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# Neurophysiology of gaze orientation: Core neuronal networks

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# 6 Neurophysiology of gaze orientation: 7 Core neuronal networks

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## 13 Summary

14 The appearance of an object in the visual field triggers a shift of gaze toward its location. This  
15 orienting response consists of a rapid rotation of the eyes, the saccade, which can be  
16 accompanied by a rotation of the head. If the target moves, the saccade is followed by a slow  
17 movement of the eyes and a catch-up saccade. In this chapter, instead of describing the path  
18 leading from the target-evoked retinal activity to the changes in muscle tension, we shall take  
19 the reverse path. Starting from the muscle contractions, we shall proceed upstream and  
20 describe the tremendous organization that, in the brainstem and cerebellum, enables us to  
21 rapidly and accurately orient the foveae towards visual targets located at different  
22 eccentricities and depths. This chapter is an attempt to synthesize the considerable  
23 knowledge that neurophysiologists and neuroanatomists gathered in the monkey during the  
24 last six decades.

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27



57           The situation is more complicated when gaze moves vertically. Vertical movements  
58 involve not only steady tension of LR and MR muscles, but also a complex cooperation  
59 between the four other muscles. The contraction of superior and inferior rectus muscles  
60 elevate and depress each eye, respectively. These actions are stronger when the eye is in  
61 abduction. The contraction of oblique muscles causes torsional movements but also elevate  
62 or depress the eye, more strongly when the eye is in adduction. If we consider the movements  
63 made when the eyes are centered in the orbit, in addition to elevating the optic axis (turquoise  
64 arrows in Fig. 1B), the contraction of the superior rectus (SR) muscle fibers causes adduction  
65 (black arrows) and intorsion (blue arrows) of the eyeball. Likewise, in addition to lowering the  
66 optic axis (yellow arrows in Fig. 1B), the contraction of the inferior rectus (IR) muscle fibers  
67 causes adduction and extorsion (green arrows). These secondary actions can be counteracted  
68 by the contraction of oblique muscles, for the contraction of inferior oblique (IO) muscle fibers  
69 causes elevation, abduction and extorsion of the eyeball, whereas the contraction of superior  
70 oblique (SO) muscle fibers causes depression, abduction and intorsion.

71           Binocular conjugate movements are made when the head rotates while a visual target  
72 is being fixated (vestibulo-ocular reflex), when the visual surround is moving (optokinetic  
73 reflex) and whenever a target appears or is imagined in the peripheral visual field (saccades).  
74 We shall first examine the neurophysiology of saccade generation when the head does not  
75 move. Then, we shall study the case when a head rotation accompanies the saccade. During  
76 these combined eye-head movements, two couplings can happen: the eyes and the head  
77 move either in the same direction or in opposite directions. Next, we shall see the  
78 neurophysiology of disconjugate movements of the eyes, which occur when gaze is shifted  
79 between targets located at different depths (vergence eye movements). Finally, we shall have  
80 an overview of the complex network that enables one to fixate and track a moving target, i.e.,  
81 an object whose spatial coordinates keep changing. (smooth pursuit eye movements).

## 82   Binocular conjugate movements

### 83   Horizontal saccades

84           Figure 2 schematizes the current view of the premotor neurophysiology of horizontal  
85 saccades in the pontine and mesencephalic reticular formation. During leftward saccades (Fig.  
86 2A), the fast-twitch muscle fibers of the right eye's MR and of the left eye's LR contract while

87 those of antagonist muscles (right eye's LR and left eye's MR) relax. Motor neurons in the  
88 abducens nucleus (ABD, located in the pontine reticular formation) and in the oculomotor  
89 nucleus (OMN in the midbrain tegmentum) emit bursts of action potentials that respectively  
90 cause the phasic contraction of muscle fibers. The burst discharge of cells in the OMN is  
91 triggered and supported by spikes emitted by internuclear neurons (AIN) also located in the  
92 abducens nucleus. In return, the bursts of abducens motor (MN) and internuclear (AIN)  
93 neurons are driven by afferent input from excitatory burst neurons (EBN) located in the  
94 ipsilateral paramedian pontine reticular formation (PPRF, synapses a). The abducens neurons  
95 also receive excitatory input from internuclear burst-tonic neurons in the contralateral  
96 oculomotor nucleus (not shown). Discharging during saccades and increasing their firing rate  
97 during convergence, these cells are possibly involved in the motor drive for conjugate  
98 saccades because in addition to cause exophoria, lidocaine injection in the medial rectus  
99 subdivision of the oculomotor nucleus causes hypometria and slowing of abducting saccades  
100 of the contralateral eye.

101           Otherwise silent, the EBN fire trains of action potentials whose interspike interval is  
102 smaller for larger saccades. Contrary to statements found in numerous review articles, the  
103 instantaneous firing rate of EBN is not a replica of instantaneous eye velocity. For each  
104 saccade, the interspike interval is much more constant than expected if this claim were true  
105 (i.e, that EBN rate equals instantaneous eye velocity). The suggestion that the firing rate of  
106 motor neurons would alone determine the instantaneous eye velocity is also brought into  
107 question by a study in the cat, which showed that a model factoring in muscle tension and its  
108 first derivative accounted for the firing rate of motor neurons better than a model factoring  
109 in eye position and its first and second derivatives (velocity and acceleration).

110           Regarding the relaxation of antagonist muscles, it results from a pause in the firing of  
111 motor neurons innervating them. This pause is itself caused by inhibitory input from burst  
112 neurons (IBN) located in the ipsilateral dorsal paragigantocellular reticular formation (dPGRF,  
113 synapses b). In addition to bursting during ipsiversive horizontal saccades (so called "on-  
114 direction" response), approximately half of these inhibitory burst neurons also emit spikes  
115 during contralateral horizontal saccades (off-direction response). Thus, the agonist motor  
116 drive is a combination of excitatory and inhibitory presynaptic input from the ipsilateral EBN  
117 and contralateral IBN, respectively. The relative strength of these antagonist premotor inputs

118 is under the descending influence of saccade-related burst neurons located in regions involved  
119 in other functions, such as the left and right caudal fastigial nuclei (located in the medial  
120 cerebellum) and the contralateral deep superior colliculus (in the midbrain tectum). The  
121 bilateral fastigial input exerts an influence that is more modulatory than the collicular  
122 influence because, contrary to lesions in the superior colliculus, fastigial lesions do not  
123 suppress or delay the generation of saccades.

124

### **Figure 2 about here**

125 During rightward saccades (Fig. 2B), the active circuit is mirror reversed. The agonist  
126 muscles are the right eye's LR and the left eye's MR, whereas the antagonist muscles are the  
127 right eye's MR and the left eye's LR. IBN in the right dPGRF cause the relaxation of antagonist  
128 muscles. Under the excitatory influence of EBN in the right PPRF and the inhibitory influence  
129 of IBN in the left dPGRF, motor and internuclear neurons in the right abducens nucleus provide  
130 the motor commands to the ipsilateral LR and contralateral MR, respectively. The circuits  
131 producing rightward and leftward saccades are presumably not completely symmetric insofar  
132 as the number of active neurons and the number of synapses and neuromuscular junctions  
133 likely differ between them. By contrast, we shall see next that the networks involved in the  
134 generation of downward and upward eye movements are not at all symmetrical with respect  
135 to each other.

### 136 Vertical cardinal saccades

137 The neuronal network underlying the generation of vertical saccades is located in the  
138 midbrain tegmentum. For upward saccades (Fig. 3A), the agonist muscles are the IO and the  
139 SR and the antagonist muscles the IR and the SO. As reported above, in addition to elevating  
140 the eye, the contraction of SR muscle fibers causes intorsion, whereas contraction of IO  
141 muscle fibers causes extorsion. Thus, the intorsion caused by the motor commands to the SR  
142 combines with the extorsion caused by the commands to the IO. The observation of negligible  
143 torsional component during upward saccades suggests that the two torsions cancel each other  
144 out. Such a balance of force likely involves bilateral activity in the midbrain because for each  
145 eye, the motor neurons innervating the SR muscle are located in the contralateral OMN  
146 whereas the motor neurons innervating the IO muscle are located in the ipsilateral OMN. The

147 two sets of commands during upward saccades must be adjusted in a timely manner, and any  
148 asymmetry in the bilateral motor drive would engender a torsional component.

149 **Figure 3 about here**

150 The excitatory commands responsible for generating upward saccades are issued by  
151 burst neurons located in the left and right rostral interstitial nucleus of the medial longitudinal  
152 fasciculus (RIMLF). These commands are doubly bilateral. Indeed, on the one hand, the burst  
153 emitted by premotor neurons (uEBN) in the left RIMLF excite the motoneurons innervating  
154 the SR muscles of *both* eyes (black synapses a) and motor neurons innervating the IO muscles  
155 of *both* eyes as well (black synapses b in Fig. 3). On the other hand, the burst emitted by uEBNs  
156 in the opposite RIMLF excite the same motoneuronal group (blue synapses a and b).  
157 Moreover, in addition to recruiting the motor neurons, the uEBN also excite neurons that  
158 inhibit the motor neurons that innervate the antagonist muscles (IR and SO, synapses c).  
159 Located in the interstitial nucleus of Cajal, these cells (uIBN) inhibit the motor neurons in the  
160 contralateral oculomotor nucleus, i.e., cells responsible for the contraction of the IR of the  
161 contralateral eye (synapses d) and motor neurons responsible for the contraction of the SO of  
162 the ipsilateral eye (synapses e). However, contrary to uEBN, uIBN do not send bilateral  
163 projections to the motor neurons innervating the SO muscle fibers. Their projection make  
164 synaptic contacts only with motor neurons on the contralateral side.

