Training the Conductor of the Brainwave Symphony: In Search of a Common Mechanism of Action for All Methods of Neurofeedback

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Abstract

There are several different methods of neurofeedback, most of which presume an operant conditioning model whereby the subject learns to control their brain activity in particular regions of the brain and/or at particular brainwave frequencies based on reinforcement. One method, however, called infra-low frequency [ILF] neurofeedback cannot be explained through this paradigm, yet it has profound effects on brain function. Like a conductor of a symphony, recent evidence demonstrates that the primary ILF (typically between 0.01–0.1 Hz), which correlates with the fluctuation of oxygenated and deoxygenated blood in the brain, regulates all of the classic brainwave bands (i.e. alpha, theta, delta, beta, gamma). The success of ILF neurofeedback suggests that all forms of neurofeedback may work through a similar mechanism that does not fit the operant conditioning paradigm. This chapter focuses on the possible mechanisms of action for ILF neurofeedback, which may be generalized, based on current evidence.

Keywords: EEG biofeedback, neurofeedback, electroencephalography, infra-low frequency [ILF], infra-slow oscillations [ISO]

1. Introduction

Neurofeedback is biofeedback for the brain. It is a method that developed out of research curiosity and demonstrated efficacy as a therapeutic modality for improving brain function, although it has taken more than half a century to gain some level of acceptability into the Western medical establishment. Now that it has gained some respectability as a therapy for symptoms of brain and mental health disorders, it is becoming increasingly important to develop a concise theory of the mechanism of action for how neurofeedback causes its effects. There have been many proposed mechanisms, but they are often very narrowly applicable to the particular method of neurofeedback discussed. Furthermore, some lines of investigation have provided evidence to suggest that most of the proposed, straightforward mechanisms are likely incorrect, which may actually explain some of the inconsistent results that have plagued the research literature. Thus, it is important to consider that there may be one overarching mechanism of action explaining how neurofeedback works, which takes into account and applies to all the various methods of neurofeedback.

In this article, several hypothetical mechanisms of action are presented, which were derived from the various methods of neurofeedback, from which a single hypothesis is proposed that attempts to incorporate all of the common features of the other mechanisms in order to more generally explain how all neurofeedback may work.

2. Neurobiology underlying mechanisms of neurofeedback

Since the field of neurofeedback essentially co-developed with our modern understanding of neurobiology, the neurobiological concepts underlying the mechanism(s) of neurofeedback that are presented here are as putative as the neurofeedback mechanisms, themselves. In many ways, the application of neurofeedback, itself, has helped to elucidate the underlying neurobiology. Therefore, it is important not to over-commit to any particular theory or hypothesis, since, in the future, after more information is revealed through rigorous scientific investigation, it may be proven wrong. Scientists must always be willing to pivot from one model to another and not hold too tightly to any piece of "knowledge". Herein, a non-exhaustive description of the current neurobiological foundations in which neurofeedback works to produce its effects are presented.

2.1 The brain as a prediction device

To understand how the brain works, it's necessary to consider some basic functions of the brain and the obstacles it needs to overcome in order to perform such functions. As we all know, the brain is how we perceive and function in our physical reality/world. Everything we are and do is controlled by the brain, such as sensory perception, motor activity (voluntary and involuntary), and cognition/executive functions. Those are the three basic forms of brain function, covering *everything* that we perceive and do. For example, the only way we know that there is a tree in front of us is because we see it (i.e. visual perception), we smell the bark and leaves (i.e. olfactory perception), and maybe we even touch it (i.e. tactile perception), which are all sensory percepts that are processed in the brain. Does that tree really exist outside of the brain? Well, of course, that's a question for philosophers. It's essentially the same question as: If a tree falls in the forest but nobody sees or hears it, does it really fall? Most of us would say, yes, but we have no way to "prove" it (not to mention that the concept of "proof" is also moot in science, but that's another topic), because that requires some sort of observation or exchange of information, which is lacking in the given scenario.

In order to perceive and function in the world, the brain must be able to take in the information from the environment via our senses, process it ("bottom-up processing"), make a decision on how to react, then implement that action (often involving motor output or "top-down processing") [1]. These processes are not instantaneous, but take time, which is a critical obstacle if a quick response is necessary, such as when a lion attacks or a child runs into oncoming traffic. Thus, the brain needs to overcome this relatively slow processing speed by not *re*-acting to the world, but *pro*-acting to it, or predicting it [1, 2]. Prediction is based on prior information about the regularities or patterns in the environment, and it is a key feature of brain function that helps create an accurate representation or model of the sensory environment and any actions required to navigate it [1].

One way in which the brain is able to make predictions is through constant, ongoing activities, such as waves of electrical potentials that are created by oscillations of local field potentials (LFPs) throughout neural networks in the cerebral cortex and subcortical structures, which commonly called brainwaves [3–5].

Anything cyclical or periodic is inherently predictive. While oscillatory activity lends itself easily as a mechanism for temporal prediction (i.e. predicting 'when'), it is also an effective mechanism for predictive coding (i.e. predicting 'what') [3, 6].

Another way in which the brain predicts future activity is through prepotent models of the sensory environment and prepotent models of actions that it forms based on patterns from past situations/scenarios/contexts from which it learned [2]. For instance, in the GO/NOGO task employed for the analysis of event-related potentials, the subject is instructed to press a button every time they see a target for the GO condition, for which the brain creates a prepotent model of the action of pressing a finger down on a button as soon as the target stimulus is presented [7]. Then, once the target is shown, that activity encoded in the prepotent model is easily and quickly performed without much effort since it was pre-planned. However, if a non-target is shown, instead, such as in the NOGO condition, the brain needs to actively put the brakes on that pre-planned action, which actually takes more energy than following through on that action [7, 8]. This brain function is called "response inhibition" and is carried out by the prefrontal cortex, which is primarily an inhibitory cortex, and the primary inhibitory neurotransmitter is gamma aminobutyric acid (GABA) [7, 8].

People whose prefrontal cortices are not fully developed, such as children, teenagers, some young adults, and those who have been diagnosed with attention deficit/hyperactivity disorder (ADHD), have difficulties with response inhibition [7]. These difficulties may manifest in impulsive behaviors, compulsive behaviors, obsessive thoughts, inappropriate remarks or behaviors, etc. [7]. A couple of other examples of brain dysfunction that shed light on the ongoing functions of the brain are automatisms and alien hand syndrome [9, 10]. Automatisms are behaviors that sometimes occur during an epileptic seizure where a set of motor behaviors occur in a particular sequence without conscious thought or agency but may appear purposeful, except for the fact that they do not achieve any particular function and the individual is usually in an altered state of consciousness [9]. Most of the time, those of us who have excellent functioning prefrontal cortices are able to inhibit automatic behaviors that do not have a purpose, but sometimes, particularly when inebriated with mind-altering substances, the brain becomes disinhibited, allowing these behaviors to come out [11].

