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Review

Functional maps within a single neuron

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Narayanan R, Johnston D. Functional maps within a single neuron. *J Neurophysiol* 108: 2343–2351, 2012. First published August 29, 2012; doi:10.1152/jn.00530.2012.—The presence and plasticity of dendritic ion channels are well established. However, the literature is divided on what specific roles these dendritic ion channels play in neuronal information processing, and there is no consensus on why neuronal dendrites should express diverse ion channels with different expression profiles. In this review, we present a case for viewing dendritic information processing through the lens of the sensory map literature, where functional gradients within neurons are considered as maps on the neuronal topograph. Under such a framework, drawing analogies from the sensory map literature, we postulate that the formation of intraneuronal functional maps is driven by the twin objectives of efficiently encoding inputs that impinge along different dendritic locations and of retaining homeostasis in the face of changes that are required in the coding process. In arriving at this postulate, we relate intraneuronal map physiology to the vast literature on sensory maps and argue that such a metaphorical association provides a fresh conceptual framework for analyzing and understanding single-neuron information encoding. We also describe instances where the metaphor presents specific directions for research on intraneuronal maps, derived from analogous pursuits in the sensory map literature. We suggest that this perspective offers a thesis for why neurons should express and alter ion channels in their dendrites and provides a framework under which active dendrites could be related to neural coding, learning theory, and homeostasis.

active dendrite; ion channel; intrinsic plasticity; efficient encoding; map; neuromodulation; synaptic plasticity

A QUESTION THAT HAS BEEN CENTRAL to several defining debates in neuroscience is whether neurons and their dendrites are simple integrate-and-fire units or machines capable of complex computational tasks. A few critical instances where this question has been central are the rate vs. temporal coding debate (Branco and Hausser 2011; Shadlen and Newsome 1995, 1998; Softky 1995; Softky and Koch 1993), the debate on whether dendritic nonlinearities play a critical role in neuronal information processing (Chen et al. 2011; Jia et al. 2010; Kitamura and Hausser 2011; Losonczy and Magee 2006; Losonczy et al. 2008; Lovett-Barron et al. 2012) and the origins of extracellular field potentials (Buzsaki et al. 2012). The literature presents a diversity of opinions spanning a large spectrum, including those that present extreme standpoints (see references above) and those that constitute subtle differences in terms of what molecular/cellular processes mediate specific dendritic nonlinearities (Angelo et al. 2007; Hoffman et al. 1997; Magee 1998, 1999; Narayanan and Johnston 2007; Stuart and Sakmann 1994; Stuart and Spruston 1998). Here, we present a case for viewing dendritic information processing through the lens of the sensory map literature and argue for a potential convergence of the literature toward viewing dendrites and their ion channels as facilitators of the two conjoined goals of efficiently encoding incoming local information and maintaining homeostasis through this process.

Functional maps across neurons constitute a common design principle in various regions of the central nervous system. These topographic maps are systematic and continuous spatial representations of information within a brain region, where adjacent neurons represent adjacent points along a parametric space (Luo and Flanagan 2007; Schreiner and Winer 2007). For example, topographic maps of the visual world exist along the primary visual pathway, starting at the retina, through the visual thalamus to the primary visual cortex. Similar somatotopic in primary somatosensory cortex and of tonotopic order in primary auditory cortex extend this topographic order to other sensory modalities (Petersen 2007; Schreiner and Winer 2007). Functional maps of numerous other properties such as direction selectivity, color, or stereo processing, in the visual cortex (DeAngelis and Newsome 1999; White and Fitzpatrick 2007; Xiao et al. 2003) and echo delay and sound source location in bats (Schreiner and Winer 2007) also have been reported. Apart from these, maps of grid cell spacing (Moser et al. 2008) and intrinsic oscillatory frequency (Giocomo et al. 2007) in the entorhinal cortex, maps in the motor cortex (Graziano and Aflalo 2007), and olfactory glomerular maps

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(Luo and Flanagan 2007) have also been reported, establishing the commonality of this design principle across numerous brain regions. In this cross-literature review, we extend this map metaphor to single neurons and submit our argument that several functional parameters that are known to possess orderly gradients within a single neuron can be investigated from the perspective of topographic functional maps. Expanding on this extended metaphor, we present our thesis that explorations into this emerging field on intraneuronal maps are bound to benefit by drawing direct equivalents from the well-developed literature on interneuronal sensory maps. Specifically, we present analogies spanning maps in these two scales in terms of their functions, underlying mechanisms, plasticity, activity dependence, and neuromodulation, apart from comparing their computational, developmental, and genetic facets. In this process, we establish straightforward equivalences across these two scales of maps with respect to the theoretical bases and the experiments that have been performed, and we present directions for future research that emerge as an outcome of this simple allegory.

Background on Functional Maps Within a Neuron

What constitutes a functional map? We define a functional map within a neuron as an orderly progression of a functional parameter on a topograph of the neuron. Specifically, a systematic distribution of a physiologically relevant parameter mediated by active mechanisms along a spatial axis within the neuron would constitute a functional map. A striking example of a functional map within a neuron is the recently reported map of resonance frequencies that exists within a single CA1 pyramidal neuron (Narayanan and Johnston 2007). There, it was demonstrated that adjacent compartments along the apical trunk maximally respond to higher frequencies in an orderly progression, forming a topographic map of resonance frequencies within a CA1 pyramidal neuron (Narayanan and Johnston 2007). Such a map, although much smaller in terms of scale, is similar to the tonotopic maps that exist within the auditory system, where adjacent neurons are progressively tuned to higher frequencies of audible tones (Graziano and Aflalo 2007; Schreiner and Winer 2007).

A growing body of experimental evidence has revealed the existence of numerous functional maps within a neuron, with respect to local (Fig. 1*B*) as well as propagating properties (Fig. 1*C*). Prominent examples of these include those of the amplitude of backpropagating action potentials (bAPs) (Hoffman et al. 1997; Spruston et al. 1995), excitatory postsynaptic potential (EPSP) amplitude (Magee and Cook 2000), input resistance (Magee 1998; Narayanan and Johnston 2007), resonance frequency (Hu et al. 2009; Narayanan and Johnston 2007), and intrinsic phase response (Narayanan and Johnston 2008). It should be noted that different neurons exhibit different map structures for the same parameters, and the set of maps that exist within a neuron also depends on the neuronal subtypes. Numerous recent reviews provide excellent overviews of these functional maps from multiple perspectives (Lai and Jan 2006; Migliore and Shepherd 2002, 2005; Nusser 2011; Sjostrom and Hausser 2006; Spruston 2008).

What mediates these maps? By our definition (above) of functional maps, we suggest that these maps are maintained by active mechanisms; passive attenuation of voltage signals as a function of distance (Rall 1977) would thus not be called a map. These functional maps are largely maintained by gradients in densities of one or various ion channels within the topology of the neuron. Whereas gradients in K^+ channels contribute to a map of bAP amplitude (Hoffman et al. 1997; Spruston 2008), gradient in the h channel contributes to the maps of resonance frequency (Narayanan and Johnston 2007) and phase response (Narayanan and Johnston 2008). However, it should be noted that passive properties and morphology of the neuron could play a significant role in the existence of such maps (Narayanan and Johnston 2007, 2008; Vetter et al. 2001; Williams and Stuart 2003).