165 As for the upward saccades, the discharge of neurons located in each side of the brain  
166 is capable of causing a downward movement of *both* eyes (Fig. 3B). The premotor excitatory  
167 burst neurons leading to downward saccades (dEBN) are also located in the RIMLF. However,  
168 unlike the uEBN, the dEBN do not send bilateral projections to the motoneurons; their  
169 projection is ipsilateral only. During downward saccades, the SO and IR muscle fibers of *both*  
170 eyes contract because the dEBN excite 1) the motor neurons in the ipsilateral OMN, which  
171 cause the contraction of IR muscle fibers of the *ipsilateral* eye (synapses a), and 2) the motor  
172 neurons which, in the ipsilateral trochlear nucleus, cause the contraction of SO muscle fibers  
173 of the *contralateral* eye (synapses b). Moreover, in addition to lowering the eyes, the  
174 contraction of SO muscle fibers causes an intorsion of the eye while the contraction of IR  
175 muscle fibers causes their extorsion. The commands from the ipsilateral OMN for extorsion  
176 combine with commands from the contralateral trochlear nucleus for intorsion. Precisely how

177 these opposite torsional components cancel each other out during downward saccades  
178 remains unexplained. A bilateral adjustment at the level of premotor burst neurons seems  
179 inevitable. Moreover, the neural processes in charge of the relaxation of antagonist muscles  
180 during downward saccades remain to be characterized.

181 Even though the number of cells and the number of synaptic boutons likely differ  
182 between the left and right sides of the reticular formation, the connectivity patterns involved  
183 in generating leftward and rightward eye movements are symmetrical with respect to the  
184 brainstem midsagittal plane (see Fig. 2 and 5). By contrast, the networks involved in the  
185 generation of downward and upward eye movements are not symmetrical with respect to the  
186 midsagittal plane (Fig 3).

187 During vertical saccades, the EBN involved in the generation of horizontal saccades do  
188 not fire. Some IBN in the dPGRF emit action potentials whose number increases with the  
189 saccade size. For vertical saccades to remain straight while their size increases, one possibility  
190 is that the motor and internuclear cells in the abducens nucleus emit additional spikes, thus  
191 reducing the contrapulsive effect of IBN spikes. This does not seem to be the case because  
192 MN and AIN in the abducens nucleus do not emit action potentials during vertical saccades. A  
193 more likely possibility is that the contrapulsion exerted by IBN in the left and right dPGRF  
194 cancel each other out. If no perfect symmetry exists between the set of active neural elements  
195 (number of neurons and of synaptic boutons) located on each part of the reticular formation,  
196 then the observation of strictly vertical saccades leads us to infer that a process adjusts the  
197 bilateral activity of IBN during vertical saccades.

198 This bilateral control is not restricted to the group of IBNs, which are primarily involved  
199 in the generation of horizontal saccades. In addition to elevating both eyes, the discharge of  
200 motor neurons in the right OMN causes, as a secondary action and via the contraction of the  
201 right eye's IO and the left eye's SR, a rightward deflection of both eyes during vertical saccades  
202 while the discharge of motor neurons in the opposite side causes a leftward deflection (Fig.  
203 3A, top row). Likewise, in addition to lowering both eyes, the dEBN in the right RIMLF lead to  
204 the contraction of the left eye's SO and the right eye's IR, causing a leftward deflection of their  
205 trajectory while dEBN in the left RIMLF cause a rightward deflection during vertical saccades  
206 (Fig. 3B, top row). The observation of straight vertical saccades (with no horizontal deviation)



207 implies that the horizontal deflections caused by the secondary action of the muscles elevating  
208 or depressing the eyes are also canceled in the motor drives.

209           Therefore, the generation of straight vertical saccades rests upon a balance of bilateral  
210 motor activation, which itself depends upon an adjustment of premotor commands that takes  
211 into account the structural (neurons and their connectivity) and functional (firing properties,  
212 secondary and tertiary consequence of muscle contractions) asymmetries between the  
213 oculomotor territories that are distributed on either side of the brain stem. The saccade-  
214 related neurons in the left and right fastigial nuclei and in the oculomotor vermis regulate this  
215 bilateral balance. Indeed, most of them burst during vertical saccades and their asymmetrical  
216 perturbation horizontally deflects the trajectory of vertical saccades. Bilateral activity in the  
217 two deep superior colliculi is also involved with their medial halves for driving upward  
218 saccades and their lateral halves driving downward saccades. The contribution of the deep  
219 superior colliculi and of the caudal fastigial nuclei differ insofar as horizontal saccades involve  
220 activity of bursting cells in only the superior colliculus on the contralateral side, whereas  
221 saccade-related neurons burst in the caudal fastigial nuclei on both sides.

## 222 Combined horizontal and vertical saccades

223           When a target appears off the cardinal visual axes, the orienting response does not  
224 consist of horizontal and vertical saccades made in sequential order. Both horizontal and  
225 vertical components are generated in such a manner that their onset and offset are relatively  
226 simultaneous. These combined horizontal-vertical saccades are conventionally called  
227 “oblique” saccades. Considering the muscle diversity (lengths, contractile properties and  
228 orbital attachments) involved in the horizontal and vertical components and the fact that their  
229 motor innervations are not located in nearby regions of the brainstem, their simultaneous  
230 onsets and the limited curvature of their spatial trajectory are empirical observations  
231 suggesting coupling mechanisms.

232           In the medial pontine reticular formation, the nucleus raphe interpositus (RIP) hosts a  
233 population of cells that exhibit a sustained firing rate during intersaccadic intervals but pauses  
234 during all saccades, regardless of their direction and amplitude. These cells are called  
235 omnidirectional pause (or omnipause) neurons (OPN) and are thought to prevent the eyes  
236 from moving during visual fixation through their inhibitory post-synaptic influence upon the

237 premotor burst neurons (Fig. 2). Moreover, with their pause, OPN could also be responsible  
238 for the synchronous onsets of horizontal and vertical saccades, as they project to burst  
239 neurons in both the horizontal and vertical gaze centers. So far, however, experimental  
240 studies have failed to document onset asynchronies during inactivation or lesion of RIP. No  
241 fixation instability was reported either. The absence of deficits in visual fixation may have  
242 resulted from the particular testing conditions. Indeed, the consequence of suppressing OPN  
243 sustained activity during delayed or memory-guided saccade tasks was not tested. Indeed, the  
244 observation of irrepressible saccades to the peripheral target during the delay interval would  
245 unambiguously confirm the role of OPN in visual fixation; a result that electrical  
246 microstimulation studies have suggested. Unfortunately, these stimulation studies are not  
247 sufficiently conclusive because it is possible that the interruption and the delaying of saccades  
248 by electrical stimulation result from undesired retrograde recruitment of inhibitory burst  
249 neurons.

250 Turning back to the generation of combined horizontal and vertical saccades, one  
251 study reported crucial observations signaling a process that couples their time course during  
252 oblique saccades. When the horizontal component is experimentally slowed by the local  
253 injection of a pharmacological agent in the pontine reticular formation, the vertical  
254 component was also slowed. In some of these experiments, the duration of both components  
255 was prolonged and the accuracy of saccades was preserved, supporting further the  
256 persistence and preservation of the target-related commands. The neural connectivity  
257 underlying this “component stretching mechanism” have not yet been elucidated.

## 258 Combined eye and head movements

259 Saccades are frequently associated with a head movement when the target  
260 eccentricity approaches and exceeds the limits of the oculomotor range. Moving the head  
261 enable to look at targets located more eccentrically in the visual field, and to re-centers the  
262 eyes in their orbit. The directions of the eyes in the orbit and of the head relative to the trunk  
263 add together to determine the direction of gaze.

264 Two functional modes characterize orienting gaze movements toward a static target:  
265 a mode during which both eyes and the head rotate in the same direction and a mode during  
266 which they move in opposite directions. The second mode happens sometimes when the head

267 movement precedes the eye saccade, mostly when the target location is known or  
268 foreseeable. More frequently, it happens later because the eyes move much faster than the  
269 head. The equilibrium of bilateral activity that characterizes visual fixation has been reached  
270 before the head has terminated its movement. Before describing how gaze is stabilized at the  
271 end of orienting movements, we shall examine the first mode, i.e., how despite the vestibulo-  
272 ocular reflex, the eyes and the head can move in the same direction during horizontal gaze  
273 shifts (Figure 4).

## 274 Combining a head movement with a saccade

275 In this section, we limit our description to the horizontal eye movements that are made  
276 while the head also moves horizontally. Whether the head is moving or not, behavioral studies  
277 show that the gaze movements are equally accurate. In the monkey, around twenty muscles  
278 are involved to change the orientation of the head. Among them are the muscles whose  
279 contraction changes the orientation of the head relative to the trunk, the muscles that  
280 stabilize the head during its rotation and the muscles that do not exhibit any change. The co-  
281 contraction of the left and right *rectus capitis posterior minor* (RCPm) stabilize the atlas while  
282 the contraction of the *rectus capitis posterior major* (RCPM) and *obliquus capitis inferior* (OCI)  
283 produce an ipsilateral horizontal rotation of the head. The observation that the contralateral  
284 muscles exhibit no electromyographic change indicates that stopping the head rotation is not  
285 caused by muscle co-contraction. For movement amplitudes greater than 20 degrees, the  
286 contraction of the *splenius capitis* muscle adds to that of the RCPM and OCI muscles. At the  
287 end of the orienting movement, the co-contraction of the RCPm, RCPM, OCI and *obliquus*  
288 *capitis superior* (OCS) muscles altogether stabilizes the head.

289 Thus, orienting gaze shifts mobilize several muscles in parallel when a movement of  
290 the head accompanies the saccade. The synergy results from activities distributed within a  
291 complex set of motor and premotor neurons located in the reticular and vestibular nuclei.  
292 Contrary those involved in the cat, the premotor processes remain incompletely characterized  
293 in the monkey. Contemporary knowledge is not sufficient to reach a synthetic understanding  
294 that is comparable to the neurophysiology of saccades.

295 The recruitment of EBN and reticulo-spinal neurons (RSN) by descending commands  
296 from bursting cells in the deep superior colliculus (grey-colored synapses a in Fig. 4) leads to

297 the excitation of the pools of extraocular motoneurons (ABD) in the abducens nucleus and  
298 neck motoneurons (NMN) in the cervical spinal cord (green and blue synapses b), and thus, to  
299 the contraction of the agonist extraocular and neck muscle fibers, respectively. Contrary to  
300 the cat, collicular connections with EBN do not seem to be direct in the monkey. The EBN and  
301 RSN also excite the IBN (synapse a'), thereby suppressing the activity of cells that otherwise  
302 act to facilitate the contraction of antagonist extraocular (synapses c) and neck muscles  
303 (synapse g), respectively. Finally, they also excite secondary vestibular neurons which are  
304 inhibitory (IVN-2; blue and green colored synapses d) and located in the ipsilateral medial  
305 vestibular nucleus. Within the vestibular nuclei, the discharge of IVN-2 inhibits the secondary  
306 vestibular neurons, IVN-1 and EVN-1 (purple-colored synapse e). By inhibiting IVN-1, the  
307 motor neurons innervating the agonist extraocular and neck muscles fibers (red synapses f  
308 and f') are disinhibited, and the contraction of these muscles is facilitated. By inhibiting the  
309 EVN-1, the IVN-2 prevent the primary vestibular neurons (PVN), whose firing is enhanced by  
310 the head movement, from causing a counter-rotation of the eyes in the orbits (synapse h).  
311 The contraction of antagonist neck muscles through vestibulospinal pathways is also  
312 prevented (synapse h').