Alien hand syndrome is probably one of the most fascinating phenomena that reveals brain and body function in a unique and strange way. Some people with intractable epilepsy have surgery that severs the connection between the two hemispheres of the brain – these people are often called "split-brain" patients [12]. Some of these "split-brain" patients, or others who have had a stroke or some other injury or insult, have severed connections between the pre-supplementary motor area (pre-SMA), the anterior and medial cingulate cortices (ACC and MCC), and the sensorimotor cortex (SMC) in either hemisphere [10, 13, 14]. This severance releases the hand contralateral to the SMC lesion from conscious, voluntary control, allowing it to behave as if it has a mind of its own [10, 13, 14]. What is particularly interesting is that this usually does not mean that the hand does nothing and just sits listlessly at the side of the person. Instead, the hand literally behaves as if it has a mind of its own, revealing what a hand would do if it was not told to stop – that is, to grab or clutch [13, 14]. A hand without conscious control will grab anything it "sees" (although it does not actually "see", but since the feedback connection between the visual cortex and the SMC is not severed, information from the visual cortex can directly drive hand motor action since it cannot be inhibited by the dominant prefrontal cortex), such as a glass, a pencil, or even a woman's breast (if you are someone who likes women's breasts) [14]. One of the only ways to get the alien hand to stop grabbing things is to put something in it to hold so it is occupied and unable to grasp anything else [10].

2.1.1 Feedback as general mechanisms of learning and neuroplasticity

A second major characteristic of the brain is its ability to learn and adapt. The neurobiological mechanism of learning is called neuroplasticity, which means that the brain changes – it's considered malleable like plastic, as opposed to something that cannot change easily, like a rock or metal. Learning requires information to be remembered, but it also requires error correction to make sure that the information retained matches the information taught. It is also the mechanism by which we fine tune our performance, which is just another form of learning. For instance, in order to walk, we must move our legs, but in order to know that we are walking, we must get information from our feet that they have met the ground and maybe also from our eyes to see it touch the ground. If all of these bits of sensory information agree they are then integrated together in a feedback loop with the motor action to confirm that what was pre-planned (the motor activity of taking a step) is what actually occurred. This mechanism of feedback is called the sensorimotor loop and is a form of predictive processing, which is a primary mechanism by which the brain is able to respond to the environment and self-correct when errors or perturbations occur [2–5].

Based on feedback loops, predictive processing can be considered a strategy of control systems [2–5]. If the body is a collection of bodily systems, the brain is the control system, defined as a stable system in which its elements interact to preserve stability for both internal control and response to perturbations from external sources [4, 5]. Control systems are characterized by feedback loops, which can either be closed or open [4]. Negative feedback loops in closed systems create oscillatory activity, which are generated in the brain by coupling excitatory and inhibitory neuronal activity in circuits [4, 5]. These oscillatory activities, which can be measured in LFPs, regulate the excitability of the cortex, which regulates the ease with which long-term potentiation (LTP) or learning can occur [15].

A key aspect of learning (i.e. neuroplasticity) is timing. Learning, which requires memory formation, occurs through LTP and is primarily established through spike-timing dependent plasticity (STDP), the conventional form of which is through Hebbian plasticity [16]. Nearly all of our synaptic connections are weakly formed in the first two years of life [17]. After this period of neurogenesis and synaptogenesis, our brains go through nearly two decades of experience-dependent synaptic strengthening and both experience- and neglect-dependent synaptic pruning [17, 18].

According to Hebb's postulate, the strengthening of a synapse requires the precise timing of the activation of two neighboring synapses on the same post-synaptic neuron such that a pre-synaptic signal from the weak synapse is quickly followed by a stronger, post-synaptic signal (coming from an established synapse upstream of it), causing the weaker synapse to appear to co-fire with the stronger synapse, linking them to create an action potential that propagates down the neuronal axon [19, 20]. The timing of these coordinated signals must be very precise, such that the signal from the pre-synaptic neuron into the weak synapse must fire within milliseconds (ms) (generally around 20–40 ms) before the stronger, established synapse on the post-synaptic neuron fires in order for LTP to occur [21]. If the post-synaptic neuron fires first, however, long-term depression (LTD) can occur, which further weakens the synapse, ultimately resulting in synaptic pruning [21]. The typical timeframe for LTD requires that a spike from the presynaptic neuron reaches the weak synapse within 20–40 ms after the spike from the postsynaptic neuron [21]. To complicate the matters, different neuronal populations in different brain regions have their own specific temporal patterns of STDP [16]. The brainwave most frequently implicated in LTP and memory formation is the theta (θ) band [15], which

has a phase-amplitude cross-frequency coupling with the gamma (γ) [22] band in the hippocampus. This θ-γ coupling is believed to play complementary functions in memory formation: θ oscillations are involved in encoding whereas γ oscillations (which form ripples) are involved in consolidation [23].

2.1.2 Functional networks

Due to technological advances in imaging, neuroscience has grown exponentially in the past few decades. Using a technique called functional magnetic resonance imaging (fMRI), researchers identified networks of metabolic activity in the brain that work together at the same time (i.e. synchronously) over spatially distant regions, which are connected via white matter tracts [24–27]. These networks are called *functional networks*. Furthermore, there are both task-positive and task-negative networks (a.k.a. resting state networks), meaning that some networks are associated with some sort of voluntary endeavor or task whereas other networks are not associated with a particular activity but are active during times of "rest" or non-directed thought [27]. Eventually, researchers discovered that many of these resting state networks are shared with task-positive networks, with one exception, the default mode network (DMN), which will be discussed in more detail later [25]. Researchers were surprised to see that functional networks continue to be active during times of rest, but those of us who have thoughts streaming through our heads nonstop already knew this about our brains! Even those who do not have thoughts constantly streaming through their brains, however, also have resting state network activities. In fact, the only time when the brain does not seem to be flowing through different functional networks is during states of unconsciousness, or at least the networks during unconsciousness show less connectivity, and the dynamics between networks are slower [28]. The brain continues to switch between resting state networks even during sleep, which is an altered state of consciousness, although their dynamics are also slower than during wakefulness, but not as slow as during unconsciousness or coma [29].

The key aspect of fMR imaging, which differentiates it from regular MR imaging, is the additional signal analyzed, which is the blood oxygen level dependent (BOLD) signal that causes the magnetic resonance to shift in intensity by approximately 1% depending on oxygen-rich or oxygen-poor blood in the region [24, 25]. Essentially, the premise of fMRI that gives it its functionality is the notion that where there is oxygen-rich blood in the brain neural activity is occurring. Furthermore, the BOLD signal fluctuates or oscillates at a typical frequency which is between 0.01–0.1 Hz, or one cycle per every ten seconds to one cycle every 100 seconds [24, 26]. This frequency is the same as the primary infra-low frequency (ILF) that can be measured by electroencephalography (EEG) [26, 30, 31].

