Chapter 2

How the Brain Works: Perspectives on the Future of Human Neuroscience Research

Ramesh Srinivasan

Abstract

Many books and review articles have been written about the structure and function of the brain. That is beyond the scope of this one chapter or, indeed, of this entire volume. Instead, this chapter will emphasize general principles and salient features of *human* brains and attempt to provide a useful theoretical framework for considering how to design experiments and perform data analysis that yields a better understanding of the vast amounts of information being obtained about the function of the human brain by neuroscientists using EEG, MEG, ECoG, fMRI, NIRS, etc. The details of these techniques can be found in other chapters in this volume, and I will not consider the strengths and weaknesses of these methods in detail. Rather, I will try to assess what kind of questions we can ask with non-invasive measures of brain function in humans. In my view, the field of cognitive neuroscience has to grow beyond the marriage of experimental psychology to brain mapping, and I consider some potential directions.

Key words Theoretical neuroscience, Neurocognitive models, Complex systems

1 A Brief Quantitative Anatomy of the Human Brain

The three primary divisions of the human brain are the *brainstem*, *cerebellum*, and *cerebrum*. The brainstem (the brain's stalk) is the structure through which nerve fibers relay signals (*action potentials*) in both directions between the spinal cord and higher brain centers. The *thalamus,* composed of two egg-shaped structures at the top and to the side of the brainstem, is a relay station and important integrating center for all sensory input to the cortex except smell. The *cerebellum*, which sits on top and to the back of the brainstem, has long been associated with the fine control of muscle movements. More recently, the cerebellum has been shown to play additional roles in cognition, especially learning.

The large part of the brain that remains when the brainstem and cerebellum are excluded is the *cerebrum*, which is divided almost equally into two halves. The outer portion of the cerebrum, the *cerebral cortex* (or *neocortex* in mammals), is a folded structure

Mirko Grimaldi et al. (eds.), *Language Electrified: Principles, Methods, and Future Perspectives of Investigation*, Neuromethods, vol. 202, https://doi.org/10.1007/978-1-0716-3263-5_2,

varying in thickness from about 2–5 mm, having a total surface area (in humans) of roughly 1600–4000 cm^2, and containing about 10^{10} *neurons* (nerve cells) [1]. Cortical neurons are strongly interconnected. For example, the surface of a large cortical neuron may be covered with as many as 10^4–10^5 *synapses* that transmit inputs from other neurons. The synaptic inputs to a neuron are of two types: those which produce *excitatory postsynaptic potentials* (EPSPs) across the membrane of the output neuron, thereby making it easier for the target neuron to fire an *action potential*, and the *inhibitory postsynaptic potentials* (IPSPs), which act in the opposite manner on the output neuron. EPSPs produce local membrane *current sinks* with corresponding distributed passive sources to preserve current conservation. IPSPs produce local membrane *current sources* with more distant distributed passive sinks. The cortex is also believed to be the structure that generates most of the electric potential measured on the scalp with EEG and the magnetic field recorded with MEG [2].

Much of our conscious experience must involve, in some largely unknown manner, the interaction of cortical neurons. The cortex is composed of *gray matter*, so-called because it contains a predominance of cell bodies that turn gray when stained by anatomists; but gray matter is actually pink when alive. Just below the gray matter is a second major region, the *white matter*, composed of nerve fibers (*axons*). In humans, white matter volume is somewhat larger that of the neocortex. White matter interconnections between cortical regions (*association fibers or cortico-cortical fibers*) are quite numerous. A patch at the boundary of gray and white matter of area one cm^2 may contain 10^7 input and output fibers, mostly cortico-cortical axons interconnecting different regions of the cortex. Early attempts to map these connections in humans were relatively rare studies in deceased brains [3, 4]. Recent advances in neuroimaging have allowed for in vivo estimates of some of the white matter connections of the brain using diffusion-weighted imaging. Figure 1 shows an example of a *structural connectome* estimated by a tractography analysis of the group average of diffusion imaging from 842 subjects from the HCP 842 dataset [5]. We combined the resultant streamlines (estimated axon fiber bundles) with the Lausanne parcellation [6] to define 114 cortical regions of interest (ROI) and identify the cortico-cortical and callosal connectivity between these regions.

