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How Do Cortical Dynamics Organize an Anatomy of Cognition?

Abstract: *Freeman's pioneering work — and neurodynamics in general — has largely ignored specification of an anatomical framework within which features of coherent objects are represented, associated, deleted, and manipulated in computations. Recent theoretical work suggests such a framework can emerge during embryogenesis by selection of neuron ensembles and synaptic connections that maximize the magnitude of synchrony while approaching ultra-small-world connectivity. The emergent structures correspond to those of both columnar and non-columnar cortex. With initial connections thus organized, spatio-temporal information in sensory inputs can generate systematic and specific patterns of synchronous oscillation, with consequent synaptic storage. The theoretical assemblies of connections resemble experimentally observed 'lego sets', while facilitation and interference among synchronous patterns, particularly when executed by fast synapses under metabolic entanglement, imply powerful parallel computation.*

Keywords: synchronous oscillation; cortical embryogenesis; synaptic dynamics; cortical computation; cortical variation.

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1. Introduction

In his highly innovative career, Walter Freeman's achievements were based on his experimentally derived equations for the transfer of synaptic pulses to dendritic waves, and dendritic waves to axonal pulses (Freeman, 1975). Working with the olfactory bulb of rabbits, he identified travelling and quasi-static waves with learned perceptions of the subjects — crucially recognizing that these were not merely direct responses to sensory stimuli (Freeman and Schneider, 1982). His life's work was concerned with linking theoretical and experimental aspects. He recognized the significance of oscillation between excitatory and inhibitory neurons (Freeman, 1992), and their transition, when sufficiently excited, to a limit-cycle state, differing from the background firing, and comparable to a thermodynamic phase change. He carried this to a high degree of development in his latter career (e.g. Freeman, 2004a,b; 2005; 2006; Buzsaki and Freeman, 2015) and, in many publications with his colleagues, developed conceptions emphasizing highly nonlinear and far-from-equilibrium neural interactions.

Walter strongly encouraged alternative efforts to mathematically specify the dynamics of cortical neurons. In this issue, several influential lines arising from his work are described (Mannino and Bressler; Tsuda; Vitiello) and more, by Liljenström (2017). These bodies of work share in common a motivation to move neural field theory to a more physiologically realistic basis than generally pertains in artificial neural networks, but they each differ, in some cases fundamentally, in the simplifying assumptions upon which they are based. Thus the interpretations of similar data made by each differ, and a major challenge for his successors is to compare, contrast, and test these proposals, and, if possible, integrate them. It is not at all clear how that might be achieved. None of these theories specify neuroanatomical detail above the 'K-sets' proposed by Walter.

Characteristically, Walter Freeman took a course independent to the dominant stream of cortical neurophysiology, by regarding the exact details of connections and activity of single cells as subordinate to the dynamic properties of the medium — a viewpoint that can be traced back to Lashley and Hebb (Orbach, 1998) and earlier — and contrasts notably with (e.g.) Hubel and Wiesel (Hubel and Wiesel, 1959; Hubel, 1981), who sought to determine function within the classical anatomical order — of the organization of parts of the cortex into columnar patterns (Gilbert and Wiesel, 1979; 1989: Bosking *et al.*,

1997; Girman, Sauve and Lund, 1999; Issa, Rosenberg and Husson, 2008; Muir *et al.*, 2011) and of the response properties of single cells to stimulus 'features' — the orientation, spatial, and temporal frequencies of visual inputs (Hirsh and Gilbert, 1991; Angelucci, Levitt and Lund, 2002; Horton and Adams, 2005; Kascube *et al.*, 2010; Martin, Roth and Rusch, 2014; Bauer *et al.*, 2014; Ji *et al.*, 2015).

The cell-by-cell reductionist agenda has encountered difficulties. Stimulus feature responses were initially thought of as independent, atomistic, and inherent response properties of individual neurons. Early theories for the origin of neuronal responses presumed feature 'tuning' must emerge consequent to stimulation by visual objects (Swindale, 1996). It was soon realized that neurons could exhibit stimulus preferences before they were ever exposed to external stimuli (Wiesel and Hubel, 1974), yet could also fail to exhibit responses when deprived of early postnatal stimulation (Blakemore and van Sluyters, 1975). So, some innate organization existed that later was sustained or modified by external stimuli. Further, the elemental response properties were not independent, but interdependent — *viz.* the orientation response of neurons to a stimulus varies not only with orientation *per se*, but is different with changing speed of the stimulus, orientation to the direction of motion, and other factors (Basole, White and Fitzpatrick, 2003).

Thus, it is not just parody to suggest that theories of neural dynamics have been developed without more than very general anatomical underpinning, and anatomical theories have foundered without a sufficiently general foundation in neural dynamics.

A union between Freeman's dynamical approach and cellular neurophysiology seemed imminent with the discovery of synchronous oscillation in individual cortical neurons each activated by separate features of a single stimulus (Eckhorn *et al.*, 1988; Gray and Singer, 1989; Singer, 1994; 1999), so that synchrony became proposed as the solution to the 'binding problem'. This line of research, too, is rooted in the work of Walter Freeman (Liljenström, 2017). But an explanation of the origins and interrelationships among feature responses and their significance within perceptual wholes remains elusive, and it is uncertain why, or even if, oscillation and synchrony are essential to the operation of the cortex (Varela *et al*., 2001; Merker, 2016).

A reasonably satisfactory explanation would provide sufficient and general rules for learned representation of a single perceptual object, explain how representations of different objects were distinct from each other, yet similar for closely related perceptual wholes, how

perceptual wholes could be partially correlated, and how deletion of errors and 'forgetting' could occur without disruption of the whole. Ideally, a substrate for large-scale parallel computation should emerge. It is unclear whether such demands could all be met in real cortex by *ad hoc* linking of features in a random field, or would necessarily require an anatomical order. This bears on the relevance, if any, of why the cortex is columnar in some sites and non-columnar in others — a classical anatomical conundrum (Horton and Adams, 2005). Although anatomically specific, such a system might not be completely identified by traditional anatomical methods, as the orderliness might lie in the pattern created by very large numbers of synapses that cannot be exhaustively tracked by standard means, rather than in the positions of cells that may, or may not, show orderly arrangement of their cell bodies.

Here we extend our efforts (Wright and Bourke, 2013; 2016; Wright, Bourke and Favorov, 2014) to unify anatomical order and neural dynamics. Our group used neural field equations similar to Freeman's equations to explain spatial and frequency properties of electro-cortical potentials (summarized in Wright, 2016) and attributed synchrony to dissipative equilibrium in the exchange of electro-cortical waves. The ubiquity of synchrony led us to consider a possible role of synchronous oscillation in the embryological development of the cortex. Our conviction is that the mechanisms governing the regulation of neural growth in the embryo should be sufficient to explain the operation of the cortex in the postnatal environment. A successful theory of cortical neurogenesis and emergent structure ought, therefore, to imply a theory of cortical function, and might also go some way to resolve other neurophysiological uncertainties; frequency versus rate coding (Gerstner *et al.*, 1997); the impact of dynamic changes in synaptic efficacy (Wu, Wong and Tsodyks, 2013); the effect of competitive selection of cells by apoptosis (Chambers *et al.*, 2004; Elmore, 2007; Ryu *et al.*, 2016) and of competition between synapses (Antunes, Roque and Simoes de Souza, 2016), as well as the formulation of Hebbian learning rules.