Each publication on resting state functional networks seems to characterize a different number and general description of networks, although some networks appear to be consistent across reports, such as the dorsal and ventral attention networks (DAN; VAN), the central executive network (CEN), the salience network (SN), the basal ganglia/limbic network (BGLN), and a series of sensory-related and motor networks [27, 32]. The most consistently characterized network in all reports is the DMN, making it the network in which the brain spends most of its time and energy [30]. The DAN, VAN, CEN and sensory- and motor-related networks are all considered "task-positive" networks as they are associated with specific attentional, executive, sensory, and motor tasks, but they have also been detected at times of rest, as well [26]. The DMN, however, is exclusively associated with times of rest and relaxation, self-reference, and projecting into the mind of others (i.e. "theory of mind"), which are all considered part of the "core self" [30, 33, 34]. The DMN

has particular significance in the mechanism of neurofeedback, and its role may be to integrate the self with the three-dimensional body and world in which it inhabits [30, 33, 34].

2.1.2.1 Inter-network dynamics

These functional networks break up into two basic systems of internally-focused (i.e. the DMN) and externally- or task-focused (the so-called "task-positive networks, which essentially refer to all of the other networks) [26]. Since these networks are very dynamic, even at rest, their very characterizations have been relatively elusive, depending heavily on statistical analyses of correlated activities at different nodes or hubs [24]. The characterization of the DMN, however, seems to have great consensus among researchers, revealing it as probably the most important network, which anti-correlates with all of the other networks with little exception [26, 35]. This anti-correlation means that when the DMN is activated, the task-positive networks are deactivated or inhibited [26, 30, 35].

Studies on network inter-dynamics suggest preferential directionalities in these dynamics where certain networks tend to be activated before or after other networks and how different networks modulate the activity of other networks [35–38]. Specifically, the DMN and the SN regulate switching between internally-generated, self-referential/self-focused processing (in the DMN) and externally-generated information processing (such as from the senses) or other cognitive functions that are not self-focused or self-referential (such as math, reading, etc.) in the attention networks, the sensory networks, and the executive networks, etc. (i.e. the "task-positive" networks) [38]. Some of the same network hubs that overlap between the DMN and the SN are also part of the executive networks, which make their differentiation somewhat ambiguous, but both models - where the DMN interacts exclusively with the SN and where the DMN interacts with both the SN and the executive networks – reflect the same underlying mechanism whereby the SN regulates switching between the DMN and task-positive networks, including executive functions [37]. Furthermore, both models make intuitive sense when considering that when you are internally focused you cannot also be externally focused since these are mutually exclusive states.

Network dynamics may be a good neurophysiological measure of neuroflexibility, which can manifest as cognitive and behavioral flexibility, particularly for networks involving the frontal lobes [39]. The level of dynamic switching between networks and their interactions also appears to be more strongly correlated to conscious processes, as opposed to intra-network connectivity, alone [28]. Greater dynamics in functional connectivity correlates with better behavioral responses and results in cognitive tasks, as well as better mental health [40–43]. These results imply that a more flexible brain, one which easily engages and disengages in brain states, is a better functioning brain.

The variation in network participation at inter-network hubs correlates with retrospective self-generated thoughts, which are considered correlates of unhappiness and are precursors for a negative mood [44]. This variation in membership at inter-network hubs, as well as the stability of densely interconnected nodes (considered to be the 'rich club') diminish with age [44–46]. This reduction in network modularity with age suggests less distinct functional divisions between networks, resulting in less information sharing and processing across networks [46]. Furthermore, there are specific changes in inter-network dynamics which also change with age, but the developmental trajectories are specific to the particular interacting networks and may also be specific to certain functions that depend on the particular activities and interests of the individual over their lifetime [45, 47].

2.1.3 Glial cells

Neurons get all of the attention when it comes to the brain and the nervous system, but they can only do what they do because glial cells provide protection, nutrients, neurotransmitters, insulate axons (creating myelin), assist in synapse formation and remodeling, protect against foreign attack, clean up extracellular debris, maintain structural integrity of the tissue, etc. [48–50]. The ratio of glial cells to neurons in the human brain has typically been reported as anywhere from 4 to even 50, although these numbers are inaccurate due to the region-specific ratios, while total numbers of neurons and glia have a ratio of nearly 1:1 [51]. Despite the variability in these regional ratios, an argument could be made that glial cells, as opposed to neurons, are the most important cells of the brain.

The term, *glia*, is derived from the Greek word meaning glue, and reflects the original function that these cells were believed to do, which was essentially holding neurons together in the brain like glue [48, 49]. In recent years, however, scientists have discovered that these cells provide substantially more functions than just structural integrity of the brain. For instance, astrocytes or astroglia, which are named for their star shape, help create and maintain the blood brain barrier, regulate the formation, maturation, maintenance, and stability of synapses, and regulate specific neuronal network activities through the inhibition of local, non-specific activities [18, 52, 53].

Astrocytes, in fact, play a central role in regulating neuronal activity through metabolic coupling and neurotransmitter recycling [52]. Through their foot processes that wrap around the endothelium of the capillaries and their intimate contact with synapses (creating the *tripartite synapse*), astrocytes play crucial roles in neurovascular coupling [54]. This coupling allows astrocytes to regulate the metabolic activity of the neurons associated with these synapses through the release of ATP, as well as the removal of metabolites and the recycling of ions and neurotransmitters into the synapse [52, 53].

Recent studies on astrocytes have revealed their heterogeneity in the human brain, which may be as diverse as all of the different neural circuits and networks [55, 56]. In fact, astrocytes are implicated in the development, plasticity, and function of neural circuits [18]. Furthermore, astrocytes have bioelectrical properties that are created by calcium fluctuations across its membrane, which couple with neuronal firing and are likely the source of LFPs, which create the brainwaves that can be detected by EEG [57, 58].

The two other glial cell types in the central nervous system, microglia and oligodendrocytes, play important roles in neurodevelopment, neuronal signaling, neuroplasticity, and neuroprotection [49]. Oligodendrocytes create the myelin sheath on neurons, allowing for faster and more efficient propagation of the action potential down the axon, while microglia are critical for neuroprotection as the resident phagocytic immune cells of the brain [49]. Microglia also play critical roles in neurodevelopment and neuroplasticity (particularly during synaptic pruning), and their dysfunction is implicated in the etiology of many neurodevelopmental disorders and neuroinflammation [59]. Despite the critical functions that these cells play in the brain, no significant and/or unique roles have been ascertained for them at this time in the possible mechanisms of neurofeedback.

2.2 Clinical benefits of neurofeedback training

There have been many reports on the clinical benefits of neurofeedback training but describing in detail all of the studies on the efficacy of different neurofeedback methods in improving the multitude of brain-related symptoms reported in the

literature is beyond the scope of this chapter. Therefore, the reader is referred to some recent reviews of the subject [60–64]. Briefly, a general description of neurofeedback effects that modify different symptoms are presented here.

