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Opinion

Where Does EEG Come From and What Does It Mean?

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Electroencephalography (EEG) has been instrumental in making discoveries about cognition, brain function, and dysfunction. However, where do EEG signals come from and what do they mean? The purpose of this paper is to argue that we know shockingly little about the answer to this question, to highlight what we do know, how important the answers are, and how modern neuroscience technologies that allow us to measure and manipulate neural circuits with high spatiotemporal accuracy might finally bring us some answers. Neural oscillations are perhaps the best feature of EEG to use as anchors because oscillations are observed and are studied at multiple spatiotemporal scales of the brain, in multiple species, and are widely implicated in cognition and in neural computations.

Electroencephalography (EEG, see Glossary) and magnetoencephalography (MEG) are the most powerful techniques for noninvasively studying the electrophysiological dynamics of the brain, and linking those dynamics to cognition and disease. The term 'EEG' is used throughout this paper for convenience, but the discussion applies equally to MEG. EEG has many advantages, including high temporal precision and direct measurement of population-level neural activity in humans. Perhaps the main disadvantage is that EEG is limited to large, synchronous populations of neurons; small-scale and asynchronous activity is difficult or impossible to measure.

What Is the Answer to the Title Question?

When the question in the title of this paper is posed to colleagues, textbooks, or the Internet, the answers often involve some combination of a description of Maxwell's equations regarding volume conduction of electrical potentials and mathematical descriptions of anatomical localization algorithms [1,2]. The assumption behind this answer is that understanding the significance of EEG requires solving the ill-posed inverse problem: given an observed topographical distribution of voltage values, what were the active locations in the brain that produced that topography (Figure 1)?

Anatomical localization is reasonably accurate at the centimeter scale [3–7], and localization methods are widely and increasingly used in cognitive electrophysiology [8–10]. But does identifying an *XYZ* coordinate help us understand how the brain works? To some extent the answer is 'yes', and clearly some anatomical localization is important. But consider Figure 1B, where the EEG topography could be accounted for by a dipole in one of two locations. Would the researcher make fundamentally different claims about brain function based on these two possibilities? Most likely not. Certainly there are exceptions where precise localization is crucial – two examples are retinotopic mapping [11] and identifying the source of epileptogenic activity for surgery [12]. But the vast majority of conclusions drawn in the cognitive electrophysiology literature require localization only on the order of many centimeters. In other words, the mathematical, physical, and practical aspects of anatomical localization – while important to know – do not answer the title question.

Trends

EEG is one of the most important noninvasive brain imaging tools in neuroscience and in the clinic, but surprisingly little is known about how activity in neural circuits produces the various EEG features linked to cognition.

The 'standard model' of EEG states that simultaneous postsynaptic potentials of neural populations produces EEG, but this explains only the existence of EEG, not the meaning of the content of the EEG signal.

No 'grand unified theories' are presented, because there is unlikely to be a single 'neural correlate of EEG'. More experiments, analyses, and models that span multiple spatial scales are necessary.

Recent advances in neuroscience knowledge and technologies make this an ideal time for new discoveries about the origins and significances of EEG.

This research will benefit fundamental neuroscience, cognitive neuroscience, clinical diagnoses, and data analysis development.

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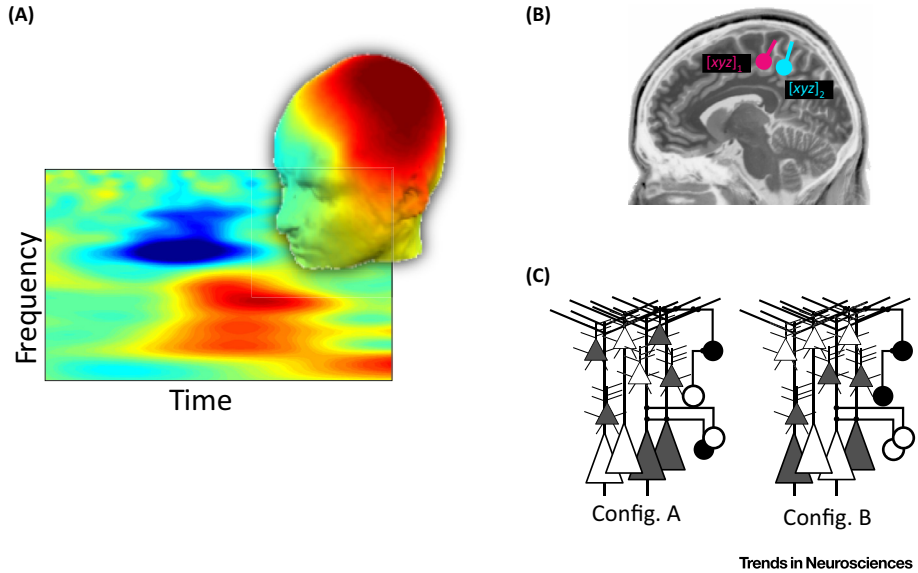