Physiological Roles of the Intraneuronal Functional Maps

Why should these physiological measurements be organized systematically within a single neuron? What roles do these maps play? In general, different maps are known to play different functions. The map of increasing local EPSP amplitudes in CA1 pyramidal cells, for instance, appears to reflect and compensate for the passive filtering properties of the dendritic cable. Specifically, the density of AMPA receptors as a function of distance from soma seems to be organized such that the somatic EPSP amplitude remains relatively independent of the dendritic location of individual synapses (Magee and Cook 2000). The gradient in A-type K^+ channel and the consequent bAP map play distinct roles in modulating synaptic plasticity (Chen et al. 2006; Sjostrom et al. 2008). The functional gradient in h channels (Magee 1998), while contributing to the map in resonance frequency (Narayanan and Johnston 2007) and the phase-response map (Narayanan and Johnston 2008), also contributes to a distance-independent normalization of temporal integration in CA1 pyramidal neurons (Magee 1999). Furthermore, morphologically induced impedance gradients coupled with the expression of NMDA receptors, a major active component in dendritic physiology (Larkum et al. 2009; Schiller and Schiller 2001), have been demonstrated to enable neurons to respond specifically to certain spatiotemporal patterns of dendritic activation (Branco et al. 2010; Branco

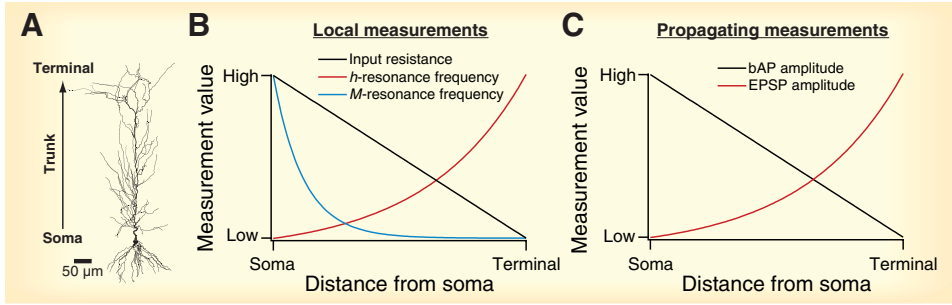

Fig. 1. Pyramidal neurons express numerous functional maps along the somato-apical trunk. *A*: typical CA1 pyramidal neuronal morphology (http://www.neuromorpho.org) (Ascoli et al. 2007), depicting the somato apical trunk. Various physiologically relevant measurements vary along the trunk, forming functional maps on local (*B*) as well as propagating (*C*) measurements. bAPs, backpropagating action potential; EPSP, excitatory postsynaptic potential.

and Hausser 2011). Thus, in general, various functional maps within a neuron are critically reflective of various aspects of intraneuronal filtering and/or activity patterns of the network.

Plasticity of Intraneuronal Functional Maps

The intraneuronal functional maps are not static entities; they are highly dynamic and can undergo either local or global plasticity. All the major well-characterized map systems mentioned above have been demonstrated to undergo either local or global modulations, depending on the kind of activity patterns. The oldest and most well-established system of plasticity is that associated with EPSP amplitude. Bidirectional regulation of EPSP amplitude has traveled a long distance since the initial demonstration of long-term potentiation (LTP) by Bliss and Lomo (1973). The biochemical signaling mechanisms involved (Lisman et al. 2002; Thomas and Huganir 2004), the bidirectional trafficking and phosphorylation of AMPA receptor (Shepherd and Huganir 2007), the relevance of synaptic plasticity to various learning tasks (Martin et al. 2000; Neves et al. 2008), and several theoretical aspects of synaptic plasticity (Haykin 1998; Kotaleski and Blackwell 2010) have been thoroughly studied. Although homosynaptic LTP and long-term depression (LTD) are pathway specific, rendering the plasticity in the EPSP amplitude map to be local, various mechanisms have been reported where plasticity in this map could be global. Prominent among these is what has been called synaptic scaling (Turrigiano 2011), where excitatory synapses in a neuron are globally up or downregulated. Synaptic scaling has been demonstrated under both physiological and pathological conditions (Chang et al. 2006; Turrigiano 2011), thus suggesting that the EPSP amplitude map can undergo both local and global plasticity.

The map of bAPs has been shown to undergo both local (Frick et al. 2004; Losonczy et al. 2008) and global plasticity (Bernard et al. 2004; Shah et al. 2010). The map of bAP amplitude has been demonstrated to undergo localized plasticity around the synapses that are subjected to LTP, where the amplitude of the bAP changes only around a region of these potentiated synapses and remains unchanged at other places (Frick et al. 2004). Furthermore, under a pathological condition, the bAP map has been demonstrated to undergo spatially widespread changes, with widespread channelopathy reported as the underlying mechanism (Bernard et al. 2004). The h channels, which mediate the resonance frequency map, have also been demonstrated to undergo either local (Campanac et al. 2008; Narayanan et al. 2010; Wang et al. 2003) or spatially widespread plasticity (Brager and Johnston 2007; Chen et al. 2002; Kole et al. 2007; Narayanan and Johnston 2007; Shah et al. 2004). Whereas some of these reported studies have shown changes in h channels to accompany synaptic plasticity, others correspond to a pathological downregulation of the h channels (Shah et al. 2010). Thus the well-characterized maps within a hippocampal neuron can undergo either local or spatially widespread plasticity under physiological or pathological conditions.

Plasticity in these maps not only alter the way the neuron would process information but also change the way the neuron encodes future information and the way these maps themselves would be plastic in future. This is because the ion channels that mediate these maps have been shown to affect the rules of synaptic plasticity; in other words, they mediate metaplasticity (Chen et al. 2006; Frick and Johnston 2005; Sjostrom et al. 2008). Furthermore, because synaptic and intrinsic plasticity mechanisms can be induced by similar plasticity induction protocols (Lujan et al. 2009; Shah et al. 2010; Sjostrom et al. 2008), such metaplasticity would affect intrinsic plasticity mechanisms as well, thus altering various intraneuronal maps, either locally or globally, in an intricately coupled manner.

Several common themes emerge by comparing plasticity in these intraneuronal maps to plasticity in sensory maps. For instance, studies involving the effects of dark rearing on various visual maps could be metaphorically related to the studies involving activity blockade to a neuronal map. In both cases, the maps respond to changes in the environment by changing their own characteristics. Similar to the case where multiple maps in the visual system respond differently to the same environmental deprivation (Chalupa and Rhoades 1978; Fregnac and Imbert 1978; Wiesel and Hubel 1963), different maps within the neuron could be responding differently to the same environmental deprivation. It would certainly be of interest to catalog the effect of inactivity on all maps that exist within a single neuron and also to study the responses of these maps with respect to specific changes in that environment. In this context, selective alteration to the environment (rather than complete inactivity/deprivation), a standard set of techniques in sensory map physiology (Chalupa and Rhoades 1978; de Villers-Sidani et al. 2007; Hirsch and Spinelli 1970; Wiesel and Hubel 1963), could be employed in understanding the interactions between these maps and the environment (the network) they reside in. Studies involving blockade of activity along one pathway (Shin and Chetkovich 2007), studies involving locally increasing or decreasing activity to one set of synapses (all LTP and LTD experiments could be considered to belong to this category), studies of the response of these maps to various activity patterns, or possible studies involving an artificial increase of specific inputs frequencies fed to a neuron would all belong to this broad category of selective alteration to the environment. Similar to the sensory maps, it is known that some of such microenvironmental alterations do change the structure of intraneuronal maps (Frick and Johnston 2005; Shah et al. 2010; Shin and Chetkovich 2007; Turrigiano 2011), but a more systematic approach involving each of these maps, with various alterations to the environment, with the alterations guided by the functions of the various maps, would provide novel insights into single-neuron function and memory encoding.