2.2.1 Seizures

The first clinical effect of neurofeedback was the reduction of seizure incidence, duration, and severity in cats, which was then recapitulated in humans [65–67]. This original protocol, which trains the so-called sensorimotor rhythm (SMR), which was originally developed for cats, is still used for the treatment of seizures in humans today, but the seizure-reduction benefits are not exclusive to that method and can be achieved using other forms of neurofeedback, as well [63, 68, 69]. Furthermore, the method is generally the same no matter what kind of seizures the subject has, including psychogenic non-epileptic seizures (PNES), unless it's a focal seizure, which could require specific electrode placements to target the focus [68, 69, personal experience].

2.2.2 Attention/focus

Most of the research in the field of neurofeedback has centered around its benefits for improving executive functions in people who have been diagnosed with ADHD [60, 65, 66]. In fact, in 2013, the American Association of Pediatrics endorsed neurofeedback at level 1 effectiveness for the treatment of ADHD, which is the same level endorsed for ADHD medications [70]. Due to the fact that the literature is over-saturated with these reports on the efficacy of neurofeedback for ADHD, the reader is directed to some excellent, recent reviews [71–73]. The main point is that neurofeedback has been used to improve symptoms of ADHD, particularly executive dysfunctions such as inattention and difficulty shifting tasks, etc., but also hyperactivity and impulsivity [71–73]. Improving symptoms of ADHD, however, is merely the tip of the iceberg of what neurofeedback training can achieve.

2.2.3 The multitudes of symptoms improved by neurofeedback

It's truly difficult to describe all of the symptoms, behaviors, and other effects that neurofeedback has affected, and even more difficult to show evidence of these effects via randomized, controlled trials (RCTs), which are the gold standard for determining evidence-based practice in our Western healthcare system. However, despite the challenges of designing, obtaining funding, implementing, then publishing such studies, the field of neurofeedback has continued to progress due to the very real benefits that clients continue to gain from it, spreading the word to others who then try it and also witness its benefit [74, 75]. Of course, the issue is that this method of utility and expansion of the field is unsustainable in a healthcare system dependent on insurance where insurance will only pay for what the Western medical establishment considers evidence-based practice.

Clearly, evidence-based practices are ideal in order to demonstrate efficacy and build trust in the field, but the only way to get evidence is to practice. It's been a bit of a Catch-22 to reach the level of evidence-based practice when grant lending agencies have been reluctant to fund studies in the field of neurofeedback, but in order to get funding, the clinicians need to establish some level of efficacy of the practice to recruit enough subjects for the gold standard RCTs. In the meantime, the clinicians have done their best on their own to optimize neurofeedback for its benefits to their clients in the absence of funding for these gold standard studies [66, 74, 75].

In addition to its benefits in reducing seizures and improving ADHD symptoms, some of the multitude of benefits of neurofeedback training are reductions

in headaches, migraines, anxiety, irritability, post-traumatic stress symptoms, etc., and improvements in sleep regulation, pain management, mood, peak performance, etc. Most of these effects have been documented in case studies and/or experimental trials that are less rigorous than RCTs [61–63, 74, 76]. Essentially, any function of the brain can be modulated using neurofeedback, which theoretically means that everything we do, think, and feel can be improved using neurofeedback.

3. A very brief history of neurofeedback

Neurofeedback originated as EEG biofeedback and developed nearly at the same time as EEG, itself, beginning in the 1930s with Hans Berger and his colleagues toying around with this new machine to watch how their brainwaves changed with different perturbations [60, 65, 66, 77, 78]. However, neurofeedback as a therapy did not start until the 1960s after Barry Sterman discovered that neurofeedback training could protect cats against jet fuel-induced seizures [67]. Around the same time, another scientist, Joe Kamiya, was also conducting neurofeedback using alpha (α) training, which he found was able to reduce anxiety [77, 78]. After publishing an article about his experience with α training, public awareness and interest was piqued, so more people decided to try it out. Some people who tried α training had a spiritual experience, which is great for them, but, unfortunately, it did not bode well for the reputation of the emerging field of neurofeedback since the spiritual effects were seen as contrary to true medical treatment or therapy [66, 77, 78].

Although the remainder of the history of neurofeedback is quite interesting and provides a good background for why the field is so divergent today (primarily due to in-fighting between pioneering researchers), it is not within the scope of this article to present. Therefore, the reader is directed to many other resources where they might find a history of the field [65, 66, 77, 78]. The main points here are that neurofeedback began as EEG biofeedback, which developed out of pure curiosity about how one might be able to control their brainwaves through visual feedback of their activities, and the original methods that were developed were α training and SMR/beta (β) training.

3.1 A very brief history of electroencephalography

Neurons communicate quickly through electrical impulses that travel down long axon tails, ending at a synapse, which is where the electrical signal changes to a chemical signal between neurons [19]. Neurons can also communicate directly through electrical synapses, as well, although this is not as versatile of a signal (i.e. it cannot be regulated to the same degree as a chemical signal) [19]. We can detect the electrical signal in the brain using EEG, which is a technique that detects changes in electrical potential via electrodes that are placed on the scalp [7]. Since the electrodes are several millimeters away from the cerebral cortex, and their surface area is thousands-to-millions of times larger than the surface area of a single neuron, they are actually picking up the summed electrical field potentials from millions of neurons and their surrounding glial cells, both cell types of which can establish an electrical potential across their membrane [7, 52, 57].

Hans Berger was the first person to publish an article with the first human EEG in 1929 [65, 77, 79]. After placing an electrode on the back of the head, Berger observed a wave of electrical potential with an approximate frequency of ten cycles per second or 10 Hertz (Hz), which he coined as α waves [60, 77, 79]. After this initial discovery, several other brainwave bands were discovered, which will be discussed in more detail in the next section [77].

3.1.1 Brainwaves

As mentioned in the previous section, the invention of EEG led to the discovery of ongoing electrical oscillatory activity in the brain, which could be detected using electrodes placed on the scalp. Following the discovery of α waves, β waves (≥ 13 Hz) were then discovered, then delta (δ) waves (1–3 Hz), and θ waves (4–7 Hz) [77]. γ waves are a subset of very high β waves (> 30 Hz) [79]. Collectively, we have dubbed these *brainwaves* [57]. These brainwave bands show specific patterns of activity at specific times, locations, and during specific brain activities, although their precise functions are not abundantly clear [57, 79]. Furthermore, the origins or oscillators that generate the brainwaves are also not very clear or easily defined, although studies suggest key oscillatory roles for the thalamus, the reticular activating system (RAS) of the brainstem, and specific layers of pyramidal neurons and astroglia in the cortex [57, 79, 80].