313 **Figure 4 about here**

## 314 Stopping gaze while the head terminates its motion

315 The second mode of combined eye head movements is reminiscent of the vestibulo-  
316 ocular reflex recorded when the head is passively rotated while subjects maintain their gaze  
317 directed toward a visual target. During active eye and head movements, the premotor input  
318 to motor neurons makes a transition from commands fed by target-related (visual or auditory)  
319 signals to commands fed by head movement-related signals. The latter consist of trains of  
320 action potentials that originate in the three semicircular canals buried within the temporal  
321 bone. Each semicircular canal consists of a ring within which a fluid (endolymph) flows and  
322 mechanically deflects the stereocilia of multiple cells whenever the head rotation accelerates  
323 or decelerates. This deflection either increases or decreases the discharge of primary  
324 vestibular neurons (PVN) with a rate proportional to head velocity.

325 The two lateral canals are located in the left and right inner ears and lie roughly in a  
326 "plane" which is tilted not only relative to the Reid plane, but also to the "plane" passing

327 through the medial and lateral rectus muscles. These canals are often called “horizontal”  
328 because they are primarily activated during head rotations about the Earth gravity axis. During  
329 such rotations, PVN on the side toward which the nose is rotating (ipsilateral side) increase  
330 their firing rate while those on the contralateral side decrease their firing rate. These bilateral  
331 changes modify the firing rate of post-synaptic neurons (secondary vestibular neurons)  
332 located in the medial and superior vestibular nuclei. On either side of the brain’s midsagittal  
333 plane, these nuclei are bilaterally organized and house two categories of neurons: type 1 and  
334 type 2 neurons. Type 1 neurons increase their firing rate during head rotations toward the  
335 side (left or right) containing the nucleus in which their discharge is recorded. During  
336 contraversive head rotations, they decrease their discharge. In addition, they pause during  
337 saccades. In the monkey, these neurons have been called Position Vestibular Pause (PVP)  
338 neurons. Type 2 neurons exhibit the opposite pattern, increasing their firing rate during  
339 contraversive head rotations and decreasing it during ipsiversive head rotations.

340 **Figure 5 about here**

341 Figure 5 schematizes the mechanism by which vestibular signals contribute to ending  
342 a leftward movement of gaze toward a visual target. The end of the orienting movement is  
343 characterized by a time interval during which the gaze direction remains stationary relative to  
344 the trunk while the head slowly terminates its motion. The saccades by both eyes give way to  
345 their rotation in the opposite direction. As the head rotates, the primary vestibular neurons  
346 (PVN) excite the type I vestibular neurons (EVN-1) in the ipsilateral medial and ventrolateral  
347 vestibular nuclei. In turn, the EVN-1 initiate and drive the counter-rotation of both eyes in the  
348 orbit by exciting the motor (LRMN) and internuclear (AIN) neurons in the contralateral  
349 abducens nucleus (red-colored synapses a). Thus, the abducens neurons can resume their  
350 activity from the pause imposed by the inhibitory input from IBN in the left Med RF (see blue-  
351 colored synapses b in Fig. 2). The LR muscle fibers of the right eye can contract, as well as the  
352 MR muscle fibers of the left eye, which are activated via motoneurons located in the OMN.  
353 The latter cells (MRMN) are also excited by neurons in the ipsilateral nucleus of the ascending  
354 tract of Deiters (ATDN; green-colored synapse b). In parallel, the spikes emitted by other type  
355 1 vestibular neurons (IVN-1) choke the activity the LRMN and AIN in the abducens nucleus  
356 (red-colored synapses c), preventing them from responding to any residual descending  
357 (target-related) commands. The recruitment of type 2 neurons (IVN-2) in the contralateral

358 vestibular nuclei (red-colored synapse d) complements the cessation of agonist commands by  
359 inhibiting the activity of EVN-1, thereby reducing their excitatory influence upon the motor  
360 and internuclear neurons (synapses e). IVN-2 also inhibit the activity of IVN-1, which in turn  
361 favors the disinhibition of cells (synapses e) in charge of the counter-rotation of the eyes under  
362 the influence of EVN-1 (synapses a).

363         The functional anatomy schematized in Fig. 5 enables us to see how the disinhibition  
364 of type 1 vestibular neurons can quickly arrest the eye saccade during ipsilateral orienting  
365 movements. The spikes of IVN-1 (inhibitory synapses c) choke the burst commands while the  
366 spikes of EVN-1 order the eyes to counter-rotate as the head terminates its motion (excitatory  
367 synapses a). This mechanism also helps us to understand the hypometria of contralateral eye  
368 and head movements after unilateral lesion of the caudal fastigial nucleus (for instance the  
369 right nucleus). Contralateral (leftward) saccades are hypometric because the agonist drive  
370 from EBN lacks of the excitatory input from inactivated (right) fastigial cells, and because the  
371 saccade-related burst of neurons in the opposite (unaffected) fastigial nucleus excite IBN in  
372 the contralateral (right) reticular formation. These IBN inhibit IVN-2 in the opposite (left)  
373 vestibular nuclei, disinhibiting the excitatory influence of EVN-1 (initiating the counter-  
374 rotation of the eyes) and the inhibitory influence of IVN-1 upon ipsilateral motor neurons  
375 (inhibiting the saccade-related drive). The latter mechanism also explains the hypometria of  
376 head movements. Their amplitude is truncated because the IVN-1 inhibits the ipsilateral neck  
377 motor neurons (NMN; synapse e) while the EVN-1 facilitates the contraction of contralateral  
378 neck muscles (synapse f).

379

#### **Figure 6 about here**

380         As for the generation of upward and downward saccades (Fig. 3), the neural  
381 connectivity involved in the generation of downward and upward slow eye movements are  
382 not symmetrical. Figure 6A schematizes the network that stabilizes gaze during downward  
383 gaze movements. While the head pitches down and slowly terminates its motion, both eyes  
384 rotate upward in the orbits. The upward eye movement is the outcome of contracting SR and  
385 IO muscles fibers. Driven by the increased firing of PVN connected with the left anterior canal,  
386 excitatory vestibular neurons (EVN-U) in the left medial vestibular nucleus activate the motor  
387 neurons innervating the left eye's SR and the right eye's IO muscle fibers (synapses a).

388 In addition to elevating both eyes, the contraction of these fibers causes an intorsion  
389 of the left eye and an extorsion of the right eye, as if both eyes were counteracting a tilt of the  
390 head toward the left shoulder. This clockwise torsion of both eyes can be attenuated by the  
391 torsion caused by the excitatory input from EVN-U in the right MVN. Because of their  
392 excitation by the right anterior canal, PVN drive the firing rate of EVN-U, which in turn excite  
393 the motor neurons that innervate the right eye's SR and the left eye's IO muscle fibers  
394 (synapses b), causing the right eye's intorsion and left eye's extorsion. The absence of torsion  
395 during strictly upward slow eye movements suggests that the output of the left and right  
396 vestibulo-oculomotor channels have been adjusted so that the torsional signals balance out.

397 Regarding the antagonist muscles, their inhibition is promoted by IVN-U located in the  
398 superior vestibular nuclei. These cells inhibit the motor neurons innervating the IR of the  
399 ipsilateral eye (synapses c) and those innervating the SO muscle of the contralateral eye  
400 (synapse d). Contrary to the network involved in horizontal eye and head movements (Fig. 5),  
401 the neural mechanisms triggering the counter-rotation of the eyes when the head pitches  
402 down are not yet elucidated. However, the inputs are necessarily bilateral and balanced since  
403 the eyes move by the same amount and their torsion canceled.

404 Finally, figure 6B schematizes the neuronal network involved in stopping an upward  
405 gaze shift while the head slowly terminates its upward motion. Both eyes rotate downward in  
406 the orbits because of the contraction of IR and SO muscle fibers. This is driven by the increased  
407 firing of primary vestibular neurons (PVN) connected with the left posterior canal. Excitatory  
408 vestibular neurons (EVN-D) in the left medial vestibular and ventral lateral vestibular nuclei  
409 activate the motor neurons innervating the fibers of the right eye's IR and the left eye's SO  
410 muscles (synapses a).

411 As above, in addition to depressing both eyes, the contraction of these fibers cause an  
412 extorsion of the right eye and an intorsion of the left eye, as if the eyes are counteracting a tilt  
413 of the head toward the right shoulder. Once again, the binocular torsion is attenuated by a  
414 torsion made in the opposite direction and caused by excitatory input from the right posterior  
415 canal to the motor neurons innervating the left eye's IR and the right eye's SO muscle fibers  
416 (synapses b). Inhibitory vestibular neurons (IVN-D) located in the superior vestibular nuclei  
417 prevent the antagonist muscles from contracting by inhibiting the motor neurons innervating

418 the SR of the contralateral eye (synapses c) and possibly also the motor neurons innervating  
419 the IO muscle of the ipsilateral eye (synapse d). As for the neural mechanisms ending  
420 downward gaze shifts, the neural mechanisms triggering the counter-rotation of the eyes  
421 when the head pitches up are not completely identified. Nevertheless, if the eyes do not  
422 exhibit any torsional component, the motor commands are necessarily bilateral and balanced.

423 In summary, by studying the networks underlying the generation of slow eye  
424 movements, we discover a complexity that radically differs from the straightforward solutions  
425 that human engineers would have designed. One puzzling question concerns the constraints  
426 that led the torsional components caused by the contraction of elevator or depressor muscles  
427 to cancel each other out. Moreover, the connectivity that we have described is not complete,  
428 because new eye movements can be produced in response to “unusual” combinations of head  
429 rotations and visual stimulation. Experiments in the cat have shown that the visual stimulation  
430 exerts a significant influence on the functional connectivity yielding vestibulo-oculomotor  
431 responses. Horizontal compensatory eye movements can be generated during vertical head  
432 rotations in the dark after training sessions during which the visual field moved horizontally  
433 whenever the head rotated vertically.