Neuromodulators and Intraneuronal Functional Maps

An aspect of neuronal map representations that is closely related to plasticity is their modulation through neuromodulators. Neuromodulation has been demonstrated to play a crucial role in remodeling cortical maps of sensory information, with reference to the behavioral significance of stimuli (Bao et al. 2001; Bear and Singer 1986; Froemke et al. 2007; Kilgard and Merzenich 1998). The basis for functional maps within single neurons are ion channel gradients, and the modulation of ion channel properties by neuromodulators is well established (Marder and Thirumalai 2002). Thus neuromodulation should be expected to alter or remodel functional maps within single neurons. The modulation of intracellular maps through neuro-

modulators would be dependent on various parameters that include intraneuronal gradients in receptor subtypes for specific neuromodulators, the properties of channel subtypes, and the associated signaling mechanism present across various compartments along the neuron, the volume of neuromodulatory projections onto various subregions of the neuron, and the state of the neuron during the arrival of neuromodulatory inputs. For instance, different neuromodulatory substances have been demonstrated to modulate dendritic action potentials along different directions through various pathways (Hoffman and Johnston 1999; Sjostrom et al. 2008), and the effect of dopamine on h channels in entorhinal cortical pyramidal neurons is dependent on the state of the neuron and dopamine receptor subtype (Rosenkranz and Johnston 2007). Systematic analyses of the impact of different neuromodulators on maps that span the same neuronal topograph could provide insights into the state-dependent processing machinery that is dependent on these maps and their interactions.

Coexistence of and Interaction Among Intraneuronal Functional Maps

Although individual maps seem to reflect different aspects of neuronal information processing and perform distinct functions, they are colocalized in the same neuron and process information as a cohesive unit. Furthermore, the different maps within a single neuron interact with each other functionally and in terms of the signaling mechanisms underlying them. Functionally, the map of bAPs is known to interact with the map of EPSPs in multiple ways in terms of accompanying and regulating synaptic plasticity (Chen et al. 2006; Frick et al. 2004; Sjostrom et al. 2008). Similarly, the interactions between and cross-regulations of A-type K^+ current and the h current, which are known to regulate the bAP and the resonance frequency maps, respectively, have also been established both experimentally (MacLean et al. 2003) and theoretically (Burdakov 2005). Furthermore, the h channel has also been shown to modulate bAP amplitude by altering somatodendritic coupling (Kole et al. 2007). Finally, the h channel contributes to EPSP amplitudes (Magee 1998; Stuart and Spruston 1998), is modulated by synaptic plasticity mechanisms that affect EPSP amplitudes (Brager and Johnston 2007; Fan et al. 2005), and has been suggested to be involved in metaplasticity and thus in the regulation of the EPSP map (Brager and Johnston 2007; Fan et al. 2005; Narayanan and Johnston 2007).

Although the biochemical signaling mechanisms that are responsible for the origins and sustenance of these maps remain largely unknown, it is clear that many maps could be downstream to the same biochemical pathway. For instance, activation of the MAPK pathway leads to changes in the maps of EPSP and the bAP amplitudes (Thomas and Huganir 2004; Yuan et al. 2002), and activation of the CaMKII pathway leads to changes in the maps of EPSP amplitude and the resonance frequency (Fan et al. 2005; Lisman et al. 2002; Narayanan and Johnston 2007). Thus the map systems are not only cross-regulating each other but also are coregulated by underlying biochemical signaling mechanisms.

What are the functional consequences of colocalization of and interactions among the various maps within a single neuron? Recent studies have demonstrated that a target network activity or a target neuronal activity can be achieved through a variety of combinations of conductances (Marder and Goaillard 2006). If that is the case, what constrains specific neuronal classes to exhibit specific intracellular map structures? Why cannot another set of map structures replicate the same target behavior of the cell? Is it the map structure that guides the activity levels of the network, or vice versa, or does the modulation exist on both ways? Although the answers to these questions are certainly unknown and are worth rigorous exploration, three broad hypotheses come about as possible answers.

Efficient Coding and Intraneuronal Functional Maps

The first could be considered as an extension of what is known as the efficient coding hypothesis, which states that a group of neurons should encode information as compactly as possible, to utilize the available resources most effectively. Extending this to a cellular neurophysiology perspective, we may simply state that a single neuron should encode information as compactly as possible, to utilize the available resources most effectively. Under such a governing principle, single-neuron information processing would be heavily constrained by coding efficiency and hence would depend on the statistics of the environmental (the network surrounding it) activity, because the efficiency of the neural code depends both on the transformation that maps the input to the neural responses and on the statistics of the input (Simoncelli and Olshausen 2001). Specifically, guided by the sensory literature and extending the principles outlined there to the microenvironment of a single neuron, we postulate that the development and maintenance of the intraneuronal maps could be driven by three fundamental components (Simoncelli and Olshausen 2001): *1*) the integration and action potential generation tasks that the single neuron must perform, *2*) the arborization of the axons and the dendrites, the constellation of ion channels, their properties, gradients, and plasticity, all of which guide the computational capabilities and limitations of neurons, and *3*) the network in which the neuron resides in (Fig. 2). Although single-neuron information processing has focused on the first two aspects, the microenvironment of a single neuron and its role in neuronal adaptability has been largely ignored (Stemmler and Koch 1999). This is especially important because input signals that one set of neurons receive could be completely different from another, and it is possible that neurons adapt themselves to process their respective signals in an efficient manner. Thus the formation of such intraneuronal maps and their adaptability could be contingent on the statistics of inputs that each region of its dendritic arbor receives. Because these statistics could change in response to learning- or pathology-induced activity patterns, the functional maps within a neuron adapt their response statistics to these altered network statistics (Narayanan and Johnston 2007). Along the lines of the role of natural scene statistics in arriving at receptive field properties of single neurons (Simoncelli 2003; Simoncelli and Olshausen 2001), we postulate that natural network statistics sculpt the functional maps within a single neuron and play crucial roles in efficient encoding of various inputs signals.

