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"Multiplexing" cells of the visual cortex and the timing enigma of the binding problem

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Abstract

In this opinion essay, I address the perennial binding problem, that is to say of how independently processed visual attributes such as form, colour and motion are brought together to give us a unified and holistic picture of the visual world. A solution to this central issue in neurobiology remains as elusive as ever. No one knows today how it is implemented. The issue is not a new one and, though discussed most commonly in the context of the visual brain, it is not unique to it either. Karl Lashley summarized it well years ago when he wrote that a critical problem for brain studies is to understand how "the specialized areas of the cerebral cortex interact to provide the integration evident in thought and behaviour" (Lashley, 1931).

KEYWORDS

asynchronous perception, functional specialization, multiplexing cells, visual integration

1 | INTRODUCTION

The term binding has been used in different contexts (see Burwick, 2014; De Kamps & Van der Velde, 2001). Treisman (1996) defines seven different categories of the binding problem "which may not all share the same solution." Of these, I concentrate here on the problem of "Property Binding" which arises because "...different properties (e.g. shape, colour and motion) must be bound to the objects that they characterize… [and these different properties] are coded in specialized visual areas" (Treisman, 1996). Underlying this statement is the principle of functional specialization within the visual cortex, in which primary visual attributes such as colour, form and motion are processed in separate visual areas (see Zeki, 1978; Zeki, Watson, & Lueck, 1991) or in separate modules within areas such as V1 or V2 (Livingstone & Hubel, 1984; Hubel & Livingstone, 1987; Shipp and Zeki, 1985; DeYoe & Van Essen, 1985). Here, I address the "Property Binding" problem from another viewpoint, and specifically with respect to the so-called "multiplexing" cells (Leventhal, Thompson, Liu, Zhou, & Ault, 1995) whose activity in relation to binding is not clear; these cells respond to three (or two, at least) of the cardinal visual attributes, namely form (orientation), colour and directional motion and have been reported in areas V1, V2 and V3 of the primate visual brain. Some have seen in their responses a mechanism for integrating or binding separate visual attributes to give us a coherent and holistic visual image, where colour, form and motion are seen in precise spatial and temporal registration and are assigned to a particular object. They have thus seen in such cells the solution to the binding problem or rather to its non-existence. Friedman, Zhou, and von der Heydt (2003), for example, state that "a binding problem does not exist for the representation of colour and orientation in the visual cortex" because it is nothing more than a relic of old times (for which read 1970s to 1990s) when neurobiologists believed, in the words of Di Lollo (2012), in "modular specificity and independence" which, in his view, "has been

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Abbreviations: fMRI, functional magnetic resonance imaging.

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disconfirmed by advances in neuroanatomy and neurophysiology. Instead of coding for single features, neurons *throughout the visual cortex are now known to code for multiple features*, thus rendering the binding question moot" (my emphasis). Hence, in this view, there is no "Property Binding" problem because there is no functional specialization in visual cortex; the properties are already "bound" in the responses of such "multiplexing" cells, prior to onward transmission. My main aim here is to discuss the extent to which multiplexing cells can account for the bound image. But I also address two other related issues: when, after the appearance of a multi-attribute visual stimulus, does binding (whether mediated through the non-specialized "multiplexing" cells or by actual physiological interaction between cells specialized to process different visual attributes) occur? And to what extent is it legitimate to dismiss a category of cell belonging to a minority (~10% of cells in an area) from playing a leading role in visual perception—and ultimately raising the binding problem in a different way—if that category belongs to a minority?

2 | THE BOUND STATE

That we perceive three of the cardinal attributes of the visual world—forms, colours and directions of motion—in precise spatial and temporal registration is common experience, so common in fact that, for a long time after the discovery of the primary visual cortex (area V1) in the 1870s, it was generally supposed that a picture of the visual world is imprinted on the retina and subsequently relayed to V1 to be "analysed" there. Flechsig (1905) concluded from Salomon Henschen's work that V1 constitutes "the [sole] entering place of the visual radiation into the organ of psyche" while Henschen himself called V1 the "cortical retina," implying that it receives the retinal image, quite literally as on a photographic plate (Henschen, 1910). Henschen's terminology, now out of use, implied to most, if not all, neurologists that we see with V1; indeed as late as 1945 Gordon Holmes (1945) called V1 the "visual perceptive centre" and conceived of it as the sole "seeing" cortex. Like Henschen before him, Holmes disliked accounts of specific visual defects following specific cortical lesions, as was provided by Louis Verrey for colour and by George Riddoch for visual motion, in significant part because they seemed to imply that there may be other visual areas beside V1; these accounts thus disappeared from the literature for over 70 years (see Zeki, 1990; Zeki, 1991 for reviews). Holmes asserted, somewhat impatiently, that "My observations…tend to show that an isolated loss or dissociation of colour vision is not produced by cerebral lesions" while he considered Riddoch's findings to be "certainly incorrect" since "in all my cases…the blindness was total" (Holmes, 1918). But, if the terminologies used by the early neurologists passed out of fashion a long time ago, their implications were with us until the 1970s; in some quarters, they are still around today.