2. Synchrony Can Orchestrate an Anatomical Order

2.1. The origin of synchronous oscillation

Figure 1 highlights the mechanism generating gamma oscillation as described by Freeman (1992) — placed within the context of overall

cerebral organization. Excitatory neurons and inhibitory neurons are closely intertwined in the cerebral cortex, and when sufficiently excited by pulses from external sources, their interactive firing becomes surging, as excitation and inhibition alternately predominate (Douglas and Martin, 1991). Groups of cells pulsing at the gamma frequency (about 40 Hz) transmit bursts of pulses to-and-fro to other groups via synaptic couplings to the surrounding cells, which, when firing at a low background rate, act as a stochastic medium for transmission of waves (Wright and Liley, 1996). As pulses from different sources sum at dendritic membranes of each neuron, pulses out of synchrony exert little effect, whereas pulses in synchrony summate (Chapman, Bourke and Wright, 2002). Thus, the exchange of signals between excitatory cells quickly reaches a dynamic equilibrium at which the excitatory cells all fire simultaneously, and exchange bursts of excitatory pulses. This synchronous oscillation is of greatest amplitude where the cells are strongly and reciprocally coupled. The exchange of pulses between excitatory and inhibitory cells also reaches an exchange equilibrium, but the opposite effects of the pulses exchanged requires them to fire at alternate times (Wright, 2010). The graphical representation of zero-lag cross-correlation of excitatory pulses, and out-of-phase excitatory/inhibitory cross-correlation, are also shown in Figure 1, and the dynamics are described in Appendix 1.

If all excitatory cells were strongly coupled at all times, then all the cells in the cortex would fire synchronously. This does not occur, partly because different subsets of cells receive different inputs, and partly because synapses change their efficacy (the strength of current connection) continuously. This means there are a very large number of ways different subsets of cells can enter synchrony, while other subsets remain firing at the low background rate. Which subsets are active defines the current, but continuously changing, brain state.
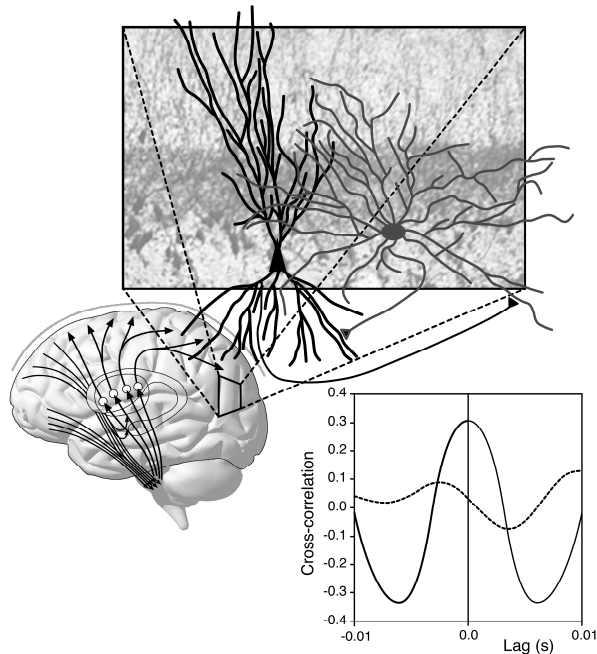
Figure 1. At bottom left a system of ascending and descending neural pathways, sending signals to and from the cortex is shown. Top, a slice through the cortex is shown in microscopic detail, with an excitatory pyramidal cell emphasized, and alongside it, an inhibitory cell — the excitatory and inhibitory cells being closely entwined. When sufficiently excited, excitatory and inhibitory cells begin oscillatory, to-and-fro, excitatory–inhibitory firing, at the gamma rhythm frequency, and excitatory cells begin to fire synchronously. Inset bottom right are cross-correlograms of pulses in a pair of excitatory cells, versus an excitatory and an inhibitory cell. The solid line, peaked at zero milliseconds, indicates that excitatory cells are firing simultaneously, the dashed line shows that excitatory and inhibitory cells fire a quarter-cycle out of phase with each other.

2.2. Synapses adjust their strengths to maximize synchronous amplitude by increasing connection symmetry

Aspects of Hebb's (1949) famous rule have been recently unified (Izhikevich and Desai, 2003) (see Appendix 2). Synaptic connections strengthen if the pre-synaptic cell pulses before the post-synaptic cell (long term potentiation — LTP) and is depressed (LTD) if the cells fire in the reverse order (Bear and Malenka, 1994). These effects combine as spike-timing dependent plasticity (STDP) (Markram *et al.*,

1997). The mathematical form of STDP is compatible with a further rule — the Bienenstock-Cooper-Monroe (BCM) rule (Bienenstock, Cooper and Monroe, 1982), which describes slower changes in synaptic strength.

The unification of STDP and BCM applies under two provisos. Firstly, on very rapid timescales, synapses must change their strength pulse-by-pulse, with minimal effect of prior pulses on the change in strength, although predominance of LTP over LTD slowly leads to increasing synaptic strength, and vice versa. Secondly, when pre- and post-synaptic neurons fire with high correlation, then a stable synaptic state cannot persist for long, implying that strongly synchronous firing of coupled neurons must be self-limiting. Synapses interact directly with their neighbours, probably by many different mechanisms, and compete for essential metabolic components — calcium ions being one component of established importance (e.g. Vernino *et al.*, 1992; Antunes, Roque and Simoes de Souza, 2016). Together, these effects would force continual switching between different subsets of strongly and synchronously pulsing neurons.

On longer timescales, the BCM rule imposes a refractoriness upon the effects of LTP, so the stronger the synapse, the smaller subsequent change becomes, while conversely, the weaker the existing connection, the more steeply the synapse increases its strength as fresh afferent pulses are received — an effect described as 'floating hook'. The 'floating hook' effect implies that two excitatory cells bidirectionally coupled and exchanging pulses would tend to come into equilibrium with each other, with equal firing rates, and equal, symmetric, strength of the synapses involved — and, more generally, such bidirectional connection symmetry might also be exerted over several intermediate synapses.

2.3. Maximization of synchrony and the development of small-world connections in columnar and non-columnar cortex

Embryonic neurons divide rapidly, spreading their long axonal connection trees, and generate pulses as they grow (Friauf, McConnell and Shatz, 1990; Downes *et al.*, 2012; Shi *et al.*, 2012). A large fraction of the dividing cells die (apoptosis) (Elmore, 2007; Ryu *et al.*, 2016) and, although apoptosis is a complicated process, involving suicide signals, we assume that access to and competition for resources plays a part in the selection of survivors. Ensembles of cells will survive better if the ensemble is connected by axons of minimum

length, to establish the necessary connections at lowest metabolic cost, so surviving ensembles will form 'small-world' systems, and that is found experimentally to be the case (Downes *et al.*, 2012). In the limit, the ensemble would form an 'ultra-small-world' (Cohen and Havlin, 2003) — a topology of connections in which distance of separation is proportional to the number of synaptic steps between neighbouring cells via which any two neurons are interlinked. For this to be the case, the average probability of connection between individual cells must decline with distance as a power function.