## 434 Fixating a static visual target

435 Considering the line of sight as the direction of gaze measured when a subject fixates  
436 a visual target, the binocular fixation point designates the intersection between the two lines  
437 of sight. Of course, the quantification of movements must be distinguished from their  
438 neurophysiological correspondence. On the retinal side, looking at a visual target obviously  
439 does not reduce to the excitation of one single photoreceptor on the fovea of each eye. On  
440 the oculomotor side, the orientation of the eyes is maintained steady thanks to the discharge  
441 of a tonic neurons distributed in the nucleus prepositus hypoglossi (NPH), the vestibular nuclei  
442 (in the medullary reticular formation) and in the interstitial nucleus of Cajal. The more  
443 deviated the eyes in the orbit, the higher their firing rate. In addition to connective tissues  
444 that stabilize each eyeball relative to the orbit, two neuronal networks are involved in  
445 maintaining the rotation axes of the eyes within Listing’s plane and deviating them  
446 horizontally and vertically. These networks are relatively independent from each other insofar  
447 as a lesion in the NPH primarily affects the ability to maintain gaze direction within the



448 horizontal plane, with marginal effects on vertical gaze direction. After the saccades, whose  
449 amplitude is unaffected, the eyes exhibit an exponential drift toward their primary orientation  
450 (roughly straight ahead). By contrast, lesion in the NIC causes a failure to hold vertical  
451 deviations of the eyes (i.e. both upward and downward) but not horizontal deviations. A  
452 torsional drift of the eyes is also observed when the lesion is unilateral.

453           Considering now the case when the foveation changes between targets or locations  
454 situated at different depths in the three-dimensional physical space, three visuomotor  
455 processes occur: 1) vergence, 2) accommodation and 3) variation of pupil diameter.  
456 Convergence designates the symmetrical eye movements made when the MR muscle fibers  
457 of both eyes contract, diminishing the distance of the binocular fixation zone relative to the  
458 head. Divergence designates those movements made when the distance increases because of  
459 a binocular relaxation of MR muscle fibers. The contraction level of intraocular muscles also  
460 changes. During convergence, the contraction of ciliary muscles (CM) reduces the tension in  
461 zonular fibers, changing the refractive power of the lens as its anterior surface bulges forward  
462 (increase in convexity). Thus, the target images are brought into focus on the foveae. This  
463 accommodation is associated with a myosis, i.e., the constriction of the iris and the reduction  
464 of the pupil diameter, thereby increasing the depth of field. The myosis itself results from the  
465 contraction of the sphincter pupillae (SP) combined with the relaxation of the dilator pupillae  
466 (DP). Altogether, these three visuomotor processes constitute the so-called the near response  
467 (or near triad).

468           Although these processes are generated jointly, clinical studies report pathological  
469 cases in which they are dissociated and the neuroanatomy helps us to understand why. Figure  
470 7 shows that the contraction of MR muscle fibers is controlled by the firing rate of motor  
471 neurons (MRMN) located in the oculomotor nucleus whereas the intrinsic musculature of each  
472 eye is controlled by motor neurons located in the ciliary ganglions (CG) and premotor neurons  
473 in the Edinger-Westphal preganglionic nucleus (EWpg). In both cases, the innervation is  
474 ipsilateral. The binocular control and the near triad starts with their afferent input from two  
475 major regions of the midbrain tegmentum: the supraoculomotor area (SOA) and the central  
476 mesencephalic reticular formation (cMRF).

477

**Figure 7 about here**

478           The SOA is primarily involved in the generation of the slow near response and its  
479 sustained maintenance. Therein, we find burst neurons and tonic neurons, with separate  
480 subgroups characterized by different discharge patterns during the generation of diverging  
481 and converging eye movements. More common just lateral to the MLF, four categories of  
482 neurons are found: convergence burst neurons, divergence burst neurons, convergence tonic  
483 neurons and divergence tonic neurons. Whether divergence neurons exert an inhibitory  
484 influence upon the firing rate of convergence neurons is not known yet. Neurons in SOA send  
485 projections to the medial rectus MN that are ipsilateral, whereas the projections to the EWpg  
486 are bilateral.

487           In the cMRF, we find neurons that emit a burst discharge whenever the near response  
488 accompanies a saccadic eye movement: saccade convergence burst neurons and saccade  
489 divergence burst neurons. The former fire during asymmetrical saccades associated with an  
490 increase of the vergence angle and the latter fire during asymmetrical saccades associated  
491 with a divergence. Each cMRF innervates the SOA and the EWpg bilaterally. It also sends  
492 ipsilateral projections to the sites in the OMN in which the motor neurons that innervate the  
493 singly-innervated muscle fibers are located.

494           The bilateral projections from SOA to the EWpg, and from the cMRF to both EWpg and  
495 SOA, are completed by bilateral afferents from caudal fastigial nuclei (CFN) whose  
496 contribution in converging eye movements has been reported by unit recording and lesion  
497 studies. In addition to send bilateral projections to the midbrain tegmentum and contralateral  
498 projections to the pontomedullary reticular formation (where EBN and IBN are located, Fig.  
499 2), the CFN also project bilaterally to the rostral part of the deep superior colliculi, with a  
500 contralateral predominance. Therein, some cells either increase (convergence neurons) or  
501 decrease (divergence neurons) their firing rate during vergence eye movements.

502           In addition to this role in vergence, recording studies in the rostral superior colliculi  
503 (SC) also revealed the presence of cells that burst during miniature saccades (also called  
504 microsaccades), just like more caudal cells discharge during larger saccades. Local  
505 pharmacological inactivation confirmed a causal role in the generation of microsaccades.  
506 However, it also unraveled an implication of rostral SC in specifying the direction of gaze when  
507 a target is presented (or even imagined) in the central visual field, static or moving.

508 Unbalanced activity between the two rostral SC causes a fixation offset: gaze direction is not  
509 directed to the target center but toward an offset location. The same deficit happens after  
510 unilateral pharmacological perturbation of CFN, suggesting that the sustained firing rate of its  
511 neurons adjusts the balance of activity between the two rostral SC during visual fixation. Thus,  
512 the direction of gaze would correspond to an equilibrium of commands that counterbalance  
513 with each other, involving fastigial projections to the left and right rostral SC but also to the  
514 left and right nuclei *reticularis tegmenti pontis* (NRTP). Through their projections to NRTP, the  
515 two rostral SC and CFN have access to neurons which, in the flocculus and paraflocculus,  
516 influence the firing rate of tonic neurons that innervate the motor and internuclear neurons  
517 in the abducens nuclei.

518 In summary, the knowledge of the detailed neuronal circuitry underlying the  
519 generation of disjunctive eye movements is not advanced as much as the circuitry for  
520 conjugate saccades. However, significant progress has been made during the last decade,  
521 helping to better understand the neurophysiology of vergence eye movements and  
522 strabismus.

## 523 Tracking a moving visual target

524 A target drifting in the visual field often elicits a primary saccade (called interceptive  
525 saccade) at the end of which gaze does *not* land ahead of the moving target. Interceptive  
526 saccades either accurately capture (foveate) or fall behind the target. Then, a slow eye  
527 movement follows with a velocity that rarely matches the target's. A textured background  
528 (yielding visual motion in the direction opposite to the eye movement) does not seem to be  
529 responsible for the pursuit slower than target velocity because the consequences of its  
530 suppression are very weak. A subsequent correction saccade (called catch-up saccade)  
531 restores the foveation. Thus, unless the target trajectory is already known and foreseeable,  
532 gaze lags behind the target most of the time, especially when the target is small: the visual  
533 tracking is mostly composed of catch-up saccades interspersed by intervals during which the  
534 eyes drift roughly in the same direction as the target and with a lesser speed. In well-trained  
535 subjects, the catch-up saccades can be eliminated. Moreover, increasing the target size  
536 enhances the velocity of slow eye movements and reduces the size and number of catch-up

537 saccades. This point is important because most experimental studies use a small spot of light  
538 as a target.

539           Contrary to a static target which yields a bounded activity, a moving spot evokes on  
540 the retina a streak of activity the tail of which corresponds to past locations of the target and  
541 the leading edge the most recent location. In the deep superior colliculus, the population of  
542 saccade-related burst neurons is expanded as for a static target. However, it does not recruit  
543 cells that fire during saccades to future target locations. The population consists of a  
544 continuum of cells ranging from neurons issuing commands related to past locations of the  
545 target to neurons issuing commands related to its current location. At the level of motor  
546 neurons, other input must therefore complement the collicular signals. This input stems, at  
547 least in part, from motion signals processed in area MT because its lesion leads to saccades  
548 landing at locations that the target crossed earlier. Thus, the ability to capture the visual target  
549 here and now (at the time of saccade landing) may consist of adding a “predictive” component  
550 based on the integration of putative target-related “velocity” signals. However, an alternative  
551 explanation is possible. Accurate saccades toward a moving target may result from  
552 attenuating the synaptic weight of spikes emitted by cells that were the earliest to be excited  
553 by the passage of the target across their response field combined with promoting the synaptic  
554 weight of action potentials emitted by the cells that are more recently excited.

555           The dorsolateral pontine nucleus (DLPN) is one of the nuclei that relays signals from  
556 motion-related areas of the cerebral cortex to the cerebellum. When a chemical lesion is  
557 placed in the DLPN, saccades toward a moving target are hypometric whereas saccades to a  
558 static target remain unchanged. The hypometria suggests that the saccades were directed  
559 toward the past location of the target. Neurons in DLPN project to the floccular and medio-  
560 posterior regions of the cerebellum. Ablation of the floccular region (flocculus and  
561 paraflocculus) impairs the velocity of slow eye movements, seemingly without affecting catch-  
562 up saccades. By contrast, unilateral inactivation of the output nucleus of the medio-posterior  
563 cerebellum, the caudal fastigial nucleus, impairs both contralesional saccadic and pursuit eye  
564 movements. Gaze direction always lags behind the moving target because the saccades are  
565 hypometric and the pursuit velocity slowed. Unfortunately, the interpretation of the  
566 hypometria is complicated by the fact that saccades toward a static target are also

567 hypometric. More experiments are required to refine the neuronal mechanisms underlying  
568 the generation of these two saccade categories.