Optimal Wiring and Intraneuronal Functional Maps

A second possibility arises from linking the coexistence of these map structures to optimality in wiring diagrams of neuronal

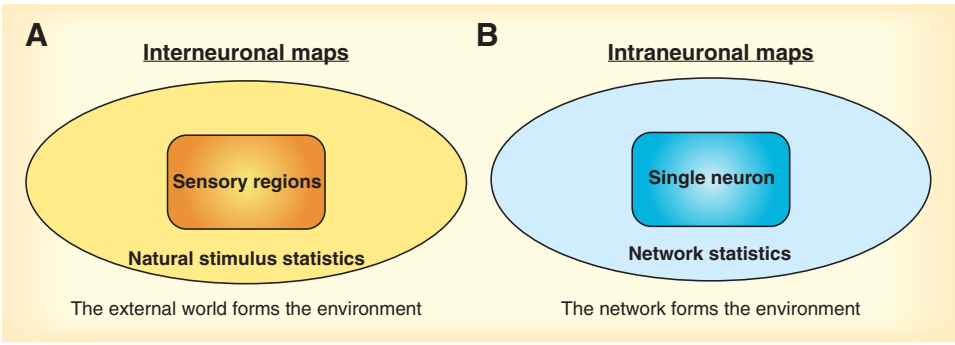

Fig. 2. Efficient coding hypothesis from a cellular neurophysiology perspective. *A*: from a systems neuroscience perspective, neurons in sensory areas efficiently encode natural stimulus statistics corresponding to sensory information in the external world. *B*: from a cellular neurophysiology perspective, compartments within neurons in different brain regions encode network statistics that are naturally impinging on them, with the network forming the microenvironment where this neuron resides.

networks within and across brain regions, similar to what has been postulated with interneuronal maps (Chklovskii and Koulakov 2004). A standard paradigm that has driven neuroscience research over the years has been that structure and function are closely related (see Buzsaki 2006 for a historical treatise of this paradigm). Consistent with this, it has been argued that cortical maps form a solution for an evolutionary pressure to place connected neurons as close to each other as possible, and thus contribute to wiring optimization (Chklovskii and Koulakov 2004). Taking a cue from this suggestion, we postulate that the coexistence of functional maps within a single neuron also could contribute to the wiring within and across brain regions. To elaborate, assume that a single neuron receives inputs from various brain regions at different dendritic locations, and the signal statistics of these inputs demand certain localized neuronal response properties for efficient encoding. Aligning functional gradients within a neuron then may be an easier way to achieve matched functional characteristics than to undergo complex and energy-consuming rewiring of the circuitry. As an example, let us consider the CA1 pyramidal neuron, which receives inputs from the CA3 and the entorhinal cortex at proximal and distal dendritic segments, respectively. Given the anatomical organization and axonal pathways, this arrangement fits well for innervations of the entorhinal cortical inputs to various units of the hippocampal formation. Under this constraint of wiring, it may be easier to provide intracellular functional gradients than to reorganize wiring so that the entorhinal inputs are received at proximal dendrites. On the other hand, if the presence of these maps were to regulate the manner in which connections to the neuron are organized, the connections would have to be present in a certain order for achieving efficiency in encoding. Thus it could be efficiency in encoding that drives wiring to the neuron, or optimality in wiring could be driving these functional gradients, which in turn could contribute to efficient encoding. Such concerted synergy between wiring and these intraneuronal maps would also suggest that plasticity in one should affect plasticity in the other. Specifically, any changes in the wiring would change the activity patterns and hence induce plasticity in these maps, whereas any change in these maps may lead to retraction or addition of synapses, thus changing the wiring diagrams. An example for the former is the finding that an intact entorhinal cortex, which projects to distal dendrites of CA1 pyramidal cells, is critical for the establishment and maintenance of distal dendritic enrichment of h channels (Shin and Chetkovich 2007). Any instance of long-term synaptic potentiation/depression is an example for the latter, with either retraction or formation of new synapses and spines. This postulated synergy between wiring diagrams and intraneuronal maps is thus a rich avenue for further exploration, with focus on the roles of these maps in determining network and circuit level properties including energy-efficient wiring, oscillatory synchrony, and information storage (Buzsaki 2006; Chklovskii and Koulakov 2004; Chklovskii et al. 2004; Laughlin and Sejnowski 2003).

Parametric Variability, Homeostasis, and Intraneuronal Functional Maps

The final of the three hypotheses on what specific constraints could lead to specific interactions between functional maps arises from the examination of plasticity in these maps. We had earlier noted that these intraneuronal maps are plastic in response to activity and to neuromodulators. If these maps are so dynamic, what maintains stable neuronal function in the face of such variability and plasticity? How do the maps remain largely intact across neurons, and how do neurons maintain characteristic electrophysiological signatures? Although these questions have not been asked specifically in the context of maps, a large number of studies have concentrated on homeostasis in neurons and networks. It could be argued that the maps, their coexistence and coregulation, are all essential components in maintaining a neuron's characteristic electrophysiological signature and activity levels. Thus it could be postulated that these coexisting maps are a solution to a homeostasis problem across the network where there is a heavy interdependence of these functional attributes on each other so that the neuron can maintain its characteristic electrophysiological signature. Under such a framework, changes in one map structure would affect the structures of other maps, effectively using the coexistence of the map structures to maintain the requisite activity levels in the face of a changing environment (Marder and Goaillard 2006; Turrigiano 2011). Future studies could concentrate on elucidating links between network statistics and the nature of specific maps, their links to efficient coding and wiring diagrams, and their relationships to homeostasis in the neuron. Finally, significant functional insights could be garnered from systematic investigations on the biochemical signaling mechanisms underlying the origins and the sustenance of these various maps. More importantly, a catalog of how various maps are related to the same upstream pathways could provide important insights into the necessity for the coexistence of these maps (Kotaleski and Blackwell 2010; Lai and Jan 2006).

Development of Intraneuronal Functional Maps

The developmental origins of sensory maps and the influence of genetics and environment on their early development form central themes in the interneuronal map literature and have contributed heavily to our understanding of neural plasticity at the molecular, cellular, and systems levels in the context of the external environment (Chalupa and Rhoades 1978; de Villers-Sidani et al. 2007; Fregnac and Imbert 1978; Hirsch and Spinelli 1970; Petersen 2007; Wiesel and Hubel 1963). What mediates the developmental formation of the intraneuronal maps? What are the relative genetic and environmental (network activity) influences on the development of these intraneuronal maps? Is there an early developmental period, a critical period, during which these maps are more plastic? Answers to these questions lie in understanding the developmental profile of the ion channel gradients that underlie these maps (Bender and Baram 2008; Marcelin et al. 2012; Spigelman et al. 1992; Turrigiano 2011; Tyzio et al. 1999), apart from the molecular mechanisms that mediate dendritic morphogenesis (Gao 2007; Jan and Jan 2010). In this context, developmental changes in neurons, their circuitry and activity patterns (Lahtinen et al. 2002; Mohns and Blumberg 2008), could be employed as a means for experimental verification of our postulate that the intraneuronal functional maps are reflections of afferent network statistics.

Computational Considerations

Computational models have been widely used in analyzing and understanding the development and physiological properties of interneuronal sensory maps (Douglas and Martin 2007; Goodhill 2007). With reference intraneuronal functional maps, although the physiological roles of dendritic ion channel expression gradients have been explored using computational techniques (Angelo et al. 2007; Migliore et al. 1999; Migliore and Shepherd 2002, 2005; Narayanan and Johnston 2007, 2008), they have been limited to questions on information integration within these neurons. Models that explore the physiological roles of the these maps, their interactions with each other and plasticity to broader questions involving learning theory, information encoding, and to network wiring, are rare (Poirazi and Mel 2001; Stemmler and Koch 1999; Wu and Mel 2009). Although plasticity in intrinsic excitability and intrinsic dynamics of a neuron are now acknowledged as putative cellular correlates of learning and memory, and the role of these intraneuronal maps in regulating intrinsic excitability and dynamics are well established (Kim and Linden 2007; Mozzachiodi and Byrne 2010; Shah et al. 2010), systematic theories relating the two have not emerged.