A complication is introduced by differences in the extension of the axonal trees of different types of excitatory neurons. We can consider the cells in a given cortical area as composed of a group with longer axons (here called alpha cells), and a group with shorter axons (beta cells). In different cortical areas the disparity of axonal lengths may vary, and, depending on the degree of disparity, different ratios of alpha to beta cells must be selected to ensure an equivalent overall connection-density versus distance power function.

It has also been shown experimentally that cells prevented from firing in synchrony are prone to apoptosis (Heck *et al.*, 2008). A plausible explanation for this is that as they fire in synchrony the neurons pump critical metabolites from the extracellular fluid collectively, outcompeting cells that fire asynchronously and uncooperatively. (The ratio of the pumping power could be as strong as N/square-root N, for N neurons in the synchronous and asynchronous groups.) So, selection of surviving neurons is toward cooperative, synchronous ensembles of cells, joined together in ultra-small-world configuration, and adjusting their synaptic contacts as much as possible towards reciprocal symmetry, so as to maximize synchrony. The principle of competition for resources can be assumed to operate within the cells as well as between the cells; thus surviving cells must find an efficient distribution of resources to their developing synaptic connections, such that synchronization is maximized in the ensemble to which they belong.

Figure 2 shows the outcomes of the interplay of these factors in simulations of the growth of cortical connections, and contrasts the outcome of two extremes in the ratio of lengths of beta and alpha cells. These simulations took place in three stages. In the first stage, the surviving cell bodies were arranged so as to form an ultra-small-world system of connections. In the second stage, the cells' positions were further arranged under the assumption that the forming synapses were adjusting their strengths according to the synaptic learning rules

discussed in the prior section, so that the surviving cells were forming reciprocally symmetric connections and attempting to compromise between both criteria — maximum synchrony and minimal total axonal length. In the final stage, which had little effect on the arrangement of the cell bodies themselves, synaptic resources were deployed so as to push the theoretical amplitude of total synchrony to a maximum.
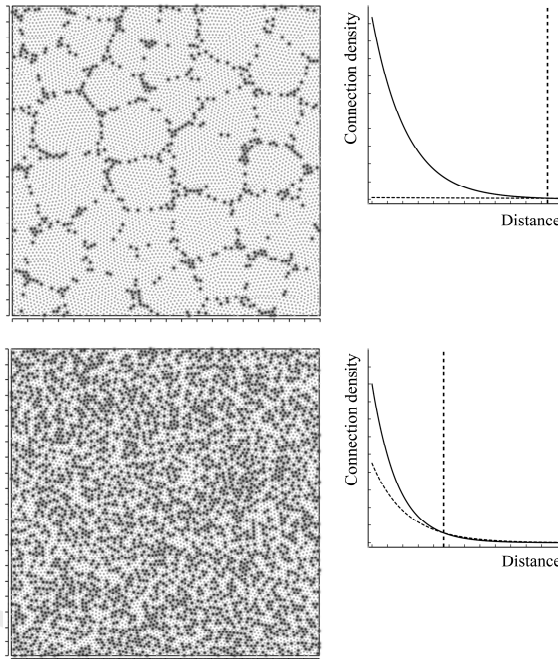

Figure 2. Simulation of cortical antenatal growth. In the left-hand figures, cell bodies of neurons with relatively long axons (alpha cells) are marked in black, and those of cells with relatively short axons (beta cells) in grey. In the top result a columnar structure emerges, where the cells with long axons are both much longer and much fewer in number than in the lower result, where short and long axons are more approximate in length, and the numbers of each type of cell closer to equality. In the right-hand figures, corresponding to the simulation results, the density (as a function of distance) of synapses generated by the cells with long axons are shown in the black curves, and the synapses generated by the short-axon cells as a dashed curve. In the respective cases, the average synaptic density versus distance approximates the same power function. The vertical dashed lines indicate the crossover distance, X, from the cell bodies beyond which the longer-axon alpha cells generate more synapses than do the short-axon beta cells.

It can be seen that when the long-axon, alpha, cells have much longer axons that the short axon, beta, cells, the outcome is a pattern in which the cells are arranged in columns — that is, clusters of beta cells surrounded by a meshwork of alpha cells. When the axon tree lengths are more nearly approximate, no such clear columnar arrangement is apparent.

The reason for these distinct outcomes can be seen in the accompanying plots, on the right-hand side of the figure, showing the respective distribution and numbers of alpha and beta cells required for the power function approximation in each case. Where most of the cells are beta cells, maximization of synchrony depends on tight packing of beta cells, yielding a columnar structure. Conversely, where long-axon alphas are present in more nearly equal numbers to the beta cells, optimization of the alpha–alpha connections plays a more nearly equal role, forcing a non-columnar outcome.

2.4. Formation of synaptic patch connections, and winding of local cell synapses about a singularity

Following the early embryological development, resulting in deployment of surviving cells near optimal positions, later synaptic development would continue, also under the constraint of limited resources. Thus synaptic connections must develop so pulsation exchanges resonate as much as possible — that is, maximize synchrony. Figure 3 illustrates the geometric effects determining the optimum synaptic positions.

To contribute appropriately to the power function/distance relationship, synapses between alpha cells must be deployed at distances from the alpha cell bodies greater than the distances at which alpha cell axonal density exceeds that of beta cells. This forces alpha cells to form synapses in skipping patches. The alpha network must resonate not only within itself, but also with the clusters of beta cells. This has the effect of generating an image of the alpha network projected upon each cluster of beta cells — a 'local map'. Each of the beta clusters must also interact with its neighbours so that local maps in adjacent beta clusters also achieve maximum co-resonance, and this is optimal if adjacent local maps are arranged in approximate mirror symmetry.

Also to increase resonance, the connections within the beta cluster must themselves be deployed so that the beta cell connections are as dense as possible, while consistent with the reception of a one-to-one map of alpha cell inputs. This condition is met when the beta cells'

synapses form into an array somewhat like a Möbius strip. The Möbius-like arrangement can occur with the local map arranged with either left- or right-hand chirality, which, in turn, facilitates the arrangement of adjacent beta clusters in mirror symmetry.

