make a saccade toward the transient 340 moving target (like in the study of Quinet and Goffart, 2015a). They were used to continue their 341 tracking after the target reappearance, until the end of the trial. In other words, it is possible 342 that additional central factors contributed to the robustness of interceptive saccades. Fig. 4 343 indeed shows that the monkey made catch-up saccades when the target was not visible, during 344 unperturbed trials (green arrows) but also during perturbed trials (blue arrows). Following the 345 target disappearance, the diffusion of residual signals could merge with prelude signals related 346 to the upcoming target reappearance. Thus, the interval of invisibility would be "filled" by a kind 347 of interpolation, driving the activity of premotor neurons and guiding the eve movement 348 (saccadic or slow) in the absence of target-related retinal signals. Therefore, the command 349 which encodes at best the expected and current (here-and-now) location of the target and 350 drives the premotor neurons when a visual target is being temporarily occluded corresponds 351 to a combination of signals related to the recent past with mnemonic signals carrying an 352 expectancy built upon the past and repeated experience.

353 5. BEYOND THE NOTION OF INTERNAL MODEL

Several studies show cases where the eyes rotate smoothly and in spatial synchrony with the motion of a visual object, as if no delay separated the time-varying changes of target location and the time-varying changes of extraocular muscle tension. The gaze direction seems to be locked onto the present location of the target, i.e., where it is here and now. Obviously it is not the retinal signals yielded by the external target which drive this spatiotemporal coincidence.

360 According to the most popular view, the ability to perform visually guided eye 361 movements which are spatiotemporally accurate rests upon a putative internal model of the 362 moving target. The major concern of this explanation is that it leads to a dead end insofar as it 363 refers to an entity which is neurophysiologically intractable. Nowadays, the notion of internal 364 model is used like a shortcut, barely helpful to identify and characterize the underlying 365 neurophysiology. The major obstacle which compromises this possibility is the distributed 366 nature of the representation of a visual target in the brain activity (e.g., Nowak and Bullier, 367 1997; Schmolesky et al., 1998; Sparks et al., 1976). A moving visual target involves flows of 368 neural activity which do not remain local but propagate both "vertically" (i.e., across the 369 successive relays interposed between the retina and the extraocular MNs) and "horizontally" 370 (diffusion within each relay). In other words, in the brain activity, the neural image (in the 371 mathematical sense) which corresponds to an object in the external world, even static, is not 372 reducible to a vector with independent spatial and temporal coordinates (Pellionisz and Llinas, 373 1982). It involves entangled flows of neural activity which are spatiotemporally distributed in 374 the brain, from the retinal ganglion cells to the oculomotor neurons. Furthermore, the 375 involvement of a measurable movement (like a saccade) is critical to guarantee that the 376 associated neural activity corresponds to a real object and not to an illusion. The interceptive 377 saccades have indeed been shown to be immune to strong visual illusions: they aim at the 378 physical, not the perceived location of the target (Lisi and Cavanagh, 2015).

379 The neurophysiological characterization is also complicated by the changing location 380 of the object. The time course of the motion can indeed look smooth and continuous, but such 381 retrospective evaluation does not guarantee that the neural image follows a similar dynamics. 382 In the case of tracking a moving target, we will see in the next section that the visuo-oculomotor 383 brain does not spontaneously transform the smooth motion of a small object into a continuous 384 smooth movement of the eyes. A complete dynamic morphing requires several days of training 385 (Bourrelly et al., 2016a,b). Synchronizing the eye movements with the motion of a target is the 386 outcome of a gradual process during which the brain activity assimilates the combination of 387 visual and oculomotor signals. Contemporary habits of language and the Newtonian 388 mechanics lead us to consider that an object is moving within a three- dimensional, 389 homogeneous, isotropic and neutral "receptacle," changing discretely its location in such a way 390 that when it is here and now, it is not anymore where it was before, nor where it will soon be. 391 In the brain activity corresponding to this object, there is no such thing as a "here and now" 392 local point (Pellionisz and Llinas, 1982). The neural image obviously does not change as fast 393 as its associated object in the external world; some residual activity persists "behind" (Goffart 394 et al., 2016, 2017a; Keller et al., 1996). It also expands toward neighboring cells, driving the 395 gaze toward locations in the external world where the target never went (Mitrani and Dimitrov, 396 1978; Quinet and Goffart, 2015a). Given the complexity of the problem when one considers 397 the neural image of a real object moving in front of our eyes, how do we address the problem

of a putative internal model without doing disappointing parodies of the neurophysiologicalprocesses and their oculomotor expression?