Figure 1. Many Features in Electroencephalography (EEG) Data Are Localized in Time, Frequency, and Space, As in Panel (A). Where do these features come from and what do they mean? Traditionally, this question is interpreted to indicate an *xyz* coordinate in the brain that could have produced a given topography (B). However, does one or the other solution shown here provide meaningful insights into how these EEG features arise from or are related to neural computations? Perhaps a more meaningful answer to the question 'what does EEG mean?' would come from determining the underlying microcircuit configurations (Config.) (C) that give rise to the features of the EEG landscape and that are consistently linked to cognitive processes. In other words, important advances in neuroscience will come from determining which functional/anatomical configurations in (C) could produce EEG features such as those illustrated in (A).

What then is the answer? Perhaps we should start with the right question. For EEG to be useful in understanding how the brain works, we need to know the functional and anatomical configurations of neural circuits that produce the large-scale voltage fluctuations that we measure as EEG. Therefore, the right question is: what are the **neural microcircuit** functional/anatomical configurations – the dynamics within and among different classes of cells, different layers within the cortex, and different columns across the cortical sheet – that produce the various spatial/spectral/temporal **EEG features** that have been linked to cognitive processes?

To be clear, the issue under consideration here is not the physical principles by which electromagnetic fields propagate from brain tissue to the scalp; this issue is solved to a reasonable degree of accuracy by forward models used by anatomical localization algorithms. Instead, the question is how one can interpret specific patterns in the EEG signal that are consistently linked to cognition, such as frequency band-limited power, phase perturbations (e.g., phase-reset or phase slips), phase- or power-based connectivity, cross-frequency coupling, and so on. Thus, it is the content of the EEG signal, not the existence of electromagnetic waves, that we know very little about. It is remarkable to think that EEG has been a dominant tool in studying healthy and diseased brain function, and for diagnosing medical conditions, for a century – and we still do not have answers to this fundamental question.

The Ultimate but Ultimately Unattainable Goal: One-to-One Mapping between EEG Feature and Microcircuit Configuration

EEG could be a much more powerful and insightful brain measurement tool if only we could identify one-to-one mappings between EEG feature and neural microcircuit configuration, as in Figure 1C. In truth, the relationship between EEG feature and microcircuit configuration is likely to be at best 'few-to-some', meaning that a small number of EEG features may correspond to a

Glossary

Electroencephalography (EEG): the measurement of brain electrical fields via electrodes (which act as small antennas) placed on the head. The electrical fields are the result of electrochemical signals passing from one neuron to the next. When billions of these tiny signals are passed simultaneously in spatially extended and geometrically aligned neural populations, the electrical fields sum and become powerful enough to be measured from outside the head. EEG is often attributed to Hans Berger, who was trying to discover a 'mechanism' for extra-sensory phenomena. It was known since the late 19th century that the brain produces electrical fields, and that these fields exhibit oscillations; Berger's great contributions included demonstrating that these fields could be measured in humans from outside the brain, and demonstrating that neural oscillations were related to cognitive phenomena such as sensory processing and solving mathematical equations.

EEG feature: this term is used here as shorthand for an idiosyncratic spatial/temporal/spectral pattern that is associated with a particular sensory or cognitive process, similar to a 'fingerprint' [17]. Examples include midfrontal theta and response conflict monitoring, and posterior alpha power and spatial attention.

Multiscale (or cross-scale): brain function can be measured at many spatial scales, ranging from individual synapses (~10 nm) to whole-brain networks (~10 cm). Although neuroscience research in general spans all these spatial scales, there is little understanding of how the dynamics are related across spatial scales. Is understanding multiscale dynamics important for understanding brain function? No-one really knows, but multiscale dynamics are hypothesized to be necessary for the complexity required for higher cognitive functioning including consciousness [93]. Studying multiscale interactions presents conceptual, mathematical, and technological challenges, and scientists tend to like challenges.