3 | THERE IS NO BINDING PROBLEM

In the "photographic" schema proposed by Henschen and accepted for so long, there was no reason to postulate any binding problem at all, for all the features were registered simultaneously just as they would be on a photographic plate, or so it was implicitly assumed. To most today, this is an outdated view; its resurrection here may seem surprising and superfluous had it not been for the fact that a similar picture—really an updated cellular version of the old one—has been recently proposed, based on the demonstration—with which not all would agree (see below)—that most cells in the visual brain, and particularly in areas V1 and V2, are "multiplexing" ones which register simultaneously the colour, form and direction of motion of a moving stimulus, thus obviating the necessity for binding. But those who have thus dismissed the binding problem have not addressed a seemingly serious issue that needs to be considered in the context of binding by multiplexing cells—especially if binding, or rather its non-existence, is to be accounted for in terms of such cells. That crucial issue revolves around the temporal asynchrony in the processing and perception of different visual attributes (see below). This is surprising because the psychophysical experiments that challenge the notional role of multiplexing cells in binding, or in rendering the binding issue superfluous, are over a quarter of a century old.

Reports of multiplexing cells are thus a central issue in the discussion that ensues; this issue does not concern the veracity of these reports. Accepting these reports at face value, the operation of such multiplexing cells fails to meet the challenge of binding. The problem is one of timing.

4 | THE ASYNCHRONOUS PERCEPTION OF DIFFERENT VISUAL ATTRIBUTES

While there is little doubt that we ordinarily appear to perceive all the different visual attributes of the world in precise spatial and temporal registration, there are also conditions in which we do not (Moutoussis & Zeki, 1997a). The latter might be considered trivial: exceptions encountered only under rigorous laboratory conditions and hence without general validity or interest. Alternatively, they may provide important insights into the operations of the visual brain. Either way, they raise important questions, which need to be addressed, about the role of "multiplexing" cells in binding.

I refer here to the fact that, as demonstrated in psychophysical experiments, different cardinal attributes of vision, which are processed in parallel within distinct visual areas of the brain (Brouwer & Heeger, 2009; Lafer-Sousa & Conway, 2013; Wade, Augath, Logothetis, & Wandell, 2008; Zeki, 1978;

Zeki et al., 1991, *inter alia*) are not necessarily either processed or perceived simultaneously in time (Arnold, Clifford, & Wenderoth, 2001; Holcombe & Cavanagh, 2008; Linares & López-Moliner, 2006; Moutoussis & Zeki, 1997a, 1997b; Self, 2014; Viviani & Aymoz, 2001; Žaric, Yazdanbakhsh, Nishina, De Weerd, & Watanabe, 2015). Psychophysical pairing experiments show, instead, that the colour of an object is perceived before its form (orientation) or its directional motion, the temporal advantage of colour over orientation being about 40 ms and over directional motion about 80 ms. Because the time taken to perceive these different attributes differs, it follows that over brief periods of time, amounting to less than 100 ms, human subjects perceive different visual attributes of the same object asynchronously; they "bind" the colour of the object that they perceived at time *t* to its directional motion that they had perceived some 80 ms earlier and therefore "misbind" the two in terms of veridical reality; in other words, two visual attributes that are presented simultaneously are not necessarily perceived as having occurred simultaneously.

Interestingly, and though not related to Property Binding but to the question of whether perceptual asynchronies are determined by differences in processing time (see below), a perceptual asynchrony can also occur within the same visual attribute. For example, if the task is to pair upward or downward motion (i.e. vertical) with motion that is either up, or up-and-to-the-right, the temporal advantage lies with the latter (Lo & Zeki, 2014); furthermore, the degree of asynchrony between motion in different directions can be modified by asking subjects to pair moving colour stimuli that are equiluminant to the background with identical stimuli that differ in luminance from the background (Lo & Zeki, 2014).