Because of all these complications, we will avoid considering the notion of internal model to understand how the brain endows the animals with the ability of maintaining the direction of their gaze toward the present location of the target, i.e., where it is here and now. Instead, our working hypothesis is that spatiotemporally accurate actions result from an adaptive process which consists in synchronizing the outcome of visuomotor flows of activity with the target dynamics.

406 6. LEARNING TO TRACK THE CHANGING LOCATION OF A MOVING 407 TARGET

A target moving in the visual field triggers an interceptive saccade that brings the target image onto the fovea. Then, this foveation is more or less efficiently maintained by two types of eye movements: low-velocity (pursuit) and high-velocity movements (catch-up saccades). Fleuriet and Goffart (2012) hypothesized that the oculomotor system is driven by an estimate of the expected current target location, and subsequent experiments indicated that this command is merging signals from the recent past with mnemonic signals carrying an expectancy built upon repeated experience.

415 It is indeed obvious that the ability to continuously encode, in spite of neural conduction 416 and stabilization delays, the "here-and-now" location of a moving target, requires that its 417 trajectory is already known. To further develop this hypothesis, we studied how inexperienced 418 monkeys learned to track a target which always moved along the same path. During these 419 experiments, each trial started with the foveation of a central target which, after a variable 420 interval, stepped on the vertical meridian (upward or downward) and immediately after, moved 421 horizontally with a constant, increasing or decreasing velocity (Bourrelly et al., 2016a,b). The 422 target moved toward the left or the right for 800 ms before disappearing. The monkey was 423 rewarded if, after making a saccade in the appropriate visual quadrant, it tracked the target 424 until its ultimate location. During the first days, the tracking was composed of saccades 425 separated by periods during which gaze moved slowly in the same direction as the target. 426 Except for the brief periods during which fairly accurate saccades occurred, the gaze lagged 427 behind the target most of the time.

< Figure 5 approximately here >

428

429 Fig. 5 illustrates qualitatively with example trials recorded in five monkeys, how the 430 oculomotor tracking changed between the first and last sessions of the training procedure, 431 when the target moved with a constant speed. During the first session (left column), after the 432 interceptive saccade, the eye followed the target with a velocity which was not sufficient to 433 maintain its image on the fovea. The velocity of the postsaccadic movement did not match the 434 target speed. Contrary to the experiments where the target moved with an increasing speed 435 (Fig. 6), the eye did not increase the velocity of its movement before the subsequent catch-up 436 saccade. After several daily training sessions (right column), the monkey was able to smoothly 437 track the target immediately after the interceptive saccade; the catch-up saccades either 438 disappeared or their amplitude was largely diminished. This saccade-free tracking was rarely, 439 if ever, observed during the first session. The reader will find in Bourrelly et al. (2016a) a 440 detailed description of how tracking eye movements changed during the course of one trial, 441 during the course of the first and last sessions and across the successive sessions. Fig. 6 442 illustrates the same evolution when an accelerating target is tracked (Bourrelly et al., 2016b). 443 After the interceptive saccade, contrary to the experiments which tested the tracking eye 444 movements made in response to a target moving with a constant speed, the postsaccadic eye 445 movements could accelerate when the target accelerated, but not sufficiently to match the 446 increasing target speed. With repeated practice, i.e., with a larger number of trials and over 447 the consecutive days, the pursuit gain (ratio of eye to target velocities during the intersaccadic 448 intervals) enhanced while the number and amplitude of catch-up saccades diminished 449 (Bourrelly et al., 2016a). The evolution of tracking from an intermittent to a continuous "here-450 and-now" mode is actually inevitable because the saccades exert a facilitative influence on 451 pursuit eye movements. This facilitation is twofold, visual and motor. On the one hand, 452 saccades bring the target image within the central visual field, where the visual motion signals 453 are more effective for driving slow eye movements compared with signals from the peripheral 454 field (Lisberger and Westbrook, 1985). On the other hand, the slow eye movements match the 455 target speed better when they are preceded by a saccade (Lisberger, 1998). We will see in the 456 next section the neurophysiological process which possibly underlies this facilitation.