A much smaller fraction (perhaps less than 1%) of axons that enter or leave the underside of the human neocortical surface radiates from the thalamus (*thalamocortical fibers*) [7]. This fraction is only a few percent in humans, but substantially larger in lower mammals [1]. This difference partly accounts for the strong emphasis on thalamocortical interactions (versus cortico-cortical interactions), in the animal electrophysiological literature. The extreme dominance of cortico-cortical over thalamocortical

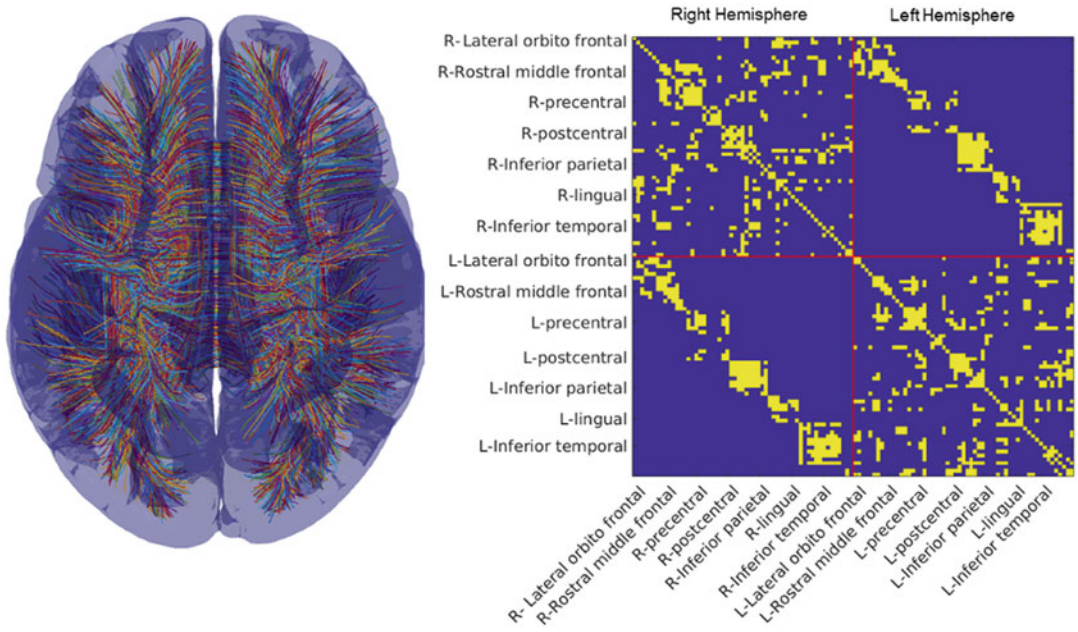

Fig. 1 Structural connectome: We show the streamlines derived by probabilistic tractography analysis of diffusion-weighted imaging of 842 individuals [5] on the left and the structural connectome for the 114 areas of the Lausanne parcellation of the cortex [6] on the right. We have labeled a subset of areas each with one to three subdivisions (see [6] for all subdivisions of the Lausanne parcellation). We show the binarized structural connectome, with any non-zero edge being shown in yellow

connections may be the critical distinction of human brains. The implications of this admittedly oversimplified anatomical picture are that in humans, the connections between neocortical neurons are mostly with neurons in other regions of the neocortex. The brain is mostly operating on input signals emanating from other areas of the brain rather than sensory inputs and mostly sending outputs to other parts of the brain rather than the motor systems of the body!

2 Circuits, Networks, and Fields

A common view of brain operation is that of a complex circuit or *neural network*. In this view, groups of cortical cells are imagined as analogous to electric circuit elements. Cortical columns, i.e., organization of cortical activity across the layers of the cortex, at several scales are candidates for such local cell groups (cf. Fig. 5 in Chapter 1). The smallest scale is a *minicolumn* which has been identified as (potentially) the smallest processing unit in the brain [8–10]. When a sensory signal enters the cortex via the thalamus, it activates a canonical circuit involving interactions between excitatory pyramidal cells and both excitatory and inhibitory

interneurons, producing a functional unit with both strong excitation across layers and inhibition of surrounding tissues. The details of this fundamental structure have been elucidated over the past 40 years by a number of prominent investigators. The most important point is that columnar organization is a *functional* property of the activity of neurons rather than a fixed wiring diagram like a circuit. Columns form and dissipate dynamically in response to input to the cortex that excites pyramidal cells and interneurons. The interneurons in a minicolumn have axons that remain within the white matter and only synapse of neighboring cells. The pyramidal cells within a minicolumn have axons with diverse targets as discussed below.

Neocortical neurons within each cerebral hemisphere are connected by short intracortical fibers with axon lengths mostly less than 5 mm. The *macrocolumn* of typical radius of 3 mm reflects the extent of the intracortical axons of pyramidal cells and is another level of circuit definition. The macrocolumn typically contains hundreds or thousands of minicolumns which often share functional properties. For example, in the visual cortex, the macrocolumn (or hypercolumn, per [11]) contains all the cells that respond to different stimulus features in one location of space. The macrocolumn is potentially a much more useful functional unit than the minicolumn for the modeling of human brain data. Macrocolumns are comparable in size to a typical voxel ($5\ mm^3$) in MRI research. Macrocolumns are also a reasonable size of tissue for modeling the current sources of EEG/MEG as a dipole source [2].