These arrangements correspond to observed cortical synapses, as is next discussed — except for the Möbius configuration, which has thus far not been directly observed, although its presence has been inferred. Our earlier papers discuss the full range of correspondences between theory and experimental data (Wright and Bourke, 2013; 2016; Wright, Bourke and Favorov, 2014).
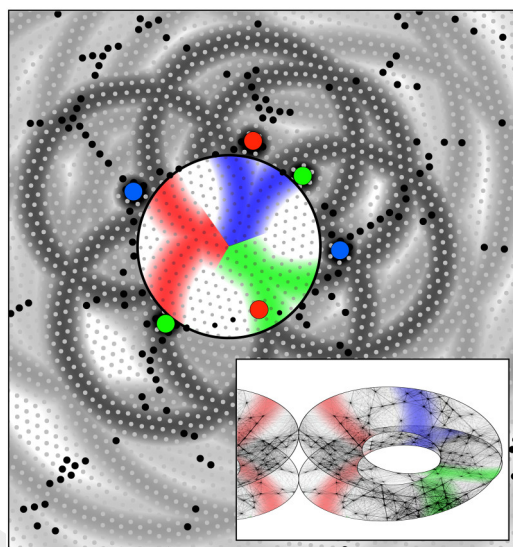

Figure 3. From the top simulation in Figure 2, six alpha cells surrounding a zone of beta cells have been picked out each at distances of separation from their nearest neighbours roughly the crossover distance, X. The fields of optimal synaptic connection of these six alpha cells with beta cells and other alpha cells have been emphasized in dark grey, and the alpha cells themselves, marked in red, blue, and green, generate optimal connections to beta cells within the central zone, coloured red, green, and blue according to their origins from diametrically opposite alpha cells. Consequent to restriction of synaptic resources, connections have become established over only half the potential field, and these are arranged so diametrically opposite alpha cells make connections outwards at similar angles from a 'singularity'. The inset shows the corresponding form of connections among the beta cells within the zone. The beta cells have established connections so they form a connected system analogous to a Möbius strip. The inset also shows the mirror-image arrangement of connections in an adjacent column of beta cells.
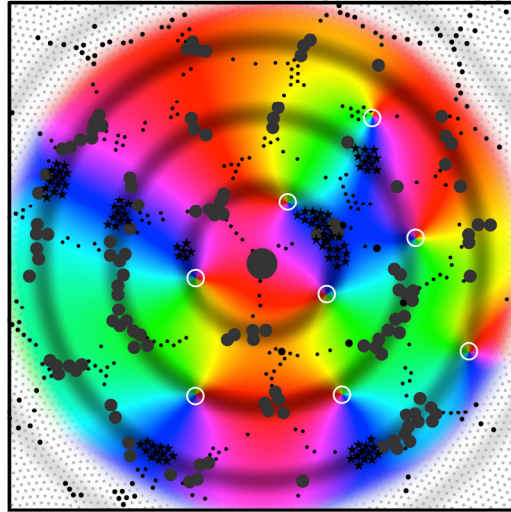
Figure 4. This image is centred on one of the original six alpha cells in Figure 3. The organization of connections shown in the inset of Figure 3 leads to a distribution of conventionally measured Orientation Preference (OP) of the enclosed beta cells, from 0 to 180° over 360° about an OP singularity, indicated by continuous colours on the colour spectrum. The emergence of OP in adjacent systems of beta cells is shown by arrange-ment of OP in mirror-image array in adjacent columns. Those alpha cells to which the central cell makes strong connection are shown as enlarged black-filled circles, and those beta cells with common OP connected to the central alpha are marked with black stars. These patterns reproduce the anatomical phenomena of patch cell connections, and 'like to like' connections, respectively.

2.5. Final configuration in primary visual cortex.
Patch connections, 'like to like' connections, and orientation-preference maps

Figure 4 shows the way the formation of synaptic connections diagrammed in Figure 3 reproduces established anatomical findings. The connections of a single central superficial patch cell (an alpha cell, in the simulation convention) is distributed in rings to other patch cells at a regular distance of separation (e.g. Gilbert and Wiesel, 1979; 1989), while not necessarily being connected to all patches in its axonal domain. The short-axon local cells are shown tinged with all the colours of the rainbow surrounding central pinwheels marked with small white circles about which all the colours are focused. These

focal points in the primary visual cortex are orientation preference 'singularities' and each colour demarcates response to *slowly moving* bars at a continuum of angles from 0–180 degrees — i.e. the range of angles as a bar is rotated to reverse its ends — around 360 degrees at the singularity (e.g. Bosking *et al.*, 1997) — reflecting the way the 'local map' of projections from the alpha cells to the folded beta cluster are arranged Möbius-fashion. Synaptic connections from the central patch cell are made only to local cells of similar orientation preference in areas surrounding different singularities, forming 'like to like' synaptic connections (Gilbert and Wiesel, 1989; Muir *et al.*, 2011).

Although these, and other, consistent anatomical features are most clearly seen in strongly columnar systems — most typically the primary visual cortex — there is reason to believe that a very similar system of organization may exist in all cortical areas, as next shown.

2.6. Sparsity of connections permits functional similarity in columnar and non-columnar cortex

Figure 5 shows a blown-up segment of the network of alpha cells from the non-columnar simulation outcome in Figure 2. Inset is shown a segment from the columnar simulation outcome. Both segments have been scaled so that the distance X — the crossover of density for beta versus alpha axonal trees, equal to the distance of separation of alpha (patch cell) clusters — is equal in the two cases. A subset of alpha cells have been connected with emphasized black lines each distance X long, and it can be seen that the same type of intermingled connection systems can be present in both, the difference being only in the magnitude of X, and the degree to which patch and local cells systems are clearly defined. This is consistent with anatomical findings in non-columnar cortex, which nonetheless exhibit patches, and occasional areas of local cell organization analogous to columnar cortex (Girman, Sauve and Lund, 1999; van Hooser *et al.*, 2006; Ko *et al.*, 2011; Garrett *et al.*, 2014). Connections between neurons in the cerebral cortex are very sparse — i.e. any two randomly chosen cells have low probability of connection, so many similar connection systems may be intertwined. This generalization of columnar structure permits us to extend our account from the primary visual cortex to the cortex at large.
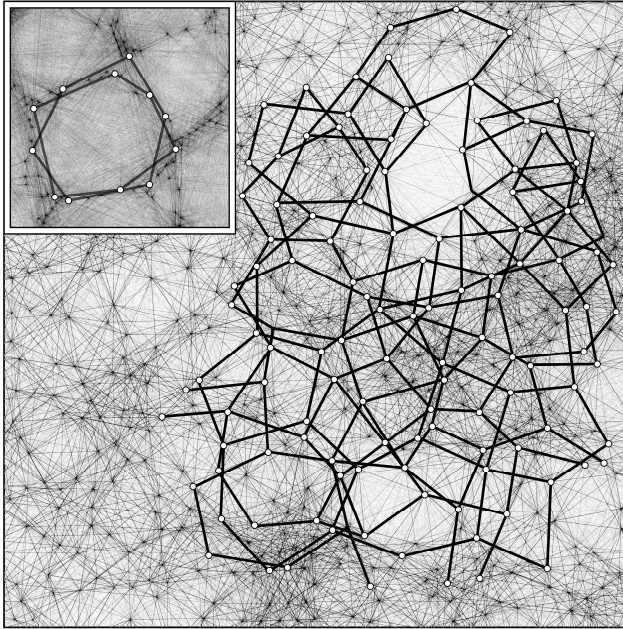
Figure 5. A section of the bottom simulation result from Figure 2, with the detail of the top simulation of Figure 2 used in Figure 3 inserted as an inset. The crossover distance, X, is normalized between the section and the inset. Alpha cell connections approximately distance X from near neighbours are then picked out by emphasis in black, in both the section and the inset.