457

< Figure 6 approximately here >

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7. NEURAL BASIS OF SACCADIC AND PURSUIT EYE MOVEMENTS

459 The gaze direction is determined by the cooperative action of six muscles attached to 460 each eyeball. These muscles are called extraocular muscles, to distinguish them from those 461 located inside the eye and which influence the diameter of the pupil or the lens curvature. Two 462 pairs of muscles are involved during horizontal rotations of the eyes (i.e., rotations about a 463 vertical axis through the eyeball): the lateral rectus (LR) and medial rectus (MR) muscles. 464 Orienting gaze toward the right is accomplished in the right eye by the contraction of the LR 465 and the relaxation of the MR, while in the left eye the MR is contracted and the LR relaxed. 466 Conversely, orienting gaze toward the left is produced in the left eye by the LR contraction and 467 MR relaxation concomitantly with the MR contraction and the LR relaxation in the right eye. 468 Vertical movements of the eyes (rotations about a horizontal axis) are slightly more complex 469 than the horizontal ones because they are the result of a synergy between the other four 470 extraocular muscles. The joint contraction of the superior rectus (SR) and inferior oblique (IO) 471 muscles of both eyes, combined with the relaxation of the inferior rectus (IR) and superior 472 obligue (SO) muscles, rotate the eyes upward. The bilateral contraction of the IR and SO, 473 combined with the relaxation of SR and IO, rotates them downward. Oblique saccades are 474 generated by tensions simultaneously developed by the muscles rotating the eye horizontally 475 and those rotating the eye vertically. The contraction of extraocular muscles is driven by the 476 activity of MNs located in cranial nerve nuclei III (oculomotor), IV (trochlear), and VI 477 (abducens).

478 Different populations of premotor neurons in the reticular formation are involved in the 479 generation of saccadic and slow eye movements. The generation of saccadic eye movements 480 involves burst discharges by neurons located in the pontomedullary and mesencephalic 481 reticular formation, respectively, for the horizontal and vertical movements (see Goffart, 2017 482 for a brief review and references). Because they emit a burst of action potentials within a very 483 short-time interval, these neurons have been called saccade-related burst neurons. Although 484 it can be preceded by a prelude firing, it is the burst which drives the MNs and yields the rapid 485 rise in the tension of extraocular muscles during saccades. Lesions of the regions where the 486 burst neurons are located abolish the ability to generate saccades without compromising the 487 ability to make slow eye movements toward a moving target (Henn et al., 1984). The 488 generation of pursuit eye movements involves other groups of neurons called tonic neurons 489 which are located in distinct nuclei of the reticular formation (Sharpe, 2008).