In addition to the intracortical axons, each pyramidal cell projects an axon which enters the white matter and synapses at one (or more) distant locations in the brain. Thus, each of the pyramidal cells in the cortex receives excitatory input from (possibly many) cells at other locations. If this input is sufficient to depolarize the cell, the cell transmits action potentials to other locations in the brain. Thus, the neocortex is densely interconnected by about 10^{10} *cortico-cortical* axons with axon lengths in roughly the 1–15 cm range. Cross-hemisphere interactions occur by means of about 10^8 *callosal axons* through the corpus callosum and several smaller structures connecting the two brain halves. A comparably small number of fibers project to and from subcortical structures such as the thalamus and basal ganglia. The cortico-cortical, callosal, and subcortical axons might then be analogous to wires connecting the circuit elements. In this oversimplified (and probably mostly wrong) electric network picture, "circuit elements" are also under external control by means of electrical and chemical input from the brainstem neuromodulatory systems. More detailed computational models that retain the essential aspects of this picture but provide more intricate anatomical details *are still gross approximations*. For one thing, even a single neuron is far more complex and diverse

than the most complex model of neural networks likely to be created in the near future [12].

Transmission times for action potentials along cortico-cortical axons may range from roughly 10–30 ms between the most remote cortical regions. Local delays due to capacitive-resistive properties of single neurons are typically in the 1–10 ms range, but may also be longer. As the brain's awareness of an external event seems to require multiple feedback between remote regions [13], perceptual consciousness may take several hundred ms to develop as a consequence of brain network activity. The multiple mechanisms by which neurons interact across and within brain areas in integrative brain functions are often labeled by the term *cell assemblies* [14]. The label "cell assembly" denotes a diffuse cell group capable of acting briefly as a single structure. We may reasonably postulate cooperative activity within cell assemblies without explicitly specifying interaction mechanisms or relying on the specificity of a neural network.

Brain processes may involve the formation of cell assemblies at several spatial scales [1, 15]. At smaller spatial scales, corresponding to recordings from individual cells, such groups of neurons may be described by neural network models that can incorporate details of physiologically realistic features such as feedforward and feedback connections [9, 16]. Such anatomical specificity may not have a direct bearing on recordings at a macroscopic scale of human neural data. That is, while these detailed anatomical models (largely derived from animal models) have a strong influence on the behavior of individual cells, they may not be easily related to the coarse-grained variables at macrocolumn or larger spatial scales accessible in non-invasive recordings in human subjects. Even the coarse-grained measures of anatomy such as structural connectome shown in Fig. 1 and network dynamics measured in EEG, MEG, and fMRI signals have complex relationships which are an active field of research.

Field descriptions of brain dynamics may be required to model dynamic behavior and make contact with macroscopic data measured in humans such as EEG, MEG, or fMRI. In this context, the word "field" refers to mathematical functions expressing, for example, the numbers of active synaptic or action potentials in macroscopic tissue volumes. Alternatively, probability of neural firing in a tissue mass may be treated as a *field variable*. In this view, *cell assemblies are pictured* as *embedded within synaptic* and *action potential fields* [1, 17]. Electric and magnetic fields (EEG and MEG) provide large-scale, short-time measures of the *modulations* of synaptic and action potential fields around their background levels. Similarly, fMRI or fNIRS provides information about the modulation of blood flow or oxygen consumption from a background level. These fields are analogous to common physical fields, for example, *sound waves, which are short-time modulations of*

pressure or mass density about background levels. We distinguish these short-time modulations of synaptic activity from long-time scale (usually minutes but sometimes seconds) modulations of brain chemistry controlled by *neuromodulators.*

3 Relationship Between Brain Structure and Measurements of Brain Function

Figure 2 shows a conceptualization of the complexity of relating brain measurements in humans (fMRI and EEG) to each other and to behavior [2]. If we imagine there are cell assemblies distributed in different cortical regions that give rise to behavior, with an fMRI or EEG experiment, we can establish correlations between the behavior and the fMRI and/or EEG signals. Both fMRI and EEG are spatial and temporal filtered representations of the activity of the cell assemblies with the details of the filtering depending on the specific characteristics of the recording method. For instance, it is well known that the EEG has excellent temporal resolution but poor spatial resolution, providing a representation of space-averaged synaptic activity [2] (see however the discussion in Chapter 7). This makes EEG especially sensitive to synchronous synaptic activity in populations of neurons and insensitive to asynchronous activity. fMRI is sensitive to the metabolic demand and consequent blood flow also resulting from synaptic activity of the cell assemblies; however, some of the cell groups contributing to fMRI, e.g., inhibitory basket cells, produce no external electric field. Thus, in general, different cell groups can be expected to generate the EEG or fMRI signals.