Characterizations of the classic brainwave bands are primarily derived from sleep studies and studies of patients with epilepsy [81]. Early neurofeedback studies also attempted to functionally characterize these brainwave bands, but their functional characterization has been elusive due to the promiscuity of associated activities [57, 79, 81]. One intriguing theory posits that the different brainwave bands are evolutionarily related and similar in categorization as the *triune* model of brain structure and function [82]. In this model, δ oscillations are analogous to the brainstem's basic functions, representing the evolutionarily oldest structures and functions of the brain, while θ and α oscillations are analogous to the limbic system and basal ganglia, dominating in lower mammals, and the fastest brainwaves, β and γ, are analogous to the neocortex, which is the evolutionarily newest structure with associated functions such as higher order cognitive processing and self-awareness [82]. Although this model is very intriguing, it remains to be substantiated with experimental evidence.

A more complex picture of brainwave activities has emerged in recent years that describes different ways in which brainwaves interact with each other through cross-coupling [22]. Much like functional networks, researchers discovered different coupling patterns in ongoing activity that spatially organize in networks similar to and often overlapping with the intrinsic functional networks that were discovered by fMRI [22]. These intrinsic coupling modes (ICMs), as they have been dubbed, demonstrate more precise correlations with function than single brainwave bands, indicating a much more richly complex structural and functional architecture to the electrophysiology of the brain [22]. For example, a specific difference in visual perception – whether two lines appear to bounce away from each other or pass through each other – correlated with the percentage of coherence in a β phase ICM in specific visual processing regions (i.e. those with higher β coherence perceived bouncing, whereas those with lower coherence perceived passing) in a study using the bounce-pass paradigm [83]. Delineating function to specific brainwave bands is challenging because: (1) the function can be highly specific, which means each specific brain function would require definition by experimentation, (2) each brainwave band is associated with many different specific functions with little generalizability between them, and (3) functions of brainwaves are spatially and temporally specific, and may be specific to certain cross-frequency couplings [22, 57, 79].

3.2 Modern neurofeedback

Today, there are many methods of neurofeedback using different technologies, data, and protocols (for some reviews, see [61, 63–65, 84]). Different researchers group the methods in different ways. For instance, some researchers group the

methods according to their neuroimaging technology (i.e. EEG or fMRI) [75]. Other researchers group the methods according to the temporal structure of the data, such as methods that use *discrete* events (e.g. frequency training, fMRI, etc.), in which there are periods of target activity and periods of rest, and methods that use *continuous* "events" (e.g. ILF), in which the target signal is continuous and the goal is not necessarily to modulate its activity [65]. Two general categories of methods have emerged in the field of neurofeedback, those that employ a *directive*, operant conditioning approach, which require explicit awareness and learning by the subject, and those that are *non-directive* in nature, employing a passive approach, which only require *implicit* learning of self-regulation of which the subject is likely unaware [84, 85]. The directive methods are the most abundant and commonly used neurofeedback methods, and the theories behind them are the easiest to understand and explain. Thus, the directive methods are presented first.

3.2.1 Directive methods

Directive methods of neurofeedback refer to the methods that require the clinician to *direct* the subject to consciously control specific brainwaves by learning what it feels like to modulate the brainwaves during the session. These methods have also been called *explicit* methods of neurofeedback, which refers to the fact that the subject learns to become consciously aware of their brain states [84]. The purpose of the directive methods is to learn to voluntarily regulate specific brain activities and, by reinforcing them, these specific activities increase, altering the pattern of brain activity. Thus, there are two outcomes for directive methods of neurofeedback: (1) how well the subject *learned* to regulate their own specific brain activities, and (2) improved symptoms and behaviors [84, 86].

These directive methods are based on assumptions of how the brain *should* work, using these assumptions to tell the brain what it needs to correct and how to correct it, using an operant conditioning model to "fix" the broken brain. Developed by the pioneering behaviorist, B.F. Skinner, operant conditioning is a method of learning that is based on positive reinforcement and punishment or rewards and inhibits, respectively [87]. When the subject does the desired behavior or learns the desired skill, then they receive some sort of reward, which may or may not have anything to do with the new behavior or skill. Since the reward is desirable, the subject will then repeat such behavior or skill with greater frequency. The behavior or skill is considered learned when the subject can perform it even without the reward. The original neurofeedback methods and most methods still employed today use this operant conditioning model to both direct the procedure as well as to explain how neurofeedback works [61, 64].

3.2.1.1 Conventional EEG-based training

As mentioned previously, the original neurofeedback training protocols used operant conditioning to train the brain to modulate the power of conventional EEG bands, such as the SMR, which is in the low β band, and α training [65]. These protocols continue today, but now they have expanded to include more brainwaves and different properties of the EEG, such as coherence (also called "synchronization") and phase [63]. With the development of quantitative EEG (QEEG) methods, where a cap of 19 electrodes on the head records all channels simultaneous and the activities in each region can be quantitatively compared to others, databases have been created using both normative data from healthy controls as well as comparative data from brains with different symptomologies and diagnoses [7, 74]. These databases can be used as a resource to determine the significant differences between

a subject's QEEG activity and that in the normative database, providing a statistical score called a "z-score", which indicates how significantly different the activity is and in what direction (i.e. increased or decreased) [7, 74]. Some methods utilize this resource as part of their protocol to train the brain closer to the norms, presuming that the most common QEEG patterns are preferred for better functioning [60, 61, 63, 88, 89]. These additional methods are discussed briefly in this section, although full and complete descriptions are not within the scope of this article and the reader is directed to the previously mentioned review articles and their references within for a more in-depth understanding.

3.2.1.1.1 Frequency training

As mentioned, there are a plethora of conventional EEG-based neurofeedback protocols. These protocols range from single frequency trainings to whole frequency-band trainings to two or more frequencies or frequency band trainings at the same time, etc., training in different directions –"up" or "down" - meaning increasing or decreasing the power and incidence of that frequency or frequency band [61, 62, 64]. Sometimes the protocols are designed based on differences in the QEEG from the normative database, while other times the protocols are determined based on symptom presentation [7, 60]. Some classic frequency training protocols are SMR for epilepsy, as previously mentioned, but also for ADHD, α-θ training for trauma reorganization, midline θ training and θ/β training for focus/concentration, as well as training each individual conventional EEG band for various conditions [7, 60–64, 74].

3.2.1.1.2 Other EEG-based methods

As mentioned at the top of the section, other EEG-based methods of neurofeedback use different aspects of the EEG data to train the brain. For instance, QEEG-based training uses z-scores as the substrate for the feedback, where the brain is rewarded as the QEEG pattern normalizes closer to a z-score of 0 [60, 61, 63, 88, 89]. The issue with this method is that it presumes that the most common QEEG patterns in healthy individuals reflects the best, most optimal pattern of brain function. However, just because something is typical or common does not mean it is the best. In fact, one might hypothesize that anyone who has an exceptional brain, maybe with a very high I.Q. or great talent, might also show differences from the norms – quite possibly significant differences, in fact – but we might presume that these particular differences confer their exceptional abilities as opposed to pathology.

