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# 1 Revisiting horizontal connectivity rules in V1: from like-to-like towards 2 like-to-all

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## 9 Abstract

10

11 Horizontal connections in the primary visual cortex of carnivores, ungulates and primates  
12 organise on a near-regular lattice. Given the similar length-scale for the regularity found in  
13 cortical orientation maps, the currently accepted theoretical standpoint is that these maps are  
14 underpinned by a like-to-like connectivity rule: horizontal axons connect preferentially to  
15 neurons with similar preferred orientation. However, there is reason to doubt the rule's  
16 explanatory power, since a growing number of quantitative studies show that the like-to-like  
17 connectivity preference and bias are mostly observed at short-range scale, are highly variable  
18 on a neuron-to-neuron level and also depend on the origin of the presynaptic neuron. Despite  
19 the wide availability of published data to this effect, the accepted model of visual processing has  
20 never been revised. We review three lines of independent evidence supporting a much-needed  
21 revision of the like-to-like connectivity rule, ranging from anatomy to population functional  
22 measures, to computational models and theoretical approaches. We advocate an alternative,  
23 distance-dependent connectivity rule that is consistent with new structural and functional  
24 evidence: **from like-to-like bias at short horizontal distance to like-to-all at long horizontal**  
25 **distance**. This generic rule accounts for the observed high heterogeneity in interactions  
26 between the orientation and retinotopic domains, that we argue is necessary to process non-  
27 trivial stimuli in a task-dependent manner.

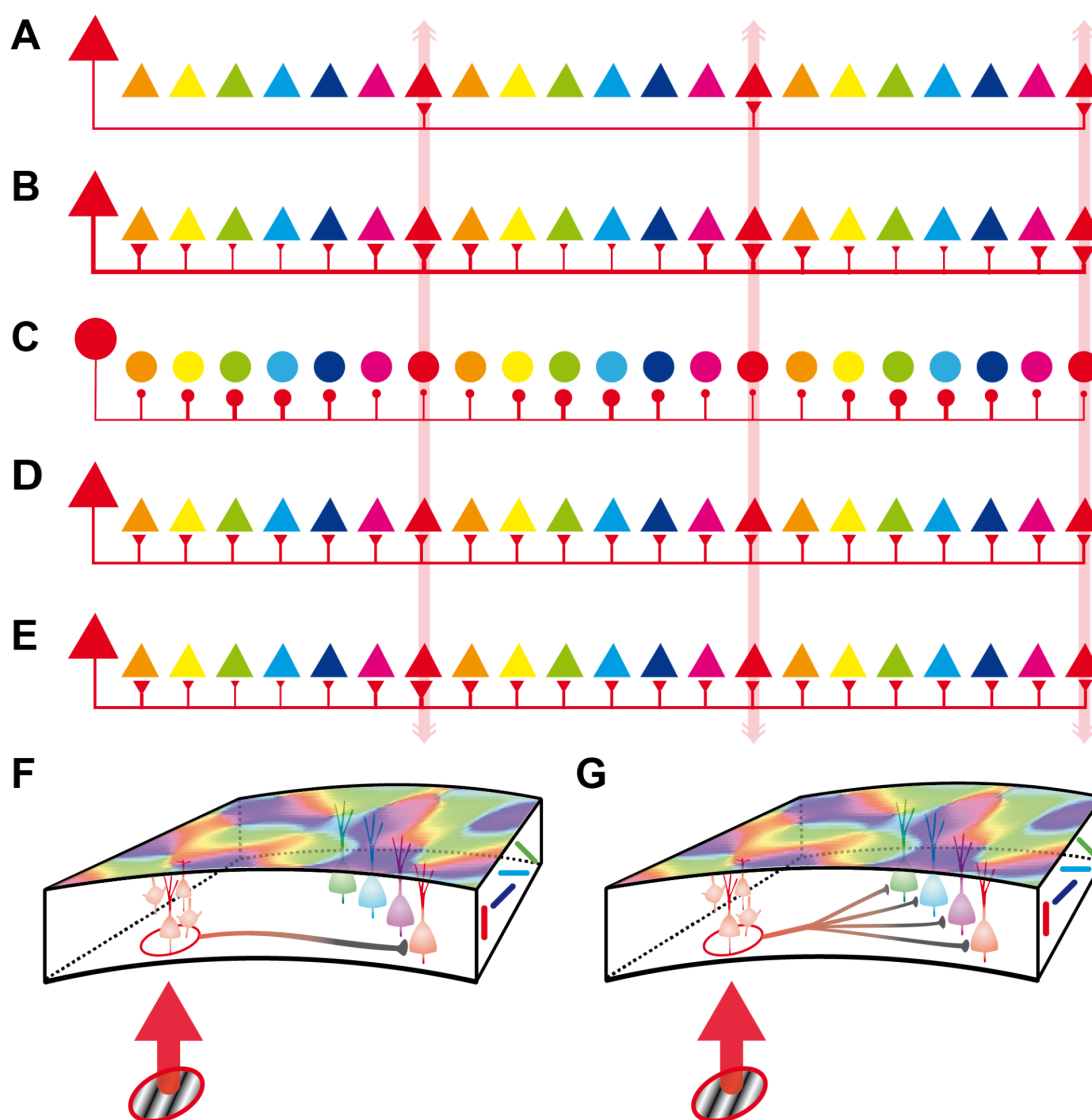
## 28 INTRODUCTION

29 Retinotopy and orientation are two of the main features processed and topographically  
30 organized into maps in primary visual cortex (V1) of carnivores, ungulates and primates.  
31 Anatomical connections between neurons separated on the cortical sheet, through the so-called  
32 *intrinsic, intra-cortical or horizontal* axons have a crucial theoretical importance for  
33 understanding the computational operations that V1 can perform. Indeed, these axons connect  
34 different points in the retinotopic and orientation maps and thereby generate a set of possible  
35 topological interactions within a multidimensional representation of space, orientation and time.  
36 It is therefore critical to characterize structural horizontal interactions in order to understand their  
37 functional relevance. The vast majority of presynaptic contacts in cortex originate from neurons  
38 located in the same area as the postsynaptic target (>80% in macaque V1, (Markov et al. 2011),  
39 thus forming an intra-cortical network. In the primary visual cortex, the feedforward  
40 thalamocortical inputs drive the cortical network, which in turn strongly shapes the evoked  
41 response through major excitatory and inhibitory recurrent circuits within the column (Douglas et  
42 al. 1991), a canonical circuit that constitutes nearly  $\frac{2}{3}$  of intra-cortical connectivity (Markov et al  
43 2011). The rest of the intra-cortical network connects neurons in adjacent columns separated  
44 laterally over distances up to several millimeters, the so-called horizontal network. Early  
45 anatomical observations reported that the horizontal connectivity of carnivores, ungulates and  
46 primates is spatially distributed into regular clusters (Fig. 1A, (Braitenberg 1962; Fisker et al.  
47 1975; Creutzfeldt et al. 1977; Gilbert and Wiesel 1979; Rockland et al. 1982) forming a radially  
48 projecting pattern that resembles a daisy's petals (Douglas and Martin 2004). Since orientation  
49 maps are also regular with comparable spatial frequency, the currently accepted theoretical  
50 standpoint is that these maps are underpinned by a **like-to-like connectivity rule**: cortical  
51 columns are connected by horizontal connections only if they share similar orientation  
52 preference (Fig. 1A), an hypothesis originally put forward by Mitchison & Crick (Mitchison and  
53 Crick 1982). Correlative studies, comparing bouton labelling with autoradiography, or with  
54 optical imaging maps, qualitatively supported the like-to-like rule (Gilbert and Wiesel 1989).  
55 Later quantitative anatomical combined with optical imaging studies confirmed the existence of  
56 an orientation preference bias (Fig. 1B, in the range of 1.5-2 times greater than chance, [Bosking](#)  
57 [et al. 1997](#), [Kisvárdy 1997](#); [Schmidt et al. 1997](#); [Malach et al., 1993](#), [Rocheffort et al., 2009](#)),  
58 with high cell-to-cell variability. Probably due to its simplicity and its elegant topological  
59 implications, the highlighted iso-orientation biases have led to a general acceptance of the  
60 hypothesis of a simplified and unique like-to-like connectivity. One consequence is that  
61 theoretical and computational models have implemented it as a strict rule, not as a bias (e.g.  
62 (Bressloff et al. 2001; Raizada and Grossberg 2003; Rangan et al. 2005; Sarti et al. 2008; Baker  
63 and Cowan 2009; Kaschube et al 2010; Rubin et al. 2015; Carroll and Bressloff 2016).  
64 However, we believe such an over-simplified schema may impair the development of our  
65 theoretical understanding of the primary visual cortex function.