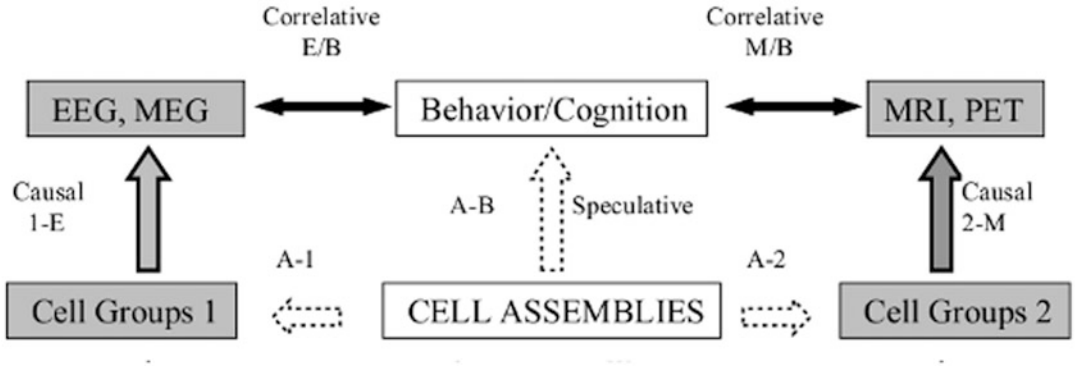

Fig. 2 Conceptual framework for brain signals in cognitive experiments. Double arrows indicate experimental correlative relationships between behavior/cognition and EEG, MEG, MRI, or PET. By definition, Cell Groups 1 generate EEG or MEG, and Cell Groups 2 generate MRI or PET. While theoretical models of Cell Groups 1 are well developed (see [2]), Cell Groups 2 are not known, but are the subject of intensive study in animal models [18]. But in actuality, there exist unknown cell assemblies that underlie the behavior/cognition which are not directly accessible with either recording technique. Cell Groups 1 and 2 may be part of this cell assembly or may be influenced by this cell assembly producing the observation of correlations between EEG and fMRI signals and behavior/cognition

Early efforts to combine separately measured EEG and fMRI signals focused on using source localization of EEG signals to obtain information about the dynamics of each fMRI activation. This is a *spatial model* that assumes that the cell groups generating EEG and fMRI signals are at identical positions. Methods ranging from the simple (equivalent dipoles) to sophisticated (distributed Bayesian solutions with fMRI informed priors) have been developed and applied to localize EEG signals to the activation sites detected with fMRI. Although the technical problems of EEG inverse solutions remain a formidable challenge, this approach suffers from far more significant conceptual problems. As indicated in Fig. 2, fMRI and EEG are recording from different cell groups, and there is no reason to expect a simple spatial correspondence between the cell groups that generate fMRI and EEG signals. Even with the same stimulus and task conditions, EEG and fMRI emphasize different neural populations and may lack substantial spatial or temporal overlap.

Structure-function relationships for macroscopic field variables have been the subject of intense study with the discovery of diffusion-weighted imaging, which provides estimates of the structural connectivity at a macroscopic scale (as shown in Fig. 1) which is more readily comparable to fMRI or EEG/MEG data. The integration of such structural and functional data is a crucial step in establishing the physiological basis of network models of brain function.

4 What Does Localization of "Brain Activity" Really Mean?

A considerable amount (perhaps the majority) of cognitive neuroscience research is concerned with documenting the relationship between "brain activity" and cognitive functions usually by obtaining experimental evidence that the signal recorded from some region of the brain has been modulated by a cognitive task. Clever task manipulations, gleaned from experimental psychology, are used to generate contrasts for statistical tests to associate brain activity with hypothesized cognitive processes. This "spatial" model of brain function takes an overly simplistic view of brain networks as a series of "activations" in brain areas – the strength of the fMRI is to tell us where to find these activations, and the job of EEG (or usually evoked responses, ERP) is to tell us when the activation occurred.