3. Within the Anatomical Order, Synchrony Can Perform Cognitive Operations

3.1. A time-varying stimulus created by a moving object becomes represented by a set of simultaneously activated neurons

As well as explaining anatomical findings, the model of cortical growth presented above has succeeded in explaining the way the orientation preference of visual cortex neurons changes with the speed, angle of orientation relative to direction of motion, and length of stimulus objects (Basole, White and Fitzpatrick, 2003) — findings unexplained any other way except by matching to Fourier properties of the stimuli (Issa, Rosenberg and Husson, 2008); an explanation that is an equivalent solution (see Appendix 3). In turn, this phenomenon enables us now to explain how, after birth, the antenatal pattern of

synaptic development can be modified in response to external sensory input in an orderly manner. Figure 6 shows how the image of a line projected to the visual cortex will be projected by the alpha cell (superficial patch) network to the 'local maps' in a representative set of clusters of beta cells, whether columnar or non-columnar. Each local map receives the image of the moving line with different time-lags of conduction for each position on the line, and for each local map. The set of inputs to the local maps are thus a sample of the line's movement through space and time. If a substantial number of the neurons in the local maps are activated above threshold, they can then enter into synchronous oscillation with each other, and the synchronous firing of the cells at any moment represent the moving object not as a static image at that moment, but as a sample of the line in motion, over some short epoch. (See Appendix 3.)

Although the duration of the synchronous firing is self-limiting, as earlier discussed, repeated short bursts of firing would result in permanent synaptic consolidation. Consequently, activation of the group of cells by other inputs would generate the same effect as the original sensory image. However, if long-term consolidation of synapses is not maintained, the connections between the activated cells will revert to their embryological pattern, and the input will be 'forgotten'. Also, similar stimuli moving through similar parts of the sensory field will generate similar, partially overlapping, synchronous sets. Synaptic bridges, if later developed between initially distinct connected sets, would create new object representations — the new representation having some characteristics of each initial object.

In the examples that follow emphasis is placed upon vision, but it should be noted that inputs in all sensory modalities can be similarly characterized as spatio-temporal sequences, whatever the way the primary stimulus has been modified by the input pathways. As previously noted, although orderly arrangements in macrocolumns like those of the primary visual cortex are used for illustration, similar mechanisms are applicable in all cortical areas.
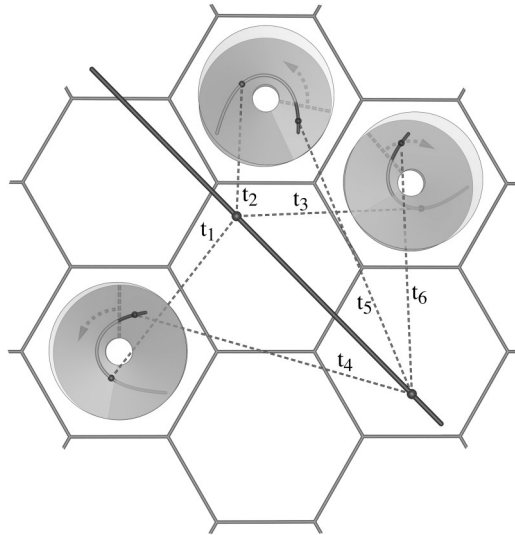
Figure 6. Mapping of a moving object onto a set of synchronous neurons. An object in the visual field is projected to the cortical surface, and is here represented by the black line. Lateral transmission from the receptive fields of input takes place via the patch cell (alpha) system, to many of the macrocolumnar local maps, composed of short-axon (beta) cells. The Möbius strip-like organization of the local maps is indicated as formations of synaptic connections analogous to a clam-shell. The dashed lines on each clam-shell indicate mapping of the horizontal axis in the larger field, in each map, with dashed arrows indicating the chirality of the map. The projection of the line to each macrocolumn winds onto the 0–2π, or 2–4π 'limbs' (or 'skeins') of each local map. Projection from input points on the cortex to corresponding points on each local map take place with different conduction delays, marked t_1–t_3, and t_4–t_6. The simultaneous activation of a set of cells in the local maps, and their entry into synchronous oscillation, represents a space-time sampling of a moving object over a short epoch.

Figure 7 shows the progress of the inputs to a single idealized macro-column in the primary visual cortex, generated by the same object travelling at a variety of different speeds. The laterally travelling waves of input signals do not raise the local cells above threshold for firing until the moving stimulus directly stimulates the macrocolumn over the direct pathway from the optic nerve and lateral geniculate body. Then a characteristic set of the cells close to threshold are excited beyond their threshold.
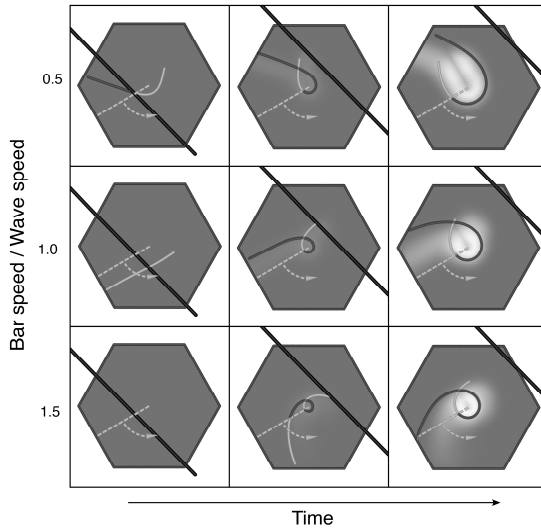
Figure 7. In accord with the mechanism diagrammed in Figure 6, the moving stimulus generates subthreshold activation of cells in each macrocolumn in a pattern that is updated as the progress of the visual stimulus continues. When the particular macrocolumn receives direct input to its classic receptive field (cRF) the cells are triggered above threshold, and can enter synchrony. This effect is shown for a sequence, arranged left to right, of epochs in a single macrocolumn, as the visual stimulus (black line) moves left to right. Top to bottom the sequence is shown for stimulus inputs moving at half the speed of wave transmission through the patch system, at equal speed of stimulus and waves, and where stimulus speed is 50% greater than wave speed. The right-hand epoch shows, in white highlighting, the approximate area within which cells are triggered above threshold in each case.