66

67 Actually, there are reasons to doubt the explanatory power of a global and strict like-to-like  
68 connectivity rule. First, a growing number of quantitative studies show that there is a wide  
69 variety of connectivity biases (like-to-like bias, no bias, like-to-unlike bias) depending on cell  
70 type (Fig. 1C, excitatory vs inhibitory neurons, see [Kisvárdy et al. 1994](#); [Buzás et al. 2001](#)),

71 layer origin (Fig. 1D, no bias in layer 4 or layer 6, see Yousef et al. 1999; Karube and Kisvarday  
72 2010; Karube et al. 2017), and position in the orientation map (Yousef et al. 2001, iso-  
73 orientation domain vs pinwheels). Second, the effect is mostly observed at short-range where  
74 most of the connectivity arises (<1-1.5mm), but connections can connect neurons over  
75 distances of a few millimeters. The rare analyses over larger cortical distances (more difficult  
76 because far fewer boutons are present) showed a global tendency for the iso-orientation bias to  
77 reduce with distance (Fig. 1E) due to wider selectivity or deviation from the iso-orientation bias,  
78 as observed in Buzás et al. (2006, fig8C), Kisvarday et al (1997, Fig9 - area 17) and Bosking et  
79 al (1997, Fig 5); however, see a counter example for area 18 in Kisvarday et al (1997, Fig10 –  
80 area 18). As a consequence, the effective functional selectivity of horizontal axons beyond the  
81 short-range distance is not very clear. Lastly, the functional impact of the structural organisation,  
82 as described by anatomy, is far from being trivial to predict. Indeed, any visual stimulation will  
83 activate a neuronal mass encompassing all layers, both excitatory and inhibitory neurons and at  
84 least a full hypercolumn composed of pinwheels and iso-orientation domains (see Fig1D in  
85 Chavane et al 2011). Furthermore, not only neurons with preferred orientation matching the  
86 orientation of the stimulus will be significantly activated, but a distribution of neurons with say,  
87 +/-15 deg around the stimulus orientation. The intra-cortical horizontal network triggered by this  
88 functionally activated neuronal mass will forcibly contact a diversity of orientation tuned neurons  
89 (ranging from an iso-orientation, Fig. 1F, to an omni-orientation interaction, Fig. 1G) with an  
90 overall net effect beyond short-range distance that is particularly difficult to predict.



91

92 **Fig. 1: Illustration of different connectivity rules from literature and possible outcomes for**  
 93 **functional activation.** In A-E the local neuron (large on left) connects to neighbours in a radially  
 94 approximated schema spanning outwards over three hypercolumns (where the same preference is  
 95 encountered, as indicated by the vertical arrows). Colors indicate the orientation preference of neurons.  
 96 **(A)** Strict like-to-like connectivity (extends to long distances). **(B)** Modulated like-to-like bias (extends to  
 97 long distances). **(C)** Like-to-unlike bias as exhibited by inhibitory interneuron. **(D)** Like-to-all as exhibited  
 98 by neurons in layer 4 and 6. **E:** Like-to-like bias that reduces with distance resulting in like-to-all at  
 99 distances beyond adjacent hypercolumns. **(F-G)** Two extremes hypothesis for the net outcome of  
 100 functionally driven connectivity rule at long-range distance. In response to a local oriented stimulus, all  
 101 neurons that have a receptive field in overlap with the stimulus will be activated, for excitatory and  
 102 inhibitory neurons, different lamina and positions in the orientation map. Such functional activation can  
 103 lead either to a strict iso-orientation activation of neighboring neurons through the horizontal network (like-  
 104 to-like rule, F) or omni-orientation activation (like-to-all rule, G).

105 In this review, we present a body of recent evidence from anatomy, physiology and  
106 computational modeling, leading to the conclusion that horizontal interactions do not forcibly  
107 conform with a like-to-like orientation preference. In the last decade, structural (Hunt et al. 2011;  
108 Martin et al. 2014, see Kisvarday 2016 for review), and functional (Chavane et al. 2011; Huang  
109 et al. 2014) studies have shown that the rule is not valid for long-distance connections. Chavane  
110 et al (2011) proposed revisiting the connectivity rule as a function of horizontal distance: from  
111 like-to-like at short distance towards like-to-all and long distances (Fig. 1E; see discussion in  
112 (Alonso and Kremkow 2014a, b). In their computational modelling study, (Rankin and Chavane  
113 2017) show that this behavior is in fact to be expected based on the anatomical observations  
114 made by Buzas et al (2006). The functional implications of such evidence is further discussed in  
115 the framework of natural scenes analysis (Perrinet and Bednar 2015; Boutin et al. 2021). In light  
116 of converging evidence from a range of approaches, this review argues for a timely, in-depth  
117 revision of V1 horizontal connectivity rules. Revisiting this textbook mindset is an important  
118 prerequisite to better understand the relationship between structure and function in the visual  
119 cortex.

## 120 NEW PHYSIOLOGICAL EVIDENCE

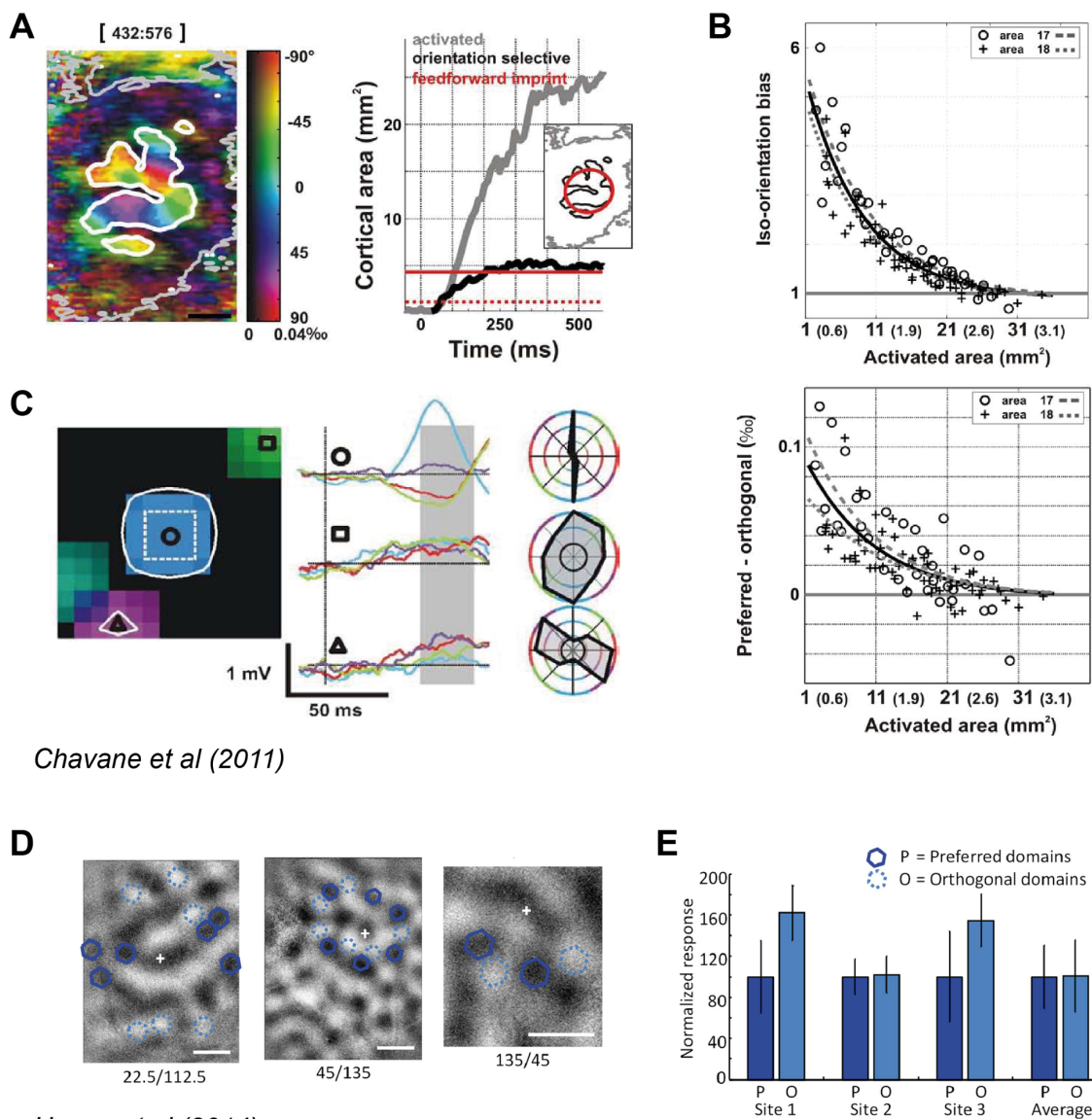
### 121 *Neuronal population activity measures*

122 Here, we review more recent evidence for versatile connectivity rules reported in different  
123 species and with different recording techniques. Importantly, one should keep in mind that long-  
124 range horizontal axons only have a subthreshold influence on their postsynaptic targets  
125 (Bringuier et al. 1999). In order to study the selectivity of the postsynaptic target of these axons,  
126 it is therefore important to use methods that are sensitive to subthreshold membrane potential  
127 changes. Indeed, methods that only record spiking activity necessitate experimental protocols  
128 that co-activate the presynaptic source and postsynaptic target of the horizontal network, to  
129 study cross-correlation between neurons (Michalski et al. 1983; Ts'o et al. 1986; Schwarz and  
130 Bolz 1991; Das and Gilbert 1999). Under these conditions, it is hard to tease apart the direct  
131 effects of the horizontal axons rather than secondary activation of recurrent columnar circuits.