However, a fundamental unknown (and in many cases unknowable) in any neurophysiological study is whether observed modulations of neural responses at one location in the brain by cognitive processes should be interpreted only as the action of a *local* network in the specific cortical region or due to the interactions between this cortical region and the rest of the brain in *global*

networks. Non-local interactions between cortical regions are mainly mediated by connections of the cortico-cortical (also labeled association) fibers. The axons range in length from less than 1 cm (the U fibers connecting adjacent gyri) to the total length through the white matter between frontal and occipital lobes. The total number of cortico-cortical fibers is roughly equal to the number of pyramidal cells, about 10^{10}. Thus, the issue of global networks interacting in cognitive processes is salient to the interpretation of physiological signals obtained from the brain with any technique – EEG, MEG, fMRI, LFPs, or even spiking activity of a single neuron.

The physiology and anatomy of the brain indicate that our model of the underlying cognitive processes should favor global networks over local networks unless there is strong evidence of functional localization. *This is the great strength of human neuroscience!* Studies in animal models necessarily place electrodes in a limited number of hypothesized brain regions, while human neuroscience research views the function of the whole brain, allowing us to understand how brain networks give rise to intelligent brain function. This dense network connectivity suggests that it is far less common for brain function to be a purely local operation in one location of the brain. Examples of such local processing might include feature extraction in the processing of sensory systems. However, if we consider the entire processing stream involved in figure-ground segregation of (perceptual) objects such as a written or spoken word, we find that the processing involves feedforward and feedback processing along anatomical pathways linking neurons distributed in different cortical areas into a functional network [13]. Thus, even "low-level" perceptual and motor processes involve distributed brain function in hierarchically organized neural systems whose complexity is beyond the simple measures of localized brain activity that predominate studies of brain function. The future of human brain research is in the study of whole brain systems.

5 Neurocognitive Models

The study of the human brain has been closely linked to advances in cognitive science, which provides the theoretical foundation for studies of human brain function. In recent years, cognitive science has married mathematical theories of behavior with experimental data via computational modeling. More recently, neurocognitive models have been developed that formally integrate neural signals into mathematical theories of cognitive function [19].

Computational models of behavior usually propose a mechanistic or algorithmic description of the computations that may be happening in the brain to support behavior. These models usually

have parameters (e.g., drift rate or learning rate) that quantitatively modulate the computations made by the model. Model fitting techniques allow us to infer the parameters that are most likely to give rise to the observed behavior. Then, given a set of parameters for a model, it is also possible to obtain the latent variables that are part of the models' computations and putatively are the underlying variables needed to account for the observed behavior.

Thus, cognitive modeling may provide two types of benefits to relate behavior and neural signals. First, fitting computational models to behavioral data allow researchers to extract model parameters that are related to mechanisms underlying behavior – rather than an implicit specification of a cognitive process being manipulated, an explicit model is made of how the behavioral data is generated. These parameters may or may not capture variability (between conditions or individuals) better than raw behavioral data, but are more scientifically meaningful as the generative mechanisms are specified. Second, model fitting also allows researchers to extract latent variables that putatively reflect the computations supporting behavior. These variables may then be better candidates to reflect the trial-by-trial neural signal.

Perhaps the most active area of neurocognitive modeling are models of perceptual decision-making [20, 21]. The drift-diffusion model (DDM) is a specific model of perceptual decision-making that has been integrated with neural signals. The DDM is used to account simultaneously for accuracy and reaction time observations in binary perceptual decision tasks, such as the random dot motion task [22]. Specifically, the DDM formalizes decision as a noisy accumulation of evidence to one of two bounds; it assumes that once the decision variable reaches the bound, the corresponding choice is made. The DDM is usually parameterized with three parameters: non-decision time, drift rate, and decision threshold. The non-decision time reflects a fixed period of time during which no information is accumulated; mechanistically, it may include both initial perception latency and motor command latency after the decision is made. The drift rate reflects the rate at which information is accumulated or the strength of each new piece of evidence. The threshold indicates the level the evidence should reach prior to a decision being taken. Other parameters are sometimes included in the DDM to better capture behavior; for example, a bias term may be needed to capture participants' tendency to select one option more than another.

Using the DDM of quick decision-making as an example, single-trial estimates of evidence accumulation rate during quick decision-making and non-decision time (time in milliseconds of a human reaction time not related to a decision) have been obtained using hierarchical Bayesian modeling with ERP amplitude estimates on single trials, time-locked to the onset of visual stimuli [23, 24]. Hierarchical Bayesian modeling (HBM) of human

cognition is one of the most powerful methods to integrate EEG and behavior, since these datasets are linked with respect to the *cognitive* function specified by the model and shared relationships are estimated simultaneously. The hierarchical Bayesian modeling (HBM) framework is ideally suited for the joint analysis of multiple modes of data. In addition, the EEG data can also provide new and additional information about the cognitive process that cannot be discerned with just behavior alone. This flexible framework can inform building and testing theoretical models of the relationship of neural signals from the human cortex (EEG, fMRI, etc.), human cognition, and human behavior.

