



Perspective article

Cytoelectric coupling: Electric fields sculpt neural activity and “tune” the brain’s infrastructure

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ABSTRACT

We propose and present converging evidence for the Cytoelectric Coupling Hypothesis: Electric fields generated by neurons are causal down to the level of the cytoskeleton. This could be achieved via electrodiffusion and mechanotransduction and exchanges between electrical, potential and chemical energy. Ephaptic coupling organizes neural activity, forming neural ensembles at the macroscale level. This information propagates to the neuron level, affecting spiking, and down to molecular level to stabilize the cytoskeleton, “tuning” it to process information more efficiently.

1. Electric fields, ephaptic coupling and LFPs

Ephaptic coupling describes direct influences of the brain’s electric fields to individual neurons. It is different from the influence of one neuron to the other through synapses (Anastassiou et al., 2011). The activity of populations of neurons generates electric fields near each neuron and in extracellular space as currents flow in their dendrites, somata and axons. In turn, these electric fields influence the activity of individual neurons and their parts.

Detailed imaging of brain anatomy and structure at the microscopic level allows us to understand the currents and electric fields. Advances in super resolution imaging (Novak et al., 2013; Hochbaum et al., 2014), multiphoton brain imaging (Denk and Svoboda, 1997) and computational studies have revealed the contribution of different electric and geometric properties of individual neurons to the electric fields. Besides synaptic and intrinsic currents, the fields depend on microscopic processes like gap-junction activity and neuron-glia interactions. They also depend on large scale properties, like the inhomogeneity of extracellular tissue and the anatomy of grey matter (Kotnik et al., 1997; Gimsa and Wachner, 2001; Jeong et al., 2016; Jia et al., 2016). In brief, knowing the brain’s anatomy, it is possible to understand properties of emerging electric fields.

Here, we aim to understand the reverse: How the fields influence individual neurons. Whether electric fields are an epiphenomenon of

neural activity or not is unknown. Some studies suggest that fields are coupled to neural activity (Anastassiou et al., 2011; Anastassiou and Koch, 2015). They are thought to have very small amplitudes (about 0.5 mV) (Faber, 2010). Spikes from individual neurons are unlikely to affect firing of nearby neurons unless a large number of neurons are firing synchronously (Anastassiou and Koch, 2015; Fröhlich and McCormick, 2010). Also, isolating fields is difficult: ephaptic coupling co-occurs with electrochemical processes. But they can be studied using the theory of electrodiffusion from chemical physics. This examines how electric fields and concentration gradients change the flow of ions in electrolytes and conductors (Savtchenko et al., 2017).

Electric fields change the flow of currents and information transfer at the local circuit level. One way to study ephaptic coupling is via computational modelling. Models have described field effects on synapses and changes in the flow of neurotransmitters (Savtchenko et al., 2004). Electrodiffusion studies have used the Nernst Planck (NP) equations (Planck, 1890; Lu, 2013) to study ephaptic effects on local field potential (LFP) waveforms (Pods et al., 2013), the voltage distribution in spines (Cartailler et al., 2018) and membrane bound aqueous compartments known as Ranvier nodes (Loppreore et al., 2008). Input currents to bipolar neurons can feed back to membrane potentials (Gardner et al., 2015). Diffusive currents in extracellular space generate electric field gradients that alter the soma potential (Perram and Stiles, 2006; Sokalski and Lewenstam, 2001), an effect known as liquid

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junction potential (Velumian et al., 1993).

Direct evidence of ephaptic coupling has been found in slices (Anastassiou and Koch, 2015; Chiang et al., 2019; Jefferys et al., 2012). Ephaptic coupling has been shown to change spike response latencies (Schmidt et al., 2021), increase spike synchronization, and affect synaptic interactions (Anastassiou and Koch, 2015; Traub et al., 1985). Eccles and Jaeger (1958) showed ephaptic effects on ion currents in synaptic cleft. Externally applied fields were found to regulate network dynamics (Deans et al., 2007). Endogenous fields can form a feedback loop that modulates the very activity that generates them (Fröhlich and McCormick, 2010). Changes in the average membrane potential of the population influenced synaptic currents and the ionic flux in the synapse, along with its plasticity and conductance (Vöröslakos et al., 2018; Kronberg et al., 2017; Ye and Steiger, 2015). Experimental evidence for ephaptic coupling is reviewed in (Anastassiou and Koch, 2015).

In vivo ephaptic effects are difficult to isolate. But evidence is consistent with ephaptic coupling in the intact, functioning brain. This is found in local field potentials (LFPs). LFPs capture spatially distributed activity over patches covering a few square millimetres of cortical surface (Buzsáki et al., 2012). Experiments have shown that LFP signals coordinate individual neuron spiking (Fröhlich and McCormick, 2010). They also contain oscillations thought to be produced by coordinated activity of groups of neurons. Application of external electric fields resulted in membrane potentials oscillating at the same frequency as the drive (Anastassiou et al., 2011). LFP oscillations during epilepsy affect structure and contribute to pathogenesis and maladaptive myelination (Knowles et al., 2022).

In brief, properties of LFPs oscillations are consistent with ephaptic effects. We will come back to this later. Before this, we discuss the neural sources (ensembles) that generate LFPs.

2. Mesoscale organization and neural ensembles

Ephaptic coupling to the LFP oscillations suggests large-scale organization of neural activity on the level of millions of neurons. Is mesoscale organization useful for brain function? The short answer is yes. The idea has a long history going back to the work of Semon (Semon et al., 2018), Hebb (Hebb, 1949) and Hopfield (Hopfield, 1982). Studies by us (Miller et al., 2018; Antzoulatos and Miller, 2016; Buschman et al., 2012; Kornblith et al., 2015; Pinotsis and Miller, 2020; Pinotsis et al., 2018, 2017a) and others (Fujisawa et al., 2008; Benchenane et al., 2010; Obien et al., 2014) exploiting multielectrode arrays support the conclusion that oscillations can form neural ensembles via synchronous activity at the LFP level. They seem to mediate the processing of incoming stimuli (Gray, 1999), attention (Desimone and Duncan, 1995; Fries, 2009), encoding of rules, memory encoding and recall (Buschman et al., 2012) or the binding of sensory inputs to representations (Singer and Gray, 1995).