132 In 2011, Chavane and collaborators used complementary recording tools that specifically record  
133 the subthreshold activity of a mesoscopic population (voltage-sensitive dye imaging, VSDI), and  
134 of individual neurons (intracellular recordings) in area 17 and 18 of the anesthetized cat. The  
135 first method allowed us to visualize and quantify the orientation selectivity of the laterally  
136 spreading activity evoked by a local stimulus (Jancke et al. 2004). The second method enabled  
137 a precise measurement of the impact of this subthreshold spread of activity on individual  
138 neurons. Using VSDI in the cat area 17 and 18, the authors showed that a local oriented  
139 stimulus evokes a spread of activity along the horizontal dimension, extending up to three mm  
140 laterally (see also (Bringuier et al. 1999; Reynaud et al. 2012; Muller et al. 2014, 2018). It is to  
141 be noted that the spread of activity did not show any patchiness, contrary to the anatomical  
142 observations. However, we believe that this is to be expected considering the large variability in  
143 the patches that will be activated from different neurons, varying as a function of a neuron's

144 type, layer and position in the orientation map. As a consequence, and in sharp contrast to the  
145 extended horizontal activation, the orientation-selective component of this spread remains  
146 confined to the cortical feedforward imprint of the stimulus (Fig. 2A). The feedforward imprint  
147 being defined in Chavane et al (2011) as the population of neurons directly or partially activated  
148 by the feedforward stream. This effect was systematically observed in both areas 17 and 18 and  
149 quantified using complementary methods to quantify the decrease of the orientation selectivity  
150 with horizontal distance. Both at the level of orientation preference and orientation selective  
151 response, the bias towards like-to-like activation (and therefore functional connectivity)  
152 decreases exponentially with horizontal distance with a similar characteristic cortical space  
153 constant of about one mm or one hypercolumn (Fig. 2B). Importantly, this signifies, that, for a  
154 lateral radius of about 1.5 mm, the iso-orientation bias (Fig2B) was in the same range as that  
155 observed in the anatomy for similar lateral distance (Bosking et al. 1997, Kisvarday 1997;  
156 Schmidt et al. 1997; Malach et al., 1993, Rochefort et al., 2009). However, VSDI is a population  
157 measure of the subthreshold activation that pools activity from all neurons (excitatory and  
158 inhibitory), all compartments (dendrite, soma and axons) and mostly the upper layer (see  
159 Chemla et al 2017). Therefore, VSDI offers a unique population view of the functional activation  
160 but it is less precise than anatomical studies: it is for instance possible that the lack of overall  
161 bias comes from the mix of tuned and untuned subpopulations (see Kisvarday 2016 for further  
162 discussion). Chavane et al (2011) therefore used intracellular recordings to confirm the VSDI  
163 observations and further showed that this loss of orientation selectivity actually arises from the  
164 diversity of converging synaptic inputs originating from outside the classical RF (Fig. 2C). The  
165 conclusion from this work is that the lateral spread of cortical activity gradually loses its  
166 orientation iso-preference at a distance of around one hypercolumn and that there exists a  
167 range of strategies for different post-synaptic neurons.

168 In a more recent work, Huang et al (2014) provided similar and complementary results in a  
169 different species, V1 of the tree shrew, and using a different methodological approach. The  
170 authors used optical imaging of intrinsic signals to monitor the impact of intra-cortical  
171 optogenetic stimulation under various stimulation configurations. In particular, their results show  
172 that the optogenetic stimulation of excitatory neurons within a set of orientation domains in the  
173 cortex generated the same response amplitude for either iso- or orthogonal domain stimulation  
174 (Fig. 2D, E). The responses actually depended primarily on intra-cortical distance (similar to the  
175 results obtained via cross-correlation in (Das and Gilbert 1999). Using their innovative  
176 approach, the authors also tested stimulation along an axis in the retinotopic map, either  
177 collinear with the preferred orientation or orthogonal to it. The authors found no bias in either  
178 direction. Huang et al (2014) therefore provides independent and complementary evidence that  
179 the horizontal network, when probed with functional measures, does not show a bias for iso-  
180 orientation preference in V1. It should be noted however that using optogenetic stimulation of  
181 excitatory neurons may drive complex dynamical activation of the cortex (Li et al 2019), mixing  
182 excitatory and inhibitory recruitment of the lateral network with different dynamics. Since the  
183 authors have used intrinsic optical imaging, they could not access to the dynamics of the lateral  
184 activation that would be averaged out in the observed activation maps (see Kisvarday 2016 for  
185 further discussion).

186  
187

Chavane et al (2011)

Huang et al (2014)

188  
189 **Fig. 2 : Probing for the orientation selectivity of the horizontal network with functional imaging.** A-  
190 C Taken from Chavane et al (2011) and D-E from Huang et al (2014). **(A)** Voltage-Sensitive Dye Imaging  
191 of the orientation selective response evoked by local oriented gratings, example from area 17 of an  
192 anesthetized cat. (Left) Polar orientation map averaged over the final 145 ms of the response (time  
193 stamps indicated above the frame). Color hue and brightness code respectively for the preferred  
194 orientation and the strength of the orientation tuning. Contours delineate the outer border of the cortical  
195 domain within which significant activation level (thin gray contour) or significant orientation selective  
196 response (thick white contour) are observed. (Right) Spatial extent of the activated area (gray) and of its  
197 orientation-selective component (black) as a function of time. Red line indicates the expected limit of the  
198 feedforward imprint, defined and estimated from Albus (1975) as the population of neurons directly or  
199 partially activated by the feedforward stream. Dotted red line indicates the retinotopic area of the stimulus  
200 representation. Inset: The spatial extent of the activation spread (gray) and the orientation-selective



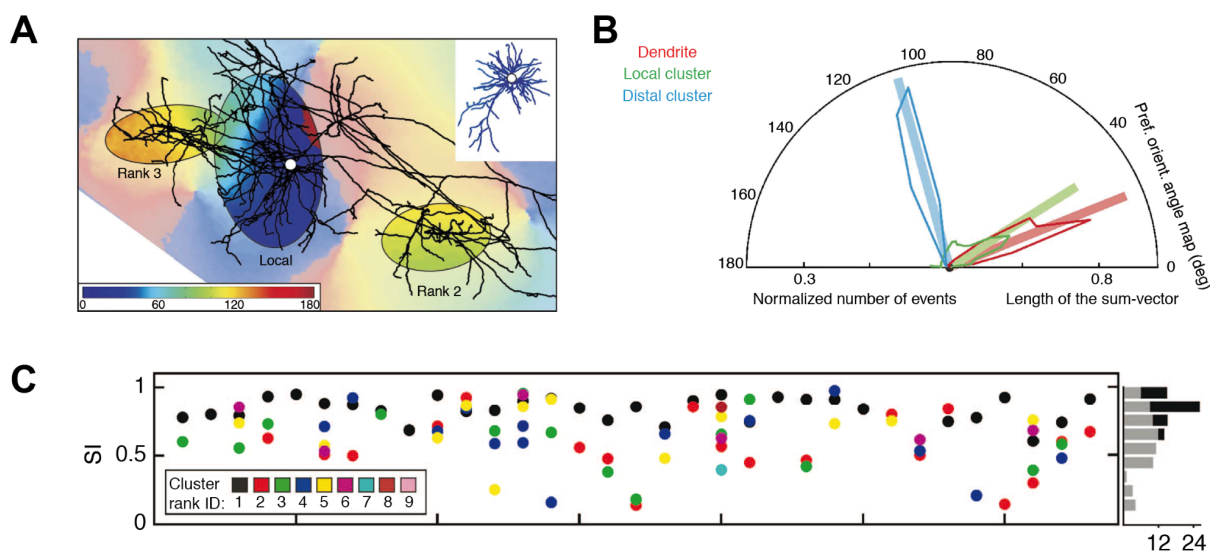
201 activation (black) are shown in comparison with the expected limit of the feedforward imprint (red). **(B)**  
202 Population analysis over nine hemispheres [three in area 17 (o) and six in area 18 (+)] of the horizontal  
203 distance-dependent decrease of orientation selectivity. (Top) Iso-orientation bias as a function of the  
204 spatial eccentricity of the lateral spread. The first point corresponds to the area of the initial cortical  
205 activation. Exponential fit is shown in black. (Bottom) Decrease in condition-wise modulation depth with  
206 lateral propagation distance. **(C)** Visuotopic orientation polar map of an intracellular subthreshold  
207 response; Color hue and brightness code respectively for the preferred orientation and the strength of the  
208 orientation tuning. The white contours delineate the significant responsive regions when combining both  
209 amplitude and orientation selectivity criteria. Middle: averaged subthreshold responses to four different  
210 orientations (same color code) presented for particular locations (circle, triangle, and square); scale bars:  
211 50 ms and 1 mV; Right: normalized orientation-tuning curves, integrated within a fixed temporal window  
212 (shaded area of middle panel). The black circle indicates the spontaneous level for the depolarizing  
213 integral measure. **(D)** Three orientation maps measured with optical imaging of intrinsic signals (Huang et  
214 al 2014) with the extracellular recording site (white “+”). Optogenetic layout stimulation sites that were  
215 centered over orientation domains with the same orientation preference (blue solid hexagons) as the  
216 recording site (+), and stimulation sites that were centered over domains with the orthogonal preference  
217 (light blue dashed hexagons). Scale bars: 500  $\mu$ m **(E)** Extracellular responses to optogenetic stimulation  
218 of preferred domains (dark blue) and orthogonal domains (light blue) in the three example cases shown in  
219 D, and the average responses to stimulation of preferred or orthogonal domains across all cases  
220 examined (n = 10).