Finally, the principle of self-organization where local computations lead to the emergence of global order in map formation, through interactions between adjacent computational elements, has been very useful in understanding neuronal computations and their interactions in sensory maps (Goodhill 2007; Kohonen and Hari 1999; Swindale 1996). With reference to intraneuronal maps, we postulate that similar self-organizing schemes would play a critical role, with the difference that the global order in terms of the emergence of these functional maps would be consequent to local computations in dendritic compartments, enabled through interactions between ion channels present in these compartments. In this context, it was recently demonstrated that voltage-gated ion channels (VGIC) or receptors have influences on physiological measurements of adjacent compartments, in a distance- and measurement-dependent manner (Gidon and Segev 2012; Rathour and Narayanan 2012). Such non-local influences of VGICs could form the intraneuronal counterparts to the Mexican-hat interactions across neurons (Fig. 3) that play a critical role in translating local computations to global order in the interneuronal sensory map literature (Goodhill 2007; Swindale 1996). The spatial spread of the influence of a VGIC or a receptor on several physiological measurements lays the foundation for understanding the emergence of intraneuronal maps through cooperation and competition between different ion channels and receptors. It should be noted that the cooperations arise between similar types of channels/receptors (restorative or regenerative channels; inhibitory or excitatory receptors), whereas competitions are across opposing types of channels/receptors (Rathour and Narayanan 2012). The emergence of computational theories relating to the formation and the function of intraneuronal map systems would provide a strong basis for understanding ion channel gradients and their roles in network connectivity and information encoding.

Beyond

In this review, we have largely dealt with maps of electrically measurable functional parameters. However, there could be other maps within the neuron in terms of, say, calcium signaling or any other biochemical signaling mechanisms. Any

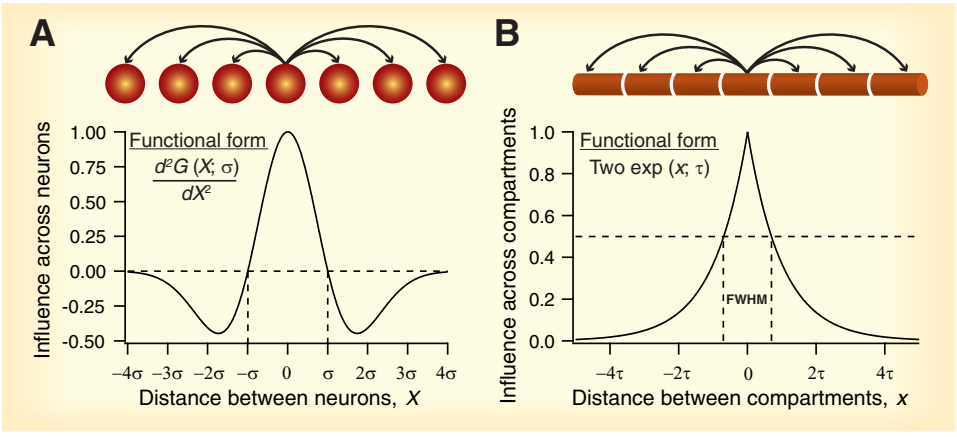

Fig. 3. Non-local influences foster global order from local computations. *A*: Mexican-hat interactions between adjacent neurons have been postulated to bestow self-organization capabilities on interneuronal sensory maps. *B*: voltage-gated ion channels influence physiological measurements at adjacent compartments and could bestow self-organization capabilities on intraneuronal sensory maps. $G(X; \sigma)$ represents a Gaussian function of variable X, with standard deviation σ.

orderly progression of signaling mechanisms within a neuron would also constitute a map by our initial definition of a functional map. It is quite possible that the maps that we have described here have their basis in some biochemical signaling map within the neuron, in terms of expression profiles of, say, different kinases and phosphatases. For instance, the mammalian target of rapamycin (mTOR), a serine/threonine kinase that controls protein synthesis, plays a critical role in certain forms of synaptic plasticity and in regulating local translation of ion channels (Kelleher et al. 2004; Raab-Graham et al. 2006). Similarly, there are numerous examples of enzymes that are critically involved in synaptic plasticity also playing a very important role in regulating dendritic VGICs (Lujan et al. 2009; Shah et al. 2010; Sjostrom et al. 2008), thus suggestive of potential coregulation of several maps by underlying biochemical signaling gradients.

Although we have focused on mechanisms that mediate intraneuronal maps, mechanisms that modulate these maps also are critical in defining the specific configuration of these maps. For instance, inhibitory synapses and their plasticity can critically regulate the EPSP and the input resistance maps, dependent on the spatial location of the inhibitory synapse (Gidon and Segev 2012; Jadi et al. 2012; Lovett-Barron et al. 2012; Mody 2005). Thus future investigations should thus focus not just on the molecular mechanisms that mediate intraneuronal maps but also on those that modulate them. Finally, because the literature has been largely focusing on the apical dendritic shaft, most of the maps we have described fall on the somatoapical trunk of neurons. Since recent technical advances have allowed access to thin structures like the basal and the apical tuft dendrites (Larkum et al. 2009; Losonczy et al. 2008; Nevian et al. 2007), it would be worthwhile to look into the thinner oblique dendrites to understand whether there is a map structure in terms of distance from the apical trunk. This is important because most of the excitatory synaptic connections fall onto the obliques, and the response properties of these thin branches are very important in understanding the neuronal responses to the synaptic inputs that impinge there.

Conclusions

In this review, we argue that a variety of functional maps exist within a single neuron, with each serving a basic function that is potentially reflective of intraneuronal filtering or the statistics of activity in the network that the neurons reside, or a combination of both. Relating the existence and plasticity of these maps to sensory maps in various regions of the brain, we postulate that the coexistence and coregulation of these maps could possibly play roles in efficient encoding, optimal wiring, and homeostasis within the neuron or their networks. Under this postulate, we hypothesize that different brain regions are endowed with neurons with specific morphology and specific ion channel gradients so that they could efficiently encode the statistics of network activity impinging on these neurons at different dendritic locations. We believe that the metaphorical link between intraneuronal and sensory maps provides a fresh conceptual framework for analyzing and understanding single-neuron information processing. Future experiments could be geared toward harnessing this link to the mature literature on sensory maps and could assess the role of dendritic ion channels in efficiently encoding inputs driven by afferent statistics under different physiological and pathophysiological conditions. These experiments could provide potential convergence of various lines of investigation including neural coding, dendritic information processing, sensory integration, homeostasis, wiring optimization, channelopathies, and network pathology.