This can be connected to the neuron level. With the advent of super resolution imaging (Tønnesen et al., 2014) and modern engram imaging techniques (Tonegawa et al., 2015a), including immediate early gene labelling (Reijmers et al., 2007) (IEG) and optogenetics (Deisseroth, 2011), neurons participating in ensembles can be identified and their activity can be recorded. Their dendrites, spines, organelles and other biophysical details can be mapped (Liu and Tao, 2022) along with their electrical activity. Transgenes allow the activity of a target neuron to be visualized during production of proteins needed to perform cognitive functions. Optogenetics allows for control of neural firing during various functions, including memory storage and recall.

LFPs seem to play a role in selecting neurons representing memories (neural ensembles). Using ensemble (engram) imaging, the authors of (Tonegawa et al., 2015b) suggested a dissociation between memory storage and recall that indicates a role for LFPs. Storage relies on long term potentiation (LTP) that includes a late phase of protein synthesis for consolidation aided by NMDA receptors. During learning, neural ensembles are formed. Neurons participating in ensembles have

increased spine density and higher synaptic strength. Increased strength seems to be required only for memory recall, not storage. Under drug-induced amnesia, direct activation of ensemble neurons is sufficient to overcome impaired synaptic potentiation and leads to memory recall (Ryan et al., 2015).

Importantly, memory storage seems to depend on connectivity patterns (which neurons are connected to which), not how strong the connection is. Ephaptic coupling via LFPs could produce detailed connectivity patterns that allow specific memory content to be stored. This is also consistent with a wide variety of work showing that not only memory but cognition in general depends on the mesoscale organization of neural activity. Studies in monkey and rat IT (Gross et al., 1972), PFC (Miller and Cohen, 2001) and hippocampus (Opris et al., 2015) have found cognitive maps (Behrens et al., 2018) with multidimensional representations (Fusi et al., 2016). Increased mesoscale activity has also been recorded in vivo in humans with PET (Cabeza et al., 1997) and fMRI (Nolde et al., 1998) during memory tasks.

Neural oscillations are a natural way to organize activity on the mesoscale. Oscillations underlie many cognitive functions (Buzsáki et al., 2012; Kahana, 2006) including working memory (Miller et al., 2018; Pinotsis et al., 2018), attention (Fiebelkorn and Kastner, 2019; Buschman and Miller, 2007; Lakatos et al., 2008; Pinotsis et al., 2014; Fries et al., 2001; Gregoriou et al., 2009), and predictive coding (Bastos et al., 2020; Pinotsis et al., 2017b). Waves of LFP activity across cortex serve many functions (Muller et al., 2018) including regulating spike-timing dependent plasticity (Muller et al., 2016). Gamma LFP oscillations organize spiking activity to odours in the olfactory bulb (Kay et al., 2009). Rhythms in the cortex entrain to the rhythms of the outside world (Schroeder et al., 2010; Fries, 2015), which are exploited for focusing attention. In cortex, oscillations can bind together networks (Singer, 1993). They organize activity to produce computation (Lundqvist et al., 2023). In short, mesoscale organization of neural activity underlies many brain functions. Ephaptic coupling seems like a good way for the brain to produce this organization.

3. The cytoelectric coupling hypothesis

The brain infrastructure that connects neurons is collectively referred to as the cytoskeleton. It includes proteins, neurotransmitters, filaments, microtubules etc. Above, we saw how electric fields generated by neurons and other parts of the cytoskeleton carry information being used for behavior. Here, we propose the Cytoelectric Coupling Hypothesis: Electric fields help organize components of the cytoskeleton in order to “tune” it to process information efficiently.

Direct tests of this hypothesis would require linking LFP recordings to molecular level imaging. Still, many components of cytoskeleton themselves support information processing, learning and memory (Lee et al., 2000; Queenan et al., 2017; Nikolić, 2023). Microtubules form electric circuits that are stabilized during memory formation (Craddock et al., 2010, 2012). Cytoskeletal proteins regulate neuronal inputs and outputs and are remodelled with learning (Priel et al., 2010). Proteins at synapses enable spike timing dependent plasticity (STDP) (Caporale and Dan, 2008) along with long term potentiation and depression (Teyler and DiScenna, 1987). Proteins in the extracellular space also play a role in learning. They form the extracellular matrix (ECM). The ECM is a network of macromolecules that holds neurons together (Yue, 2014). Proteins anchor the neuron-ECM junctions and allow neurons to communicate (Herrmann et al., 2007). The ECM allows for cell adhesion and communication and maintains the links between them, despite protein changes within each neuron and extracellular space (Brockman, 2006; Tsien, 2013). Both synapses and ECM are built from scaffold proteins. These form sites to which neurotransmitter receptors are inserted. They are important for synaptic functions like the trafficking and clustering of glutamate receptors and adhesion molecules (Kim and Sheng, 2004). They hop in and out of the ECM and synapses similarly to the way that electrons move within semiconductors (Queenan et al.,

2017).

This flexibility endows the neurons and extracellular space with homeostatic stability. Stimulation perturbs the ECM via mechanical forces in neurons, other cells, and ECM proteins. Filaments and microtubules are subject to them—and use them to interact with other cytoskeleton structures through a process known as mechanotransduction (Iskratsch et al., 2014). A well-known example is sound perception in inner ear hair cells. The cytoskeleton is subject to similar forces generated by motor proteins (Sweeney and Holzbaur, 2018). At the same time, mechanosensitive proteins convert these forces back to chemical energy. An important example of an ECM protein is talin. It is known to underlie neuron adhesion and cytoskeleton stabilization (Goult et al., 2018). Besides ECM, ion channels in neurons also change as a result of mechanotransduction (Gu and Gu, 2014). In response to these perturbations, the cytoskeleton seeks to return to a stable configuration. Protein filaments and microtubules in the ECM are only a few nm long. But homeostasis requires organization on a much larger scale, i.e. meso- and macroscale (Ingber, 2003).