That the degree of perceptual asynchrony between two attributes, say colour and motion, can be varied or significantly reduced (and even abolished) by manipulating the stimuli (Arnold & Clifford, 2002; Holcombe, 2009; Holcombe & Cavanagh, 2008; Lo & Zeki, 2014; Moutoussis & Zeki, 1997b; see above) suggests that perceptual asynchronies can be traced to differences in neural processing times for different visual attributes. Hence, activity arising in different groups of cells in different or the same processing system, or even the same visual area, may acquire a conscious correlate at different times (Zeki, 2015a). Equally significantly, these experiments also suggest that there is a disjunction, at the micro time scale, between brain (or perceptual) time and veridical time since two events that occur simultaneously in real time are not necessarily perceived to have occurred simultaneously.

There are other interpretations of the causes of this perceptual asynchrony; Holcombe and Cavanagh (2008), for example, believe that the asynchrony, which can be manipulated by introducing exogenous attention, can be explained by supposing that access to colour transients is stronger than that to motion transients while Nishida and Johnston (2002) rely on an hypothetical "time marker" in the brain to account for the observed asynchronies. These interesting alternative interpretations are nevertheless variants of the interpretation based on differences in processing times; I do not agree with them and do not discuss them here because they are irrelevant to a discussion of whether multiplexing cells render "binding" superfluous. If it is indeed the multiplexing cells that are at the basis of our conscious perceptual capacities to gain a holistic experience of the visual world, in which colour, form and motion are bound together, then it follows that the same single multiplexing cells must be processing these different attributes at different times, depending on the conditions of the stimulus and the task and that the times taken to process these attributes by these single cells can be made to vary independently, depending upon the characteristics of the stimulus. There is, unfortunately, no current account of how these perceptual findings can be accommodated within the known physiological properties of multiplexing cells and no account either, in terms of multiplexing cells, of how the processing times for different attributes can vary independently when the characteristics of one—or all three—attributes change.

It is worth noting that, where subjects are asked to pair changes that occur in two different attributes (for example whether a change in colour and a change in direction of motion occur at the same or different times, without naming the colour or the direction of motion, as in the experiments mentioned above), there does not appear to be a perceptual asynchrony (Bedell, Chung, Ogmen, & Patel, 2003; Arnold & Clifford, 2002; but see also Viviani & Aymoz, 2001). In such experiments, subjects only have to report a change in colour or a change in the direction of motion, without identifying the colour or the direction of motion; hence, they are only required to report that they were aware of a change in one domain or the other, of both of which they are presumably conscious. To report such changes does not require binding and there is no perceptual asynchrony in pairing the changes. The difference between such a condition and one in which mis-binding occurs through perceptual asynchrony has been accounted for by the supposition that the temporal advantage that activity in a given area or system has over activity in another (or other) area(s) is task and stimulus dependent (Adams & Mamassian, 2004; Zeki, 2016). In brief, event awareness appears to be spread out in (micro) time; hence, knowing something happened and knowing what has happened are not simultaneous. This difference, too, has yet to be accounted for in terms of the physiology of multiplexing cells.