Neural microcircuit: a microcircuit refers to a spatial scale of brain anatomical/functional organization that is larger than a single neuron but

larger (but hopefully not very large) number of microcircuit configurations. In part, this is necessarily true because EEG can measure only large-scale synchronous events produced by geometrically aligned pyramidal cell populations [2]; there may be different microcircuit configurations that produce the same macroscopic feature.

On the other hand, there is justification to be optimistic about a feasible EEG-to-microcircuit mapping: although the theoretical dimensionality of neural activity space is so huge that it might as well be infinite, populations of neurons seem to occupy a relatively small subset of all configurational possibilities, and this 'low-dimensional principle' seems to characterize brain activity at multiple spatial scales [13–15]. Furthermore, focusing on EEG features that can be theoretically linked to neurophysiological principles put further constraints on EEG-to-microcircuit mapping [16].

EEG Oscillations Are an Excellent Link to Neurophysiology

Neural oscillations are the most prominent feature of EEG data, and countless studies over many decades have demonstrated that perceptual, cognitive, motor, and emotional processes are tightly linked with specific patterns of oscillations [17]. Oscillations are observed throughout the nervous system and at multiple spatial and temporal scales [18], and they seem to be ubiquitous across species [19]. Taken together, this suggests that oscillations have important functions that have been preserved over the course of evolution. Furthermore, neural oscillations have been investigated using *in vitro*, *in vivo*, and *in silico* techniques, producing a large and growing understanding of the principles and significances of oscillations. Therefore, the motivation for studying neural oscillations is that they can provide insights into the computational principles, as well as the temporal precisions and limitations, of the neural computations that implement perception, cognition, and action.

On the other hand, we must appreciate that 'neural oscillation' is an umbrella term that is useful mainly as a generic reference to a collection of phenomena. Neural oscillations arise from different biophysical mechanisms that depend on intrinsic properties such as ion channels, neurite lengths, and wiring, as well as on extrinsic properties such as input strength and noise levels [20–23]. Neural oscillations produced by different microcircuits and in different cognitive contexts may have different computational significances and cognitive implications. It is not clear whether a functional principle of, for example, visual cortex alpha oscillations applies equally to, for example, lateral prefrontal cortex theta oscillations.

What Then Do We Know about Where EEG Comes From?

From a biophysics perspective, much is known about the origins of the local field potential (LFP) and EEG [23]. The (here termed) 'standard model' states that LFP and EEG are the extracellular currents reflecting summed dendritic postsynaptic potentials (the exchange of electrochemical signaling across the synapse) in thousands to millions of pyramidal cells in parallel alignment [2,24,25]. Although postsynaptic potentials make the largest contributions, other neural processes including calcium and sodium spikes, glial cells, active as well as passive currents, and mono/quadripolar sources also contribute to some extent to the LFP [23,25–31]. These various aspects may contribute differently to LFP versus EEG, in part because EEG reflects a larger spatial scale of activity, and in part because the relationship between LFP and EEG depends on several factors that are imperfectly understood [32,33].

Nonetheless, statements such as 'EEG reflects the integration of postsynaptic potentials across neural populations' contain no explanatory power for scientists trying to decipher the spatial/spectral/temporal features they observe in their EEG data such as frequency band-limited power modulations, various manifestations of functional connectivity, cross-frequency coupling, event-related potential components, and so on. These features reflect

smaller than an fMRI voxel. Microcircuits can take several forms; the term 'microcircuit' often connotes a bundling of dozens or hundreds of cells of various classes that are more densely interconnected than they are connected to neighboring microcircuits, and that work together towards a common function [57]. Orientation-tuned columns in primate V1 is an example of a microcircuit.

Neural oscillations: the EEG activity of a living brain is not flat, nor is it random. Instead, EEG is dominated by rhythms that are grouped into a small number of characteristic frequencies. These rhythms are driven by fluctuations in excitability of populations of neurons, and have complex spatiotemporal patterns that vary in amplitude, timing, and frequency. These variations are known as nonstationarities, and the general goal of cognitive electrophysiology is to understand how and why these nonstationarities are related to various cognitive and perceptual processes.

the dynamics of neural microcircuits that implement cognitive computations, and it is these computations that are of great interest to neuroscientists and psychologists. In other words, the 'standard model' explains the existence of EEG but not the content of the EEG signal; the former is a prerequisite for the latter, but the latter is more important in cognitive electrophysiology.