Another method that uses a full cap of 19 electrode placements is low resolution electromagnetic tomography [LORETA] training [61, 75, 88]. LORETA is a method by which QEEG data is analyzed using blind source separation methods like independent component analysis (ICA) to localize the neural source of the signal in the brain and projects that source onto a three-dimensional map of the brain, including subcortical nuclei [7, 88]. The EEG substrates that can be monitored via LORETA are EEG band power, coherence, and/or phase, as well as z-scores [60, 61, 90].

Low-energy neurofeedback system (LENS) is another method of neurofeedback based on EEG data, but it diverges from all other methods in that it actually delivers a very weak electromagnetic pulse into the subject's brain while they lay motionless with their eyes closed [61]. LENS is a very quick treatment and does not require months of sessions, but it is the only neurofeedback methodology that activity adds an exogenous signal to the subject, so it may be considered less "non-invasive" than the other techniques [60]. The basic hypothesis behind LENS is that it perturbs the

brain's typical activity by delivering the weak electromagnetic pulse in order to get it "unstuck" [60].

3.2.1.2 Hemodynamics-based training

Since neuronal activity is tightly coupled to hemodynamics (blood flow), several forms of neurofeedback use hemodynamics as a measure of brain activity in specific regions of the brain as substrates for feedback [61, 63]. The most well-known method is fMRI training, which monitors the BOLD signal in brain structures with high spatial resolution [91–93]. Other hemodynamic-based methods that are less well-known are hemoencephalographic (HEG) training and functional near-infrared spectroscopy (FNIRS) training, which have less spatial resolution than fMRI but greater than that of EEG [67, 94, 95]. FMRI neurofeedback has the greatest number of gold standard RCTs, likely due to the fact that the principal investigators on those studies typically are medical doctors and tend to receive more funding than non-medical doctors [91, 93].

3.2.2 Non-directive methods

Non-directive methods of neurofeedback, which have also been called *implicit* neurofeedback, do not rely on directions from a clinician to the subject, nor do they rely on the subject to consciously regulate their brain activity [84, 85]. In fact, the subject does not need to do anything to receive the benefits of these methods of neurofeedback as they are entirely passive processes. These methods have only been in development over the past 10–15 years or so, partly due to their dependency on technological advances of the neurofeedback equipment and software [65, 96, 97].

3.2.2.1 Infra-low frequency training

ILF training grew out of conventional EEG frequency training [65, 74, 76, 97]. It is based on rewards and inhibits, which are aspects of conventional EEG frequency training, but these concepts no longer make sense at such low frequencies (the current Cygnet software, version 2.0.7.4, can now filter out frequencies as low as 0.0001 mHz, which is approximately one cycle per 116 days). Even though there are biorhythms that are as slow and slower than the current limit of detection by this EEG amplifier [95], there are no known neural or glial origins of these very slow oscillations, causing controversy over the source of the signal [65, 76, 97]. However, a recent study demonstrated that 20 sessions of ILF neurofeedback training increased the power of all of the ILFs (≤ 0.1 Hz), including the typical peak around 0.01–0.1 Hz, which is called the infra-slow oscillation (ISO) and correlates with the BOLD signal [98, 99].

One of the differences between ILF and conventional EEG training is that ILF training cannot work through an operant conditioning model since there are no discrete events to reward [65]. Interestingly, though, there is a complex multi-frequency band algorithm of inhibits that follow the individual subject's regular pattern of EEG activity using thresholds that reset moment-to-moment to allow for approximately 95% success rate (which can be modulated in the software) of the signal remaining below the threshold [100, 101]. The inhibits are a summation of over-threshold signals from the different conventional brainwave bands, causing the screen to gray out and the sound volume to reduce, which essentially tells the brain not to make any sudden moves or EEG spikes [100, 101]. These inhibits, therefore, function to stabilize brain activity while the "reward" or training frequency provides continuous information on cortical excitability.

3.2.2.2 Dynamical neurofeedback (i.e. NeurOptimal®)

The final method of neurofeedback that requires some mentioning due to its proliferation in recent years uses a nonlinear dynamical approach and is implemented with equipment and software called NeurOptimal® [102]. Unfortunately, there are no peer-reviewed publications that describe this method and only a very few publications were found of studies using it [103, 104]. Thus, it is hard to describe this method due to the fact that the details on what it is are murky and based entirely on non-peer-reviewed content on the NeurOptimal® website [102]. Descriptions of the method, however, suggest a similar form of training as described for the inhibits used in ILF neurofeedback in the previous section.

Based on theories developed by Val Brown, who originally came up with a five-phase model of neurofeedback training [105], and empirical experimentation performed by his wife, Susan Cheshire Brown, NeurOptimal® claims to train neural dynamics by providing feedback information on how these dynamics change [102]. This information is obtained through threshold boxes on either filtered or fast Fourier transformed EEG frequency bands that set both a minimal and a maximal power for each (several frequencies or frequency bands are monitored at once), and violations of these threshold boxes drive the feedback [102]. Essentially, when the signal power is outside of the threshold box, it causes the sound to reduce or stop in a manner to inhibit this change in activity [102]. Due to neither training frequencies directly "up" or "down", the creators claim that this method of passive observation of sudden activity changes is 100% safe and has no adverse effects [102]. However, this method requires substantially more research to verify its effects and more transparency in its process to allow other researchers to investigate its potential mechanism of action, as well.

4. Hypotheses for the mechanism of action of neurofeedback

These different methods of neurofeedback have led to the development of different hypotheses for how neurofeedback works to improve brain function. It is possible that different methods of neurofeedback work through different mechanisms to produce their effects, but the simplest model would be that all neurofeedback methods work through the same or a similar mechanism of action. Thus, the true mechanism of action of neurofeedback has yet to be determined and collectively confirmed. Here, several general hypotheses based on different methods of neurofeedback are presented, then the common denominator(s) of these hypotheses is discussed more thoroughly as a possible true underlying mechanism of action of neurofeedback, awaiting experimental designs to test and confirm its validity.

4.1 Hypotheses from directive methods: operant conditioning

Directive methods of neurofeedback, which use operant conditioning, rely on the clinician's assumptions about what is wrong with the subject's brain and how to fix it. This seems like a tall order, but it is the primary paradigm by which the Western medical establishment operates. Medical doctors spend four years of their education memorizing everything there is to know about the body, what goes wrong, and how to fix it. Thus, this same paradigm has been applied to neurofeedback with varying success.

The problem with this "clinician knows all" paradigm, however, is that it does not leave room for the unknown. In general, when a medical doctor cannot find anything "wrong" with a patient using any of their tests, they tell the patient that

there's nothing wrong and that whatever is happening to them is psychological or psychosomatic. There are even fancy terms for findings that the doctor cannot explain, such as "idiopathic", which just means that the doctor knows that there's a problem, but no one knows what it really is. Another issue with this paradigm is that knowledge changes and what if what we thought we knew for sure turns out to be wrong or at least sufficiently incomplete? In that scenario, whatever the doctor or clinician says and/or does based on this faulty knowledge will either have little to no benefit or may even be harmful for the patient. Of course, this scenario has happened in the past, as well – for example, there was a time when doctors recommended smoking cigarettes as a treatment for asthma [106], but now we know that smoking cigarettes is not only *not* healthy, but actually harmful, hastening disease and death.