One contributor to cytoskeleton organization is tensegrity (tensional integrity). Tensegrity enables mechanotransduction. It shows that multicomponent structures achieve organized stability via a pre-existing stress (some strings shorten, others lengthen to achieve isometric tension) rather than continuous deformation. It has been proposed as a principle for cytoskeleton self-organization and hierarchical integration (Ingber, 2003). This principle also endows the cytoskeleton with structural flexibility despite continuous protein changes and new stimuli. However, tensegrity is not directly linked to information processing and memory storage in the brain. It cannot, by itself, configure the cytoskeletal structure to support information processing and neural ensemble (engram) formation. In other words, structural flexibility is not sufficient to achieve cognitive flexibility. The latter depends on information processing.

Here, we propose Cytoelectric Coupling. Electric fields are the link between the information the brain is processing (Pinotsis and Miller, 2022) and a stable, organized cytoskeleton. The goal of homeostasis is efficient information processing and memory storage. It provides stability necessary for cognitive flexibility. Above, we showed that meso-scale electric fields and LFPs help form ensembles of memories being used, see also (Pinotsis and Miller, 2022, 2023). These ensembles can form, break apart and re-form on the fly to enable thoughts (Pinotsis et al., 2017a) and cognitive control (Puig et al., 2014; Buschman et al., 2011). This needs to happen fast, at the timescale of neuronal activity. Thus, it stands to reason that electric activity and fields could play a direct role by configuring and stabilizing cytoskeleton proteins. Importantly, the electrical fields carry information that the brain is processing, information that can organize the brain's infrastructure to support efficient storage and information processing needed for cognitive flexibility. Thus, Cytoelectric Coupling connects information at the meso- and macroscopic level down to the microscopic level of proteins that are the molecular basis of memory (Gallistel, 2017; Langille and Gallistel, 2020). Maybe even further. Electric fields have been linked to consciousness (Fingelkurts et al., 2012; John, 2005; McFadden, 2020; Pockett, 2000; McFadden, 2006). Penrose and Hameroff, following the pioneering work by Sherrington (Sherrington, 1951), suggested microtubules might be related to efficient information processing by exploiting quantum superposition (Hameroff, 1994; Hameroff and Penrose, 2014).

Above we discussed evidence for ephaptic coupling and the importance of LFPs and mesoscale organization of brain activity for cognition. Besides this, other support for Cytoelectric Coupling comes from results from developmental biology and known effects of electric fields on components of the ECM. Electric fields play a role in the development of multicellular organisms and invertebrates by regulating anatomy (Krüger and Bohrmann, 2015; Levin, 2021), allowing for limb and spinal cord regeneration (Durant et al., 2019; Beane et al., 2011) using electrical stimulation (Leppik et al., 2015; Murugan et al., 2022). They guide

morphogenesis (Adams et al., 2016) and can control tumorigenesis (Chernet and Levin, 2014). Fields also control neuronal migration (Bertucci et al., 2019) and sculpt neurodevelopment (Luhmann et al., 2018). Spatiotemporal patterns of transmembrane potentials during development regulate organogenesis of the brain itself (Pai et al., 2015). Cytoskeletal dynamics regulate bioelectric properties and mesoscale electric fields and result in an asymmetry of the left-right body axis (Vandenberg et al., 2013). Conversely, electric fields alter the cytoskeletal structure (Weiß and Bohrmann, 2019). All in all, there seems to be a strong influence of electric fields on the anatomy and structure of multicellular organisms.

On the level of primates, many components of the brain's ECM are affected by electric fields. This includes proteins like microtubules, actin and filaments, and scaffold proteins at synapses that allow information transmission and form the post synaptic density (PSD) (Fernández-Busnadiego et al., 2011). Microtubules form bundles that are parallel to axons and dendrites (Yamada et al., 1970). There are ions in mitochondria (Santo-Domingo and Demareux, 2010). All these proteins are affected by electric fields. Microtubules align with external electric fields (Kim et al., 2007) and change dendrite configuration and neuronal polarization (Baas et al., 2016). They also interact with actin, which changes the microtubule shape and elongation (Dent and Gertler, 2003) and modulates their electric activity (del Rocío Cantero et al., 2020). Actin has also been linked to neurotransmitter release and changes in synaptic architecture (Doussau and Augustine, 2000). Other protein filaments in PSD can form and dissolve fast and interact with neurons by responding to mechanical stimuli (mechanosensing) (Gauthier and Roca-Cusachs, 2018). We saw above that electric signals result from stimuli (mechanotransduction). Thus, stimuli change the environment around proteins and the forces they are subjected to. Ion channel probabilities change in response to different mechanical stimuli, calcium ions that diffuse through the mitochondria membrane (Jasielec et al., 2016) which, in turn, alters the ECM electric field.

This could be exploited for clinical purposes (Widge and Miller, 2019). In Brain-Computer Interface (BCI) systems, neural read-outs are used to control motor prosthetics (Hochberg et al., 2006) and employ decoding algorithms trained on LFPs and spikes (Waldert et al., 2009). The application of external electric fields (e.g., in conjunction with behavioral training) could move the cytoskeleton into stable states that support normal cognitive function. Transcranial direct current stimulation (tDCS) has been shown to affect memory storage and improve cognitive function in human subjects (Tedla et al., 2022; Widge et al., 2019). In-vitro slice experiments using tDCS have shown that entrainment, even only 5 mV (Bikson et al., 2004), affected speed of spike propagation (Chakraborty et al., 2018), the size of excitatory post-synaptic potentials (Rahman et al., 2013), and contributed to long term potentiation (Kronberg et al., 2017). New technology allows modulation on the scale of LFPs using an implantable device. Using an analogue of separated interface nerve electrode (Ackermann et al., 2011) in conjunction with the implantable freeform stimulator, it can deliver undulating and electric fields (Aplin and Fridman, 2019). Closed-loop electrical stimulation can be used to modulate endogenous oscillatory power, rather than impose outside rhythms on the brain (Widge et al., 2018). It has been shown to alter reward guided learning in the orbitofrontal cortex (Knudsen and Wallis, 2020) of animals. Closed-loop electrical stimulation has also been used to improve cognitive function in human surgical patients (Widge et al., 2019).

In sum, ECM proteins, neurons and other cells in cytoskeleton generate heterogeneous electric fields that feed back to them. To achieve homeostasis, different cytoskeleton parts should work synergistically. This includes exchanges between electrical, potential and chemical energy as a result of electrodiffusion and mechanotransduction. Electric fields can organize neural activity to form neural ensembles (engrams) used for memory and cognition. This information transmitted to the molecular level via electric fields can “tune” the cytoskeleton for efficiency, stability and enable cognitive flexibility.