The empirical literature linking EEG to neural microcircuit dynamics is under-explored, with many important questions remaining unanswered (see Outstanding Questions for a non-exhaustive list). Extant findings suggest that the origins of EEG features are complex. For example, Snyder and colleagues [34] found that the relationship between spatial integration (as measured through spike-count correlation) and EEG power is nonlinear, such that higher spike-count correlations predicted high and low EEG amplitude, while low spike-count correlations were seen during time-periods of intermediate EEG amplitudes. Another study [35] showed that LFP power and inter-electrode synchronization (used as a measure of spatial integration) made statistically independent contributions to EEG power. Interestingly, lidocaine administration decreased LFP power but increased EEG power, a dissociation that was attributable to enhanced inter-electrode synchronization. Inter-electrode coherence was not always significantly related to EEG power in the alpha band (~10 Hz), which is a strong resonant frequency of the visual cortex (where the recordings were made). Thus, EEG and LFP can provide unique insights into brain function, and spatial integration (quantified as inter-electrode coherence) may be related to EEG activity in complex ways in different frequency bands.

Two specific EEG features are worth highlighting as examples. (i) Alpha oscillations have been widely studied for a century, and modern ideas suggest that alpha is involved in coordinating temporal fluctuations in the extent of inhibition of neural networks [36–38]. Modeling and empirical studies suggest that several distinct mechanisms could produce alpha oscillations, including thalamocortical loops, rhythmically firing pyramidal cells, local interneurons, and interactions of synaptic inputs with different time-constants [20,39–43]. The lack of convergence on a single cellular mechanism of alpha suggests multiple distinct mechanisms. Indeed, features of alpha oscillations such as amplitude, time-course, and peak frequency can vary as a function of cognitive task, cortical region, and cortical layer [44–46], supporting the conclusion that there are many independent alpha generators in the brain. Different computational roles for different alpha generators is an exciting prospect that highlights the importance of neural oscillations in brain function, but it also stymies attempts at grand unified theories, and precludes simple inverse inferences from EEG to neural microcircuit configuration.

(ii) Gamma oscillations (30–80 Hz) have been implicated in active sensory processing, and computational accounts of gamma oscillations [20,47,48] have been used to account for gamma-band spike-timing correlations and LFP fluctuations [49–52]. However, direct empirical data that such cellular mechanisms produce the larger-scale gamma oscillations measurable with EEG are scarce. Indeed, researchers who study the dynamics of gamma oscillations in response to sensory stimuli have recently noted that the 'understanding of the dynamical properties of gamma oscillations *in vivo*, their appropriate quantification as well as their neurocomputational significance are still far from being fully elucidated' [53].

These examples highlight that we are not completely lost at sea when trying to link EEG features to underlying neural circuit dynamics and their computations. The most promising developments come from the intersection of macroscopic (EEG data and cognitive neuroscience theories), microscopic (neurobiology), and computational (theories and simulations) investigations. However, even for some of the most widely used EEG features there is considerable

uncertainty and ambiguity. This uncertainty emphasizes the major explanatory gap between (i) detailed investigations of one or a small number of neurons, and (ii) large-scale patterns obtained from noninvasive human electrophysiology.

Now Is the Time To Start Answering the Title Question

We are at the convergence of three developments that together provide the opportunity for new and important discoveries about the origins and significances of EEG features. The first development is the bulging of the literature that characterizes EEG features accompanying memory, perception, emotion, language, action, and other cognitive processes. One can criticize such investigations as being correlational, too macroscopic, or unable to determine whether oscillations are part of the computation or merely epiphenomenal. Further progress depends on the basic landscape first being mapped. For example, monitoring ongoing actions for errors is strongly associated with transient theta-band oscillations in the medial prefrontal cortex [54]. The origin and significance of midfrontal theta remains mysterious [55], but without such observation-based studies we would not know which of the myriad features of brain activity [56] are relevant for deeper investigation. To be sure, exploratory and 'mapping' EEG studies remain important and there are many aspects of cognition and disease whose EEG features are uncharted, but there is arguably now sufficient groundwork for more detailed investigations – including fine-grained empirical investigations and new data analyses along the lines described in the next sections.