Figure 3 summarizes the results of our studies linking EEG signals to diffusion models of perceptual decision-making. ERP measures described trial-to-trial differences in visual encoding time (a component of non-decision time during reaction time) and trial-to-trial differences in evidence accumulation rate, as described by trial-level estimates of the drift parameter [23, 24]. EEG correlates of additional cognitive processes, such as visual attention, can also add inference about the overall human cognitive process when used in combination with behavioral modeling. Nunez et al. (2015) [26] found evidence that differences in experimental participants' attention (both visual noise suppression and visual signal enhancement) as measured by SSVEPs related to some specific differences in participants' cognition during decision-making. Lui et al. 2020 [25] showed that the duration of decision-making is indexed by the readiness potential in the motor cortex.

Hierarchical Bayesian modeling also allows discovering complex relationships between multiple data types within cognitive neuroscience [27] by allowing the simultaneous estimation of posterior distributions of multiple parameters. Fitting procedures produce samples from probability distributions that display knowledge (i.e., "uncertainty") about parameter estimates and thus certainty about the effects of cognition or neural data in specific theoretical models.

6 Future Directions

Human brains are typically viewed as the pre-eminent complex systems with cognition believed to emerge from dynamic interactions within and between brain sub-systems [17, 28–33]. Here, we cite two salient anatomical and physiological features that contribute to brain complexity and, by implication, the conditions apparently required for healthy cognition. These features give rise to multi-scale spatial-temporal patterns of brain activity, revealed with imaging techniques like EEG and fMRI, which are strongly correlated with mental states. One such salient feature is anatomical and physiological nested hierarchy: as we have seen, cortical