490 A dissociation of the neural processes leading to the generation of saccadic and pursuit 491 eye movements is supported by multiple clinical and experimental lesion studies (e.g., Büttner 492 et al., 1994; Henn et al., 1984; Morrow and Sharpe, 1995; Ohtsuka et al., 1992; Pierrot-493 Deseilligny et al., 1990; Sharpe, 2008). However, this segregation is not absolute. A coupling 494 between the processes controlling each type of movement is indeed suggested by the 495 existence of neurons which modulate their sustained firing rate during both types of movement. 496 Most of these neurons have been found in the cerebellum, and more specifically in its floccular 497 and parafloccular regions (Noda and Mikami, 1986; Noda and Suzuki, 1979) and in its 498 medioposterior territories, i.e., the caudal fastigial nuclei (Fuchs et al., 1994) and the posterior 499 vermis (Suzuki and Keller, 1988). Sato and Noda (1992) also found Purkinje cells in the 500 posterior vermis which fire during saccades and pursuit eye movements, but these cells seem 501 to be rare since the activity of only 6.6% (44 units out of 663) was modulated during pursuit 502 eye movements. Of these units, less than 4% were located in the oculomotor vermis (OMV). 503 This last point is important because it led the authors to conclude that the OMV did "not qualify 504 as a structure responsible for the control of smooth pursuit," a conclusion which contrasts with 505 the recent claim that "the overwhelming majority [81%] of Purkinje cells in the OMV are 'dual' 506 PCs responding to both types of goal-directed eye movements" (Sun et al., 2017). Suzuki and 507 colleagues were the first to report neurons which, in the posterior vermis, modulate their firing 508 rate during both saccadic and slow eye movements (Suzuki et al., 1981). They report that "the 509 nature and number [of saccade-related activities in the posterior vermis] indicate that there is 510 only a slight overlap between the population of smooth-pursuit and vision-related units and the 511 population of saccade-related cells previously observed in lobules VI and VII." The observation 512 that large lesion in the posterior vermis impairs saccadic and pursuit eye movements (Takagi 513 et al., 1998, 2000) does not exclude the possibility of two or three segregated groups of 514 neurons. Therefore, the role of the medioposterior cerebellum in the control of saccadic and 515 slow eye movements requires further investigation. In the brainstem, cells modulating their 516 firing rate during saccades and pursuit have also been reported, notably in the rostral part of 517 the SC (Krauzlis, 2001) toward which the nucleus prepositus hypoglossi and the caudal 518 fastigial nuclei project (Hartwich-Young et al., 1990; May et al., 1990), as well as in the nucleus 519 raphe interpositus (RIP) where pause neurons are located. The two rostral SC participate in 520 adjusting oculomotor commands for maintaining a target within the central visual field (Goffart 521 et al., 2012; Hafed and Krauzlis, 2008; Hafed et al., 2008), a situation which is often 522 encountered when a moving target is being pursued. Concerning the pause neurons, it is 523 commonly believed that they maintain gaze steady during fixation by gating the burst of 524 saccade-related premotor neurons. Unfortunately, this idea will remain speculative as long as 525 the study of its inactivation has not demonstrated the presence of irrepressible saccades during 526 delayed saccade tasks, i.e., when a peripheral target competes with a central one. The 527 observation that pause neurons reduce their firing during the initiation of pursuit eye 528 movements led Missal and Keller (2002) to imagine an inhibitory role of these neurons in 529 pursuit. Unfortunately here again, this option requires further investigation because the 530 reduced firing could merely signal the preparation of a catch-up saccade toward the moving 531 target. Additional studies of the effects of RIP inactivation are also required to identify and 532 characterize the neural networks to which they belong.

533 8. ENLARGEMENT OF THE NEURONAL MASS FOR ACCURATE TRACKING

534 Beyond these unknowns, a general neurophysiological process can explain the 535 changes of the saccadic and slow components of oculomotor tracking during repeated 536 exercise. We propose that they result from an expansion of the "mass" of neural activity linked 537 to the visuomotor representation of the central field. Several empirical facts converge to 538 support this hypothesis. First, it is a basic fact that the saccades orient the fovea toward 539 locations situated next to the moving target (e.g., Fig. 3). As a result, neurons which are 540 sensitive to the visual stimulation of the fovea become excited by the presence of the target. 541 When the target is moving, the repeated excitation of these neurons by the catch-up saccades 542 likely contributed to delay the adaptation of their response, and the variability of saccade 543 endpoints enlarged the population of active neurons. Such an enlargement would functionally 544 correspond to an expansion of the central visual field, which is also known to involve neurons 545 in the rostral SC. Thus, the increase in pursuit velocity and the reduction of saccade size 546 observed across the learning sessions (Bourrelly et al., 2016a) could result from an 547 enlargement of the population of active neurons in the rostral portion of the SC. The 548 rostralSChas indeed been shown to be involved in both foveal and parafoveal pursuit (Basso 549 et al., 2000; Hafed et al., 2008; Krauzlis et al., 2000) as well as during fixational saccades 550 (Hafed and Krauzlis, 2012). The parallel facts that a larger target size not only improves the 551 accuracy of pursuit eye movements (Helmick, 1951; Pola and Wyatt, 1985) but also increases 552 the spatial spread of activity in the rostral SC (Goffart et al., 2012; Hafed et al., 2008) are 553 consistent with this hypothesis of enlarged population.