3.2. Each object creates a unique pattern

Figure 8 makes more explicit the process of generation of synchronous fields by a moving stimulus, in a set of idealized macrocolumns. A continuous rolling wave of subthreshold excitation reaches local cells in each macrocolumn as the movement of the visual stimulus continues. The pattern of cells entering synchrony is unique for given stimulus shape and velocity, and because of the network sparsity, many similar but distinct object representations can be anatomically intermingled.
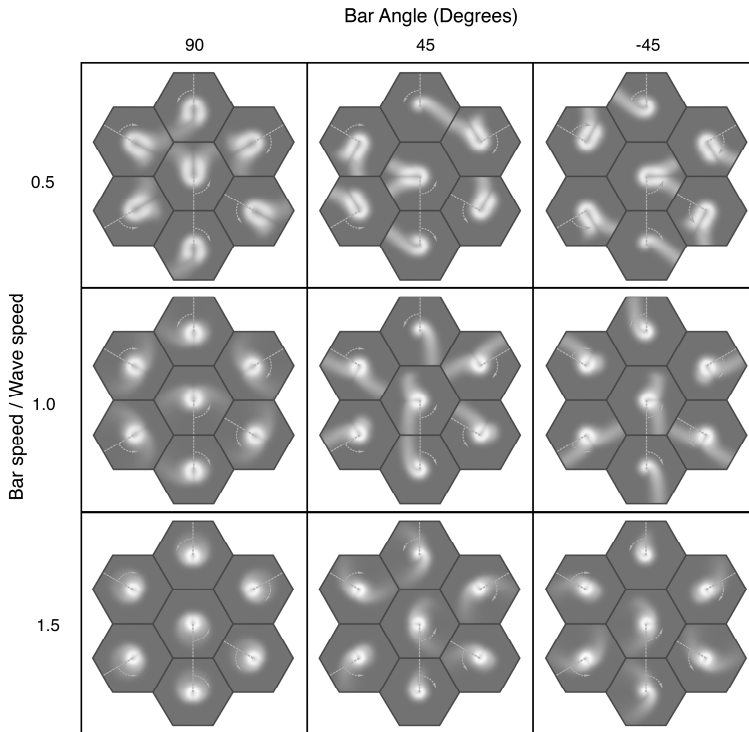
Figure 8. A complex of adjacent macrocolumns is shown, each map showing with its activation pattern in response to moving line visual inputs, aligned at 90, 45, or –45 degrees relative to the horizontal axis of the field, and at stimulus speed/wave speed ratios 0.5, 1.0, and 1.5. For each condition the field of synchronously activated cells is unique.

3.3. Separate cortical areas can interact via synchrony, to manipulate object representations and perform computations

Figure 9 indicates that interareal cortico-cortical connections can feed forward and feed backward patterns of activity between higher and lower areas in the cortical hierarchy. The signals input from the lower area would propagate laterally in the higher area according to the same rules as in the lower, generating a similar anatomical order to that of the lower, and also send return signals to the lower cortical area. According to whether the exchanged cortico-cortical signals terminate on excitatory or inhibitory cells, and which synapses are currently successfully competing for critical substrates, synchronous patterns can either mutually reinforce or suppress each other, as

shown by the in-phase and out-of-phase wave interactions at the bottom of Figure 9, and thus perform computational switching, operating as logic gates of any type. Iterative interactions among many cortical areas would be possible by similar means. As signals move up the hierarchy of cortical areas, they would contain information in increasingly abstract form, from all modalities, but always based upon the same representation of spatio-temporal moving patterns at the lower level, converted to synchronous sets at the higher level, and eventually impacting on the motor cortex and projections to subcortical systems. Conversely, as signals move down the hierarchy, higher-order motor control could be exerted to filter the incoming sensory flow.
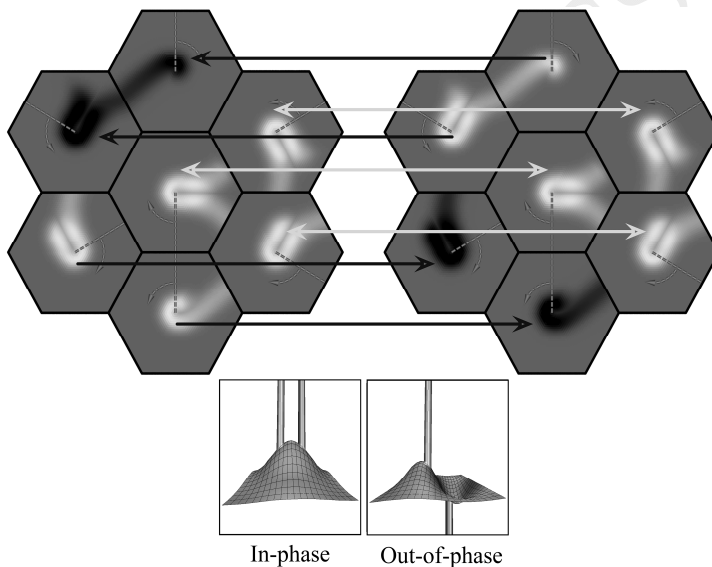

In-phase   Out-of-phase

Figure 9. Systems of adjacent macrocolumns, similar to those in Figure 8, are shown top left and right, each of which represents macrocolumns in separate cortical areas, interacting with each other via cortico-cortical fibres, as indicated by the black and white arrows linking analogous points. The arrows and the black and white shading indicate that higher and lower cortical areas can act either to reciprocally excite each other into joint synchrony, or to block synchronous activity and thus can filter and modify each other's patterns of activity by switch-like means. The bottom inset shows the mechanism of in-phase versus anti-phase interaction. The left frame shows concurrent activation of adjacent excitatory cells, generating synchrony, the right frame shows concurrent activation of an excitatory and an inhibitory cell, causing anti-phase cancellation of synchrony.

The dynamic attractors of the system are combinations of neurons firing in synchrony, each associated with a transient steady-state of synaptic activity. This requires neither exclusive pulse-frequency nor pulse-rate coding, as the most important timescale would be set by two-way synaptic adjustments in response to the pulses, and the pulses to the available synaptic resources, rather than explicit information processing by the pulses alone.

Synaptic competition for critical resources in fast synapses implies their metabolic entanglement, with some analogy to quantum entanglement, and thus, perhaps, some of the properties sought in quantum computing (Muthukrishnan, 1999). If supply problems limit critical resources to supporting 50% of fast synapses at any time the channel capacity (Shannon entropy) of synaptic states, and thus of synchronous states, would reach an immense maximum.

With this distributed and massively parallel system, reinforcement influences consolidating synaptic changes can be diffuse, if appropriately timed. Stimulation of transhypothalamic (ICSS) neurons (Olds and Milner, 1954) causes consolidation of immediately prior action sequences by a widespread diffuse action upon the cortex (Wright, 1973). Thus, interaction of the cortex with innately wired subcortical systems, providing supervision of learning in early post-natal life, would later lead to cooperative cortical control of the lower systems.

4. Conclusion

The developmental synaptic scaffold that we propose has candidate properties as a basis for an anatomy of cognition. Representations of different objects, distinct from each other yet similar and interwoven for closely related perceptual wholes, would arise from repeated episodes of synchrony, and would be associated by cross-links to form new object representations, while deletion of errors and 'forgetting' would occur by relaxation to the antenatal configuration without disruption of the whole. Of course, we have not established that the system's properties are uniquely necessary for cognitive function, but they do offer a natural pathway to self-organization and efficient operation of the cortex.

The existence of a general cortical organization, underlying the widely disparate columnar and non-columnar variations of the cortex from region to region and between species, does not imply that the rich systematic variation of structure throughout the cortex (Glasser *et*

al., 2016) is without functional significance. It does suggest, however, that at least a part of the basis of this variation may lie in variation of axonal lengths of intracortical axons in each zone of parcellation — and perhaps differences in the correlation length of signals processed in different areas. The proposal is not only compatible with localization of function to different cortical areas, but requires this.

Several independently derived theoretical ideas are unified in this proposal — *viz.*

- Synchrony is the stable state of cortical activity and requires symmetric connectivity between excitatory neurons.
- Fast-dynamic modification of excitatory synapses leads to overall symmetric connectivity, and local periods of burst firing in synchrony terminate automatically.
- Synaptic competition operating on the fast-dynamics of synapses permits a multitude of separate synchronous states.
- The metabolic entanglement of fast synapses makes possible very large-scale parallel computation.
- Consistent with the above, simulations can account for the anatomical structure of both columnar and non-columnar cortex.