Finally, returning to the question of whether dendritic ion channels and their gradients are critical to neural information processing, under our postulate on efficient coding, it is evident that the answer is dependent on the dendritic subregion under consideration. In the context of our postulate, dendritic ion channels have distinct hues and perform distinct functions depending on the statistics of the inputs that they receive at that specific dendritic location. Furthermore, because afferent statistics cover different behavioral states of the animal, and because different ion channel combinations could be coding for features that are part of different behavioral states, it is not necessary that all ion channels play a critical role in all behavioral states (Gasparini and Magee 2006). Under such a postulate, where dendritic ion channels perform state-dependent processing, it is possible to reconcile that dendritic nonlinearities and their importance to information processing tasks are critically dependent on the specific neuron, its afferent input statistics at specific dendritic locations, and the specific behavioral task under consideration. Thus a generalized conclusion on the roles of nonlinear dendritic elements on information processing across all neurons and all behavioral tasks might not be possible.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

R.N. prepared figures; R.N. drafted manuscript; R.N. and D.J. edited and revised manuscript; R.N. and D.J. approved final version of manuscript.

REFERENCES

Angelo K, London M, Christensen SR, Hausser M. Local and global effects of I_h distribution in dendrites of mammalian neurons. *J Neurosci* 27: 8643–8653, 2007.

Ascoli GA, Donohue DE, Halavi M. NeuroMorpho Org: a central resource for neuronal morphologies. *J Neurosci* 27: 9247–9251, 2007.

Bao S, Chan VT, Merzenich MM. Cortical remodelling induced by activity of ventral tegmental dopamine neurons. *Nature* 412: 79–83, 2001.

Bear MF, Singer W. Modulation of visual cortical plasticity by acetylcholine and noradrenaline. *Nature* 320: 172–176, 1986.

Bender RA, Baram TZ. Hyperpolarization activated cyclic-nucleotide gated (HCN) channels in developing neuronal networks. *Prog Neurobiol* 86: 129–140, 2008.

Bernard C, Anderson A, Becker A, Poolos NP, Beck H, Johnston D. Acquired dendritic channelopathy in temporal lobe epilepsy. *Science* 305: 532–535, 2004.

Bliss TV, Lomo T. Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. *J Physiol* 232: 331–356, 1973.

Brager DH, Johnston D. Plasticity of intrinsic excitability during long-term depression is mediated through mGluR-dependent changes in I_h in hippocampal CA1 pyramidal neurons. *J Neurosci* 27: 13926–13937, 2007.

Branco T, Clark BA, Hausser M. Dendritic discrimination of temporal input sequences in cortical neurons. *Science* 329: 1671–1675, 2010.

Branco T, Hausser M. Synaptic integration gradients in single cortical pyramidal cell dendrites. *Neuron* 69: 885–892, 2011.

Burdakov D. Gain control by concerted changes in I_A and I_H conductances. *Neural Comput* 17: 991–995, 2005.

Buzsaki G. *Rhythms of the Brain*. New York: Oxford University Press, 2006.

Buzsaki G, Anastassiou CA, Koch C. The origin of extracellular fields and currents—EEG, ECoG, LFP and spikes. *Nat Rev Neurosci* 13: 407–420, 2012.

Campanac E, Daoudal G, Ankri N, Debanne D. Downregulation of dendritic I_h in CA1 pyramidal neurons after LTP. *J Neurosci* 28: 8635–8643, 2008.

Chalupa LM, Rhoades RW. Directional selectivity in hamster superior colliculus is modified by strobe-rearing but not by dark-rearing. *Science* 199: 998–1001, 1978.

Chang EH, Savage MJ, Flood DG, Thomas JM, Levy RB, Mahadomrongkul V, Shirao T, Aoki C, Huerta PT. AMPA receptor downscaling at the onset of Alzheimer's disease pathology in double knockin mice. *Proc Natl Acad Sci USA* 103: 3410–3415, 2006.

Chen K, Aradi I, Santhakumar V, Soltesz I. H-channels in epilepsy: new targets for seizure control? *Trends Pharmacol Sci* 23: 552–557, 2002.

Chen X, Leischner U, Rochefort NL, Nelken I, Konnerth A. Functional mapping of single spines in cortical neurons in vivo. *Nature* 475: 501–505, 2011.

Chen X, Yuan LL, Zhao C, Birnbaum SG, Frick A, Jung WE, Schwarz TL, Sweatt JD, Johnston D. Deletion of Kv4.2 gene eliminates dendritic A-type K^+ current and enhances induction of long-term potentiation in hippocampal CA1 pyramidal neurons. *J Neurosci* 26: 12143–12151, 2006.

Chklovskii DB, Koulakov AA. Maps in the brain: what can we learn from them? *Annu Rev Neurosci* 27: 369–392, 2004.

Chklovskii DB, Mel BW, Svoboda K. Cortical rewiring and information storage. *Nature* 431: 782–788, 2004.

de Villers-Sidani E, Chang EF, Bao S, Merzenich MM. Critical period window for spectral tuning defined in the primary auditory cortex (A1) in the rat. *J Neurosci* 27: 180–189, 2007.

DeAngelis GC, Newsome WT. Organization of disparity-selective neurons in macaque area MT. *J Neurosci* 19: 1398–1415, 1999.

Douglas RJ, Martin KA. Mapping the matrix: the ways of neocortex. *Neuron* 56: 226–238, 2007.

Fan Y, Fricker D, Brager DH, Chen X, Lu HC, Chitwood RA, Johnston D. Activity-dependent decrease of excitability in rat hippocampal neurons through increases in I_h. *Nat Neurosci* 8: 1542–1551, 2005.

Fregnac Y, Imbert M. Early development of visual cortical cells in normal and dark-reared kittens: relationship between orientation selectivity and ocular dominance. *J Physiol* 278: 27–44, 1978.

Frick A, Johnston D. Plasticity of dendritic excitability. *J Neurobiol* 64: 100–115, 2005.

Frick A, Magee J, Johnston D. LTP is accompanied by an enhanced local excitability of pyramidal neuron dendrites. *Nat Neurosci* 7: 126–135, 2004.

Froemke RC, Merzenich MM, Schreiner CE. A synaptic memory trace for cortical receptive field plasticity. *Nature* 450: 425–429, 2007.

Gao FB. Molecular and cellular mechanisms of dendritic morphogenesis. *Curr Opin Neurobiol* 17: 525–532, 2007.

Gasparini S, Magee JC. State-dependent dendritic computation in hippocampal CA1 pyramidal neurons. *J Neurosci* 26: 2088–2100, 2006.

Gidon A, Segev I. Principles governing the operation of synaptic inhibition in dendrites. *Neuron* 75: 330–341, 2012.

Giocomo LM, Zilli EA, Fransen E, Hasselmo ME. Temporal frequency of subthreshold oscillations scales with entorhinal grid cell field spacing. *Science* 315: 1719–1722, 2007.

Goodhill GJ. Contributions of theoretical modeling to the understanding of neural map development. *Neuron* 56: 301–311, 2007.

Graziano MS, Aflalo TN. Mapping behavioral repertoire onto the cortex. *Neuron* 56: 239–251, 2007.

Haykin S. *Neural Networks: a Comprehensive Foundation*. Englewood Cliffs, NJ: Prentice Hall, 1998.

Hirsch HV, Spinelli DN. Visual experience modifies distribution of horizontally and vertically oriented receptive fields in cats. *Science* 168: 869–871, 1970.