554 This enlargement could be under the influence of the caudal fastigial nuclei, though 555 nothing excludes the participation of other deep cerebellar nuclei. Concerning the cFN, their pharmacological inactivation is known to impair the generation of pursuit and saccadic eye 556 557 movements (Bourrelly et al., 2017; Buzunov et al., 2013; Goffart et al., 2004; Robinson et al., 558 1997), as well as the direction of gaze relative to a fixated target, whether the latter is static 559 (Guerrasio et al., 2010) or moving (Bourrelly et al., 2017; Robinson et al., 1997). This gaze "positional" disorder (called fixation offset) has been proposed to involve the fastigio-collicular 560 561 connection (Guerrasio et al., 2010; May et al., 1990) because similar fixation offsets are 562 observed in the head-restrained monkey during unilateral inactivation of rostral SC (Goffart et 563 al., 2012; Hafed et al., 2008). But the fastigial involvement in generating accurate pursuit eye 564 movements is not restricted to the fastigio-collicular channel; projections to precerebellar nuclei 565 such as the nucleus reticularis tegmenti pontis or dorsal pontine nuclei have been documented 566 (Batton et al., 1977; Noda et al., 1990; Sugita and Noda, 1991). These nuclei constitute major 567 relays by which motion signals reach the flocculus and paraflocculus for the generation of 568 pursuit eye movements (Belton and McCrea, 1999; Langer et al., 1985; Mustari et al., 2009; 569 Zee et al., 1981). There again, an enlargement of the population of active neurons could also happen under the control of caudal fastigial nuclei (as recently demonstrated for the control of 570 571 the saccade size; Goffart et al., 2017b; see also Quinet and Goffart, 2015b) and possibly also 572 of other deep cerebellar nuclei (Robinson and Fuchs, 2001). More fundamentally, regardless 573 of the targeted neural region, an increase of the number of active neurons enhances the 574 probability of synchronous action potentials which, as explained in the second section of this 575 chapter, reduces the transmission delays. Thus, motion signals reach faster the tonic neurons 576 for driving the slow movements of the eyes when a moving target is being tracked.

577 9. CONCLUSION

578 In this chaper, a new line of investigation has been proposed to identify the 579 neurophysiological processes which underlie the ability to produce goal-directed eye 580 movements which are accurate, spatially and temporally. We have shown that tracking the 581 location (here and now) of a moving target is not necessarily and spontaneously smooth, that 582 such smoothness is in fact the consequence of training. Because of the visuomotor delays, the 583 ability to generate eye movements which are locked onto the current target location is 584 obviously not possible unless the upcoming trajectory is already known. Several studies have 585 shown that the velocity of slow eye movements hardly match the target speed when an 586 unpredictable target is being tracked (e.g., Bahill et al., 1980; Barnes and Collins, 2015; Deno 587 et al., 1995; Miall et al., 1986; Michael and Melvill-Jones, 1966; Mrotek et al., 2006; St-Cyr and 588 Fender, 1969). The presence of numerous catch-up saccades makes the tracking look 589 intermittent. Moreover, the absence of lead between the gaze and target directions and the 590 frequent lags tell us that the visuomotor brain works with a very short horizon of predictability 591 during visual tracking. Without assuming the existence of "predictive" signals or any encoding 592 of future target locations in the brain activity, we have explained how the spatial 593 synchronization is largely facilitated by the generation of saccades. Finally, considering that 594 "low gain smooth pursuit is a sensitive sign of chronic diffuse brain disease that can be useful 595 in the detection of neurological disorders" (Sharpe, 2008), for those disorders where the action 596 is spatiotemporally detached from the current context, the rehabilitation of neurological patients 597 may be facilitated by the development of strategies to enhance their visuomotor presence.

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FIGURE LEGENDS

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Figure 1: Effect of target contrast on the latency of saccades. Time course of the horizontal component of saccades aimed at a static target LED located 8 to the right in a dimly illuminated room. A gap interval separated the fixation of a central target from the onset of the brief peripheral target (50 ms duration). Additional methodological information can be found in Goffart et al., (2006).