## 221 *Anatomical measures*

222 In a recent anatomical study, Martin et al (Martin et al. 2014) carefully re-evaluated the  
223 orientation bias of horizontal boutons from upper layer pyramidal neurons in cat area 17 using  
224 single cell intracellular labelling, optical imaging to reveal the orientation map, and advanced  
225 cluster-by-cluster analysis of synaptic boutons. In their analysis, Martin et al (2014) compared  
226 the distribution of the preferred orientations spanned by the neuron’s dendritic arbors (used to  
227 estimate the neuron’s preferred orientation) and the preferred orientation covered by axonal  
228 clusters of the neuron (Fig. 3A). In the example of Fig. 3A-B, the preferred orientation of the  
229 dendrite (red) matched the one of the local cluster (green) but not of the distal cluster (blue).  
230 Over 33 neurons, their results revealed a very large variability in the orientation selectivity of  
231 their distal clusters (colored in Fig. 3C), as estimated by their *Similarity Index* (1 corresponding  
232 to the same orientation preference distribution with respect to the neuron’s preferred orientation,  
233 0 to an orthogonal orientation preference). Their results demonstrated the existence of a very  
234 large variance of SI (0.13-0.96) out of all 51 clusters they observed over the 25 neurons. To test  
235 whether the clusters positions within the orientation maps occur by chance, the authors made a  
236 detailed bootstrap statistical analysis of all 51 clusters, taking into account the bias that is  
237 introduced by the orientation map layout, the cluster size and position relative to the soma.  
238 Using this analysis, they found that a quarter of their clusters (14/51 clusters recently updated to  
239 17/65, personal communication from Ruesch & Martin) were not positioned randomly in the  
240 map. Interestingly, only 9% (6/65) of these clusters (see their suppl Fig10I), had a significantly  
241 high SI, above the upper bound (hence iso-oriented), and 5% (3/65) below the lower bound  
242 (hence cross-oriented). In contrast 12% (8/65) were located in position of the orientation map  
243 unlikely to occur by chance while being neither iso nor cross-oriented with the labelled cell. As a

244 conclusion, only a weak minority of clusters (9%) are significantly tuned to iso-orientation from  
 245 non-random position in the orientation map. Furthermore, as shown by Buzas et al (2006), this  
 246 bias tends to decrease with lateral distance of the clusters, which is further in accordance with  
 247 Chavane et al (2011). Finally, as observed in Huang et al (2014), Martin et al (2014) did not find  
 248 any specific alignment of the cluster distributions in the retinotopic map that could favor collinear  
 249 vs orthogonal interactions with the cell's preferred orientation. At a more macroscopic level,  
 250 diversity was also shown from animal to animal in tree shrew V1, specifically in the fine  
 251 orientation/retinotopic arrangement of extracellular anatomical labelling (i.e. a population of  
 252 neurons). In their detailed analysis (Hunt et al. 2011), showed that there is a diversity of co-  
 253 circular connectivity rules across animals, some showing a significant bias towards co-circular  
 254 rules, some towards anti-circular rules, and others without biases. Thus, as stated by Martin et  
 255 al (2014), the horizontal axons thus cannot be treated as an homogeneous network with a net  
 256 iso-oriented bias, but rather should be described as strongly heterogeneous, an heterogeneity  
 257 that may be a the core of its function (see also Kisvarday 2016).

258  
 259  
 260



*Martin et al (2014)*

261  
 262 **Fig. 3: Probing for the orientation selectivity of individual horizontal axons (from Martin et al**  
 263 **2014).** **(A)** Axon of an intracellularly labelled neuron is displayed over the orientation map. Ellipses show  
 264 clusters of boutons (not shown) for local and more distal positions. Dendritic tree (inset) was colour coded  
 265 by the orientation value of their corresponding pixels (soma ¼ white dot). Scale bar, 0.5 mm. **(B)** Radial  
 266 plots of the normalized number of boutons counted in each local (green) and distal clusters (blue) but also  
 267 the dendrite (red) for each preferred orientation (coloured curves). The individual vectors forming these  
 268 hemispheric plots were summed up to generate one sum-vector (bold vector). The length of this sum-  
 269 vector is termed as the 'tuning' of the dendrite or cluster. **(C)** Similarity Index (SI) values for individual  
 270 clusters of 33 neurons sorted by normalized depth of soma. (Top) neurons (xaxis) can have clusters  
 271 (colour coded by rank) with different SI (yaxis). The histogram on the right summarizes the SI across  
 272 clusters of all neurons (grey=distal,black=local). Note the large variance within and across neurons.  
 273

## 274 COMPUTATIONAL MODEL LINKING STRUCTURE TO FUNCTION

275 Population measures and anatomical data constrain connectivity in cortical space, however the  
276 link between known anatomical details and the resulting functional expression (in terms of  
277 neural activity) is not obvious. Computational models provide a means to explore this  
278 relationship directly. Modelling studies of V1 consider a range of connectivity rules, and these  
279 frequently allow for the shaping of connection strengths based on the difference of orientation  
280 preference between connected sites. Abstracted models of single hypercolumns implement  
281 cross-orientation interactions in local circuits that further tune selectivity derived from weakly  
282 tuned LGN inputs (Ben-Yishai et al. 1995). Similar mechanisms for orientation selectivity in V1  
283 have been explored in models with recurrent, lateral connections over short distances (between  
284 neighbouring hypercolumns in L4) (Somers et al. 1995; Kang et al. 2003; Chariker et al. 2016).  
285 Connections that extend over many mm of cortex (i.e. across multiple pinwheels) are  
286 considered in visual cortex modelling studies of contextual modulation (Rubin et al. 2015),  
287 motion illusions (Rangan et al. 2005), geometric visual patterns (Bressloff et al. 2001; Baker and  
288 Cowan 2009; Carroll and Bressloff 2016), travelling waves (Bressloff and Carroll 2015), and in a  
289 general setting (Raizada and Grossberg 2003). Whilst models do commonly feature a decay  
290 (e.g. exponential or Gaussian) in the strength of orientation-based connections with distance  
291 (Goldberg et al. 2004; Blumenfeld et al. 2006), the tuning strength is not distance dependent,  
292 rarely systematically investigated and not constrained by anatomical data. The function of  
293 patchy long-range connections has further been investigated in contexts not specific to  
294 orientation encoding (Voges et al. 2010; Voges and Perrinet 2012). In general, long-range  
295 connections feature a strong iso-orientation bias motivated by long-held assumptions that do not  
296 take into account the more recent functional and anatomical studies that motivate a modification  
297 of this rule.

298 A common modelling choice for local excitation-inhibition connectivity is a so-called Mexican-hat  
299 with inhibition extending further than excitation (Marr and Hildreth 1980; Grossberg 1983;  
300 Somers et al. 1995; Bressloff et al. 2001). This choice is known to generate stable localised  
301 patterns of activity (rather than spatial unstable dynamics that spreads across cortex) (Laing  
302 and Troy 2003), however, excitatory connections in V1 can extend many mm further than the  
303 local inhibitory footprint. In general, models that also feature long-range excitation are used to  
304 study unbounded patterns of activity rather than localised responses to inputs (Bressloff et al.  
305 2001; Blumenfeld et al. 2006). (Rankin et al. 2014) extended the results of (Laing and Troy  
306 2003) to demonstrate that localised inputs can generate stable localised activity patterns (rather  
307 than spreading activity) with a connectivity rule (as suggested in (Buzás et al. 2001), and similar  
308 to Fig. 4A) that features long-range excitation, extending much further than the local inhibitory  
309 network.