Declaration of Competing Interest

The authors declare no competing interests.

Data availability

No data was used for the research described in the article.

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References

- Ackermann Jr, D.M., Bhadra, N., Foldes, E.L., Kilgore, K.L., 2011. Separated interface nerve electrode prevents direct current induced nerve damage. *J. Neurosci. Methods* 201, 173–176.
- Adams, D.S., Uzel, S.G., Akagi, J., Wlodkowic, D., Andreeva, V., Yelick, P.C., Devitt-Lee, A., Pare, J.-F., Levin, M., 2016. Bioelectric signalling via potassium channels: a mechanism for craniofacial dysmorphogenesis in KCNJ2-associated Andersen-Tawil Syndrome. *J. Physiol.* 594, 3245–3270.
- Anastassiou, C.A., Koch, C., 2015. Ephaptic coupling to endogenous electric field activity: why bother? *Curr. Opin. Neurobiol.* 31, 95–103.
- Anastassiou, C.A., Perin, R., Markram, H., Koch, C., 2011. Ephaptic coupling of cortical neurons. *Nat. Neurosci.* 14, 217–223.
- Antzoulatos, E.G., Miller, E.K., 2016. Synchronous beta rhythms of frontoparietal networks support only behaviorally relevant representations. *Elife* 5, e17822.
- Aplin, F.P., Fridman, G.Y., 2019. Implantable direct current neural modulation: theory, feasibility, and efficacy. *Front. Neurosci.* 13, 379.
- Baas, P.W., Rao, A.N., Matamoros, A.J., Leo, L., 2016. Stability properties of neuronal microtubules. *Cytoskeleton* 73, 442–460.
- Bastos, A.M., Lundqvist, M., Waite, A.S., Kopell, N., Miller, E.K., 2020. Layer and rhythm specificity for predictive routing. *Proc. Natl. Acad. Sci.* 117, 31459–31469.
- Beane, W.S., Morokuma, J., Adams, D.S., Levin, M., 2011. A chemical genetics approach reveals H,K-ATPase-mediated membrane voltage is required for planarian head regeneration. *Chem. Biol.* 18, 77–89. <https://doi.org/10.1016/j.chembiol.2010.11.012>.
- Behrens, T.E., Muller, T.H., Whittington, J.C., Mark, S., Baram, A.B., Stachenfeld, K.L., Kurth-Nelson, Z., 2018. What is a cognitive map? Organizing knowledge for flexible behavior. *Neuron* 100, 490–509.
- Benchenane, K., Peyrache, A., Khamassi, M., Tierney, P.L., Gioanni, Y., Battaglia, F.P., Wiener, S.I., 2010. Coherent theta oscillations and reorganization of spike timing in the hippocampal-prefrontal network upon learning. *Neuron* 66, 921–936.
- Bertucci, C., Koppes, R., Dumont, C., Koppes, A., 2019. Neural responses to electrical stimulation in 2D and 3D in vitro environments. *Brain Res. Bull.* 152, 265–284.
- Bikson, M., Inoue, M., Akiyama, H., Deans, J.K., Fox, J.E., Miyakawa, H., Jefferys, J.G., 2004. Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices in vitro. *J. Physiol.* 557, 175–190.
- Brockman, J. (2006). What We Believe but Cannot Prove: Today's Leading Thinkers on Science in the Age of Certainty (Edge Question Series).
- Buschman, T.J., Miller, E.K., 2007. Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *science* 315, 1860–1862.
- Buschman, T.J., Siegel, M., Roy, J.E., Miller, E.K., 2011. Neural substrates of cognitive capacity limitations. *Proc. Natl. Acad. Sci.* 108, 11252–11255.
- Buschman, T.J., Denovellis, E.L., Diogo, C., Bullock, D., Miller, E.K., 2012. Synchronous oscillatory neural ensembles for rules in the prefrontal cortex. *Neuron* 76, 838–846.
- Buzsáki, G., Anastassiou, C.A., Koch, C., 2012. The origin of extracellular fields and currents—EEG, ECoG, LFP and spikes. *Nat. Rev. Neurosci.* 13, 407–420.
- Cabeza, R., Kapur, S., Craik, F.I., McIntosh, A.R., Houle, S., Tulving, E., 1997. Functional neuroanatomy of recall and recognition: a PET study of episodic memory. *J. Cogn. Neurosci.* 9, 254–265.
- Caporale, N., Dan, Y., 2008. Spike timing-dependent plasticity: a Hebbian learning rule. *Annu. Rev. Neurosci.* 31, 25–46.
- Cartailler, J., Kwon, T., Yuste, R., Holcman, D., 2018. Deconvolution of voltage sensor time series and electro-diffusion modeling reveal the role of spine geometry in controlling synaptic strength. *Neuron* 97, 1126–1136 e10.
- Chakraborty, D., Truong, D.Q., Bikson, M., Kaphzan, H., 2018. Neuromodulation of axon terminals. *Cereb. Cortex* 28, 2786–2794.
- Chernet, B.T., Levin, M., 2014. Transmembrane voltage potential of somatic cells controls oncogene-mediated tumorigenesis at long-range. *Oncotarget* 5, 3287.
- Chiang, C.-C., Shivacharan, R.S., Wei, X., Gonzalez-Reyes, L.E., Durand, D.M., 2019. Slow periodic activity in the longitudinal hippocampal slice can self-propagate non-synaptically by a mechanism consistent with ephaptic coupling. *J. Physiol.* 597, 249–269.
- Craddock, T.J.A., Tuszynski, J.A., Priel, A., Freedman, H., 2010. Microtubule ionic conduction and its implications for higher cognitive functions. *J. Integr. Neurosci.* 09, 103–122. <https://doi.org/10.1142/S0219635210002421>.
- Craddock, T.J.A., Tuszynski, J.A., Hameroff, S., 2012. Cytoskeletal signaling: is memory encoded in microtubule lattices by CaMKII phosphorylation? *PLoS Comput. Biol.* 8, e1002421. <https://doi.org/10.1371/journal.pcbi.1002421>.
- Deans, J.K., Powell, A.D., Jefferys, J.G., 2007. Sensitivity of coherent oscillations in rat hippocampus to AC electric fields. *J. Physiol.* 583, 555–565.
- Deisseroth, K., 2011. Optogenetics. *Nat. Methods* 8, 26–29.
- del Río Cantero, M., Gutierrez, B.C., Cantiello, H.F., 2020. Actin filaments modulate electrical activity of brain microtubule protein two-dimensional sheets. *Cytoskeleton* 77, 167–177.