Although the connections that emerge in our simulations match actual anatomical descriptions well, they predict a striking feature that has not been directly described — the Möbius strip-like winding of synaptic linkages within macrocolumns and their equivalents in non-columnar cortex. However, the demonstration of synaptic connections in 'lego sets' (Song *et al.*, 2005; Kalisman, Silberberg and Markram, 2005; Perin, Berger and Markram, 2011) is consistent with our theory. Units of lego sets appear to be linkage clusters of excitatory cortical cells, scattered over a range of up to several hundred microns — about the size of a macrocolumn. The neurons are strongly, and often reciprocally, connected by few synapses of the many possible connections their axons could have made, and are not, in themselves, small-world ensembles. Bridges between such sets could form a Möbius-like system, and have the characteristics of linkages, learned via synchrony, making up the representation of a stimulus or perceptual object. This suggests a test of theory by specification of the feature responses of a lego set, and the reconstruction from this of a stimulus object. Conversely, the embryological development of lego sets on a random basis would give rise to a postnatal cortex already primed to perceive some ensemble of elementary perceptual objects.

Much remains unspecified. We have not attempted to introduce details of biochemistry into our account, except in the most minimal form. Field equations specifying the interaction and competition of synapses are not even attempted. The role of subcortical systems in the selection of particular learning has been considered only by reference to the spirit of the work of MacLean (1973). However, the proposal appears consistent with the findings and scheme of cerebral organization described by Mannino and Bressler in this issue, and, incidentally, Tsuda's concept of chaotic itinerancy (also in this issue) might be applicable to transitions between the synchronous attractors of the present account.

Finally, on the great question of the nature of consciousness, as opposed to the nature of brain function, we remain agnostic. The implied close correspondence of the synchronous field to the representation of whole moving sensory objects, and their subsequent intermingling and generation of bottom-up and top-down information flows, ultimately generating motor outputs, represents the brain as an adaptive machine. The world within is constructed of learned relationships of concrete objects and their abstractions and associations, constrained to optimize organism survival in an environment (physical and conceptual) of ever increasing complexity. Since, in this formulation, synchronous attractors are minimum free energy states, the concept is aligned with the minimum free energy principle proposed, on more general grounds, by Friston and colleagues (Friston, 2010).

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Appendix 1.
Synchrony and equilibria in the neural field

Autoregression analysis shows electro-cortical waves resemble a near-equilibrium thermodynamic process (Wright *et al.*, 1990), frequency/wavenumber analysis reveals their widespread synchrony (Wright and Liley, 1995), and coherence analysis indicates they are long wavelength damped travelling waves, generated from multiple sources on

the cortical surface (Wright and Sergejew, 1991). Simulations indicate that the synchrony arises from symmetrical collisions with super-position of even, and dissipation of odd, components of the travelling waves (Chapman *et al.*, 2002). The limited large-scale signal com-plexity would preclude high levels of information transfer via the waves — unless there are a multitude of separate states, each with similar gross characteristics, poorly distinguished in the surface recordings. Synaptic competition would permit many such states, as partitioned equilibria, with each equilibrium requiring a different symmetry of synaptic connection.

Pulse dynamics

Pulses flow along axons until they reach pre-synapses

$$\varphi_p(\mathbf{q}, t) \leftarrow gQ_p(\mathbf{r}, t - x / v) \tag{1.1}$$

Subscript $p = e,i$ refers to excitatory or inhibitory neurons, where $\mathbf{r}$ and $\mathbf{q}$ are cortical positions occupied by single neurons.

$$x = |\mathbf{q} - \mathbf{r}|$$

$\varphi_p(\mathbf{q}, t)$ is the flux of pulses reaching pre-synapses at the neuron at $\mathbf{q}$, from the neuron at $\mathbf{r}$.
g is the slowly varying (Hebbian) synaptic gain between the neuron at $\mathbf{q}$, from the neuron at $\mathbf{r}$.
$Q_p(\mathbf{q},\mathbf{r}, t)$ are the pulse emission rates at $\mathbf{q},\mathbf{r}$. v is axonal conduction speed.

The pre-synaptic pulses produce depolarization of dendrites

$$V_p(\mathbf{q}, t) \leftarrow \sum \varepsilon_p \varphi_p(\mathbf{q}, t) \tag{1.2}$$

$V_p(\mathbf{q}, t)$ are dendritic potentials generated at $\mathbf{q}$.
ε_p is the efficacy of synaptic connection.

The dendritic depolarizations are translated back into pulses

$$Q_p(\mathbf{q}, t) \leftarrow \Theta V_p(\mathbf{q}, t) \tag{1.3}$$

Θ is a Heaviside step function for the threshold for conversion of dendritic potentials into action potentials.

Synaptic competition

The efficacy of the synapses is continually modified by the interaction of pulses with the available resource reservoir, and the competition between synapses for those resources

$$E(\overline{\varphi}) = \sum_{j,k=1}^{j,k=N} \varepsilon^j \overline{\varphi}^j + B^{jk} \overline{\varphi}^j \overline{\varphi}^k \qquad j \neq k$$

(1.4)

$E(\overline{\varphi})$ is a measure of energy of the total synaptic state.

j,k numbers the connections **qr**.

$\overline{\varphi}$ is an average of synaptic flux within a relevant time period of synaptic adaptation.

N is the number of connections.

B^{jk} is the correlation of synaptic flux in connections *j* and *k*.

ε^j is the instantaneous synaptic efficacy.

Minima of eqn. (1.4) define combined pulse and synaptic steady states. On timescales shorter than the period of oscillation, ε^j, $\overline{\varphi}^{j,k}$, B^{jk} must be represented by complex numbers. Nearby synapses are metabolically entangled, and convergence to a minimum would be rapid. This provides some analogy to quantum computing. On long timescales, ε^j, $\overline{\varphi}^{j,k}$, B^{jk} can be represented by real numbers, with analogy to Hebbian consolidation and Hopfield networks.

Requirement of connection symmetry for synchronous equilibria

Time-stationary equilibrium, either in oscillation or at a uniform low firing rate, requires the product of synaptic connection strengths and synaptic efficacies to be symmetrically equal between any two cells, and the two cells to be firing at similar rates, so that

$$\varphi_e(\mathbf{q}, t) = \varphi_e(\mathbf{r}, t) \qquad (1.5)$$

i.e. $\varphi_e(\mathbf{q}, t) - \varphi_e(\mathbf{r}, t) = 0$

That is, at stable oscillating equilibrium, excitatory cells fire in phase. The free energy of the excitatory cell neural field is at a minimum and there are no net travelling waves, whereas transitions between these steady states are associated with travelling waves. Where competition enables only about half the synapses to operate at maximum efficiency, the number of possible synchronous equilibria is necessarily very large, and the synchronous sets distinguishable, yet, within each equilibrium, thermal approximations remain applicable.