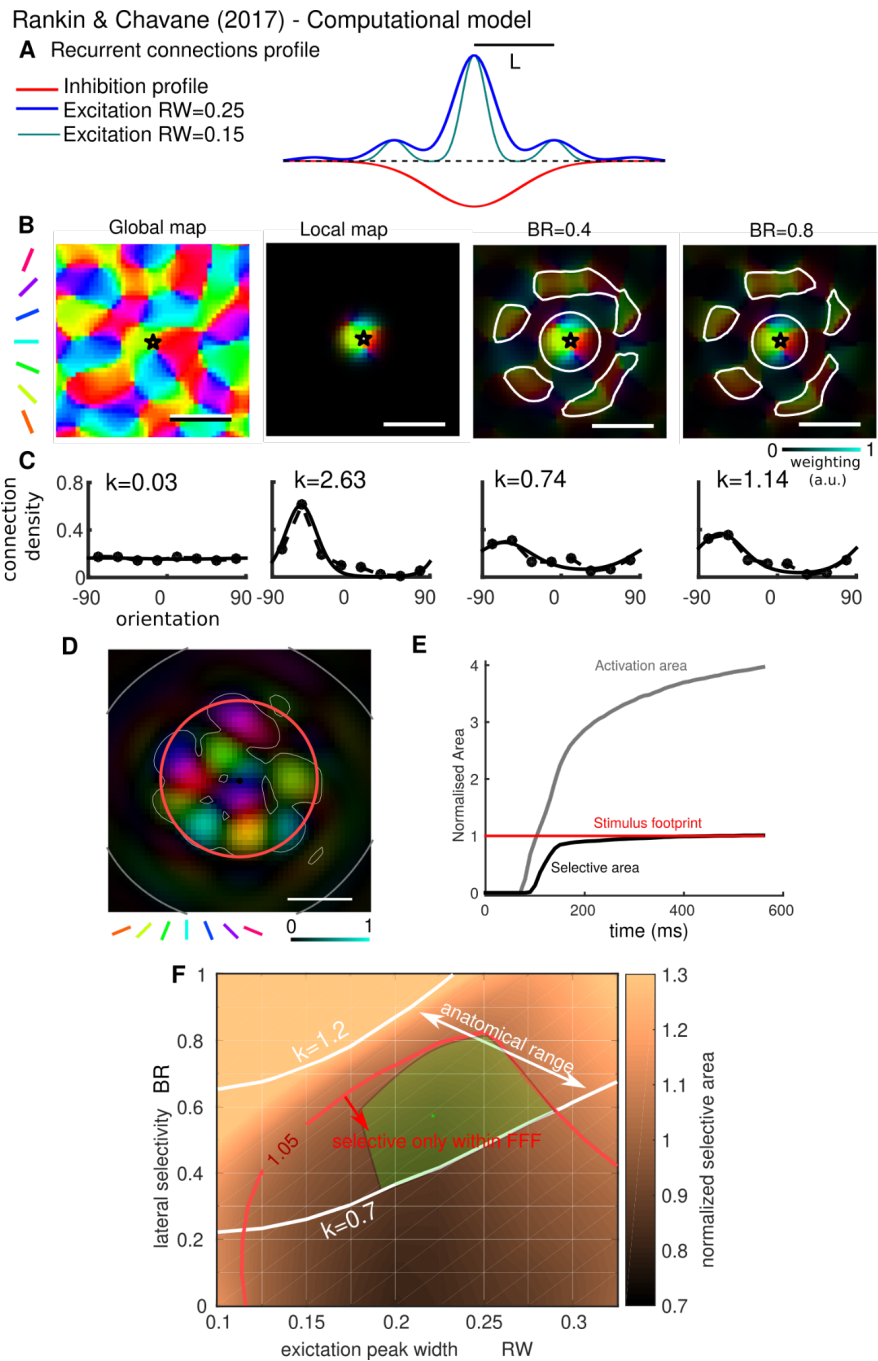
310 (Rankin and Chavane 2017) developed a planar spatial model of orientation-selective activation  
311 in V1 L2/3 with the aim of bridging between known anatomical constraints on the tuning of long-  
312 range connections (Buzás et al. 2006) and the functional expression of laterally propagating  
313 activity driven by localised stimuli (Chavane et al. 2011). A neural field architecture with  
314 orientation-specific sub-populations provides a mesoscopic description of neural activity, ideal

315 for comparison with the temporal and spatial resolution in VSDI imaging experiments. A novel  
316 connectivity function was flexibly parametrized to investigate clustering of connections, their  
317 orientation bias and balance between excitation and inhibition. We adopted the non-orientation  
318 specific nature of local excitatory connections (Buzás et al. 2006) and inhibitory connections  
319 (Buzás et al. 2001); see also (Koch et al. 2016) for a discussion of orientation specificity of  
320 excitatory and inhibitory connections. Taking motivation from (Buzás et al. 2001), longer-range  
321 excitatory connections are proposed here to, although decaying with distance, form in rings at  
322 multiples of the hypercolumn separation  $L$  (Fig. 4A). This allows for the following important  
323 features to be captured: that excitatory connections 1) drop in number at a range of  $L/2$ , 2) have  
324 a peak at a range of  $L$  (and multiplies therefore) and 3) can extend several mm across cortex.  
325 Two parameters were tuned to agree with the available data from (Buzás et al. 2006), the width  
326 of peaks in number of excitatory connections ( $RW$ ; two values shown in Fig. 4A) and their  
327 orientation bias ( $BR$ ; illustrated in Fig. 4B-C).

328 We found a significant overlap between the anatomically relevant parameter range and patterns  
329 of cortical activation consistent with imaging experiments (Chavane et al. 2011). Hence, this  
330 computational approach allowed us to reconcile the imaging results with the reported level of  
331 orientation bias from anatomical studies. Specifically, (Chavane et al. 2011) found a sharp  
332 decay of orientation selective activation at the stimulus retinotopic footprint border, resulting in  
333 peripheral activation that was not orientation selective. Our results demonstrate that this sharp  
334 decay is contingent on three factors: the diffuse clustering of long-range connections, the  
335 intermediate range (consistent with anatomy) of their orientation bias and sufficient balance  
336 between excitation and inhibition. It is worth noting that orientation-biased long-range  
337 connections can recruit a local non-orientation-biased network at the target, resulting in non-  
338 orientation specific activation (Huang et al. 2014). The modelling work illustrates that the  
339 observed levels of orientation bias in anatomical studies actually predict long-range activation  
340 beyond the retinotopic stimulus footprint with a sharply decaying orientation selectivity profile.

341 The model offers further insights into the mechanistic value of excitatory-inhibitory balance, and  
342 of intermediate levels of orientation bias in long-range connections. Long-range excitatory  
343 connections (reaching much further than the lateral inhibitory profile) could easily lead to  
344 destabilization of activity generated by localised visual stimuli. Our model was used to show that  
345 if the orientation bias of lateral connections is excessively strong, or if inhibition is particularly  
346 weak, the network operates close to an instability leading to unbounded cortical activation. This  
347 provides another line of evidence in favour of distance-decaying orientation bias in lateral  
348 connections. Diversity of long-range connections increasing with distance (i.e. decreasing  
349 orientation bias with distance) reflects a potential need to activate a broader range of  
350 orientations as we move further from a local stimulus with a specific orientation. Furthermore,  
351 the fact that, under particular circumstances, the preferred orientation of the horizontal  
352 propagation may be at odds with the underlying orientation preference map could unravel some  
353 new unexpected computational capacities of the horizontal network, which may be present in  
354 visual areas beyond V1. For instance, the ability to link information across position and  
355 orientation for non co-circular filters, which is important for processing objects with sharp angles.  
356 In line with this hypothesis, (Chavane et al. 2011) showed that the spread of orientation

357 selective activity is not fixed but can increase with increasing spatial summation generated by  
 358 annular stimuli.  
 359



360  
 361

362 **Fig. 4: Neural field model to reconcile structure with function in primary visual cortex.** Definition of  
 363 model connectivity with anatomical constraints (**A-C**) and illustration of model behaviour with operating  
 364 region in agreement with functional characteristics (**D-F**). (**A**) Radial connectivity profile for inhibition  
 365 (Gaussian decay) and excitation (locally Gaussian decay, longer range connections peak in number at  
 366 distance  $L$  and multiples thereof). Ring width ( $RW$ ) of peaks in excitatory connections illustrated for two