5 | THE MICRO- AND MACRO-PERCEPTIVE WORLDS

For simplicity, I refer to the brief time window, up to 150 ms following the appearance of a visual stimulus, as the *micro-perceptive* world. During this brief stretch of time, different attributes of the visual world are perceived consciously though separately in time, the temporal precedence of the perception of one attribute over another depending upon stimulus and task. This distinguishes the micro-perceptive world from what I shall call the *macro-perceptive world*, which is the time beyond 150 ms after the appearance of the visual stimulus; the latter is the dominant mode, when different visual attributes are apparently seen in perfect spatial and temporal registration; it is the perceptive world that almost all working on binding have been exclusively concerned with. The temptation to trace the mis-binding that occurs in the micro-perceptive world to unconscious processing or pre-attentive vision and that in the macro-perceptive world to conscious processing and attentive vision must be resisted. This is even in spite of the fact that signals may indeed be processed successively at a non-conscious level (Herzog, Kammer, & Scharnowski, 2016; Poncelet & Giersch, 2015), which of course fortifies the belief in asynchronous processing; in the experiments that reveal the perceptual asynchrony in the micro-perceptive world, subjects attend to and report the stimuli (and hence are conscious of them). The time scales I give here are only approximate; visual signals reach the visual brain (both V1 and the specialized visual areas outside it) from the lateral geniculate nucleus (LGN) much earlier than previously thought, at periods of about 28–40 ms after the appearance of the visual stimulus (Beckers & Zeki, 1995; ffytche, Guy, & Zeki 1995; Shigihara, Hoshi, & Zeki, 2017; Shigihara & Zeki, 2013, 2014). The temporal dynamics of what happens after this initial period is not clear. Most interpretations of the temporal sequence assume that there is an input exclusively to V1 first, followed by a single hierarchical cascade from area to area (Felleman & Van Essen, 1991), although this single hierarchy model of the organization of inputs to the visual brain is questionable (see Zeki, 2016) for a review). In such a hierarchical sequence, the activation of cortex specialized for objects and for faces, for example, is variably given as commencing in V1 at about 40 ms and continuing to the inferior temporal cortex, which it reaches at 170 ms (Rousselet, Husk, Bennett, & Sekuler, 2008). But the picture of how the visual brain is connected has changed considerably over the past half century. A direct input from the LGN and the pulvinar to the visual areas of the prestriate cortex has been demonstrated (Benevento & Rezak, 1976; Benevento & Yoshida, 1981; Cragg, 1969; ffytche et al., 1995; Fries, 1981; Sincich, Park, Wohlgemuth, & Horton, 2004; Yukie & Iwai, 1981), and both V1 and the specialized visual areas of the prestriate cortex have been shown to receive, in parallel, very early signals at between 28 and 40 ms after stimulus onset (ffytche et al., 1995; Shigihara & Zeki, 2014; Shigihara, Hoshi, & Zeki, 2016) [for a general review, see Zeki, 2016]; this parallel input results in a *dynamic parallelism* in the speed with which signals reach different visual areas. For example, the direct, V1-bypassing input to area V5 delivers to it signals from fast-moving stimuli at latencies of about 32 ms and therefore before signals are delivered to V1, while signals from slow-moving stimuli are delivered to V1 first (Beckers & Zeki, 1995; ffytche et al., 1995). Moreover, this direct input to V5 is potent enough to elicit and sustain a simple and conscious, if crude, experience of moving visual stimuli (Barbur, Watson, Frackowiak, & Zeki, 1993; Weiskrantz, Barbur, & Sahraie, 1995; Zeki & ffytche, 1998; Stoerig & Barth, 2001, *inter alia*). Equally, the robust peak responses for stimulation with faces, houses, oriented lines and colours occurs later, at about 150–170 ms, than the initial fast input (Shigihara & Zeki, 2013, 2014). It is therefore perhaps safe to assume that at periods less than 100 ms we are in the micro-perceptual world. The laws regulating visual brain processes during that time window may be special to the micro-perceptual world and perhaps even separate from the laws that govern cerebral operations in the macro-perceptive world. It is probably also safe to assume that the transition from the micro-perceptual to the macro-perceptive world, if there is one, occurs at about 150–200 ms after the appearance of the visual stimulus. It is hard to know how to design experiments to study this transition but it is worth enunciating the problem more explicitly.

6 | THE CONSEQUENCES OF ASYNCHRONOUS PERCEPTION

The demonstration of perceptual asynchrony was perhaps surprising enough for the great majority of those who work on the binding problem not to have taken the slightest notice of it, as is evident from several post-1997 reviews on the topic of binding, which make no mention of it (see, for example, reviews by Friedman et al., 2003; Robertson, 2003; Roskies, 1999; Sagiv, Heer, & Robertson, 2006; Shafritz, Gore, & Marois, 2002 and Di Lollo, 2012). It was not taken notice of even by those who discuss mis-binding, which is a feature of the micro-perceptive world (see, for example Zhang, Qiu, Zhang, Han, & Fang, 2014). In fact, most research that fell into the binding category, then and even now, addressed rather another question, not addressed in this article, namely how two or more cells with co-axial, oriented receptive fields modulate their response to paired stimuli that do, or do not, form part of the same object, with the implicit assumption that this occurs in the macro-perceptive world (see Engel, Fries, König, Brecht, & Singer, 1999 for a review).

It is perhaps a little more surprising that the problems raised by perceptual asynchrony have not been addressed by those who have studied multiplexing cells and, through them, dismissed the binding problem. If multiplexing cells do code for multiple features and if they are, as is implied, the basis of the simultaneous perception of different visual attributes, then it seems natural to want to learn whether there is any plausible explanation, within the physiological properties of the multiplexing cells themselves, that would account for the difference in perceptual characteristics between the micro- and the macro-perceptive worlds. Is there, in other words, any difference in the time taken by multiplexing cells to process different attributes and if so, does it match the human psychophysical data? And do such multiplexing cells change their biophysical properties with experimental design to account for the observed asynchrony where it occurs?