Second, the neurophysiological literature on the organization and operations of neural microcircuits has blossomed. Models of microcircuit structure and function have been around for decades [57], but only recently have aspects of these models become experimentally tractable in awake behaving animals. For example, we now know that specific molecularly identifiable classes of interneurons in distinct cortical layers are involved in different aspects of regulating pyramidal cells, such as blocking action potentials versus inhibiting specific dendritic branches, or releasing inhibition by blocking other inhibitory interneurons [57–61]. How these components of microcircuits are related to LFP oscillations is a new and exciting topic [21,49,62,63]; how these components might relate to specific EEG features is very much an open area of research.

These new neuroscience findings have been facilitated by the third development – the technological innovations that provide new ways to measure and manipulate the brains of small animals such as rodents. Electrodes are becoming smaller and more densely packed, allowing dozens to hundreds of measurement points throughout the depth of the cortex and across multiple cortical and subcortical regions. Indeed, the number of electrodes (and therefore the number of simultaneously recorded neurons) seems to increase exponentially, reminiscent of Moore's law [34,64]. In parallel, a wealth of optogenetic techniques offer the opportunity to combine large-scale electrophysiology with precise spatiotemporal control of subclasses of neurons identified by molecular markers [49].

Given these developments, what bottlenecks are preventing us from knowing more about where EEG comes from and what it means? One bottleneck is simply putting the right resources in the right places: research labs that have the necessary equipment and expertise tend not to focus on linking neurophysiology to EEG (there are, of course, noteworthy exceptions), while research labs that study human EEG generally lack the equipment and expertise to measure neurophysiology. Thus, important discoveries about how to interpret EEG features will come from convincing the 'human' researchers that they should expand into animal electrophysiology labs, and from convincing the electrophysiology labs (and funding agencies) that this topic is worth spending time, energy, and money on.

What Types of Data Are Needed?

To discover what EEG means, insightful experiments are likely to include empirical measurements of neural data across multiple spatial scales recorded simultaneously. The ideal dataset includes several sets of laminar probes comprising hundreds of microelectrodes that span multiple layers of the cortex and multiple cortical regions, in combination with EEG on the skull or scalp. The EEG should have sufficient density (ideally >30 electrodes) to create topographical maps and implement spatial components-based or source separation-based analyses [65,66], but even a few skull screws with wires could provide useful data about EEG. Such experiments are possible in primates but are more feasible in rodents, which has the added advantage of allowing optogenetic tools that can determine the contributions of specific classes of cells to different EEG patterns.