Hoffman DA, Johnston D. Neuromodulation of dendritic action potentials. *J Neurophysiol* 81: 408–411, 1999.

Hoffman DA, Magee JC, Colbert CM, Johnston D. K^+ channel regulation of signal propagation in dendrites of hippocampal pyramidal neurons. *Nature* 387: 869–875, 1997.

Hu H, Vervaeke K, Graham LJ, Storm JF. Complementary theta resonance filtering by two spatially segregated mechanisms in CA1 hippocampal pyramidal neurons. *J Neurosci* 29: 14472–14483, 2009.

Jadi M, Polsky A, Schiller J, Mel BW. Location-dependent effects of inhibition on local spiking in pyramidal neuron dendrites. *PLoS Comput Biol* 8: e1002550, 2012.

Jan YN, Jan LY. Branching out: mechanisms of dendritic arborization. *Nat Rev Neurosci* 11: 316–328, 2010.

Jia H, Rochefort NL, Chen X, Konnerth A. Dendritic organization of sensory input to cortical neurons in vivo. *Nature* 464: 1307–1312, 2010.

Kelleher RJ, 3rd Govindarajan A, Tonegawa S. Translational regulatory mechanisms in persistent forms of synaptic plasticity. *Neuron* 44: 59–73, 2004.

Kilgard MP, Merzenich MM. Cortical map reorganization enabled by nucleus basalis activity. *Science* 279: 1714–1718, 1998.

Kim SJ, Linden DJ. Ubiquitous plasticity and memory storage. *Neuron* 56: 582–592, 2007.

Kitamura K, Hausser M. Dendritic calcium signaling triggered by spontaneous and sensory-evoked climbing fiber input to cerebellar Purkinje cells in vivo. *J Neurosci* 31: 10847–10858, 2011.

Kohonen T, Hari R. Where the abstract feature maps of the brain might come from. *Trends Neurosci* 22: 135–139, 1999.

Kole MH, Brauer AU, Stuart GJ. Inherited cortical HCN1 channel loss amplifies dendritic calcium electrogenesis and burst firing in a rat absence epilepsy model. *J Physiol* 578: 507–525, 2007.

Kotaleski JH, Blackwell KT. Modelling the molecular mechanisms of synaptic plasticity using systems biology approaches. *Nat Rev Neurosci* 11: 239–251, 2010.

Lahtinen H, Palva JM, Sumanen S, Voipio J, Kaila K, Taira T. Postnatal development of rat hippocampal gamma rhythm in vivo. *J Neurophysiol* 88: 1469–1474, 2002.

Lai HC, Jan LY. The distribution and targeting of neuronal voltage-gated ion channels. *Nat Rev Neurosci* 7: 548–562, 2006.

Larkum ME, Nevian T, Sandler M, Polsky A, Schiller J. Synaptic integration in tuft dendrites of layer 5 pyramidal neurons: a new unifying principle. *Science* 325: 756–760, 2009.

Laughlin SB, Sejnowski TJ. Communication in neuronal networks. *Science* 301: 1870–1874, 2003.

Lisman J, Schulman H, Cline H. The molecular basis of CaMKII function in synaptic and behavioural memory. *Nat Rev Neurosci* 3: 175–190, 2002.

Losonczy A, Magee JC. Integrative properties of radial oblique dendrites in hippocampal CA1 pyramidal neurons. *Neuron* 50: 291–307, 2006.

Losonczy A, Makara JK, Magee JC. Compartmentalized dendritic plasticity and input feature storage in neurons. *Nature* 452: 436–441, 2008.

Lovett-Barron M, Turi GF, Kaifosh P, Lee PH, Bolze F, Sun XH, Nicoud JF, Zemelman BV, Sternson SM, Losonczy A. Regulation of neuronal input transformations by tunable dendritic inhibition. *Nat Neurosci* 15: 423–430, S421–S423, 2012.

Lujan R, Maylie J, Adelman JP. New sites of action for GIRK and SK channels. *Nat Rev Neurosci* 10: 475–480, 2009.

Luo L, Flanagan JG. Development of continuous and discrete neural maps. *Neuron* 56: 284–300, 2007.

MacLean JN, Zhang Y, Johnson BR, Harris-Warrick RM. Activity-independent homeostasis in rhythmically active neurons. *Neuron* 37: 109–120, 2003.

Magee JC. Dendritic hyperpolarization-activated currents modify the integrative properties of hippocampal CA1 pyramidal neurons. *J Neurosci* 18: 7613–7624, 1998.

Magee JC. Dendritic I_h normalizes temporal summation in hippocampal CA1 neurons. *Nat Neurosci* 2: 508–514, 1999.

Magee JC, Cook EP. Somatic EPSP amplitude is independent of synapse location in hippocampal pyramidal neurons. *Nat Neurosci* 3: 895–903, 2000.

Marcelin B, Liu Z, Chen Y, Lewis AS, Becker A, McClelland S, Chetkovich DM, Migliore M, Baram TZ, Esclapez M, Bernard C. Dorsoventral differences in intrinsic properties in developing CA1 pyramidal cells. *J Neurosci* 32: 3736–3747, 2012.

Marder E, Goaillard JM. Variability, compensation and homeostasis in neuron and network function. *Nat Rev Neurosci* 7: 563–574, 2006.

Marder E, Thirumalai V. Cellular, synaptic and network effects of neuromodulation. *Neural Netw* 15: 479–493, 2002.

Martin SJ, Grimwood PD, Morris RG. Synaptic plasticity and memory: an evaluation of the hypothesis. *Annu Rev Neurosci* 23: 649–711, 2000.

Migliore M, Hoffman DA, Magee JC, Johnston D. Role of an A-type K^+ conductance in the back-propagation of action potentials in the dendrites of hippocampal pyramidal neurons. *J Comput Neurosci* 7: 5–15, 1999.

Migliore M, Shepherd GM. Emerging rules for the distributions of active dendritic conductances. *Nat Rev Neurosci* 3: 362–370, 2002.

Migliore M, Shepherd GM. Opinion: an integrated approach to classifying neuronal phenotypes. *Nat Rev Neurosci* 6: 810–818, 2005.

Mody I. Aspects of the homeostatic plasticity of $GABA_A$ receptor-mediated inhibition. *J Physiol* 562: 37–46, 2005.

Mohns EJ, Blumberg MS. Synchronous bursts of neuronal activity in the developing hippocampus: modulation by active sleep and association with emerging gamma and theta rhythms. *J Neurosci* 28: 10134–10144, 2008.

Moser EI, Kropff E, Moser MB. Place cells, grid cells, and the brain's spatial representation system. *Annu Rev Neurosci* 31: 69–89, 2008.

Mozzachiodi R, Byrne JH. More than synaptic plasticity: role of nonsynaptic plasticity in learning and memory. *Trends Neurosci* 33: 17–26, 2010.

Narayanan R, Dougherty KJ, Johnston D. Calcium store depletion induces persistent perisomatic increases in the functional density of h channels in hippocampal pyramidal neurons. *Neuron* 68: 921–935, 2010.

Narayanan R, Johnston D. Long-term potentiation in rat hippocampal neurons is accompanied by spatially widespread changes in intrinsic oscillatory dynamics and excitability. *Neuron* 56: 1061–1075, 2007.