7 | THE CONSEQUENCES OF ASYNCHRONOUS PERCEPTION; WAITING FOR BINDING

That processed visual attributes are not perceived as bound has been traced to the supposition that the time taken to perceive different attributes varies (Moutoussis & Zeki, 1997a; Arnold & Clifford, 2002; but also see above). This is in spite of the fact that subjects pay attention to, and are conscious of, the characteristics of the stimulus that are to be paired. It follows that, in the micro-perceptive realm, there is no brain area (or areas) that wait(s) for all the processing systems to terminate their processing tasks; rather, the brain binds what has been processed over these brief time windows and therefore mis-binds them in terms of veridical reality. This is a surprising result, which could not have been derived from observing the nature of the apparently bound visual image in the macro-perceptive world. It is of course possible that there is no brain area that waits for all the different visual attributes of the visual scene to be processed before binding them together in the macro-perceptive world either; or, in other words, there is no cortical area tasked with resolving binding. We have argued elsewhere that activity at each processing site (node or area) can acquire a conscious correlate without the need for further processing and without the results of the processing being necessarily referred to another area or to higher areas, either for further processing or for conscious experience (Zeki, 2003; Zeki & Bartels, 1999). Indirect evidence that cortical processing in the macro-perceptive world may be asynchronous can also be derived from observing the chronoarchitecture of the cerebral, and especially the visual, cortex when subjects view complex, dynamic scenes (Bartels & Zeki, 2004; Hasson, Malach, & Heeger, 2010); the intensity of activity in different zones of the visual brain changes independently, suggesting that they are processing the incoming signals asynchronously.

What does the above say about multiplexing cells? There is more than one conclusion that could be plausibly drawn: (a) that multiplexing cells do not process different visual attributes simultaneously and, because their activity is conceived of as having a conscious perceptive correlate, the three visual attributes—of colour, form and directional motion—are perceived separately because they are processed separately by multiplexing cells; they therefore do not appear to be bound in the micro-perceptive world; (b) that the attributes, though processed by the same multiplexing cells, are not bound over these brief time windows but are bound over longer time periods, in excess of 150 ms, presumably because of a (hypothetical) shift in the physiology of such cells, which brings their responses to different attributes into temporal alignment; (c) that the multiplexing cells are perceptually impotent in both the micro- and macro-perceptive world and that their significance must be sought for elsewhere.

8 | TWO PERCEPTUAL STATES?

Another possibility is that the micro- and macro-perceptive worlds are entirely separate and that the rules that operate in one do not apply to the other; unlikely though it may seem, the co-existence of two separate and even antagonistic states is not unknown in science. An especially good, though remote, example comes from the world of physics and provides material for thought. The example is to be found in the entirely separate rules that operate in the world of gravitational physics—or macro-physics—on the one hand and of quantum physics—or micro-physics—on the other. As is well known, it is indeed for this reason that those working in the quantum world of particle physics have been able to ignore safely work in macro-physics, and vice versa—something nicely echoed in the way in which those working in macro-perception have safely ignored, or so it seems, the perceptual asynchrony that is the hallmark of visual perception in the micro-perceptive world.

Perceiving and becoming aware of separate visual attributes separately in time is in a way shocking, just as shocking as Niels Bohr found the world of quantum mechanics, when he wrote: "If you are not shocked by the world of quantum mechanics, you have not fully understood it." The psychophysical experiments referred to here become shocking because, just like the experiments in physics (though on possibly not such a grand scale), they go against common sense and experience, one in which different visual attributes appear as if they are perceived simultaneously in time, and therefore already bound. This picture of what happens in the world of micro-perception could not have been and was not, derived from our daily visual experience or from physiological and perceptual studies undertaken before 1997, which did not specifically address the psychophysics of the world of micro-perception. Though it is useless to speculate about what might have happened in a hypothetical world, it is nevertheless worth noting that had we, instead of studying uniquely what happens in the macro-perceptive world, studied uniquely what happens in the world of micro-perception, we would probably have found it equally difficult to derive the laws that operate in the world of macro-perception from the ones that operate in the world of micro-perception. But, by analogy with physics, one could also perhaps postulate, very hypothetically, the existence of two states, the major difference between them being that, in the micro-perceptive state, the processed attributes are not bound whereas in the macro-perceptive state they are. There is a temptation to equate the micro-perceptive state with the "unconscious" state and the other state as the conscious one. This temptation must be resisted because it does not take into account that we are conscious in both states, the difference between the two being that, in the micro-perceptive state, we become conscious of different attributes at different times, which is what led us to write of the "asynchrony of consciousness" (Zeki & Bartels, 1998) or the "disunity of consciousness" (Zeki, 2003). By contrast, we *appear* to become conscious of all the attributes simultaneously in the macro-perceptive state.