367 values. **(B)** Example of local preference map and resulting lateral connectivity for two values of the  
368 orientation bias of recurrent connections (BR). **(C)** Orientation tuning for each panel in **B** above (circles)  
369 with tuning parameter  $k$  from a best-fit von-Mises distribution (solid lines). Orientations are evenly  
370 represented in the global map but strongly biased at around  $-60^\circ$  for the local excitatory component (*local*  
371 *map*). The orientation bias of lateral connections increases to around  $k=1$  for  $BR>0.5$  (similar values  
372 reported in (Buzás et al. 2006)). **(D)** Model simulation snapshot at 600ms showing the orientation-  
373 selective component within a thin white contour, confined to the feedforward footprint FFF of the stimulus  
374 in red; the much broader non-orientation-specific activity falls within a grey contour extending beyond the  
375 plot limits. **(E)** Time history of the area within the non-orientation-specific contour and the orientation-  
376 selective contour. **(F)** Colour map across range of RW and BR values showing the selective area as in **D**  
377 normalised by FFF. Within the red contour the selective activation is constrained to the FFF. White  
378 contours show the anatomically constrained range for the connectivity parameters RW and BR where  
379  $k=0.7-1.2$ . In the green region other constraints on the correct orientation and the radial decay rate of  
380 orientation selectivity are also satisfied (details in (Rankin and Chavane 2017)).  
381

## 382 FUNCTIONAL ADVANTAGES OF SUCH AN ORGANIZATION

383 The insights we have reviewed at the physiological and modeling levels support a range of  
384 novel hypotheses for the organization of long-range lateral connectivity in the primary visual  
385 cortex. A functional approach, asking "*why should neurons in V1 be connected laterally?*"  
386 provides a complementary perspective. Indeed, a major argument is that the structure of V1  
387 should fulfill its function and implement principles of perceptual organization, such as the  
388 principle of *good continuation* to bring a contour's constituent edges together into a unified  
389 global percept (Wertheimer 1923). How might these principles connect knowledge across  
390 anatomy, physiology, theory, and modeling?  
391

### 392 *Principles of perceptual organization in natural images*

393  
394 A major constraint for neurons in the primary visual cortex is that information is encoded locally  
395 in their activity and must be integrated globally across the visual field. Surprisingly, perceptual  
396 principles organizing the different fragments of an image can be directly extracted by analyzing  
397 a database of natural images. One such principle is that pairs of edges in natural images are  
398 most likely organized along aligned contours, and more generally on a common circle (Sigman  
399 et al. 2001); the authors extracted edges from natural images and estimated the orientation of  
400 each edge. For each pair of active edges, they showed that the angle of maximum interaction  
401 corresponds to a configuration for which they are close to co-circular. This long-range  
402 correlation is a marker of the structure of natural images and may provide strong prior  
403 knowledge for the perceptual organization of low-level features.  
404

405 Such a structural prior can be described as a form of "association field" extending the concept of  
406 a neural receptive field to long-range local interactions. The seminal paper by Field (Field et al.  
407 1993) defines the association field as the set of local oriented elements (edges) in the visual

408 field that facilitates the detection of a central oriented target. They showed that the association  
409 field obeyed a co-circular rule. In other words, if a common circle can pass through the central  
410 target and the peripheral element, they will facilitate each other's detection, and generate  
411 suppression otherwise. This association field is invariant to translations or rotations. It extends  
412 the prior of collinearity (like-to-like) or co-circularity (Sigman et al. 2001) to a more generic  
413 description of all possible co-occurrences. In particular, by exploring the interactions of edge  
414 pairs, they showed that these association fields explain the detection of paths embedded within  
415 a field of randomly oriented edges. The association field can then be understood in light of the  
416 computer vision problem of curve tracing. Parent and Zucker (1989) described it as a diffusion  
417 process over the tangent field of oriented edges, thus suggesting a principled and biologically  
418 realistic framework for association fields using long-range interactions.

419

420 This principle can be extended to explain psychophysical experiments in humans. Geisler et al.  
421 (2001) took a similar approach by reporting the full statistics of natural image edge co-  
422 occurrences. This yields a valuable model for the statistics of neighboring edges. First, the  
423 edges are organized into parallel textures favoring parallel edges, and second, there is a bias  
424 for co-circular edges (see Fig. 5A). Using a Bayesian approach, the authors derived a clustering  
425 scheme for chaining edges into contours that was confirmed by psychophysical experiments.  
426 This approach was later extended to the high-level cognitive problem of image categorization  
427 (Perrinet and Bednar 2015). The authors showed that using supervised learning, one could  
428 derive a scheme using the association field in that image to categorize whether it contains an  
429 animal. This simple model achieved similar performance to humans and to a deep hierarchical  
430 model (Serre et al. 2007). Surprisingly, the model made similar errors to humans. This illustrates  
431 first that association fields can be used to both group edges based on different tasks or to  
432 categorize images. This also shows that for the association field reflecting the statistics of edge  
433 co-occurrences in natural images, different datasets may lead to different association field  
434 structures (see Fig. 5A). As a consequence, it seems relevant at behavioral and ethological  
435 levels that mechanisms exist to tease apart the slight differences between the co-occurrence  
436 patterns present in different images, for instance the surprising patterns of a perfect co-  
437 circularity, or that of a pair of rare but informative orthogonal edges forming a T-junction. This  
438 would then explain part of the variability in the association fields which can be involved in visual  
439 integration processes.

440

#### 441 *How do these principles translate to the cortical space?*

442

443 As Geisler (2001) states, "*the obvious hypothesis for the local grouping is a neural population*  
444 *with the receptive field structure matched to the edge co-occurrence statistics*". Yet, the  
445 emergence of receptive field properties is a combination of anatomy and the dynamics of  
446 individual neurons. Can we link the statistics of natural images to the structure of processing in  
447 the primary visual cortex?

448

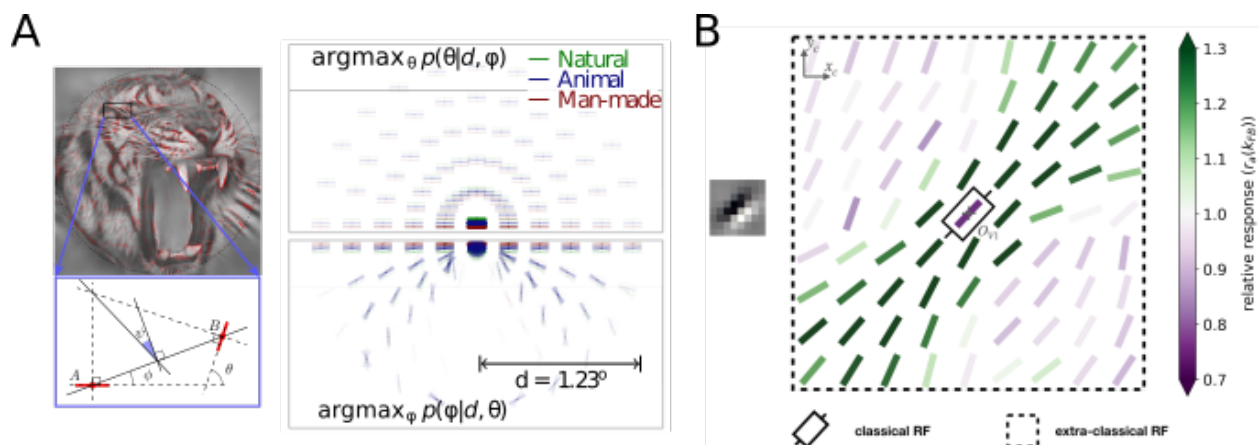
449 Olshausen and Field (1996) set out to show how the structure of V1 microcolumns can optimize

450 the efficiency of the neural representation for natural images. Hyvärinen and Hoyer (2001)  
 451 extended this to include a regularization of the representation with cortical topography.  
 452 Franciosi et al (2021) recently developed a biologically realistic, two-layered V1 sparse  
 453 predictive coding model including pooling mechanisms to impose a neighborhood prior in  
 454 cortical space, which includes by construction the possibility of representing as channels in each  
 455 layer a variety of interaction patterns. Similarly, complex cells and topographic maps emerge,  
 456 demonstrating the transfer of cortical connectivity in V1 to perceptual grouping principles. More  
 457 surprisingly, depending on the density of neurons, different structures emerge to optimize cost  
 458 efficiency: in addition to mammalian-specific features (such as topographical maps), a rodent-  
 459 specific salt-and-pepper map emerges for models with a lower cell density. Interestingly, by  
 460 focusing on this multi-channel convolutional architecture, the second layer showed a diversity of  
 461 connectivities across channels, suggesting that differing anatomical constraints may induce  
 462 different patterns of long-range lateral interactions.

463

464 A multi-layer sparse predictive coding model (Boutin et al 2020) allows for the influence of an  
 465 extrastriate cortical area such as V2 on to V1 to be modelled. The activity in the layers of this  
 466 model emerge from the recurrent interactions between neurons within and across layers (rather  
 467 than a feed-forward pass as in convolutional networks). Convergence to an efficient  
 468 representation of edge filters and interaction maps (resembling association fields) emerges after  
 469 several processing iterations. However, training on different natural image datasets can produce  
 470 different interaction maps, in accordance with Perrinet and Bednar (2015). For example, training  
 471 on images of human faces generated features resembling mouths or eyes, resulting in more  
 472 sparse and longer range interactions. This suggests that instead of a simple similarity rule,  
 473 lateral interactions between neurons reflect the variety of feature dependencies attached to the  
 474 respective neurons. In addition, similarly to physiological observations (Gilbert and Li, 2013) we  
 475 observed that the interaction becomes sharper with stronger feedback (see Fig. 5B), which  
 476 proves a synergy between the different pieces of information encoded by the network, as  
 477 illustrated by improved performance for denoising natural images.