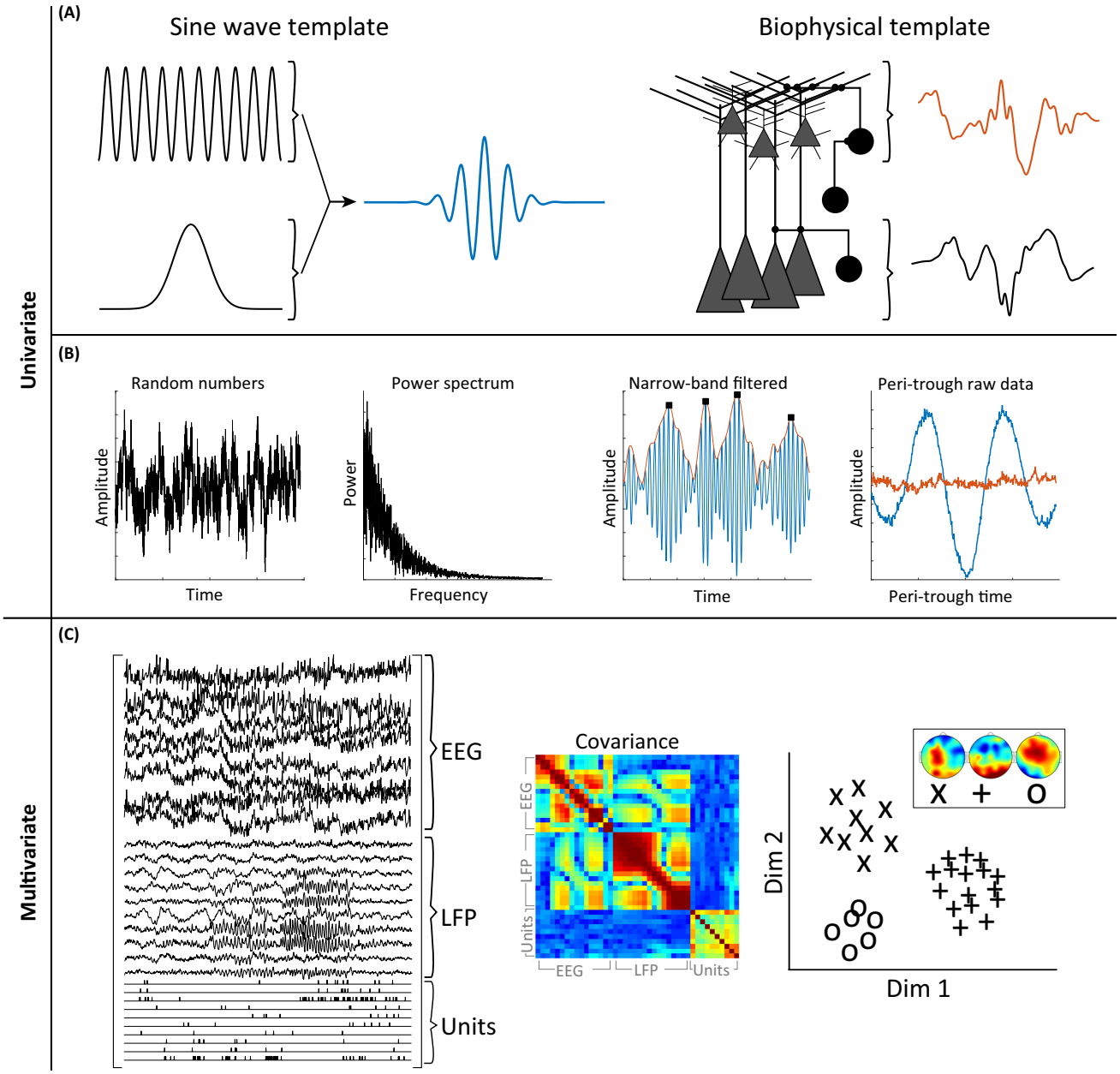
Insightful data can also be obtained in humans. For example, advances in neuroimaging allow high spatial resolution functional magnetic resonance imaging (fMRI) to be combined with EEG so as to determine how layer-specific hemodynamic activity correlates with EEG features [67,68]. Although these studies have generally focused on the relationship between EEG power and hemodynamic amplitude per voxel, additional insights might come from examining the spatial covariance structure of hemodynamic activity in relation to EEG activity (as predicted by the 'standard model' of EEG). Whole-brain coverage provides an advantage over animal studies in allowing investigations into how blood oxygen level-dependent imaging (BOLD)–EEG relationships vary over brain space and EEG topography. Layer-specific localization of non-invasively measured electromagnetic activity is also becoming feasible [69].

Nevertheless, gaining insights into EEG does not merely involve measuring cortical layers or interneuron classes; physiologically inspired data analyses can also link EEG to underlying computations and their neural implementations. For example, if the oscillatory nature of EEG activity is relevant for cognition, then phase, as an index both of timing and of fluctuations in neural states, should be related to cognitive or neural dynamics [37,38,70]. Nonsinusoidal, asymmetric, and other nonlinear features of EEG are increasingly being appreciated and linked to cognitive phenomena [71–76]. Making sense of the myriad linear and nonlinear features of EEG data requires careful analyses and clever thinking, not fancy or expensive equipment.

Computational models may also prove important. Modeling frees researchers from semantic ambiguities in ideas and predictions, and allows manipulations and investigations that are not possible in real biology – such as connectivity patterns, ratios of different neurochemicals, neuron sizes, conduction delays, and so on. The ability of computational models to account for biophysical and phenomenological aspects of EEG phenomena is already established [77–79]. Biophysical models can be more richly integrated into EEG research by using model-generated waveforms as analysis regressor templates instead of sinusoidal templates (discussed more below).

What Types of Analyses Are Needed?