9 | THE TRANSITION FROM THE MICRO-PERCEPTIVE TO THE MACRO-PERCEPTIVE STAGE

To understand when a transition from the world of micro-physics to that of macro-physics occurred, physicists project backward in time, to the moments at sub-micro-second levels starting after the Big Bang, and beyond. Assuming that there is also a transition in the perceptive world, the question for the neurophysiologist becomes one of asking at what moment after the appearance of a visual stimulus or scene the laws operating in the world of micro-perception shift to the ones operating in the world of macro-perception? The alternative is to suppose that there is no transition but only one perceptive state, with differences between the micro- and macro-perceptive worlds merely reflecting differences in experimental procedures.

If the micro- and macro-perceptive worlds are entirely separate, then those studying the one world could safely ignore the other, as indeed they have done so far. But it is worth noting that neither the majority working in the macro-perceptive world nor the minority working in the micro-perceptive world have given a remotely adequate solution to how the brain solves the binding problem as defined here, assuming that it does so by what is currently regarded as the most likely method, namely a direct physiological interaction between cells in different visual areas. In fact, no one knows if the two worlds are entirely separate, or at least as separate as the worlds of micro- and macro-physics; indeed, the question itself has not been posed. If the two are not separate then there must be a transition between them since the longer time processes must inevitably integrate the shorter ones. But to understand that transition one need not project backwards in time, as in physics. It is sufficient to learn whether such a transition occurs and, if so, what neural mechanisms are involved. I repeat that this is a problem for those who are especially interested in the transition from one state to the other, unless of course the two perceptive worlds co-exist. It does not affect those who are working in the micro- or the macro-world alone; the latter can continue their work in their field unperturbed by developments in the other field, as has indeed been the case until now.

Inspired by the quest of physicists, we can now summarize the problems to be addressed in the world of visual perception:

1. Is there a transition between the micro- and macro-perceptive worlds and do brain operations differ significantly between the two perceptive worlds. Central to this difference is that different attributes of objects and surfaces are not bound in the micro-perceptive world but are in the macro-perceptive world.
2. Assuming that there is a transition, what neural mechanisms could possibly be involved and at what moment in processing time do they come into operation? What is it that triggers the transition? Do the same neural mechanisms change over time or do novel neural mechanisms come into play as processing proceeds from the micro- to the macro-perceptive world?
3. In either case, what insights do the rules that govern the relationship of processing and perceptual time in the micro-perceptive world provide for understanding the rules that govern the relationship between the perception of different visual attributes in the macro-perceptive world
4. More specifically, if there is a transition, do the physiological properties of single multiplexing neurons, and how they code for colour, form and motion, change between one world and the other; or is it that there are cells which are dormant (or inhibited) in one perceptive world that become active (dis-inhibited) in the other (see below).
5. The properties of multiplexing cells suggest, to those who wish to dismiss the problem of binding, that these different attributes are already bound in their responses. Is there some in-built timing mechanism in the operation of multiplexing cells that allows them to combine their responses to colour, form and directional motion in the macro-perceptive world but inhibits from doing so in the micro-perceptive world?
6. A lesson to be learned from studying the micro-perceptive world is that humans can become conscious of different attributes at different times, thus leading to the notion of "micro-consciousnesses." Does this provide any insight into whether there is a "unity of consciousness" or is that a myth and that the more probable rule, even in the

macro-perceptive world, is of a "disunity of consciousness" (Zeki, 2003).