- Denk, W., Svoboda, K., 1997. Photon upmanship: why multiphoton imaging is more than a gimmick. *Neuron* 18, 351–357.
- Dent, E.W., Gertler, F.B., 2003. Cytoskeletal dynamics and transport in growth cone motility and axon guidance. *Neuron* 40, 209–227.
- Desimone, R., Duncan, J., 1995. Neural mechanisms of selective visual attention. *Annu. Rev. Neurosci.* 18, 193–222.
- Doussau, F., Augustine, G.J., 2000. The actin cytoskeleton and neurotransmitter release: an overview. *Biochimie* 82, 353–363.
- Durant, F., Bischof, J., Fields, C., Morokuma, J., LaPalme, J., Hoi, A., Levin, M., 2019. The role of early bioelectric signals in the regeneration of planarian anterior/posterior polarity. *Biophys. J.* 116, 948–961. <https://doi.org/10.1016/j.bpj.2019.01.029>.
- Eccles, J.C., Jaeger, J.C., 1958. The relationship between the mode of operation and the dimensions of the junctional regions at synapses and motor end-organs. *Proc. R. Soc. Lond. Ser. B-Biol. Sci.* 148, 38–56.
- Faber, D.S., 2010. Field effects in the CNS play functional roles. *Front. Neural Circuits* 15.
- Fernández-Busnadiego, R., Schrod, N., Kochovski, Z., Asano, S., Vanhecke, D., Baumeister, W., Lucić, V., 2011. Insights into the molecular organization of the neuron by cryo-electron tomography. *J. Electron Microsc.* 60, S137–S148.
- Fiebelkorn, I.C., Kastner, S., 2019. A rhythmic theory of attention. *Trends Cogn. Sci.* 23, 87–101.
- Fingelkurts, A.A., Fingelkurts, A.A., Neves, C.F., 2012. “Machine” consciousness and “artificial” thought: an operational architectonics model guided approach. *Brain Res.* 1428, 80–92.
- Fries, P., 2009. Neuronal gamma-band synchronization as a fundamental process in cortical computation. *Annu. Rev. Neurosci.* 32, 209–224.
- Fries, P., 2015. Rhythms for cognition: communication through coherence. *Neuron* 88, 220–235.
- Fries, P., Reynolds, J.H., Rorie, A.E., Desimone, R., 2001. Modulation of oscillatory neuronal synchronization by selective visual attention. *Science* 291, 1560–1563.
- Frohlich, F., McCormick, D.A., 2010. Endogenous electric fields may guide neocortical network activity. *Neuron* 67, 129–143.
- Fujisawa, S., Amarasingham, A., Harrison, M.T., Buzsáki, G., 2008. Behavior-dependent short-term assembly dynamics in the medial prefrontal cortex. *Nat. Neurosci.* 11, 823–833.
- Fusi, S., Miller, E.K., Rigotti, M., 2016. Why neurons mix: high dimensionality for higher cognition. *Curr. Opin. Neurobiol.* 37, 66–74.
- Gallistel, C.R., 2017. The coding question. *Trends Cogn. Sci.* 21, 498–508.
- Gardner, C.L., Jones, J.R., Baer, S.M., Crook, S.M., 2015. Drift-diffusion simulation of the ephaptic effect in the triad synapse of the retina. *J. Comput. Neurosci.* 38, 129–142.
- Gauthier, N.C., Roca-Cusachs, P., 2018. Mechanosensing at integrin-mediated cell-matrix adhesions: from molecular to integrated mechanisms. *Curr. Opin. Cell Biol.* 50, 20–26.
- Gimsa, J., Wachner, D., 2001. Analytical description of the transmembrane voltage induced on arbitrarily oriented ellipsoidal and cylindrical cells. *Biophys. J.* 81, 1888–1896.
- Goult, B.T., Yan, J., Schwartz, M.A., 2018. Talin as a mechanosensitive signaling hub. *J. Cell Biol.* 217, 3776–3784.
- Gray, C.M., 1999. The temporal correlation hypothesis of visual feature integration: still alive and well. *Neuron* 24, 31–47.
- Gregoriou, G.G., Gotts, S.J., Zhou, H., Desimone, R., 2009. Long-range neural coupling through synchronization with attention. *Prog. Brain Res.* 176, 35–45.
- Gross, C.G., Rocha-Miranda, C. de, Bender, D.B., 1972. Visual properties of neurons in inferotemporal cortex of the Macaque. *J. Neurophysiol.* 35, 96–111.
- Gu, Y., Gu, C., 2014. Physiological and pathological functions of mechanosensitive ion channels. *Mol. Neurobiol.* 50, 339–347.
- Hameroff, S., Penrose, R., 2014. Consciousness in the universe. *Phys. Life Rev.* 11, 39–78. <https://doi.org/10.1016/j.plev.2013.08.002>.
- Hameroff, S.R., 1994. Quantum coherence in microtubules: a neural basis for emergent consciousness? *J. Conscious. Stud.* 1, 91–118.
- Hebb, D., 1949. *The Organization of Behavior*. Wiley, New York.
- Herrmann, H., Bär, H., Kreplak, L., Strelkov, S.V., Aebi, U., 2007. Intermediate filaments: from cell architecture to nanomechanics. *Nat. Rev. Mol. Cell Biol.* 8, 562–573.
- Hochbaum, D.R., Zhao, Y., Farhi, S.L., Klapoetke, N., Werley, C.A., Kapoor, V., Zou, P., Kralj, J.M., MacLaurin, D., Smedemark-Margulies, N., 2014. All-optical electrophysiology in mammalian neurons using engineered microbial rhodopsins. *Nat. Methods* 11, 825–833.
- Hochberg, L.R., Serruya, M.D., Friehe, G.M., Mukand, J.A., Saleh, M., Caplan, A.H., Branner, A., Chen, D., Penn, R.D., Donoghue, J.P., 2006. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature* 442, 164–171.
- Hopfield, J.J., 1982. Neural networks and physical systems with emergent collective computational abilities. *Proc. Natl. Acad. Sci.* 79, 2554–2558.
- Ingber, D.E., 2003. Tensegrity II. How structural networks influence cellular information processing networks. *J. Cell Sci.* 116, 1397–1408.
- Iskratchk, T., Wolfenson, H., Sheetz, M.P., 2014. Appreciating force and shape—the rise of mechanotransduction in cell biology. *Nat. Rev. Mol. Cell Biol.* 15, 825–833.