478



479

480 *Fig. 5: Function and diversity of Association Fields. (A)* Following the work of (Geisler et al. 2001), one  
 481 could derive the association field from the statistics of natural images. This involves extracting edges from  
 482 images (red segments) and computing for each pair the difference of angle  $\theta$  and the relative azimuth  $\phi$  of



483 *one edge compared to the other. This allows to quantify the association field as the histogram, relative to*  
484 *a reference edge placed in the middle, for the most likely difference of angle - showing a prominent*  
485 *preference for parallel textures (top) or the relative azimuth, showing a prior for co-circular co-occurrences*  
486 *(bottom). The association field may vary for different databases with an excess of co-circularity in images*  
487 *containing animals, illustrating the variety of statistics faced by the visual system (Perrinet and Bednar*  
488 *2015; modified with permission CC-BY). (B) Boutin et al (2020) describes a biologically realistic multi-*  
489 *layer model of the visual cortex. The model is shown natural images and is optimized to represent images*  
490 *in the most efficient way. Edge-like filters emerge (see an example in the inset) and we show here the*  
491 *interaction of this edge with other edges outside the range of its classical receptive field. This pattern*  
492 *shows a large facilitatory (green) or inhibitory (purple) effect relative to a model without feed-back. This*  
493 *functional modulation of the association field shows the importance of the activity in the whole network*  
494 *and we have further shown its shape could widely vary within the network and for different types of*  
495 *images, such as images of faces (Boutin et al 2020; modified with permission CC-BY).*

#### 496 *Function and dynamics of long-range lateral interactions*

497 Overall, these theoretical models propose, as an alternative to the like-to-like structure, that  
498 there should be a wide variety of long-range lateral interaction patterns. It should be noted that  
499 most of the models described above deal with static natural images, whereas the visual world is  
500 characterized by a wealth of different dynamic scales, which raises the question of the role of  
501 neural dynamics in long-range lateral interactions.

502

503 If one imagines an edge moving in a direction parallel to its orientation, we can infer that we are  
504 following the tangent to a continuous contour. On the contrary, if the orientation of the edge is  
505 perpendicular to its direction, it is more likely that we are seeing a moving bar. This simple  
506 prototypical example shows that depending on the local intrinsic context, the optimal integration  
507 rule may change, as evidenced by intracellular recordings (Gerard-Mercier et al. 2016). If these  
508 interactions can be implemented via different contextual cues such as recurrent or feedback  
509 connections, it is also possible that the multidimensional representation of information on the  
510 cortical surface is much more than a simple topographical orientation map.

511

512 In addition, there is physiological evidence that association maps can be dynamically influenced  
513 by the task at hand. In (McManus et al. 2011), using a delayed-to-sample matching task, the  
514 authors trained monkeys to detect different patterns: a circle, a wiggle, or a line, which were  
515 embedded in a grid display of randomly oriented edges similar to that of (Field et al. 1993). They  
516 found that depending on the pattern being searched, the recorded association field adapted to  
517 preferentially exploit collinearities (for lines) or co-circularities (for circles). Such a differential  
518 processing raises an implementation problem for the unsupervised schemes described above.  
519 This problem could be solved in a supervised learning scheme (Perrinet and Bednar 2015) but  
520 raises the question of how this supervised credit is assigned in V1. A similar problem is inherent  
521 in the backpropagation rule in generic deep learning paradigms which can be solved in a  
522 predictive coding framework (Boutin et al. 2021).

523

524 Lastly, the anatomical connectivity may be patchy for different functions than just connecting  
525 like-to-like orientation patches. Indeed, patchy connections likely play an important role in

526 combining information from multiple visual cues beyond orientation, including context (Martin et  
527 al 2017). Indeed, modelling work has shown that patch-based connectivity increases the  
528 versatility of the dynamic repertoire of neural states (Voges et al, 2010). That work compared  
529 networks of realistic conductance-based neurons with a range of connectivity rules. These rules  
530 had different complexities, from a completely random connectivity, to a neighborhood-based  
531 local connectivity, and more interestingly, clustered networks including a patch-based  
532 connectivity rule. This was extended in a further modelling work (Voges and Perrinet, 2012) to  
533 include a comparison between a pure random patch-based connectivity and partially  
534 overlapping patches. As noted in (Kisvárdy 2016), these patch-based connectivity rules were  
535 sufficient to induce a large dynamic repertoire such as rhythms or travelling waves and was for  
536 instance characterized by enhanced variety in the shape of the power spectrum of population  
537 activity. In particular, such a range of dynamic behaviours is much richer when compared to  
538 those obtained with a random or local connectivity rule. Patchy connectivity rules introduce a  
539 heterogeneity in the lateral connections, which seems essential for building up an efficient  
540 population code (Martin et al 2014). In particular, this would allow the propagation of  
541 combinations of contextual cues which would reflect the richness of visual information in natural  
542 scenes.

543

544 To conclude this section, the function studied in these theoretical models hints at a solution  
545 using a superposition of different long-range connectivity profiles. The diversity of patterns and  
546 their adaptability to the task or statistics should overall improve processing efficiency in the  
547 primary visual cortex. Yet there remain open questions regarding the richness of these like-to-all  
548 patterns. Theories suggest potential strategies for addressing these open questions explicitly in  
549 neurophysiology, for example by synthesizing optimally responsive, model-driven dynamic  
550 stimuli (Walker et al. 2019).

## 551 DISCUSSION

552 In this review, we have documented convergent evidence from physiology, anatomy and  
553 computational models that the orientation selectivity of horizontal network connectivity in the  
554 primary visual cortex of carnivores, ungulates and primates is more versatile than initially  
555 proposed, leading to the necessity to revisit the like-to-like connectivity rule (Mitchison & Crick  
556 1982) still dominant today. At the anatomical level, there seems to be a diversity of connection  
557 rules between presynaptic source and postsynaptic target. At the individual cell level,  
558 anatomical studies have shown that the rule changes as a function of cell type (excitatory vs  
559 inhibitory) and layer/map locations (Yousef et al. 2001, Kisvárdy et al. 1994; Buzás et al. 2001,  
560 Yousef et al. 1999; Karube and Kisvarday 2010; Karube et al. 2017). Within one presynaptic  
561 origin, a large diversity exists with only moderate bias in the range of 1.5-2 times greater than  
562 chance (Bosking et al. 1997, Kisvarday 1997; Schmidt et al. 1997; Malach et al., 1993,  
563 Rochefort et al., 2009), More recent work by Martin et al (2014) on the upper layer pyramidal  
564 neurons of the cat V1 with a cluster-by-cluster analysis of horizontal boutons has shown the  
565 existence of a very large diversity from like-to-like, like-to-any, like-to-all and like-to-unlike  
566 connectivity rules. Altogether no net significative bias towards one of these rules could be  
567 observed in their bootstrap statistical analysis. Taken together, these anatomical results show

568 that there is diversity in the connectivity rules both within and between neuronal types and  
569 locations (see Kisvarday 2016 for an extensive review). At a more macroscopic level, it is  
570 interesting to note that Hunt et al (2011) also observed that the co-circularity rule is different  
571 from animal to animal.

572  
573 When probed with functional measures of neuronal activity, in response to a local visual  
574 stimulus using techniques sensitive to subthreshold membrane potential fluctuations (Chavane  
575 et al 2011) or an optogenetic activation of specific orientation columns (Huang et al 2014), the  
576 diversity revealed in anatomical studies leads to the absence of net bias towards like-to-like  
577 interactions along the horizontal network (see Alonso & Kremkow 2014), but also the absence  
578 of patchy activation of the horizontal spread of activation. Importantly, VSDI measures  
579 demonstrate a clear exponential decay of the like-to-like connectivity bias with horizontal  
580 distance, an effect also observed in anatomy (Buzas et al 2006, Martin et al 2014). At short-  
581 range distances, similar iso-orientation biases, as reported in anatomical studies, were  
582 observed. However, after the equivalent of one hypercolumn, no significant bias could be  
583 observed (Chavane et al 2011).