569 **Figure 8 about here**

570 Concerning the generation of slow pursuit eye movements, the figure 8 schematizes  
571 the complex neuronal network involved in their generation when the movement direction is  
572 horizontal. The schema is not complete because our current knowledge prevents from  
573 explaining how neurons in the oculomotor vermis and the rostral superior colliculi are  
574 recruited during the generation of tracking (saccadic and slow) eye movements.

575 Some cells firing tonically in the nucleus prepositus hypoglossi (NPH) and the nearby  
576 medial vestibular nucleus (MVN) increase their firing rate during ipsilateral pursuit. Although  
577 called “eye-head velocity” neurons in the monkey, we shall name them tonic neurons for  
578 simplicity and for distinguishing them from the burst neurons and EVN-1 described in the  
579 previous paragraphs. Some of the tonic neurons are believed to provide an excitatory input to  
580 the abducens neurons for contracting the agonist muscle fibers during ipsilateral pursuit.  
581 While documented in the cat, this ipsilateral excitatory tonic input (ETN) has been questioned  
582 in the monkey. Most NPH/MVN neurons seem to be inhibitory and to project to the  
583 contralateral side (synapses a and b). When the sustained firing rate of tonic neurons is  
584 considered, we understand that the reciprocal commissural inhibition between the NPH/MVN  
585 in the left and right sides yields a push-pull organization, such that a reduced firing rate on  
586 one side enhances the firing rate on the opposite side. Thus, by suppressing the activity of the  
587 neurons that innervate the antagonist muscle fibers (red synapses a), the inhibitory tonic  
588 neurons (ITN) in the NPH/MVN contribute to the relaxation of these muscles, while  
589 disinhibiting the ipsilateral abducens and internuclear neurons (blue synapses a) and  
590 promoting an ipsiversive movement of both eyes.

591 Neurons in NPH/MVN are monosynaptically inhibited by Purkinje cells in the flocculus  
592 and the ventral paraflocculus (synapse b), which receive excitatory input from the three major  
593 pontine nuclei (synapses c) involved in relaying visual motion signals to the cerebellum: the  
594 rostral part of nucleus reticularis tegmenti pontis (rNRTP), the dorsolateral pontine nucleus  
595 (DLPN) and the dorsomedian pontine nucleus (DMPN). These pontine nuclei contribute to the  
596 inhibition that Purkinje cells exert upon NPH/MVN neurons. After a chemical lesion in the

597 dorsolateral pontine nucleus (DLPN) or in the rostral nucleus reticularis tegmenti pontis  
598 (rNRTP), ipsilesional pursuit eye movements are severely impaired. The suppression of  
599 pontine input likely reduces the floccular inhibition of ITN neurons, which in turn impede the  
600 recruitment of agonist motor and internuclear neurons. The consequences of suppressing the  
601 input from DMPN have not been tested yet. However, an impairment of ipsilesional pursuit is  
602 also expected because the DMPN and the contralateral caudal fastigial nucleus exhibit strong  
603 reciprocal connections, and fastigial inactivation severely impairs the generation of  
604 contralesional pursuit eye movements.

605         The NPH/MVN are also the target of signals from neurons in the pretectal nucleus of  
606 the optic tract (NOT; synapse d) some of which are sensitive to the motion of a small visual  
607 target. These neurons fire during ipsilateral target motions and their loss severely impairs the  
608 ability to generate ipsilesional slow pursuit eye movements. NOT receives visual signals from  
609 the retina and from the middle temporal (MT) and medial superior temporal (MST) areas of  
610 cerebral cortex (synapses e and f) wherein numerous cells are sensitive to target motion as  
611 well. Projections of the frontal eye field (FEF) to NOT and to NPH have been documented  
612 (synapses e and e'). This access of frontal cortex to premotor neurons does not indicate a  
613 voluntary control of pursuit eye movements since the presence of a target is required for  
614 initiating a smooth pursuit. The NOT contributes to the maintenance of ipsilateral pursuit eye  
615 movements by its direct projections to tonic neurons in the ipsilateral NPH/MVN (synapse d),  
616 but also to the ipsilateral pontine nuclei (synapses g).

617         Through their projections to the ipsilateral rostral SC (synapse j), Gaba-ergic cells in  
618 NOT may contribute to suppression of the generation of saccades made in the direction  
619 opposite to the target motion. Simultaneously, they may depress the excitatory drive that  
620 NRTP exerts upon the ipsilateral paraflocculus (synapse k).

621         Finally, the secondary excitatory vestibular neurons (EVN-1 or PVP cells) that are  
622 involved in moving the eyes in the direction opposite to the head movement (Fig. 5) increase  
623 their firing rate during contraversive pursuit eye movements. However, as they do not seem  
624 to be inhibited by Purkinje cells located in the floccular region, the origin of the discharge  
625 modulation during contraversive pursuit remains to be identified. Direct projections from the  
626 frontal eye fields to the NPH/MVN might support this influence.

## 628 Conclusion

629 Studying orienting movements of gaze is a convenient means for investigating how  
630 intertwined networks of neurons in the central nervous system transforms sensory signals into  
631 motor commands, but also, how it enables an entire animal to visually locate and capture an  
632 object in the physical environment and to adapt when intrinsic damage or contextual changes  
633 alter their execution.

634 During the last decades, technical developments offered the possibility to measure  
635 precisely the time course of these movements and to study correlations between the firing  
636 rate of neurons and kinematic parameters such as movement amplitude, velocity,  
637 acceleration and various differences (e.g., gaze error, velocity error, etc.). However, these  
638 correlation studies should not lead us to believe that a one-to-one correspondence exists  
639 between the multiple neuronal networks within which activities propagate, and the extrinsic  
640 and homogeneous medium (mathematical space) with which we quantify the motion of rigid  
641 objects such as the eyeballs, the head and targets. Such a mapping is not at all obvious; it is  
642 even quite questionable. Contrary to the physical space, the medium of neuronal activity is  
643 neither homogeneous nor passive. Unlike most objects at which we look and that we  
644 manipulate, the corresponding brain activity is not rigid. Even the mere spot of activity that a  
645 small static object evokes on the retina yields multiple parallel flows of activity that make its  
646 correspondence in the brain spatially distributed, temporally extended and context-  
647 dependent. Moreover, reducing neurons or neuronal chains to units encoding geometric or  
648 kinematic relations between gaze and target conceals the muscle forces and the multiple  
649 antagonisms that we have described between muscles. Furthermore, the velocity profile of  
650 the movement and the time course of force development do not match. During horizontal  
651 saccades for example, the duration of the interval during which the muscle force increases is  
652 on average 60% shorter than the duration of the total change in eye orientation. A force decay  
653 happens well before the change in eye position ends and the larger the saccade, the longer its  
654 lead-time relative to saccade arrest. Finally, the temporal series of numerical values  
655 quantifying the changes during eye reorientation hides the antagonisms between those  
656 multiple channels that cause each movement. To our knowledge, no study has reported  
657 identical time courses between the kinematic and neurophysiological recordings that would  
658 support the assumption of an isomorphism.

659 In the majority of models proposed during the last decades, the movements of the  
660 eyes and the head were considered as driven by (intrinsic) error signals encoding displacement  
661 vectors in physical space. These models have definitely been useful to communicate concepts  
662 and to bring a comprehensive picture of the complexity underlying the generation of  
663 movements. However, embedding geometric and kinematic notions within the inner  
664 functioning of the brain (i.e., mapping intrinsic neuronal signals with extrinsic behavioral  
665 measurements) may be neurophysiologically misleading because different constraints  
666 characterize the neurophysiological and kinematic descriptions. In fact, rather than outcomes  
667 of processes reducing geometric or kinematic errors, the saccade and pursuit acceleration  
668 may resume merely to transitions between equilibria opposing populations of neurons whose  
669 activity leads to mutually antagonist movement tendencies.

670 Further empirical investigation is still required to determine and explain several other  
671 issues: i.e., whether and how the networks underlying orienting movements of the eyes and  
672 head interact with those generating other types of goal-directed action such as reaching  
673 movements of the hand or locomotion; whether and how they interact with the networks  
674 involved in the navigation and the memory of locations; and whether and how they support  
675 the learning of new skills and possibly the acquisition of more abstract knowledge such as  
676 geometry or counting. With the recent multiplication of cognitive studies that use eye-tracking  
677 techniques to explore the so-called "inner space" with quantitative methods, more effort is  
678 required to characterize what exactly are those covert processes that eye movements would  
679 express. At the same time, neurophysiological and neuroanatomical works must continue to  
680 reveal the fine structure of the brain connectivity and to unravel the multiplicity of channels  
681 and networks that enable a living organism to connect with its natural and cultural  
682 environments as well as to reactivate the memory of past events.

683 By studying the simple and seemingly straightforward problem of orienting the eyes  
684 toward the location of a physical object, we see how the neurophysiological and  
685 neuroanatomical studies performed with animals enables us to understand the symptoms  
686 exhibited by patients suffering from eye movement disorders. They also show that  
687 evolutionary and embryological developments led to patterns that are different from the  
688 strategies of human engineers. Contrary to the case where a design precedes the realization  
689 of a machine for solving a specific problem, the physiology teaches us that any behavioral



690 observation is the outcome of a complex network of multiple and parallel chains of neurons.  
691 It also teaches us how the multiplicity and the diversity of elements enable an organism to  
692 solve several problems in parallel and even take up new challenges.

693

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1032

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1038

## 1039 Figure captions

1040

1041 **Figure 1:** Schematic representation of the extraocular muscles (A) and pulling directions  
1042 engaged by the contraction of their fibers when the eyes are centered in the orbit (B). LR:  
1043 lateral rectus, MR: medial rectus, SR: superior rectus, IR: inferior rectus, SO: superior oblique,  
1044 IO: inferior oblique, tr: trochlea. The red arrows indicate the muscles whose contraction  
1045 abducts the eye, the black arrows the muscles whose contraction adducts the eye. The  
1046 turquoise arrows indicate the muscles whose contraction elevates the eye, the yellow arrows  
1047 those whose contraction lowers the eye. The blue arrows indicate the muscles whose  
1048 contraction causes an intorsion of the eye, the green arrows those whose contraction causes  
1049 an extorsion.