- Jasielec, J.J., Filipek, R., Szyszkiewicz, K., Sokalski, T., Lewenstam, A., 2016. Continuous modeling of calcium transport through biological membranes. *J. Mater. Eng. Perform.* 25, 3285–3290.
- Jefferys, J.G., de la Prida, L.M., Wendling, F., Bragin, A., Avoli, M., Timofeev, I., da Silva, F.H.L., 2012. Mechanisms of physiological and epileptic HFO generation. *Prog. Neurobiol.* 98, 250–264.
- Jeong, W.C., Sajib, S.Z., Katoch, N., Kim, H.J., Kwon, O.I., Woo, E.J., 2016. Anisotropic conductivity tensor imaging of in vivo canine brain using DT-MREIT. *IEEE Trans. Med. Imaging* 36, 124–131.
- Jia, W., Wu, J., Gao, D., Wang, H., Sun, M., 2016. Visualization of electrical field of electrode using voltage-controlled fluorescence release. *Comput. Biol. Med.* 75, 38–44.
- John, E.R., 2005. From synchronous neuronal discharges to subjective awareness? *Prog. Brain Res.* 150, 143–593.
- Kahana, M.J., 2006. The cognitive correlates of human brain oscillations. *J. Neurosci.* 26, 1669–1672.
- Kay, L.M., Beshel, J., Brea, J., Martin, C., Rojas-Lfano, D., Kopell, N., 2009. Olfactory oscillations: the what, how and what for. *Trends Neurosci.* 32, 207–214.
- Kim, E., Sheng, M., 2004. PDZ domain proteins of synapses. *Nat. Rev. Neurosci.* 5, 771–781.
- Kim, T., Kao, M.-T., Hasselbrink, E.F., Meyhöfer, E., 2007. Active alignment of microtubules with electric fields. *Nano Lett.* 7, 211–217.
- Knowles, J.K., Xu, H., Soane, C., Batra, A., Saucedo, T., Frost, E., Tam, L.T., Fraga, D., Ni, L., Villar, K., 2022. Maladaptive myelination promotes generalized epilepsy progression. *Nat. Neurosci.* 25, 596–606.
- Knudsen, E.B., Wallis, J.D., 2020. Closed-loop theta stimulation in the orbitofrontal cortex prevents reward-based learning. *Neuron* 106, 537–547 e4.
- Kornblith, S., Buschman, T.J., Miller, E.K., 2015. Stimulus load and oscillatory activity in higher cortex. *Cereb. Cortex*, bhv1 82.
- Kotnik, T., Bobanović, F., Miklavčić, D., 1997. Sensitivity of transmembrane voltage induced by applied electric fields—a theoretical analysis. *Bioelectrochem. Bioenergy* 43, 285–291.
- Kronberg, G., Bridi, M., Abel, T., Bikson, M., Parra, L.C., 2017. Direct current stimulation modulates LTP and LTD: activity dependence and dendritic effects. *Brain Stimul.* 10, 51–58.
- Krüger, J., Bohrmann, J., 2015. Bioelectric patterning during oogenesis: stage-specific distribution of membrane potentials, intracellular pH and ion-transport mechanisms in *Drosophila* ovarian follicles. *BMC Dev. Biol.* 15, 1–13.
- Lakatos, P., Karmos, G., Mehta, A.D., Ulbert, I., Schroeder, C.E., 2008. Entrainment of neuronal oscillations as a mechanism of attentional selection. *Science* 320, 110–113.
- Langille, J.J., Gallistel, C.R., 2020. Locating the engram: Should we look for plastic synapses or information-storing molecules? *Neurobiol. Learn. Mem.* 169, 107164.
- Lee, H.-K., Barbarosie, M., Kameyama, K., Bear, M.F., Huganir, R.L., 2000. Regulation of distinct AMPA receptor phosphorylation sites during bidirectional synaptic plasticity. *Nature* 405, 955–959.
- Leppik, L.P., Froemel, D., Slavici, A., Ovadia, Z.N., Hudak, L., Henrich, D., Marzi, I., Barker, J.H., 2015. Effects of electrical stimulation on rat limb regeneration, a new look at an old model. *Sci. Rep.* 5, 18353.
- Levin, M., 2021. Bioelectric signaling: reprogrammable circuits underlying embryogenesis. *Regen., Cancer Cell* 184, 1971–1989. <https://doi.org/10.1016/j.cell.2021.02.034>.
- Liu, Y.-T., Tao, C.-L., 2022. Digitalizing neuronal synapses with cryo-electron tomography and correlative microscopy. *Curr. Opin. Neurobiol.* 76, 102595.
- Lopreore, C.L., Bartol, T.M., Coggan, J.S., Keller, D.X., Sosinsky, G.E., Ellisman, M.H., Sejnowski, T.J., 2008. Computational modeling of three-dimensional electrodiffusion in biological systems: application to the node of Ranvier. *Biophys. J.* 95, 2624–2635.
- Lu, B., 2013. Finite element modeling of biomolecular systems in ionic solution. *Image-Based Geometric Modeling and Mesh Generation*. Springer, pp. 271–301.
- Luhmann, H.J., Kirischuk, S., Kilb, W., 2018. The superior function of the subplate in early neocortical development. *Front. Neuroanat.* 12, 97.
- Lundqvist, M., Brincat, S.L., Rose, J., Warden, M.R., Buschman, T., Miller, E.K., Herman, P., (2023). Spatial computing for the control of working memory. *Nat. Commun.* (in press).
- McFadden, J., 2006. The CEMI field theory: seven clues to the nature of consciousness. *The emerging physics of consciousness*. Springer, pp. 387–406.
- McFadden, J., 2020. Integrating information in the brain's EM field: the cemi field theory of consciousness. *Neurosci. Conscious.* 2020 niaa016.
- Miller, E.K., Cohen, J.D., 2001. An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.* 24, 167–202.
- Miller, E.K., Lundqvist, M., Bastos, A.M., 2018. Working memory 2.0. *Neuron* 100, 463–475.
- Muller, L., Piantoni, G., Koller, D., Cash, S.S., Halgren, E., Sejnowski, T.J., 2016. Rotating waves during human sleep spindles organize global patterns of activity that repeat precisely through the night. *Elife* 5, e17267.
- Muller, L., Chavane, F., Reynolds, J., Sejnowski, T.J., 2018. Cortical travelling waves: mechanisms and computational principles. *Nat. Rev. Neurosci.* 19, 255–268.
- Murugan, N.J., Vigran, H.J., Miller, K.A., Golding, A., Pham, Q.L., Sperry, M.M., Rasmussen-Ivey, C., Kane, A.W., Kaplan, D.L., Levin, M., 2022. Acute multidrug delivery via a wearable bioreactor facilitates long-term limb regeneration and functional recovery in adult *Xenopus laevis*. *Sci. Adv.* 8 eabj2164.
- Nikolić, D., 2023. Where is the mind within the brain? Transient selection of subnetworks by metabotropic receptors and G protein-gated ion channels. *Comput. Biol. Chem.*, 107820.
- Nolde, S.F., Johnson, M.K., D'Esposito, M., 1998. Left prefrontal activation during episodic remembering: An event-related fMRI study. *NeuroReport* 9, 3509–3514.