Properly analyzing the types of datasets described above may require novel, or at least different, analyses compared to the standard corpus of EEG analysis techniques (Figure 2). For one thing, the majority of time–frequency methods assume sinusoidal activity at the timescale of hundreds of milliseconds [80]. Clearly, neural oscillations are (by definition) rhythmic, but are they sinusoidal? That is less clear. There are noteworthy cases of non-sinusoidal neural oscillations, including up–down states during anesthesia and rat hippocampal theta during exploration [71,76]. These cases are clear because the oscillations are strong enough to be seen with the naked eye with no or minimal data processing. However, many oscillations are dynamic and embedded in multiplexed and noisy signals, thus necessitating offline signal processing. When this signal processing involves using sinusoidal filters, sinusoid-



Trends in Neurosciences

Figure 2. Analytical Possibilities. Most univariate-based time-frequency analyses involve matching the neural time-series data to a template. Standard templates include a pure sine wave (e.g., Fourier transform) or a tapered sine wave (e.g., Morlet wavelet convolution). Perhaps a more insightful approach would involve templates defined empirically from data, for example using spatiotemporal filters, or outputs of a computational model, as illustrated in (A). In this simulated model, deep versus superficial layers produce distinct LFP waveforms that can be used as templates. In addition to being more physiologically interpretable, such templates might reduce false positives by virtue of waveform sensitivity. (B) illustrates this using random noise data with a 1/*f* power spectrum. The blue and orange waveforms shown in (A) were used as convolution kernels, peaks in the power time-series were identified, and the nearest trough in the unfiltered data (black squares in the third panel) was taken as a center averaging point. These trough-locked waveforms (right-hand panel, average of 10 simulations) appeared sinusoidal for the wavelet kernel, reflecting time-periods in which the random noise happened to match the sine wave template. The orange template was less likely to identify noise patterns because of increased waveform specificity and complexity. (C) Multivariate analyses might involve having multiple spatial scales of data in the same matrix, and this would facilitate decomposition- or parcellation-based analyses, as well as techniques for dimensionality reduction, source separation, and classification. The covariance matrix is the starting point of many multivariate analyses. Abbreviations: Dim, dimension; EEG, electroencephalography; LFP, local field potential.

like activity will be observed, even in noise (Figure 2B). Thus, commonly used signal-processing approaches make it difficult to distinguish between sinusoidal versus nonsinusoidal oscillations (adding to the difficulty is that waveforms are typically labeled as 'nonsinusoidal' based on qualitative visual inspection).

To be clear, the assumption of sinusoidality is 'valid enough' to produce an enormous corpus of knowledge about brain function. Analytical techniques such as wavelet convolution and the Fourier transform will not (should not) become obsolete. Instead, these standard techniques could be seen as a first-pass analysis tool, a way to identify the important peaks and valleys in a large landscape of possibilities, and as a pointer to a subspace of the data in which more physiologically inspired analyses can be applied.

'Physiologically inspired' analyses can take several forms, including limiting analyses to biologically plausible hypotheses [16] or explicitly incorporating neurophysiological principles into data analyses. For example, sine waves could be replaced with physiologically defined waveform shapes in convolution-based or template-matching-based analyses (Figure 2). The main challenge is that the validity of this approach depends on the accuracy of the template. Physiology-defined templates may need to be specific for each brain region or cognitive process, and possibly for each individual. They must be either estimated from (potentially noisy) data, or derived from biophysical models that rely on sometimes unconfirmed assumptions. Using time delay-embedded spatiotemporal filtering may facilitate empirical estimates of physiological filter kernels [81–84] without the need to rely on sinusoidal templates.

A different set of analytical approaches can be applied if one has a '**multiscale** dataset', meaning simultaneously recorded neurons, LFP, and EEG. Storing such data as matrices facilitates analyses based on matrix decompositions, source separation methods, and machine-learning algorithms. For example, one could attempt to 'decode' EEG features based on single-unit and LFP activity (Figure 2C). Relatedly, source-separation techniques could be used to determine an optimal linear weighting of single units and LFPs that best differentiate, for example high versus low EEG alpha power, or transient bursts versus sustained levels of theta power.

Anticipated Challenges

Although it is not fashionable in neuroscience to highlight inter-species differences, there may be significant difficulties when trying to generalize findings across, for example, rodents and humans. Some of these difficulties may be relatively tractable. For example, differences in skull thickness and electrode size mean that a scalp electrode in humans measures activity from a larger neural population than does a screw drilled into a mouse skull. Other species differences may be more difficult to reconcile. For example, the rules that govern short-term plasticity and the roles of glial cells in regulating network activity seem to differ across species [85–88]. Furthermore, the extent to which perceptual and cognitive strategies vary across species remains debated [89–92]. Thus, the 'neural correlates of EEG' could be meaningfully different in different species.