1050

1051 **Figure 2:** Neuronal network involved during horizontal saccades toward the left (A) and the  
1052 right (B). Connecting lines ended by an arrow indicate excitatory connections; those ended by  
1053 a circle indicate inhibitory synaptic connections. Blue color indicates the agonist neuronal  
1054 elements, red color the antagonist ones. The thickness of connecting lines schematizes the  
1055 strength with which the neurons fire. OPN: omnipause neurons, EBN: excitatory burst  
1056 neurons, IBN: inhibitory burst neurons, MN: abducens motoneurons, AIN: abducens  
1057 internuclear neurons. In the bottom, the thickness of arrows attached to the eyeballs  
1058 schematizes the strength of muscle contraction. LR: lateral rectus, MR: medial rectus, SR:  
1059 superior rectus, IR: inferior rectus, SO: superior oblique, IO: inferior oblique.

1060

1061 **Figure 3:** Neuronal network involved during vertical saccades toward the top (A) and the  
1062 bottom (B). Connecting lines ended by an arrow indicate excitatory connections; those ended  
1063 by a circle indicate inhibitory synaptic connections. Blue color indicates the agonist neuronal  
1064 elements, red color the antagonist ones. The thickness of connecting lines schematizes the  
1065 strength with which the neurons fire. uEBN: upward excitatory burst neurons, dEBN:  
1066 downward excitatory burst neurons, uIBN: upward inhibitory burst neurons, MN:  
1067 motoneurons. In the top, the thickness of arrows attached to the eyeballs schematizes the  
1068 strength of muscle contraction. LR: lateral rectus, MR: medial rectus, SR: superior rectus, IR:  
1069 inferior rectus, SO: superior oblique, IO: inferior oblique.

1070

1071 **Figure 4:** Neuronal network involved during combined horizontal eye and head movements  
1072 toward the left. Connecting lines ended by an arrow indicate excitatory connections; those  
1073 ended by a circle indicate inhibitory synaptic connections. Blue color indicates the agonist  
1074 neuronal oculomotor elements, red color the antagonist ones. Green color indicates the  
1075 cephalomotor elements. The thickness of connecting lines schematizes the strength with  
1076 which the neurons fire. dSC: deep superior colliculus, RSN: reticulospinal neurons, EBN:  
1077 excitatory burst neurons, IBN: inhibitory burst neurons, ABD: abducens motor and  
1078 internuclear neurons, NMN: neck motoneurons, PVN: primary vestibular neurons, IVN:  
1079 inhibitory vestibular neurons, EVN: excitatory vestibular neurons, VIII: eight cranial nerve.

1080

1081 **Figure 5:** Neuronal network involved in ending a leftward gaze shift while the head terminates  
1082 its rotation (stabilized gaze direction). Connecting lines ended by an arrow indicate excitatory  
1083 connections; those ended by a circle indicate inhibitory synaptic connections. Blue color  
1084 indicates the agonist neuronal oculomotor elements, red color the antagonist ones. Green  
1085 color indicates the neurons of the ascending tract of Deiters (ATDN). The thickness of  
1086 connecting lines schematizes the strength with which the neurons fire. LR: lateral rectus, MR:  
1087 medial rectus, VI, abducens nerve, MRMN: motor neurons innervating the medial rectus  
1088 muscle, LRMN: motor neurons innervating the lateral rectus muscle, AIN: abducens  
1089 internuclear neurons, NMN: neck motoneurons, PVN: primary vestibular neurons, IVN:  
1090 inhibitory vestibular neurons, EVN: excitatory vestibular neurons, VIII: eight cranial nerve.

1091

1092 **Figure 6:** Neuronal network involved in ending a downward (A) and upward (B) gaze shift while  
1093 the head terminates its movement (stabilized gaze direction). Connecting lines ended by an  
1094 arrow indicate excitatory connections; those ended by a circle indicate inhibitory synaptic  
1095 connections. Blue color indicates the agonist neuronal oculomotor elements, red color the  
1096 antagonist ones. IOMN: motor neurons innervating the inferior oblique muscle, IRMN: motor  
1097 neurons innervating the inferior rectus muscle, SRMN: motor neurons innervating the  
1098 superior rectus muscle, SOMN: motor neurons innervating the superior oblique muscle, PVN:  
1099 primary vestibular neurons, IVN: inhibitory vestibular neurons, EVN: excitatory vestibular  
1100 neurons, VIII: eight cranial nerve.

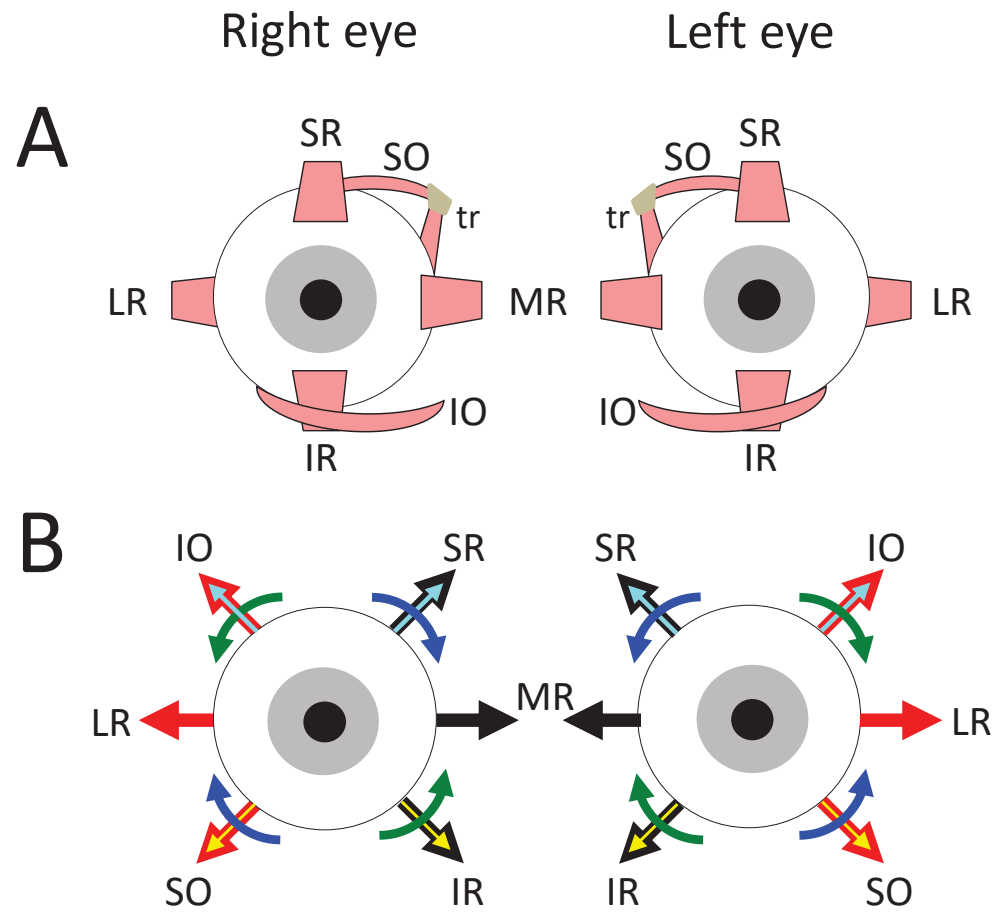
1101

1102 **Figure 7:** Neuronal network involved in the near response. LR: lateral rectus, MR: medial  
1103 rectus, SP: sphincter pupillae, DP: dilator pupillae, CM: ciliary muscle, CG: ciliary ganglion,  
1104 MRMN: motor neurons innervating the medial rectus muscle, EWpg: Edinger-Westphal  
1105 parasympathetic nucleus, cMRF: central mesencephalic reticular formation, SOA:  
1106 supraoculomotor area, cFN: caudal fastigial nucleus, SC: superior colliculus.

1107

1108 **Figure 8:** Neuronal network involved in the generation of horizontal slow pursuit eye  
1109 movements. LR: lateral rectus, MR: medial rectus, MN: motor neurons, AIN: abducens  
1110 internuclear neurons, NHP/MV: complex nucleus prepositus hypoglossi-medial vestibular  
1111 nucleus, ETN: excitatory tonic neurons, ITN: inhibitory tonic neurons, cFN: caudal fastigial  
1112 nucleus, NOT: nucleus of the optic tract, rSC: rostral superior colliculus, rNRTP: rostral part of  
1113 nucleus reticularis tegmenti pontis, DMPN: dorsomedian pontine nucleus, DLPN: dorsolateral  
1114 pontine nucleus, VPL-Th: ventroposterolateral part of thalamus, FEF: frontal eye field, MST:  
1115 medial superior temporal area of cerebral cortex.