- Novak, P., Gorelik, J., Vivekananda, U., Shevchuk, A.I., Ermolyuk, Y.S., Bailey, R.J., Bushby, A.J., Moss, G.W., Rusakov, D.A., Klennerman, D., 2013. Nanoscale-targeted patch-clamp recordings of functional presynaptic ion channels. *Neuron* 79, 1067–1077.
- Obien, M.E.J., Deligkaris, K., Bullmann, T., Bakkum, D.J., Frey, U., 2014. Revealing neuronal function through microelectrode array recordings. *Front. Neurosci.* 8.
- Opris, I., Santos, L.M., Gerhardt, G.A., Song, D., Berger, T.W., Hampson, R.E., Deadwyler, S.A., 2015. Distributed encoding of spatial and object categories in primate hippocampal microcircuits. *Front. Neurosci.* 9, 317.
- Pai, V.P., Lemire, J.M., Paré, J.-F., Lin, G., Chen, Y., Levin, M., 2015. Endogenous gradients of resting potential instructively pattern embryonic neural tissue via notch signaling and regulation of proliferation. *J. Neurosci.* 35, 4366–4385. <https://doi.org/10.1523/JNEUROSCI.1877-14.2015>.
- Perram, J.W., Stiles, P.J., 2006. On the nature of liquid junction and membrane potentials. *Phys. Chem. Chem. Phys.* 8, 4200–4213.
- Pinotsis, D., Miller, E.K., 2023. In vivo ephaptic coupling allows memory network formation. *bioRxiv* 2023, 02. 28.530474.
- Pinotsis, D.A., Miller, E.K., 2020. Differences in visually induced MEG oscillations reflect differences in deep cortical layer activity. *Commun. Biol.* 3, 1–12.
- Pinotsis, D.A., Miller, E.K., 2022. Beyond dimension reduction: Stable electric fields emerge from and allow representational drift. *NeuroImage* 253, 119058.
- Pinotsis, D.A., Brunet, N., Bastos, A., Bosman, C.A., Litvak, V., Fries, P., Friston, K.J., 2014. Contrast gain control and horizontal interactions in V1: a DCM study. *NeuroImage* 92, 143–155.
- Pinotsis, D.A., Brincat, S.L., Miller, E.K., 2017a. On memories, neural ensembles and mental flexibility. *NeuroImage* 157, 297–313.
- Pinotsis, D.A., Geerts, J.P., Pinto, L., FitzGerald, T.H., Litvak, V., Auksztulewicz, R., Friston, K.J., 2017b. Linking canonical microcircuits and neuronal activity: dynamic causal modelling of laminar recordings. *Neuroimage* 146, 355–366.
- Pinotsis, D.A., Buschman, T.J., Miller, E.K. (2018). Working Memory Load Modulates Neuronal Coupling. *Cerebral Cortex*.
- Planck, M., 1890. Ueber die Potentialdifferenz zwischen zwei verdünnten Lösungen binärer Electrolyte. *Ann. der Phys.* 276, 561–576.
- Pockett, S. (2000). The nature of consciousness: A hypothesis (IUniverse).
- Pods, J., Schönte, J., Bastian, P., 2013. Electrodiffusion models of neurons and extracellular space using the poisson-nernst-planck equations—numerical simulation of the intra- and extracellular potential for an axon model. *Biophys. J.* 105, 242–254.
- Priel, A., Tuszynski, J.A., Woolf, N.J., 2010. Neural cytoskeleton capabilities for learning and memory. *J. Biol. Phys.* 36, 3. <https://doi.org/10.1007/s10867-009-9153-0>.
- Puig, M.V., Antzoulatos, E.G., Miller, E.K., 2014. Prefrontal dopamine in associative learning and memory. *Neuroscience* 282, 217–229.
- Queenan, B.N., Ryan, T.J., Gazzaniga, M.S., Gallistel, C.R., 2017. On the research of time past: the hunt for the substrate of memory. *Ann. N. Y. Acad. Sci.* 1396, 108–125.
- Rahman, A., Reato, D., Arlotti, M., Gasca, F., Datta, A., Parra, L.C., Bikson, M., 2013. Cellular effects of acute direct current stimulation: somatic and synaptic terminal effects. *J. Physiol.* 591, 2563–2578.
- Reijmers, L.G., Perkins, B.L., Matsuo, N., Mayford, M., 2007. Localization of a stable neural correlate of associative memory. *Science* 317, 1230–1233.
- Ryan, T.J., Roy, D.S., Pignatelli, M., Arons, A., Tonegawa, S., 2015. Engram cells retain memory under retrograde amnesia. *Science* 348, 1007–1013.
- Santo-Domingo, J., Demareux, N., 2010. Calcium uptake mechanisms of mitochondria. *Biochim. Et. Biophys. Acta (BBA)-Bioenerg.* 1797, 907–912.
- Savtchenko, L.P., Kulahin, N., Korogod, S.M., Rusakov, D.A., 2004. Electric fields of synaptic currents could influence diffusion of charged neurotransmitter molecules. *Synapse* 51, 270–278.
- Savtchenko, L.P., Poo, M.M., Rusakov, D.A., 2017. Electrodiffusion phenomena in neuroscience: a neglected companion. *Nat. Rev. Neurosci.* 18, 598–612.
- Schmidt, H., Hahn, G., Deco, G., Knösche, T.R., 2021. Ephaptic coupling in white matter fibre bundles modulates axonal transmission delays. *PLOS Comput. Biol.* 17, e1007858.
- Schroeder, C.E., Wilson, D.A., Radman, T., Scharfman, H., Lakatos, P., 2010. Dynamics of active sensing and perceptual selection. *Curr. Opin. Neurobiol.* 20, 172–176.
- Semon, R., Duffy, B., Lee, V., 2018. *Mnemonic psychology*. Routledge.
- Sherrington, C. (1951). *Man on his nature*.
- Singer, W., 1993. Synchronization of cortical activity and its putative role in information processing and learning. *Annu. Rev. Physiol.* 55, 349–374.
- Singer, W., Gray, C.M., 1995. Visual feature integration and the temporal correlation hypothesis. *Annu. Rev. Neurosci.* 18, 555–586.
- Sokalski, T., Lewenstam, A., 2001. Application of Nernst–Planck and Poisson equations for interpretation of liquid-junction and membrane potentials in real-time and space domains. *Electrochem. Commun.* 3, 107–112.
- Sweeney, H.L., Holzbaur, E.L., 2018. Motor proteins. *Cold Spring Harb. Perspect. Biol.* 10, a021931.
- Tedla, J.S., Sangadala, D.R., Reddy, R.S., Gular, K., Dixit, S. (2022). High-definition transcranial direct current stimulation and its effects on cognitive function: a systematic review. *Cerebral Cortex*.
- Teyler, T.J., DiScenna, P., 1987. Long-term potentiation. *Annu. Rev. Neurosci.* 10, 131–161.
- Tonegawa, S., Liu, X., Ramirez, S., Redondo, R., 2015a. Memory engram cells have come of age. *Neuron* 87, 918–931. <https://doi.org/10.1016/j.neuron.2015.08.002>.
- Tonegawa, S., Pignatelli, M., Roy, D.S., Ryan, T.J., 2015b. Memory engram storage and retrieval. *Curr. Opin. Neurobiol.* 35, 101–109.
- Tønnesen, J., Katona, G., Rózsa, B., Nägerl, U.V., 2014. Spine neck plasticity regulates compartmentalization of synapses. *Nat. Neurosci.* 17, 678–685.