10 | THE BINDING PROBLEM IN THE MICRO- AND MACRO-PERCEPTIVE WORLDS

In principle, there is no binding problem in the micro-perceptive world because different attributes of the visual world are perceived at different times, through activity in different specialized areas of the visual brain (see references above). Paradoxically, the binding problem, in the context in which I discuss it here and in the micro-perceptive world, only occurs because of multiplexing cells. We may consider them under two hypothetical categories, distinguished by the roles in binding contemplated for them. I will refer to one category as the *Type A* multiplexing cells; these are the ones for which "cortical processing does not strive to separate form and colour information" (Friedman et al., 2003), a category that also includes the multiplexing cells which, in addition to colour and form, also apparently code for motion (Leventhal et al., 1995). I will refer to the other category as the *Type B* multiplexing cells, found in layers 2 and 3A of V2, and whose capacity to code for colour and orientation or direction of motion has been interpreted to be due to feedback connections from further, specialized visual areas (Shipp, Adams, Moutoussis, & Zeki, 2009), implementing feedback models of binding (De Kamps & Van der Velde, 2001). *Type A* cells are assumed, implicitly, to emit feedforward output. By contrast, type B cells are explicitly presumed not do so, by virtue of their laminar location (Markov et al., 2014). The possible binding action of *type B* cells may mediate a feature-attention driven modulation of *single-tuned* cells in layer 3B, a population of deeper-lying cells in V2 that do possess feedforward outputs. Hence, perceptual binding would not associate ipso facto with the activity of *Type B* cells, but be contingent upon their co-ordinating action upon populations of single-tuned, modality-specific cells in area V2 and beyond (Shipp et al., 2009). This is a very different physiological model of binding to that associated with *Type A* cells. It is one that retains separate processing of different perceptual attributes at higher levels, therefore facilitating psychophysical accounts of binding in which attentional influences are observed to modulate the exact timing of perceptual asynchrony (e.g. Holcombe & Cavanagh, 2008). Conversely, when placing a Type A interpretation upon the V2 cells to account for the observed asynchrony in the perception of colour, form (orientation) and directional motion one must invoke either some differential temporal input to, processing within, or return (feedback) output from cells in more specialized areas to the multiplexing cells in V2 (or V1) (Shipp & Zeki, 1989; Zeki & Shipp, 1989), thus also leading them to process different attributes differentially. No one has posed this question or shown that such differential temporal processing exists for these multiplexing cells; instead, the hypothetical (*Type A*) multiplexing cells are thought of as being immune from further cortical processing (see above). If they process all the attributes simultaneously, as is assumed, and are immune to feedback influences, then their physiology cannot account for the observed perceptual asynchrony if they do indeed account for perceptual properties, as is implied. Perhaps only my putative (*Type B*) multiplexing cells could, plausibly, account for the asynchronous perception of different visual attributes, the reason being traced to the equally plausible belief that different visual attributes are processed at different speeds in the more specialized visual areas which feedback onto them. Unfortunately, those who have invoked multiplexing cells to dismiss the binding problem have not addressed the question of perceptual asynchrony at all, even though it has been around for well over twenty years. Hence, none of these issues has been raised before.

Of course, it may be that the *Type A* multiplexing cells are not the ones mediating the percepts at all but, if so, what their function is needs to be accounted for; one possibility is that the orientation and wavelength- and luminance-selective double-opponent cells (Johnson, Hawken, & Shapley, 2008) may act as differencing units in a Land retinex style computation (Land, 1983; Shapley, Nunez, & Gordon, 2019), although there is no unanimity of views about the preponderance of double-opponent cells in visual cortex (Ts'o & Gilbert, 1988). It is also possible that such cells operate only in the macro-perceptive world, but that, too, needs to be accounted for.

11 | IS IT LEGITIMATE TO EXCLUDE A SMALL PERCENTAGE OF CELLS FROM PLAYING A LEADING ROLE IN PERCEPTION?

A great deal has been made of the predominance of multiplexing cells in V1 and V2 to account not only for the absence of a binding problem but for the "outdated" concept of modularity. This is evident in the view of (Di Lollo, 2012) which, reflecting that of (Shapley & Hawken, 2011), considers modularity to be "disconfirmed by advances in neuroanatomy and neurophysiology," a view that sadly neglects the contradictory results from many studies using optical imaging to demonstrate numerous aspects of functional specialization within V2 stripe modules (An et al., 2012; Chen et al., 2016; Felleman et al., 2015; Liu et al., 2016; Lu & Roe, 2008; Malach, Tootell, & Malonek, 1994; Roe & Ts'o, 1995; Shmuel et al., 2005; Wang et al., 2013). Yet even those who have emphasized strongly that the "vast majority" of cells in areas V1 and V2 of primate visual cortex are both orientation and colour selective (Friedman et al., 2003) and have suggested that such cells are not influenced by processing in further areas through feedback connections have provided percentage figures that do not sit easily with such strong statements. The percentage of cells responding to "uniform colour was about 20%" in the study of (Friedman et al., 2003) which, though a far cry from the "vast majority" (80%) of cells that are orientation selective, nevertheless represent a significant number in absolute terms. On the other hand Johnson et al. (2008) found a variable percentage of cells of the single colour opponent type of cell (which can respond to uniform colour), ranging from 2% to 31%. This, again, represents a significant number in absolute terms. The same conclusion can be drawn from the recent, extensive, study of orientation and colour selectivity in V1 cells by (Garg, Peichao, Rashid, & Callaway, 2019) who write of a "trend" in the distribution of cells with orientation and chromatic specificity to that of chromatically selective but orientationally non-selective cells, giving an overall figure of 7.5% for chromatically selective but orientationally non-selective cells. As a comparison, if one were to take the average number of 1,000 cells per sq. mm in layer 4B of V1 (which projects to area V5; O'Kusky and Colonnier, 1982) and calculate the number of cells projecting to V5 following retrograde tracer into the latter, the percentage of cells projecting from layer 4B of V1 to V5 comes to 0.6% (Shipp and Zeki, 1989); those in upper layer 6 (which also project to V5) constitute a fraction of that percentage. Yet this small percentage of cells would appear to play a crucial role in generating cardinal properties of V5, namely the capacity to respond to the global motion of complex patterns (Movshon & Newsome, 1996). Hence, there seems little justification at present for excluding cells which constitute a small minority compared with the "vast" majority from a critical and explicit participation in perception. It is worth adding that Garg et al. (2019) found that orientationally non-selective chromatic cells are "predominantly" concentrated within the cytochrome oxidase (CO)-rich zones of V1, hence seemingly lending support to earlier accounts of the separation of cells with specialized functions within different modules in V1 (Livingstone & Hubel, 1984).