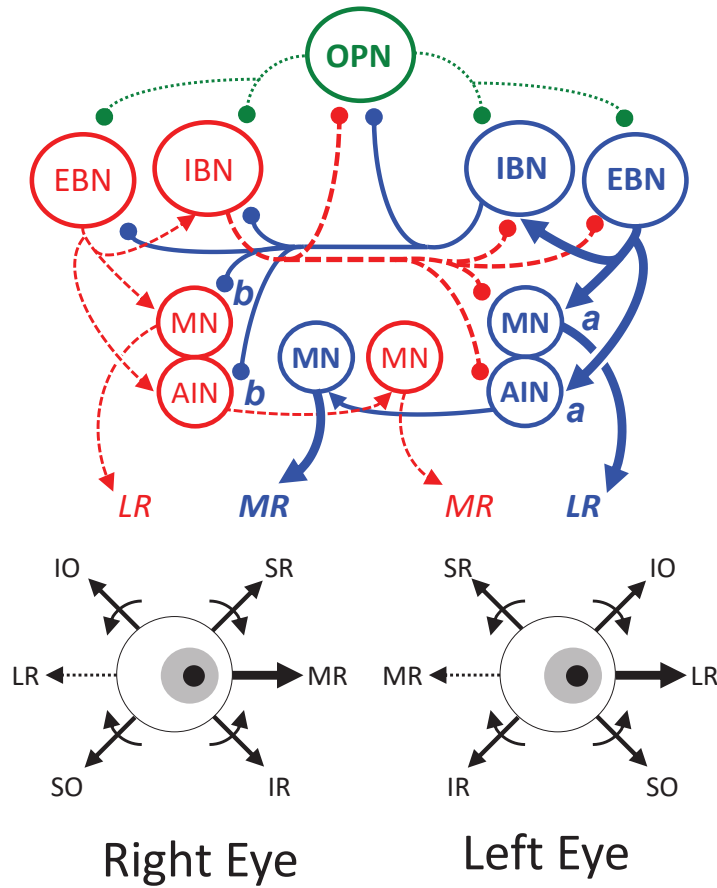
# Figure 1



# Figure 2

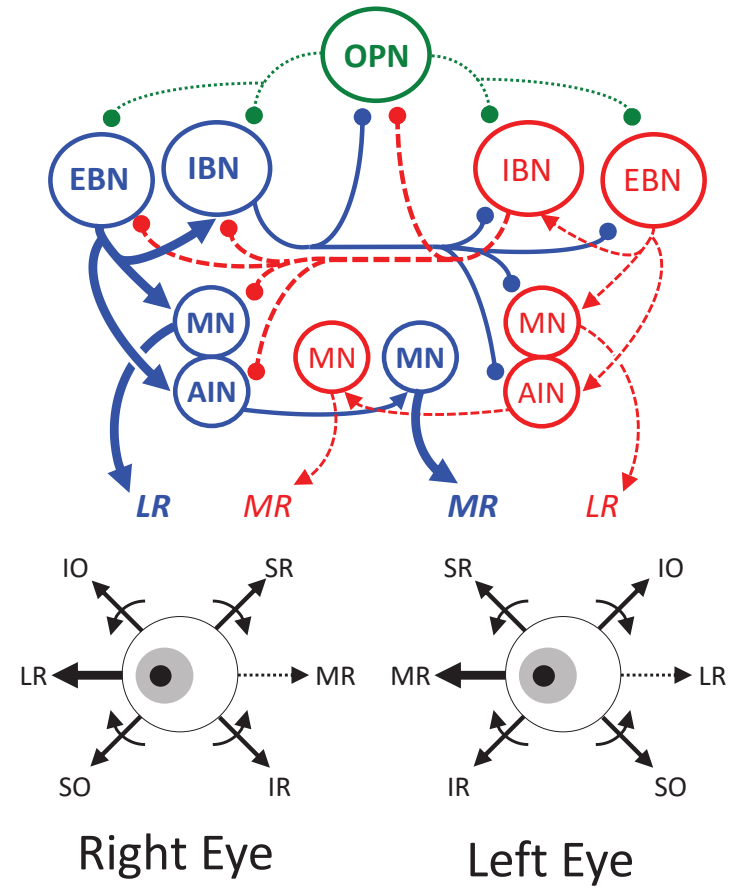
## A

### LEFTWARD



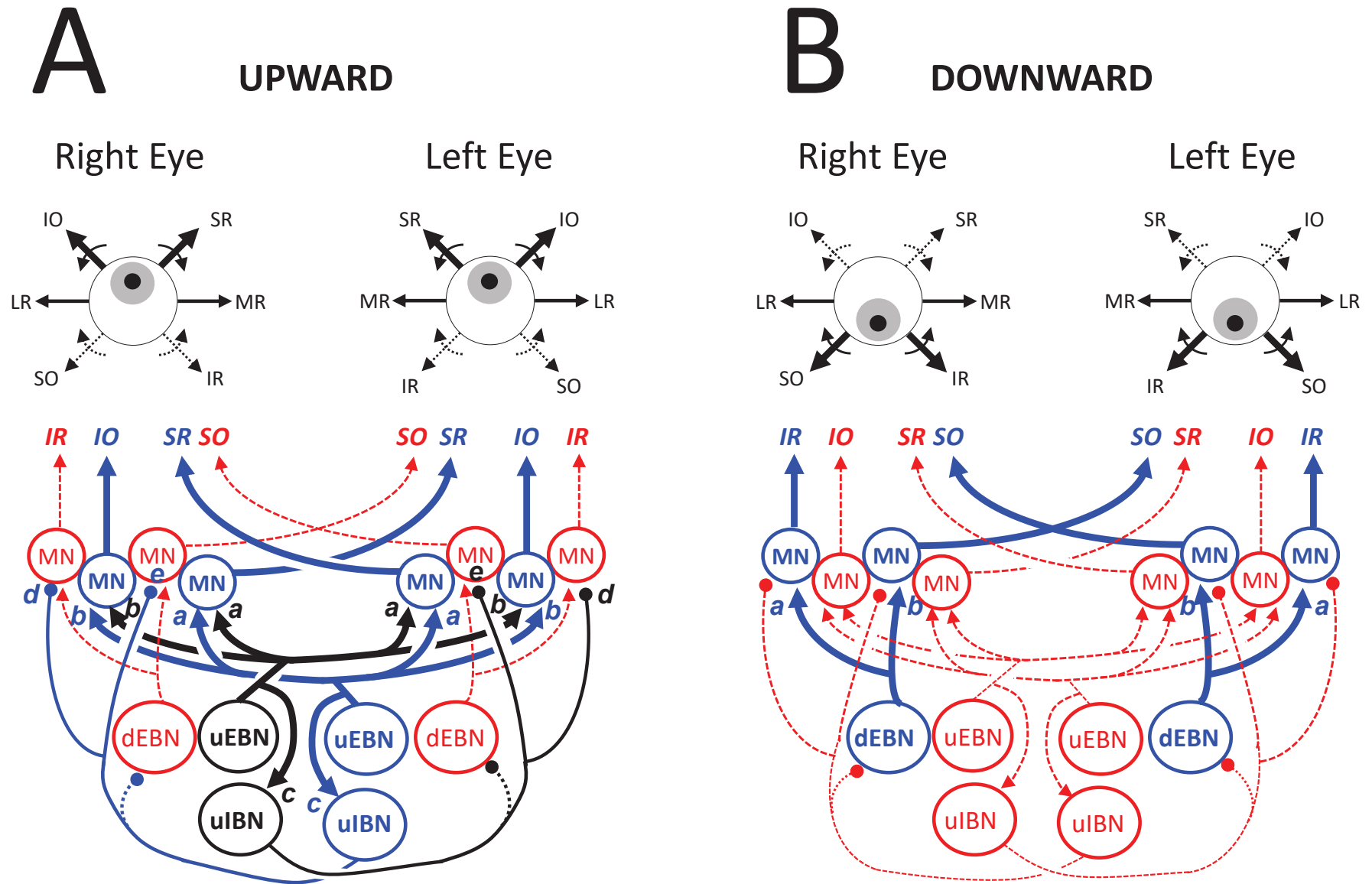
## B

### RIGHTWARD

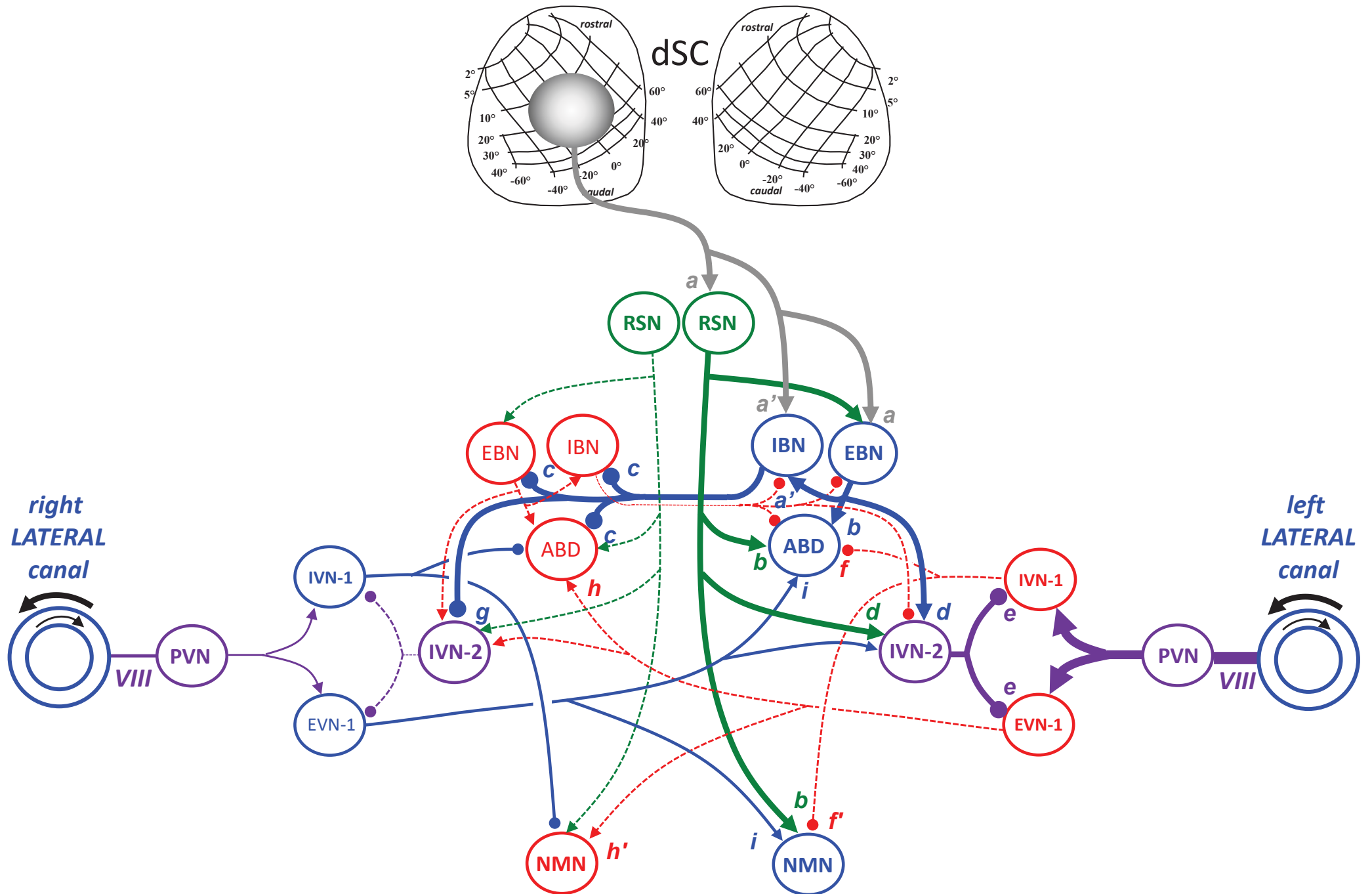