Narayanan R, Johnston D. The h channel mediates location dependence and plasticity of intrinsic phase response in rat hippocampal neurons. *J Neurosci* 28: 5846–5860, 2008.

Neves G, Cooke SF, Bliss TV. Synaptic plasticity, memory and the hippocampus: a neural network approach to causality. *Nat Rev Neurosci* 9: 65–75, 2008.

Nevian T, Larkum ME, Polsky A, Schiller J. Properties of basal dendrites of layer 5 pyramidal neurons: a direct patch-clamp recording study. *Nat Neurosci* 10: 206–214, 2007.

Nusser Z. Differential subcellular distribution of ion channels and the diversity of neuronal function. *Curr Opin Neurobiol* 2011.

Petersen CC. The functional organization of the barrel cortex. *Neuron* 56: 339–355, 2007.

Poirazi P, Mel BW. Impact of active dendrites and structural plasticity on the memory capacity of neural tissue. *Neuron* 29: 779–796, 2001.

Raab-Graham KF, Haddick PC, Jan YN, Jan LY. Activity- and mTOR-dependent suppression of Kv1.1 channel mRNA translation in dendrites. *Science* 314: 144–148, 2006.

Rall W. Core conductor theory and cable properties of neurons. In: *Handbook of Physiology. The Nervous System. Cellular Biology of Neurons*. Bethesda, MD: Am. Physiol. Soc, 1977, vol. I, part 1, p. 39–97.

Rathour RK, Narayanan R. Influence fields: a quantitative framework for representation and analysis of active dendrites. *J Neurophysiol* 107: 2313–2334, 2012.

Rosenkranz JA, Johnston D. State-dependent modulation of amygdala inputs by dopamine-induced enhancement of sodium currents in layer V entorhinal cortex. *J Neurosci* 27: 7054–7069, 2007.

Schiller J, Schiller Y. NMDA receptor-mediated dendritic spikes and coincident signal amplification. *Curr Opin Neurobiol* 11: 343–348, 2001.

Schreiner CE, Winer JA. Auditory cortex mapmaking: principles, projections, and plasticity. *Neuron* 56: 356–365, 2007.

Shadlen MN, Newsome WT. Is there a signal in the noise? *Curr Opin Neurobiol* 5: 248–250, 1995.

Shadlen MN, Newsome WT. The variable discharge of cortical neurons: implications for connectivity, computation, and information coding. *J Neurosci* 18: 3870–3896, 1998.

Shah MM, Anderson AE, Leung V, Lin X, Johnston D. Seizure-induced plasticity of H channels in entorhinal cortical layer III pyramidal neurons. *Neuron* 44: 495–508, 2004.

Shah MM, Hammond RS, Hoffman DA. Dendritic ion channel trafficking and plasticity. *Trends Neurosci* 33: 307–316, 2010.

Shepherd JD, Huganir RL. The cell biology of synaptic plasticity: AMPA receptor trafficking. *Annu Rev Cell Dev Biol* 23: 613–643, 2007.

Shin M, Chetkovich DM. Activity-dependent regulation of h channel distribution in hippocampal CA1 pyramidal neurons. *J Biol Chem* 282: 33168–33180, 2007.

Simoncelli EP. Vision and the statistics of the visual environment. *Curr Opin Neurobiol* 13: 144–149, 2003.

Simoncelli EP, Olshausen BA. Natural image statistics and neural representation. *Annu Rev Neurosci* 24: 1193–1216, 2001.

Sjostrom PJ, Hausser M. A cooperative switch determines the sign of synaptic plasticity in distal dendrites of neocortical pyramidal neurons. *Neuron* 51: 227–238, 2006.

Sjostrom PJ, Rancz EA, Roth A, Hausser M. Dendritic excitability and synaptic plasticity. *Physiol Rev* 88: 769–840, 2008.

Softky WR. Simple codes versus efficient codes. *Curr Opin Neurobiol* 5: 239–247, 1995.

Softky WR, Koch C. The highly irregular firing of cortical cells is inconsistent with temporal integration of random EPSPs. *J Neurosci* 13: 334–350, 1993.

Spigelman I, Zhang L, Carlen PL. Patch-clamp study of postnatal development of CA1 neurons in rat hippocampal slices: membrane excitability and K^+ currents. *J Neurophysiol* 68: 55–69, 1992.

Spruston N. Pyramidal neurons: dendritic structure and synaptic integration. *Nat Rev Neurosci* 9: 206–221, 2008.

Spruston N, Schiller Y, Stuart G, Sakmann B. Activity-dependent action potential invasion and calcium influx into hippocampal CA1 dendrites. *Science* 268: 297–300, 1995.

Stemmler M, Koch C. How voltage-dependent conductances can adapt to maximize the information encoded by neuronal firing rate. *Nat Neurosci* 2: 521–527, 1999.

Stuart G, Spruston N. Determinants of voltage attenuation in neocortical pyramidal neuron dendrites. *J Neurosci* 18: 3501–3510, 1998.

Stuart GJ, Sakmann B. Active propagation of somatic action potentials into neocortical pyramidal cell dendrites. *Nature* 367: 69–72, 1994.

Swindale NV. The development of topography in the visual cortex: a review of models. *Network* 7: 161–247, 1996.

Thomas GM, Huganir RL. MAPK cascade signalling and synaptic plasticity. *Nat Rev Neurosci* 5: 173–183, 2004.

Turrigiano G. Too many cooks? Intrinsic and synaptic homeostatic mechanisms in cortical circuit refinement. *Annu Rev Neurosci* 34: 89–103, 2011.

Tyzio R, Represa A, Jorquera I, Ben-Ari Y, Gozlan H, Aniksztejn L. The establishment of GABAergic and glutamatergic synapses on CA1 pyramidal neurons is sequential and correlates with the development of the apical dendrite. *J Neurosci* 19: 10372–10382, 1999.

Vetter P, Roth A, Hausser M. Propagation of action potentials in dendrites depends on dendritic morphology. *J Neurophysiol* 85: 926–937, 2001.

Wang Z, Xu NL, Wu CP, Duan S, Poo MM. Bidirectional changes in spatial dendritic integration accompanying long-term synaptic modifications. *Neuron* 37: 463–472, 2003.

White LE, Fitzpatrick D. Vision and cortical map development. *Neuron* 56: 327–338, 2007.

Wiesel TN, Hubel DH. Single-cell responses in striate cortex of kittens deprived of vision in one eye. *J Neurophysiol* 26: 1003–1017, 1963.

Williams SR, Stuart GJ. Role of dendritic synapse location in the control of action potential output. *Trends Neurosci* 26: 147–154, 2003.

Wu XE, Mel BW. Capacity-enhancing synaptic learning rules in a medial temporal lobe online learning model. *Neuron* 62: 31–41, 2009.

Xiao Y, Wang Y, Felleman DJ. A spatially organized representation of colour in macaque cortical area V2. *Nature* 421: 535–539, 2003.

Yuan LL, Adams JP, Swank M, Sweatt JD, Johnston D. Protein kinase modulation of dendritic K^+ channels in hippocampus involves a mitogen-activated protein kinase pathway. *J Neurosci* 22: 4860–4868, 2002.