874

Figure 2: Saccades evoked by electrical microstimulation of one site in the deep superior colliculus. A: Reducing the rate of stimulation pulses (from 500 to 300 pulses per second) increases the latency of evoked saccades. B: The saccades (same as in A) have identical velocity profiles. C: Reducing further the rate of stimulation pulses (from 300 to 200 pulses per second) made the latencies of evoked saccades even longer and more variable. D: Increasing the current of stimulation reduces the latency of saccades.

881

882 Figure 3: Comparison of targeting errors between saccades toward a static versus a moving 883 target. During the static target trials, the target appeared at locations comparable to those 884 travelled by the moving target. The error is plotted as a function of the duration of the largest 885 saccade component, i.e., the component orthogonal to the motion (when the target is moving). 886 In A, the target moved horizontally toward the left or the right, from locations situated 8 or 16 887 degrees along the vertical meridian. In B, the target moved vertically upward or downward, 888 from locations situated 8 or 16 degrees along the horizontal meridian. Negative values 889 correspond to a hypometria (undershoot). Data collected in one monkey (N). Additional 890 information can be found in Fleuriet et al., (2011).

891

892 Figure 4: Time course of horizontal and vertical eye movements toward a temporarily invisible 893 target. The target moved horizontally away from the vertical meridian, to the left (A,C) or to the 894 right (B,D), in the upper (tops) or lower (bottom) visual field, and with a constant speed (20°/s). 895 After a short interval of 150 ms, the target disappeared during 300 ms (grey zone) and 896 reappeared at the location where it would have been if always visible, moving at the same 897 speed. The black traces correspond to control trials, the blue traces to perturbed trials. During 898 these trials, the trajectory of interceptive saccades was perturbed by a brief electrical 899 microstimulation (30 ms, 12µA, 400 pps) in the deep superior colliculus. The black arrows 900 indicate the electrically-evoked saccade (perturbation). The green and blue arrows indicate 901 catch-up saccades made while the target is invisible during control and perturbed trials, 902 respectively. Additional methodological information can be found in Fleuriet and Goffart (2012).

903

904 Figure 5: Typical oculomotor behaviour of a monkey tracking a visual target moving horizontally 905 with a constant speed. The horizontal eye position is plotted as a function of time after the 906 target motion onset for three trials recorded during the first (left column: Beginning) and last 907 training sessions (right column: End). The time course of horizontal target position is illustrated 908 by the red line. The selected trials were recorded in 5 monkeys (A, B, C, M and G: from top to 909 bottom, respectively) when the target moved in the upper right quadrant with a constant speed 910 (20°/s). During the other randomly interleaved trials, the target moved similarly, horizontally 911 and away from the vertical meridian, but in the lower right, the lower left or the upper left 912 guadrant. Additional methodological information can be found in Bourrelly et al. (2016a). 913

914 Figure 6: Typical oculomotor behaviour of a monkey tracking an accelerating visual target. The 915 horizontal eye position is plotted as a function of time after the target motion onset for three 916 trials recorded during the first (left column: Beginning) and last training sessions (right column: 917 End). The time course of horizontal target position is illustrated by the red line. The selected 918 trials were recorded in 5 monkeys (A, B, C, M and Bi: from top to bottom, respectively) when 919 the target moved horizontally in the upper right quadrant with a speed which increased from 0 920 to 40°/s during 800ms. During the other randomly interleaved trials, the target moved similarly, 921 horizontally and away from the vertical meridian, but in the lower right, the lower left or the 922 upper left quadrant. The experimental protocol is identical to that described in Bourrelly et al. 923 (2016a).

Figure 1 Goffart, Bourrelly and Quinet *Prog Brain Res* 2017



Figure 2 Goffart, Bourrelly and Quinet *Prog Brain Res* 2017



Figure 3 Goffart, Bourrelly and Quinet *Prog Brain Res* 2017



Figure 4 Goffart, Bourrelly and Quinet *Prog Brain Res* 2017