There are basically two types of directive methods, those based on brainwave frequency information and those based on blood flow or BOLD activity. In general, brainwave data has high temporal and low spatial resolution whereas blood flow or BOLD data has high spatial but low temporal resolution [107]. However, blood flow and BOLD data are more directly and generally associated with overall brain activity in a region, while all regions of the brain have some sort of brainwave activity at all times, so the level and type of brain activity visualized in the EEG is differentiated by the particular brainwave frequencies, their amplitudes, and their cross-frequency coupling [22, 79]. Understanding the functional meaning of brainwaves in any region at any point in time has been the focus of much research for decades and remains incomplete and somewhat ambiguous [22, 57, 79, 81, 108]. Thus, neurofeedback that is based on the functional meaning of specific brainwaves identified from specific locations on the scalp remains controversial due to the controversial and non-consensus nature of the underlying science.

4.1.1 Fixing bad brainwave patterns

The first and primary hypothesis of EEG biofeedback is based on the idea that there are normal and healthy patterns of brainwave activities during rest and/or tasks and that mental illness is caused by abnormal brainwave patterns [7]. There is evidence that certain brainwave patterns, either at rest or during a task, are associated with specific symptoms and mental disorders, but their causal roles are far from established [7, 109]. Due to the fact that altering these brainwave patterns has shown moderate success in diminishing such symptoms, these hypotheses have gained some traction in the biofeedback field [7, 63]. However, there are alternative explanations for the success of the neurofeedback that are not consistent with the hypothesis of a causal role for "bad brainwaves" in symptoms of mental illness.

One hypothesis that has driven much of the neurofeedback field for use in improving attention for people with ADHD is that β waves are associated with focus and attention [7]. Although this hypothesis is likely true at times since β waves do correlate with both activating (i.e. glutamate-mediated) and inhibiting (i.e. GABA-mediated) neurotransmission [7], it is not always the case that β activity reflects a focused or attentive brain. β activity has also been associated with anxiety/agitation, so increasing β activity to improve executive functions could backfire if it increases anxiety, which, of course, inhibits executive functioning [7]. From a technical perspective, using β activity to drive feedback may also result in modulation of muscle activity due to electromyographic [EMG] artifacts in the β range of the EEG, which tend to be of greater amplitude than true β brainwave activity [64].

A more nuanced view takes into account θ power, as well, and its ratio with β power in the frontal cortex, called the θ:β ratio (TBR), which is supposedly higher

in ADHD brains compared to non-ADHD brains [110]. As the only FDA-approved biomarker for ADHD, the TBR should then be able to differentiate between individuals with ADHD and those without the diagnosis [111]. Unfortunately, there is only a very short window in childhood when the TBR can efficiently be used to distinguish between children with ADHD and those without ADHD, and it cannot differentiate ADHD from non-ADHD adults at all [110–112].

The unreliability of the TBR as a biomarker for ADHD symptoms and behaviors is exemplified in the fact that, although θ-β neurofeedback training can result in improved ADHD symptoms and behaviors, individual learning curves and increases in β power do not correlate with these behavioral outcomes, meaning that, although the neurofeedback training did work to improve ADHD symptoms and behaviors, it was not because the subjects normalized their TBR [113]. Other studies support this notion that frequency training neurofeedback *learning*, which is the measurement of how well subjects are able to consciously control their brainwaves, does not always correlate with behavioral improvements [86, 114]. These results indicate that this hypothesis of "fixing brain wave patterns" is incorrect and that there is a better explanation for the effects of neurofeedback training.

4.1.2 Increasing brain activity in specific regions

Another very simple hypothesis for the mechanism of action of neurofeedback training is the idea of increasing brain activity in specific brain regions. This hypothesis is most applicable to the hemodynamic training methods like HEG, FNIRS, and primarily fMRI neurofeedback, which has the greatest spatial resolution [107]. Specifically, the idea is to provide information on where the brain is active in real-time, and to reward the subject when the brain is active (or inactive) in the target region, such as the prefrontal cortex or the amygdala, training up for attention and down for emotional calming, respectively [93]. The straight-forward hypothesis here is that the different brain regions are associated with different functions and activating or inactivating these regions should increase or decrease those functions, respectively. There has been no evidence to negate this hypothesis, but the technology used for the greatest spatial resolution (i.e. fMRI) is not practical for use in a therapeutic setting.

4.2 Hypotheses from non-directive methods: State-based shifts

Hypotheses for the mechanism of action of non-directive methods of neurofeedback have been more challenging to define and test compared to the directive methods due to the fact that they do not follow a straightforward operant conditioning model. These hypotheses are typically fairly general, involving the concept of calming the body system by shifting from a sympathetic nervous system (SNS)-dominant state to a parasympathetic nervous system (PNS)-dominant state, improving self-regulation of regulatory biorhythms, such as the circadian and ultradian rhythms, and increasing network system dynamics and stability.

4.2.1 Biorhythm regulation

In addition to brainwaves, there are a plethora of biorhythms in the body, not to mention the global rhythms of nature, itself. These rhythms span several orders of magnitude from sub-daily rhythms (ultradian) to daily (circadian), monthly (menstrual), seasonally (circannual), into yearly, decadal (10 years), and so on [95]. If these rhythms were approximated as frequencies, these longer biorhythms fit neatly into the ILF range at 0.1 mHz (ultradian), 0.01 mHz (circadian), 0.0025

mHz (menstrual) and 0.0001 mHz (circannual, approximately 3 months), which are all within the parameters of ILF neurofeedback training using the current version of Cygnet® (v.2.0.7.4, beemedic.com, 2021). Therefore, one of the hypotheses for the mechanism of ILF neurofeedback, specifically, is that it trains and improves these biorhythms using intrinsic error correcting through feedback.

When the software could only reach as low as 0.1 mHz, which translates to an ultradian rhythm, David Kaiser proposed a mechanism through which ILF neurofeedback trains the ultradian rhythm, which is created by astrocytes [48]. Although astrocytes may be a key contributor to the mechanism, it is unlikely that the ultradian rhythm is the primary mechanism through which ILF neurofeedback works, since, as the software continues to improve, most subjects tend to have optimal training frequencies at the bottom of the register, which changes with nearly every update of the software (although it is unlikely to continue to change indefinitely) [115]. Furthermore, an electrophysiological signal corresponding to these slower, lower frequencies (< 0.1 mHz) has yet to be described, particularly with a neural or glial source. These slower biorhythms are created through clock gene feedback loops which regulate cascades of signaling pathways throughout the body, including hormonal regulation and even telomere length throughout life [95, 116]. Thus, it is unlikely that direct regulation of long, slow biorhythms, such as the ultradian, circadian, and circannual rhythms, are responsible for the effects of neurofeedback.