Also at equilibrium

$$\varphi_e(\mathbf{q}, t) = -\varphi_i(\mathbf{r}, t) \tag{1.6}$$

i.e. $\varphi_e(\mathbf{q}, t) + \varphi_i(\mathbf{r}, t)$ has a constant value (equal to twice the mean synaptic pulse rate) so inhibitory and excitatory cells fire with a ninety degree phase difference.

Appendix 2.
Synaptic learning rules and simulations
of cortical development

Unity of synaptic learning rules and emergence of synaptic symmetry (after Izhikevich and Desai, 2003)

Spike-timing dependent plasticity (STDP) (Markram *et al.*, 1997) applies to synaptic modification in the low firing rate regime, when there is not significant ongoing correlation between pre- and post-synaptic pulse rates, and is given by

$$C(\varphi_e) = \varphi_e \left(\frac{A_+}{\tau_+^{-1} + \varphi_e} + \frac{A_-}{\tau_-^{-1} + \varphi_e} \right) \tag{2.1}$$

$C(\varphi_e)$ is the change in synaptic strength per pre-synaptic pulse, at a given post-synaptic pulse rate, φ_e, and A_+, A_-, τ_+, and τ_- are parameters defining the gain and time constants of synaptic change.

When this rule is applied with appropriate parameter values and under the assumption that only 'nearest neighbour' pulses need be considered (i.e. that the effect of prior pulses is forgotten by the synapse after each post-synaptic pulse) it has the same mathematical form as the Beinenstock-Cooper-Monroe (BCM) rule, over short epochs. The complete BCM rule also includes a slower developing property — the 'floating hook' — that describes the way $C(\varphi_e)$ declines with increasing pre- and post-synaptic pulse rates. This means that the exchange of pulses between neurons tends to bring the synaptic gain of their connections (whether directly reciprocal or in the aggregate over indirect connections) and the pulse rates of the cells toward equality.

During synchronous oscillation, eqn. (2.1) becomes

$$C(\varphi_e) = \varphi_e \left(A_+ \tau_+ + \frac{A_-}{\tau_-^{-1} + \varphi_e} \right) + ac_0 \tag{2.2}$$

Where ac_0 is a time correlation function for pre- and post-synaptic pulses.

Since the exchange of synchronous pulses between neurons is highly correlated, ac_0 becomes the dominant term. Stability analysis shows the stable point is now accompanied by a high frequency unstable point, leading in time to a saddle node bifurcation that prevents synaptic stability, interfering with the exchange of synchronous pulses, and limiting the period of synchrony.

Basis of cortical growth simulations (after Wright and Bourke, 2016)

The simulations considered two populations of cells — alpha cells (that will become superficial patch cells) and beta cells (that will become local short-axon cells).

Ratio of cell types

Where N_β and N_α are the fractions of the cells that are beta or alpha, and λ_β and λ_α are the respective inverse length constants of their axonal trees, and their average of axonal tree density is an 'ultra small world' descending power function with distance, then for given λ_α and λ_β, N_α and N_β can be found by minimizing

$$\int_{x=0}^{x=\infty} [(x+\lambda_\beta^{-1/2})^{-2} - (N_\beta \lambda_\beta e^{-\lambda_\beta x} + N_\alpha \lambda_\alpha e^{-\lambda_\alpha x})]^2 \, dx$$

(2.3)

Optimum arrangement of the cell bodies must then be determined.

First stage — selection of cell positions with ultra-small-world axonal length

Up to a distance X from the cell body, beta cells have greater axonal density than alpha cells, and beyond distance X alpha cell axonal trees are denser. (See Figure 2.) Consequently, simulation of selection of cell positions during the earliest stages of embryogenesis computed an equilibrium of forces arrived at by alpha cells repelling cells at less than distance X and attracting cells at greater than distance X, while the reverse was the case for beta cells.

*Second stage — maximization of synchrony modifies final
selections of cell positions*

In the next stage, a similar equilibrium of forces algorithm was
applied, but this time under the assumption that all connections were
approaching bilateral symmetry as synapses developed to equilibrium,
maximizing synchrony. This skews the optimum cell positions into a
columnar structure. Differing ratios in the axonal lengths imply
different compromises between maximization of synchrony and ultra-
small-world axonal lengths, and thus variation in the degree of
columnar organization in cortical areas and species.

Appendix 3.
Representation of a moving object in a synchronous set

Spatio-temporal representation

Connections between the patch system and the many macrocolumnar
local maps can be represented as projection from a single complex
plane, **P**, to each of a set of complex planes, {**p**}, tiling the larger
plane

$$\mathbf{P}(P_x, P_y) \rightarrow \{\mathbf{p}(p_x, p_y, p_z)\} \tag{3.1}$$

where {**p**} are constructed from Möbius strip-like local synaptic
connections, with each map having a reference zero orientation, φ, to
the X-axis of the global field, and each centred on a singularity at a
position $\mathbf{p}_0$ so that where $|\mathbf{p} - \mathbf{p}_0| = |\mathbf{p}|$ are distances from the singu-
larity and ϑ are angles from the reference zero angle, with chirality
indicated $\pm$, then

$p_x = |\mathbf{p}|\cos(\pm\vartheta + \varphi)$

$p_y = |\mathbf{p}|\sin(\pm\vartheta + \varphi)$

$$p_z = \begin{array}{l} +1 \ if \ 0 \leq (\pm\vartheta + \varphi) \leq 2\pi \\ -1 \ if \ 2\pi < (\pm\vartheta + \varphi) \leq 4\pi \end{array}$$

the sign of p_z indicating whether **p** is located in the first or second
'limb', or 'skein', of the Möbius connections.

Thus, the image of a moving object, O, received over sensory path-
ways and relayed by lateral patch connections to any one local map
can be represented by

$$O(P_x,P_y,t-\frac{|\mathbf{P}-\mathbf{p}|}{\upsilon}) \rightarrow O(p_x,p_y,p_z,t) \tag{3.2}$$

where υ is the electro-cortical wave velocity.

Thus $\{O(p_x,p_y,p_z,t)\}$ represent a spatial and temporal sampling of the moving image over some short epoch, with distance from the singularity reflecting time-lag and global distance from the local map.
The synchronous set so generated is provided with information about the instantaneous velocities of the moving image as well as position at different lags.

Spatial and temporal frequency representation

An equivalent Fourier representation, applicable to the concept of 'feature tuning', is obtained by choosing axes X,Y so that the moving image will cross a specific macrocolumn/local map travelling at a velocity $\mathbf{V}_x$ toward that map, and $\mathbf{V}_y$ orthogonal to that map. Then wavenumbers K_x,K_y in the image are transformed to preferred-response wavenumbers k_x,k_y in the local map, consequent to Doppler effect and the orientation of the local map.

$$k_x \propto K_x \frac{\upsilon}{\upsilon \pm \mathbf{V}_x}\cos(\pm \vartheta + \varphi) \tag{3.3}$$

$$k_y \propto K_y \frac{\upsilon}{\upsilon \pm \mathbf{V}_y}\sin(\pm \vartheta + \varphi)$$

The pulses of waves arrive with frequencies of modulation, $\omega(K)$, the temporal-frequency-preference characteristic of each wavenumber of the moving image and the object velocity

$$\omega(K) = \mathbf{V}_x\sqrt{K_x^2 + K_y^2} \tag{3.4}$$