584  
585 All these papers therefore demonstrate the existence of a connectivity rule that links neurons in  
586 the primary visual cortex depending on their preferred orientation, neuronal type and position  
587 (layer and orientation map) and intra-cortical distance. This multidimensional connectivity rule is  
588 also subject to large diversity not just from neuron to neuron but also from animal to animal. Due  
589 to the difficulty in making predictions from this complex pattern, it is necessary to use  
590 computational approaches to probe for the expected functional behavior of such a network. In  
591 Rankin & Chavane (2017), we developed a neural-field model and demonstrated that the  
592 functional results observed in Chavane et al (2011) are indeed the expected mesoscopic  
593 behavior of such a network when its connectivity is constrained to match the orientation bias of  
594 connections from anatomy (Buzás et al. 2006), thus demonstrating that the functional  
595 observations are to be expected given our understanding of anatomical characteristics.

596  
597 In this review, we wish to update the accepted like-to-like connectivity rule widely assumed as  
598 the building block for connecting a local neuronal network from one position in the visual field to  
599 its postsynaptic targets. The connectivity rule should be revised to a distance-dependent  
600 formulation: **from like-to-like bias at short horizontal distance to like-to-all at long**  
601 **horizontal distance (Fig. 1E)**. The space constant of the decrease of the like-to-like bias is  
602 about one hypercolumn distance. Functionally we can speculate that this translates to an iso-  
603 orientation bias for neurons with overlapping receptive fields and no net bias for neurons with  
604 non-overlapping receptive fields.

605  
606 This may be at odds with the well-documented association field schema and co-circularity rules  
607 observed in natural scenes (Sigman et al. 2001, Geisler et al. 2001). However, it is important to  
608 differentiate the basic connectivity building block, that specifies unidirectional rules from a  
609 presynaptic region to a postsynaptic target, from lateral interactions, that are evoked by more  
610 complex stimuli that co-activate both presynaptic and postsynaptic regions (e.g., as in cross-  
611 correlation studies). The like-to-all long-distance connectivity rule can be seen as generic and

612 allows for a variety of interactions in the orientation and spatial domain. Importantly, this is  
613 possible if we take into account the large local diversity observed at neuronal level (Chavane et  
614 al 2011, Martin et al 2014, see also Monier et al 2003). Our proposition here is that such a rule  
615 could account for a wealth of interaction rules depending on the stimulus and/or the task. For  
616 instance, this would allow to account for the interactions necessary to process orientation  
617 discontinuities such as junctions or corners. Neurons in V1 have indeed been reported to be  
618 sensitive to orientation discontinuities, independent to the absolute orientation of the stimulus -  
619 set (Sillito et al. 1995, Jones et al 2001). This result could not be explained solely by iso-  
620 oriented lateral interactions. Such diversities could also contribute in shaping the orientation  
621 tuning of neurons away from primary orientation preference (i.e. horizontal and vertical  
622 orientations, Vidyasagar & Eysel 2015). More generally, using natural, stationary scenes and/or  
623 contour integration tasks may indeed favor association field interactions. However, depending  
624 on the type of natural images, Perrinet & Bednar (2015) have shown that these interactions may  
625 already differ significantly (see also Boutin et al. 2021). Moreover, dynamic non-stationary visual  
626 stimuli, such as a simple moving object, and tasks that rely on motion integration for instance,  
627 could lead to different associative rules for motion (Gerard-Mercier et al. 2016). In the case of  
628 integrating information along a coherent path for instance, visual information should be  
629 transported in the direction of motion (Perrinet and Masson, 2012) that can be in the cross-  
630 orientation dimension.

631

632 Importantly, co-circularity rules that link orientation and position with respect to a central  
633 oriented feature, are not found in the anatomy (Martin et al 2014, Hunt et al 2011), nor where  
634 they found by Huang et al (2014) using optogenetic stimulation of pattern in the horizontal  
635 network. This further supports a dynamic, context-dependent emergence of specific rules, such  
636 as co-circularity for contour integration in natural images, through higher-order network  
637 interactions. In that respect, Chavane et al (2011) observed that increasing the spatial  
638 summation of the stimulus increases the propagation of iso-orientation activity, even if the basic  
639 connectivity profile was shown to be not selective to orientation at long-range. This means that  
640 from a basic unselective building block, selective interaction can occur (for a proposition of  
641 possible mechanisms see Chavane et al (2011)). This effect could result from the fact that  
642 inhibitory neurons tend to make more horizontal connections with neurons with different  
643 orientation preference than excitatory neurons (Kisvárdy et al. 1994; Buzás et al. 2001).  
644 Increasing spatial summation could change the orientation-dependence of the  
645 excitatory/inhibitory balance and lead to the emergence of tuned activity at longer distance.  
646 More generally, the emergence of new selectivity depending on the stimulation pattern (or the  
647 task) is rendered possible by the existence of local diversity of orientation selective connections  
648 at neuronal level (Monier et al. 2003; Chavane et al. 2011; Martin et al. 2014). Therefore,  
649 different stimulation patterns will lead to activation of different recurrent subnetworks and the  
650 emergence of a variety of selectivity characteristics. It is indeed now well documented that non-  
651 trivial, paradoxical effects, can arise from recurrent balanced networks (Tsodyks et al. 1997;  
652 Ozeki et al. 2009; Pattadkal et al. 2018). In our model, we indeed observed that manipulating  
653 the balance between excitation and inhibition (i.e. reducing inhibition strength), predicts the  
654 emergence of spurious orientation selective activation through long-range lateral connections  
655 (Rankin & Chavane 2017).

656

657 Given the non-trivial effects that can arise with more complex stimuli, a number of avenues  
658 remain open to build on theoretical and modelling work. The model developed in (Rankin and  
659 Chavane 2017) could also be used to investigate selective recruitment and spatial summation in  
660 regions between localized oriented stimuli (Chavane et al. 2011; Huang et al. 2014). Indeed,  
661 increasing spatial summation increases the slope of selectivity decay at the stimulus boundary,  
662 whilst selective propagation reaches further across cortex, a property easily explored in the  
663 model by a more diverse class of localised stimuli. More generally, the model could be used to  
664 make predictions to decipher the selective functional connectivity rules that link position and  
665 orientation in cortical space. Importantly, it could also be extended to differentiate inhibitory cell  
666 subclasses as reported in (Buzás et al. 2001). As such it could generate functional predictions  
667 on e.g. the role of long-range basket cell connections that preferentially target cross  
668 orientations. Extending the framework further, a feature space including spatial frequency (SF)  
669 could be used to investigate lateral connections in light of recent work on interactions between  
670 orientation and spatial frequency maps (Romagnoni et al. 2015; Ribot et al. 2016).

671

672 In this review, we mostly focus on revisiting the connectivity rule of intra-cortical horizontal  
673 networks. However, it is important to consider that such connectivity patterns can also be  
674 influenced by feedback from higher cortical areas that provides a more diffuse and divergent  
675 input to the primary visual cortex (Salin et al., 1989, 1992). Anatomical studies in the cat,  
676 suggest that area 17 and area 18 cells are preferentially connected when they share similar  
677 preferred orientations (Gilbert and Wiesel, 1989). In the monkey, feedback from higher areas  
678 (V2 and V3) to V1 show variable level of patchiness (Stettler et al 2001; Angelucci et al 2002),  
679 unselective to orientation (Stettler et al 2001). In the cat, electrophysiological and inactivation  
680 studies of various downstream areas seems rather to influence only response amplitude or  
681 tuning width of neurons in area 17 of the cat (Martinez-Conde et al., 1999, Wang et al., 2000,  
682 2007; Huang et al., 2004; Liang et al., 2007; Shen et al., 2008, Huang et al., 2007, Galuske  
683 et al., 2002; Shen et al., 2006). However, it is important to consider that feedback will interact  
684 with horizontal network as demonstrated in monkey visual cortex, with either specific  
685 interactions as suggested by CD Gilbert (Gilbert & Li 2013 for review), or contributing to center-  
686 surround processing (Hupé et al 1998, Roberts et al (2007) Poort et al 2012, Nurminen et al  
687 2018).

688

689 In conclusion, we believe that there are enough arguments today to accept a change of  
690 connectivity rules for horizontal axons in V1, that is consistent with both new structural and new  
691 functional evidence. It remains to be established how this complex multidimensional rule  
692 (orientation x distance x neuron type x neuron location) is put into play out under different  
693 stimulus and task configurations. It would be important to understand what is the minimal  
694 stimulus design that can trigger particular tuned interactions for various spatial positions and  
695 whether it involves precisely the same neurons in the network. To test predictions that can arise  
696 from theoretical and computational approaches, new experimental tools to visualize large  
697 massive neural networks at neuronal level and sensitive to membrane potential fluctuations will  
698 be needed. Recent neuro-technological advances in awake animals, such as all-optical tools to  
699 measure and control a large set of neurons (Ju et al. 2018, Zhang et al. 2018), and the

700 development of new genetically-encoded voltage indicators that allow simultaneous two-photon  
701 microscopy subthreshold activity recording from many cells (Villette et al. 2019), provide the  
702 ideal experimental setting to probe the complex and dynamic network interactions underlying  
703 stimulus and task-dependent processing.  
704

704

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715

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