- Traub, R.D., Dudek, F.E., Snow, R.W., Knowles, W.D., 1985. Computer simulations indicate that electrical field effects contribute to the shape of the epileptiform field potential. *Neuroscience* 15, 947–958.
- Tsien, R.Y., 2013. Very long-term memories may be stored in the pattern of holes in the perineuronal net. *Proc. Natl. Acad. Sci.* 110, 12456–12461.
- Vandenberg, L.N., Lemire, J.M., Levin, M., 2013. It's never too early to get it Right: a conserved role for the cytoskeleton in left-right asymmetry. *Commun. Integr. Biol.* 6, e27155 <https://doi.org/10.4161/cib.27155>.
- Velumian, A.A., Zhang, L., Carlen, P.L., 1993. A simple method for internal perfusion of mammalian central nervous system neurones in brain slices with multiple solution changes. *J. Neurosci. Methods* 48, 131–139.
- Vöröslakos, M., Takeuchi, Y., Brinyiczki, K., Zombori, T., Oliva, A., Fernández-Ruiz, A., Kozák, G., Kincses, Z.T., Iványi, B., Buzsáki, G., 2018. Direct effects of transcranial electric stimulation on brain circuits in rats and humans. *Nat. Commun.* 9, 1–17.
- Waldert, S., Pistohl, T., Braun, C., Ball, T., Aertsen, A., Mehring, C., 2009. A review on directional information in neural signals for brain-machine interfaces. *J. Physiol.* -Paris 103, 244–254.
- Weiß, I., Bohrmann, J., 2019. Electrochemical gradients are involved in regulating cytoskeletal patterns during epithelial morphogenesis in the *Drosophila* ovary. *BMC Dev. Biol.* 19, 22, 10.1186/s12861-019-0203-y.
- Widge, A.S., Miller, E.K., 2019. Targeting cognition and networks through neural oscillations: next-generation clinical brain stimulation. *JAMA Psychiatry* 76, 671–672.
- Widge, A.S., Boggess, M., Rockhill, A.P., Mullen, A., Sheopory, S., Loonis, R., Freeman, D. K., Miller, E.K., 2018. Altering alpha-frequency brain oscillations with rapid analog feedback-driven neurostimulation. *Plos One* 13, e0207781.
- Widge, A.S., Zorowitz, S., Basu, I., Paulk, A.C., Cash, S.S., Eskandar, E.N., Deckersbach, T., Miller, E.K., Dougherty, D.D., 2019. Deep brain stimulation of the internal capsule enhances human cognitive control and prefrontal cortex function. *Nat. Commun.* 10, 1–11.
- Yamada, K.M., Spooner, B.S., Wessells, N.K., 1970. Axon growth: roles of microfilaments and microtubules. *Proc. Natl. Acad. Sci.* 66, 1206–1212.
- Ye, H., Steiger, A., 2015. Neuron matters: electric activation of neuronal tissue is dependent on the interaction between the neuron and the electric field. *J. Neuroeng. Rehabil.* 12, 1–9.
- Yue, B., 2014. Biology of the extracellular matrix: an overview. *J. Glaucoma* S20.