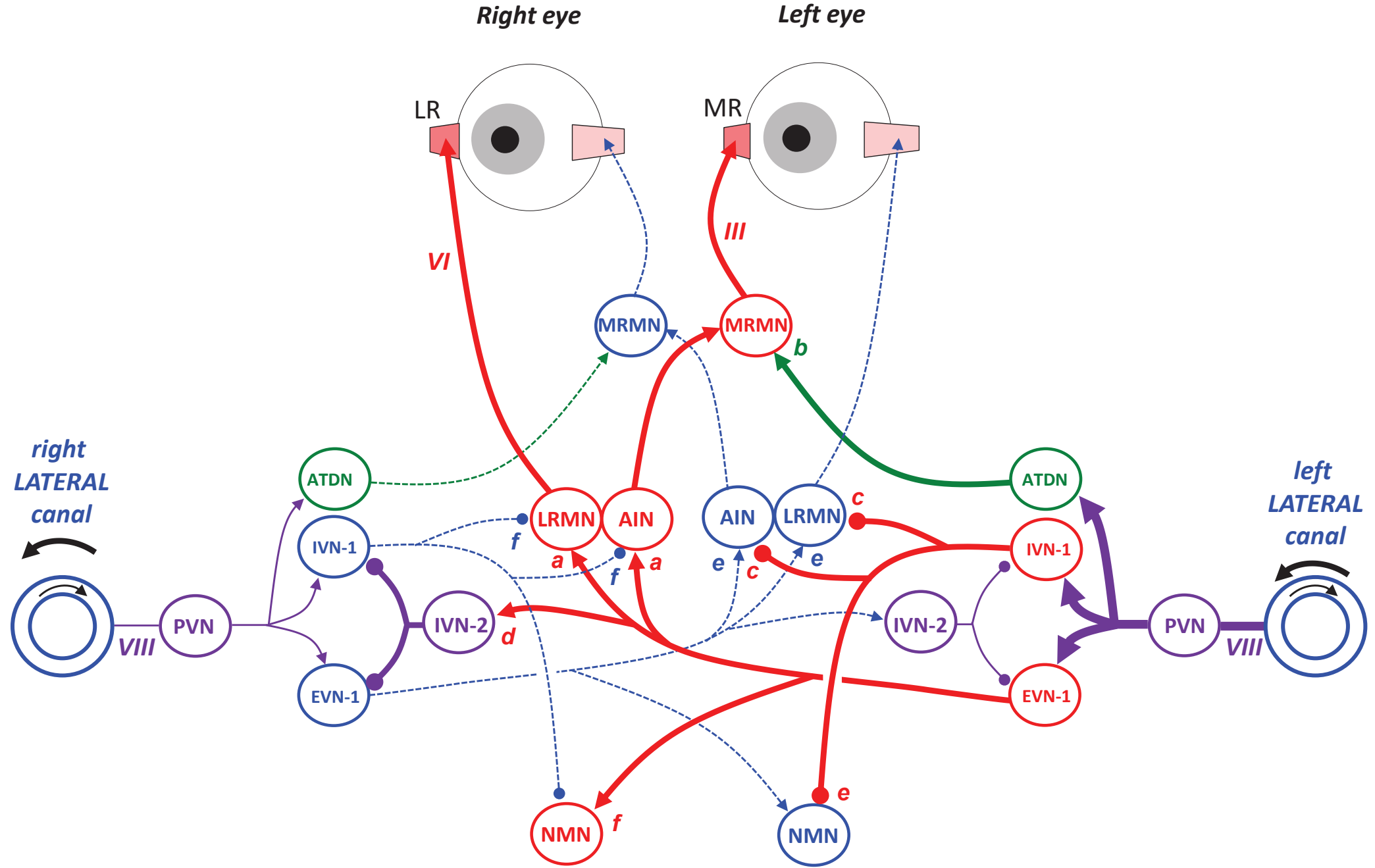
# Figure 3



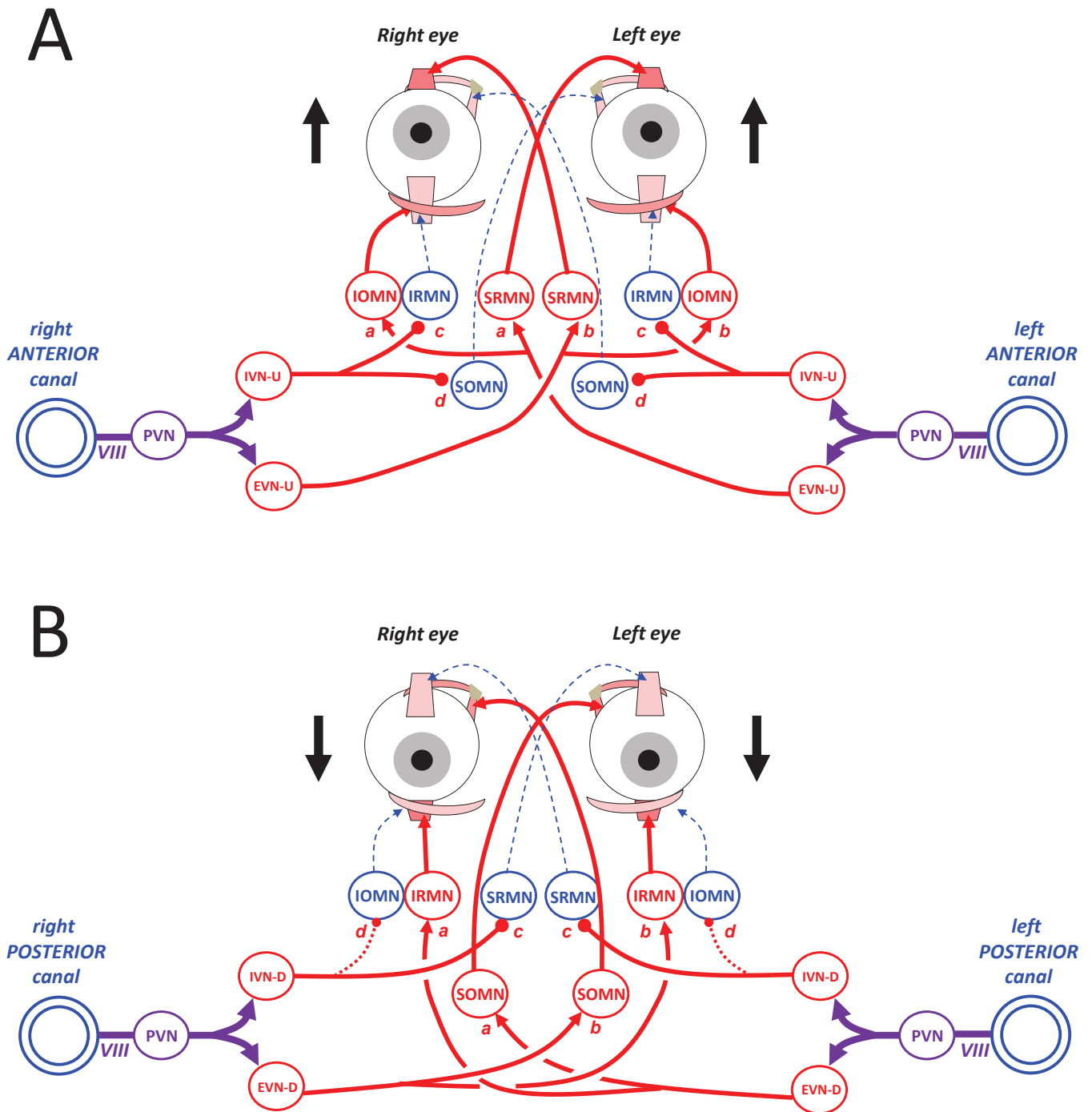
# Figure 4



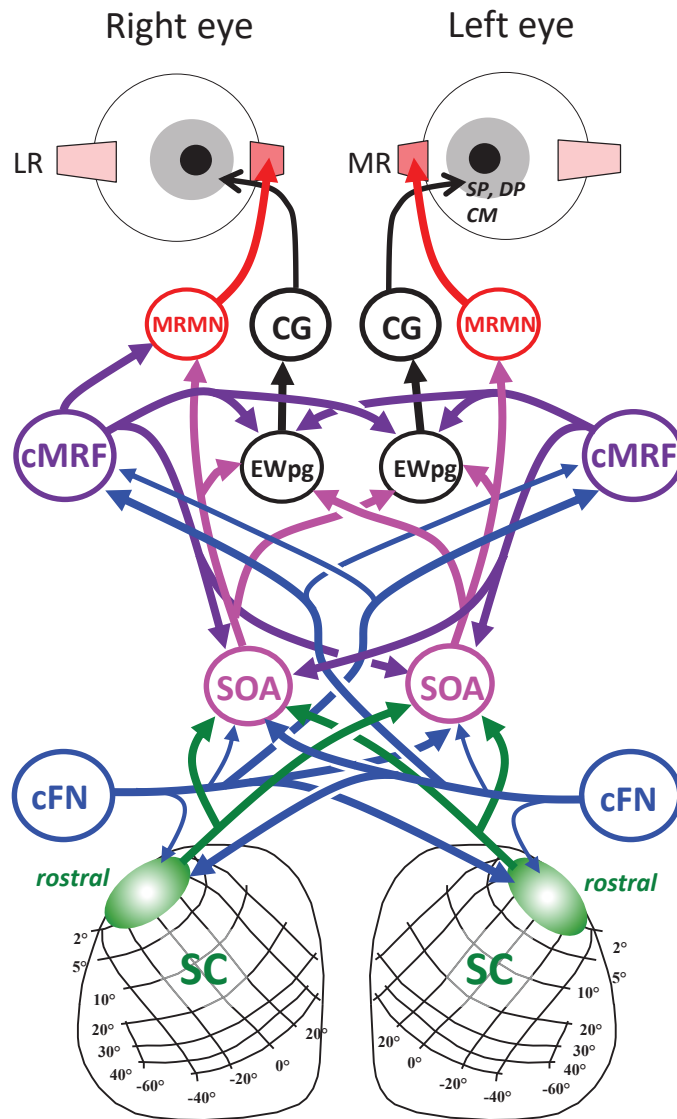
# Figure 5



# Figure 6



# Figure 7



# Figure 8