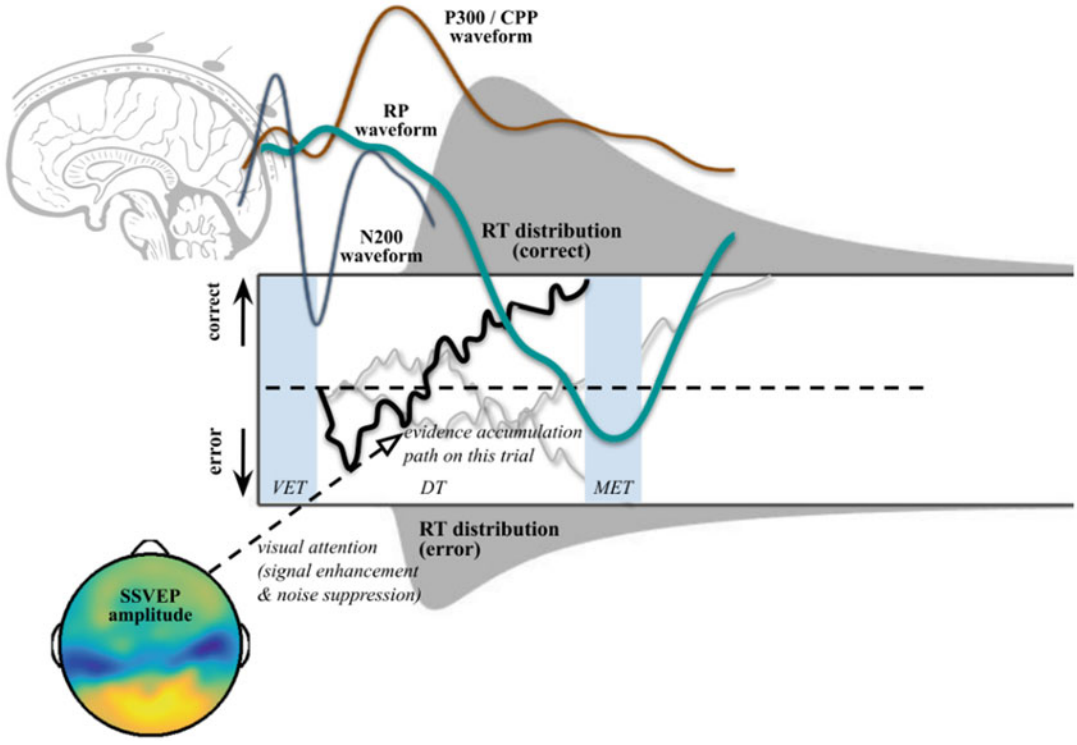

Fig. 3 A theoretical representation of some modeling studies to discover cognitive mechanisms of decision-making using neurocognitive modeling of EEG and human behavior during visual decision-making tasks. Bold text represents observed data (EEG measures or human behavioral data), while italic text represents derived cognitive parameters that can be estimated through joint modeling of time-domain EEG collected from the scalp (top left: cartoon with three scalp electrodes sitting above the brain, CSF, skull, and skin that result in time-domain waveforms), frequency-domain EEG collected from high-density arrays (bottom left: EEG amplitudes that were spline-interpolated between electrodes on a flat representation of the human scalp), and/or choice RTs (response time distributions shown for correct responses, top, and error responses, bottom flipped). Event-related potentials (ERPs) can be calculated from event-locked EEG averages and embedded in neural drift-diffusion models (NDDMs) to discover the cognitive time course of decision-making separating visual encoding time (VET), decision time (DT), and motor execution time (MET) that together add up to each trial's response time (RT) [23, 24]. Correct and error responses are described after the evidence accumulation path passes one of two boundaries during decision time (this trial is represented as a black line with two other gray lines representing other simulations from the same process that describe response times and possibly EEG potentials). Particular ERPs of interest are N200, P300/CPP, and RP waveforms. N200 waveforms are thought to reflect VET and the onset of evidence accumulation [24]. The P300 or centro-parietal positivity (CPP) are thought to reflect DT and possibly the evidence accumulation process itself. The readiness potential (RP) is a motor-related preparatory signal thought to reflect DT and MET under certain experimental conditions [25]. Steady-state visual evoked potentials (SSVEPs) can be calculated from band-limited frequency-domain EEG data using frequency-tagging experiments. Amplitude measures of SSVEPs across electrodes can then be used to estimate visual attention and, in particular, signal enhancement and noise suppression that could affect the rate and variance of evidence accumulation [26]

anatomy and physiology consist of neurons within minicolumns within modules within macrocolumns [1, 9]. Emergence and complexity generally occur in hierarchically nested physical and biological systems where each higher level of complexity displays novel emergent features based on the levels below it, their interactions, and their interactions with higher levels. Such systems may follow general principles that underlie many complex systems, including anthropology, artificial intelligence, chemistry, economics, meteorology, molecular biology, neuroscience, physics, psychology, and sociology [2, 12, 30, 32–34]. A second salient feature of many complex systems is non-local interactions in which dynamic activity at one location influences distant locations without affecting intermediate regions, as enabled in human brains by long (up to 15–20 cm) cortico-cortical fibers [1, 3, 4, 7, 35] and in human social systems by modern long distant communications facilitating small world behavior [36]. The label "small world" originates from the purported maximum six steps separating any two persons in the world; small worlds are widely studied in graph theory. The high density of short-range (mm-scale) intracortical connections coupled with an admixture of cortico-cortical axons favors small world behavior in the brain, which may be the essence of the dynamic sculpting of network architectures in brain function. For example, the path length between any pair of neocortical neurons is estimated to be no more than two or three synaptic connections [7]. Small worlds often promote high complexity; they also appear to be abundant in brain structural networks, across systems, scales, and species [32, 33].

This complex system view is critical to future genuine understanding of brain networks. However, because of the complexity of these types of analysis, to date, most of the studies that have attempted to characterize such brain networks have focused on resting-state networks in fMRI and EEG data. Very few studies of human brain function have linked network properties to cognitive operations. This is an open field with great potential for the future of brain sciences.

References

1. Nunez PL (1995) Neocortical dynamics and human EEG rhythms. Oxford University Press, New York
2. Nunez PL, Srinivasan R (2006) Electric fields of the brain: the neurophysics of EEG. Oxford University Press, New York
3. Krieg WJS (1963) Connections of the cerebral cortex. Brain Books, Evanston
4. Krieg WJS (1973) Architectonics of human cerebral fiber system. Brain Books, Evanston, p 1973
5. Yeh F, Panesar S, Fernandes D, Meola A, Yoshino M, Fernandez-Miranda JC, Vettel JM, Verstynen T (2018) Population-averaged atlas of the macroscale human structural connectome and its network topology. NeuroImage 178:57–68
6. Cammoun L, Gigandet X, Meskaldji D, Thiran JP, Sporns O, Do KQ, Maeder P, Meuli R, Hagmann P (2012) Mapping the human connectome at multiple scales with diffusion spectrum MRI. J Neurosci Methods 203:386–397