Another challenge is that the EEG–microcircuit relationships might be messy, with few or no clear links between EEG feature and microcircuit configuration. In other words, there might be a many-to-many mapping instead of a few-to-some or the Elysian one-to-one mapping. Consider, for example, empirical observations that relationships between spiking/LFP dynamics and EEG power are comparable for all EEG frequency bands [34,35]. Results such as this present a conundrum because the ~five canonical EEG frequency bands are reliably dissociable in terms of topographical distributions, temporal characteristics, and relations to specific aspects of cognition. In other words, different EEG features are telling us *something* about brain

mechanisms of cognition. It is our job to determine what that 'something' is. We have much work to do.

Why This Research Is Important

Despite (or perhaps because of) these difficulties, this type of research is important and must be done. The benefits to fundamental neuroscientific knowledge, ideas about the roles of multi-scale integration in cognition [18,93], and clinical diagnosis are myriad, including the categories listed below.

Scientific Benefits

Understanding the microcircuit dynamics underlying EEG features would put researchers in a better position to use EEG to make fundamental discoveries about the neural mechanisms underlying human cognition. Furthermore, such knowledge would form a bridge between human EEG and nonhuman neurophysiology, two literatures that should be better integrated but which often see little convergence because of differences in measurement scale.

Clinical Benefits

EEG is being explored as a biomarker of pathophysiologies and to predict treatment options and success likelihood [94–98]. Understanding where EEG comes from may increase the usability of EEG to diagnose brain disorders and predict treatment outcome success, as well as increasing the success of EEG brain–computer interfaces.

Computational Benefits

The types of empirical data described earlier would span several orders of magnitude in spatial scales of the brain: individual neurons, LFPs (hundreds to thousands of neurons), and EEG (hundreds of thousands to millions of neurons). Such datasets could be used to validate or refine computational models, and to develop new analysis methods for understanding cross-scale interactions.

Concluding Remarks

The literature linking human EEG oscillations to cognition is large and growing rapidly. It is imperative to work towards an understanding of the neurophysiological phenomena that drive those oscillations, and of the implications these oscillations have for how cognitive computations are implemented at the neural level. Linking brain dynamics across spatial and measurement scales is one of the great challenges in 21st century neuroscience.

Acknowledgments

Work in the laboratory of M.X.C. is funded by a grant from the European Research Council (ERC-StG 638589).

Supplemental information

Supplemental information associated with this article can be found online at http://dx.doi.org/10.1016/j.tins.2017.02.004.

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Outstanding Questions

How many configurations can produce a single EEG topography? In theory, the number is infinity. In reality, however, neural configurations occupy a small pocket of the theoretical neural information space. This question could be examined in models by varying mesoscopic parameters (connectivity patterns, excitation levels, etc., but only within a plausible range) in different dipoles, and then and projecting those dipole activities to the scalp.

What is the smallest neural event that can be measured with EEG? It is estimated that ~100 000 synchronous pyramidal cells are necessary to produce an EEG-measurable response. On the other hand, neurons are richly interconnected. Can stimulating a single neuron ignite a cascade that would produce a measurable EEG perturbation? What about a single synapse? Ideas from chaos theory may be relevant here.

How is EEG related to vertical versus horizontal integration? The relationship between spatial integration of neural populations and EEG is complex. Can separating spatial integration along the two dimensions of the cortex help understand its role in EEG?

What initiates and what terminates bursts of band-limited EEG power? EEG power is not constant over time, but instead is bursty. What initiates these bursts, and what terminates them?

What is the role of neurochemistry in EEG features? Phasic bursts of norepinephrine and dopamine have been hypothesized to contribute to EEG features. These types of hypotheses are difficult to test in humans because pharmacological interventions generally have tonic and nonselective effects.

How specific are microcircuit configurations to brain region, cognitive process, and frequency band? It is convenient to write 'neural correlates of EEG', but different EEG features may have qualitatively different origins and significances (e.g., occipital alpha and frontal alpha might reflect distinct mechanisms). This would make answering the title question more difficult, but it would also make EEG more insightful.

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