12 | ASYNCHRONY THROUGH FEEDBACK?

The significance of such variable percentages must be seen against physiological evidence from monkey (Bushnell & Pasupathy, 2012; Conway, Moeller, & Tsao, 2007; Zeki, 1983) and human fMRI evidence (Bartels & Zeki, 2000; Lafer-Sousa & Conway, 2013; Lafer-Sousa, Conway, & Kanwisher, 2016), which shows that colour and form are divorced from each other within the human colour centre, area V4, just as they are in the monkey (Conway et al., 2007; Lafer-Sousa & Conway, 2013; Lafer-Sousa et al., 2016; Tanigawa, Lu, & Roe, 2010; Zeki, 1983); this is, of course, in addition to the well established separation of directional motion from both form and colour in the cells of area V5 (for a review see Zeki, 2015b). Perceptual asynchrony, discussed above, shows that different attributes of vision are processed at different speeds, depending upon the experimental paradigm, at least in the micro-perceptive world; imaging evidence suggests that different specialized visual areas process different attributes at different speeds in the macro-perceptive world (Bartels & Zeki, 2004; Hasson et al. 2010). The activity of cells in these specialized areas could therefore influence, through feedback, the multiplexing cells in layers 2 and 3 of V1 and V2. I do not mean to imply that such a top-down influence is only activated once a forward going signal has been received; top down attentional influences mediated by backward connections are known to initiate before a stimulus is present; predictive coding and priors can be setting backward activity independently of forward going signals. In fact, feedback connections to account for the perceptual asynchrony in binding have been invoked before (Clifford, 2010), but by supposing a difference in latency in the feedback from the areas of the prestriate cortex to V1, which would still leave out of account what the function of Type A multiplexing cells, the ones described as immune from other cortical influences, is. It is worth considering the alternative possibility I give here, that the feedback can account for perceptual asynchronies by supposing an asynchronous processing between different visual areas that feed back their signals to cells in "lower" areas asynchronously.

13 | TWO WORLDS THAT CAN CONTINUE TO IGNORE EACH OTHER, PERHAPS

Although I have, throughout this article, given full credence to the multiplexing cells, it is only fair to add that there is no unanimity of views about them; there are many who have not encountered such "vast" majorities of multiplexing cells (see references above); their negative findings should also be taken into account when assessing the role of multiplexing cells in binding, assuming them to have any.

Hence, for the (majority) interested in the macro-world, the question is how binding is effected such that the responses of cells that are indifferent to form but concerned with colour or those of cells that are indifferent to both form and colour but specialized to detect directional motion, as in V5, come to be bound to well defined objects to give us a holistic picture of the world. The binding problem does exist in the macro-perceptual world (Holcombe & Clifford, 2012; Wolfe, 2012). But no one knows how it is solved. For the (minority) interested in the micro-perceptive stage, the task is to enquire why multiplexing cells are ineffectual in bringing about integration, thus leading to a condition in which different attributes are perceived separately in time and, if anything, are mis-bound. For the even smaller minority who are interested in both worlds, the task is to ask whether there is any transition in physiological terms between the two worlds and, if so, how and when it occurs.

The two worlds of perception, micro and macro, may in fact co-exist. The difference from the world of physics is that it is far easier, and much less expensive, to study the transition from one to the other in the world of visual perception than it is in the world of physics. Moreover, unlike the world of micro- and macro-physics, it is also much more difficult for those in the world of macro-perception to ignore the rules governing the world of micro-perception, even though to date most have done so.

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CONFLICT OF INTEREST

I have no conflict of interest to declare.

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