7. Braitenberg V (1978) Cortical architectonics: general and areal. In: Brazier MAB, Petsche H (eds) Architectonics of the cerebral cortex. Raven Press, New York, pp 443–465
8. Mountcastle VB (1979) An organizing principle for cerebral function: the unit module and the distributed system. In: Schmitt FO, Worden FG (eds) The neurosciences 4th study program. MIT Press, Cambridge
9. Szentagothai J (1979) Local neuron circuits of the neocortex. In: Schmitt FO, Worden FG (eds) The neurosciences 4th study program. MIT Press, Cambridge, MA, pp 399–415
10. Mountcastle VB (1998) Perceptual neuroscience. The cerebral cortex. Harvard University Press, Cambridge
11. Hubel DH, Wiesel TN (1977) Ferrier lecture. Functional architecture of macaque monkey visual cortex. Proc R Soc Lond B Biol Sci 198:1–59
12. Scott A (1995) Stairway to the mind. Springer-Verlag, New York
13. Lamme VA, Roelfsema PR (2000) The distinct modes of vision offered by feedforward and recurrent processing. TRENDS Neurosci 23: 571–579
14. Hebb DO (1949) The organization of behavior. Wiley, New York
15. Freeman WJ (1975) Mass action in the nervous system. Academic Press, New York
16. Lamme VA, Supèr H, Spekreijse H (1998) Feedforward, horizontal, and feedback processing in the visual cortex. Curr Opin Neurobiol 8:529–535
17. Haken H (1996) Principles of brain functioning: a synergetic approach to brain activity, behavior and cognition. Springer, Berlin
18. Logothetis NK (2002) On the neural basis of the BOLD fMRI signal. Philos Trans R Soc Lond Ser B Biol Sci 357:1003–1037
19. Turner BM, Forstmann BU, Wagenmakers EJ, Brown SD, Sederberg PB, Steyvers MA (2013) Bayesian framework for simultaneously modeling neural and behavioral data. NeuroImage 72:193–206
20. Forstmann BU, Ratcliff R, Wagenmakers E-J (2016) Sequential sampling models in cognitive neuroscience: Advantages, applications, and extensions. Annu Rev Psychol 67:641–666
21. Palmieri TJ, Love BC, Turner BM (2017) Model-based cognitive neuroscience. J Math Psychol 76(Pt B):59–64
22. Roitman JD, Shadlen MN (2002) Response of neurons in the lateral intraparietal area during a combined visual discrimination reaction time task. J Neurosci 22(21):9475–9489
23. Nunez MD, Vandekerckhove J, Srinivasan R (2017) How attention influences perceptual decision making: single-trial EEG correlates of drift-diffusion model parameters. J Math Psychol 76(Pt B):117–130. https://doi.org/10.1016/j.jmp.2016.03.003
24. Nunez MD, Gosai A, Vandekerckhove J, Srinivasan R (2019) The latency of a visual evoked potential tracks the onset of decision making. NeuroImage 197:93–108. https://doi.org/10.1016/J.Neuroimage.2019.04.052
25. Lui KK, Nunez MD, Cassidy JM, Vandekerckhove J, Cramer SC, Srinivasan R (2020) Timing of readiness potentials reflect a decision-making process in the human brain. Comput Brain Behav 4:264–283. https://doi.org/10.1007/s42113-020-00097-5
26. Nunez MD, Srinivasan R, Vandekerckhove J (2015) Individual differences in attention influence perceptual decision making. Front Psychol 8:18. https://doi.org/10.3389/fpsyg.2015.00018
27. Wiecki TV, Sofer I, Frank MJ (2013) HDDM: hierarchical Bayesian estimation of the drift-diffusion model in python. Front Neuroinform 7:14. https://doi.org/10.3389/fninf.2013.00014
28. Freeman WJ (2003) The wave packet: an action potential for the 21st century. J Integr Neurosci 2:3–30
29. Friston KJ, Tononi G, Sporns O, Edelman GM (1995) Characterising the complexity of neuronal interactions. Hum Brain Mapp 3:302–314
30. Edelman GM, Tononi G (2000) A universe of consciousness. Basic Books, New York
31. Buzsaki G (2006) Rhythms of the brain. Oxford University Press, New York
32. Tononi G, Edelman GM (1998) Consciousness and complexity. Science 282:1846–1851
33. Bassett DS, Gazzaniga MS (2011) Understanding complexity in the human brain. Trends Cogn Sci 15:200–209. Sporns O. (2011) Networks of the brain. MIT Press; Cambridge
34. Gell-Mann M, Lloyd S (1996) Information measures, effective complexity, and total information. Complexity 2:44–52. Pesenson M ed. (2013) Multiscale analysis and nonlinear dynamics. Wiley-VCH, Weinheim
35. Braitenberg V, Schuz A (1991) Anatomy of the cortex: statistics and geometry. Springer-Verlag, New York
36. Bassett DS, Bullmore ET (2009) Human brain networks in health and disease. Curr Opin Neurol 22:340–347