4.2.2 Polyvagal theory and the default space model of consciousness

Polyvagal theory is a theory describing the tripartite development of the autonomic nervous system and the functions of the resulting subsystems [116]. Through three phylogenetic stages in evolution, three subsystems of the autonomic nervous system have arisen in higher-order organisms: the sympathetic nervous system, which produces the "fight-or-flight" response, and two branches of the parasympathetic system via the vagus nerve, one branch corresponding to the ventral vagus nerve, which produces a social communication system through facial expression, vocalization, and listening, and the other branch corresponding to the dorsal vagus nerve, which produces the "freeze" response if attempts to fight or escape do not resolve the threat [116–118]. The theory further postulates that many neuropsychiatric disorders may be due to low vagal tone in one or more of these branches, particularly the ventral vagal neurons in the nucleus ambiguus [118, 119].

A key feature of the polyvagal theory is that it integrates neural circuits and rhythms of the brain with those of the heart and gut, which are relevant to all biofeedback modalities [119]. Another, similar theory that integrates these visceral functions with brainwave activities is a theory of consciousness called the Default Space Model, which proposes that at very slow oscillations, the brain synchronizes with the cardiorespiratory rhythm, activating the DMN, which integrates external and internal sensory input to create a three-dimensional conscious experience [30, 33]. Thus, according to this hypothesis, ILF neurofeedback induces the brain into the DMN, and engages the ventral vagal system, which promotes calming, self-soothing, and socially engaging behaviors [34, 118].

4.2.3 Control system dynamics and stability

Despite the lack of information on the NeurOptimal® method of neurofeedback, its description as a nonlinear dynamical neurofeedback system has been helpful in elucidating how neurofeedback training may interact and influence the dynamical system processes of the brain. As mentioned in Section 2.1.1 on feedback mechanisms in learning, control systems, such as the brain, are characterized by

feedback loops, and feedback loops create oscillatory activities, which are inherently dynamic [4]. By exercising these dynamics through neurofeedback, the brain resonates with itself, causing an amplification of this activity and creating both greater stability as well as increasing dynamics [4, 5].

4.3 The global hypothesis: self-resonance and system dynamics with microstate stability

There are two aspects that are common to all of these hypotheses: (1) self-resonance from the self-referential feedback, itself, and (2) increased system dynamics with microstate stability. All biofeedback provides self-resonance, which is subjectively calming and comfortable for the subjects [4, 120]. No matter the modality of biofeedback, the resonance of brainwaves or heart rate or baroreflex fluctuations synchronize with each other, ultimately settling comfortably in a PNS-dominant or ventral vagal state, which is restorative, clarifying, and energy-efficient [30, 33, 116, 120].

The second part of the global hypothesis refers to the increasing dynamics of the neuroelectric functional network system. Each method of neurofeedback relies on sensory information to provide the feedback, which requires the brain to enter into the various sensory functional networks in order to process it. However, the information, itself, may not reflect activity in the sensory networks, and the calming aspect of the self-resonance will activate the DMN, which is mutually exclusive with the sensory networks [26, 30, 35]. In fact, several studies show that neurofeedback training increases DMN connectivity, supporting this hypothesis of activating the DMN [34, 121–123].

Acquiring the neurofeedback, itself, requires dynamic shifts between task-positive networks and the DMN, thus strengthening this shifting ability or network dynamics. These effects can be seen in emergent subnetworks that are present immediately after neurofeedback training that combine hubs from the SN, basal ganglia/reward network, and the visual network (presumably due to visual feedback) [85]. Furthermore, the specific brain location or brainwave that is the substrate for the feedback strengthens and stabilizes that brain activity or microstate [5, 123]. They are called 'microstates' because they are short-lived due to the nature of dynamics, but their stability is in the strength of their connections (in the case of functional networks) or peak power intensity (in the case of brainwaves), conferring the brain resiliency against perturbations [5]. These effects translate to improved brain function in the same manner that increased inter-network dynamics improves brain function, as described in Section 2.1.2.1.

Essentially, this common hypothesis combines general mechanisms of biofeedback that confer a calm, parasympathetic-dominant state with specific mechanisms of neurofeedback that exercise inter-network dynamics while stabilizing intra-network connections. As described earlier, these increased dynamics result in improved cognition and mental wellbeing, while the increased stability results in greater resilience. Thus, all methods of neurofeedback improve overall brain self-regulation, where some methods may achieve this more globally and other methods achieve it through more specific detailed aims, such as training very specific brainwave patterns or regions of activity.

4.3.1 The regulatory functions of the infra-slow oscillations

As mentioned in Section 3.1.1, different brainwaves can interact with each other and become coupled, meaning that their activities correlate [22]. These correlations may occur according to phase (where the phase of the slower brainwave regulates the discrete activity of the faster brainwave) or envelope (where the envelope of the slower brainwave modulates the amplitude of the faster brainwaves) [22].

Thus, these forms of cross-frequency coupling of electrical oscillations in the brain suggest that information about one brainwave automatically provides information about another, usually slower, brainwave, which is embedded in its fluctuating activity. However, the resolution of the information of the slower brainwave embedded in the information of the faster brainwave is lower than if the slower brainwave was observed directly.

Although there are many reports on the significance of the cross-frequency coupling of conventional EEG brainwave bands, such as θ-γ in the hippocampus or δ-θ-γ in the auditory cortex or δ-α in the left and right homologous regions of the attention networks, these are short-lived interactions that are both spatially and functionally-specific [22]. One cross-frequency interaction that is constant, however, is between the ISO (typically between 0.01–0.1 Hz) and all of the faster, conventional EEG brainwaves, including δ through γ bands (~1–40 Hz) [99]. This interaction is a phase-amplitude coupling where the amplitudes of all of the faster frequencies are regulated by the phase of the ISO [99].

Studies show that the ISO and the BOLD signal from fMRI correlate and may be part of the same activity, representing the fluctuations of oxygenated and deoxygenated blood [30, 31]. Since neither oxygen nor blood, themselves, create LFPs, the source of the ISO is likely calcium fluctuations across astrocyte membranes as they provide energy and neurotransmitters to local neuronal circuits and regulate their activity [50, 58]. Furthermore, these oscillations also correlate with cognitive performance as well as sleep patterns [31, 99].

These findings suggest that all brainwaves and bodily rhythms, such as the cardiorespiratory rhythm, baroreflex fluctuations, and oxyhemoglobin/deoxyhemoglobin fluctuations, etc., are correlated, particularly when calm and relaxed, which occurs with self-resonance [30, 33]. This means that information from one rhythm contains embedded information about other rhythms, albeit at varying levels of resolution. Therefore, each biofeedback modality can work through a similar mechanism of action to effect change, while the differences in intensities of the effects may be due to the level of resolution of the underlying master regulatory rhythm as conferred by the particular form or substrate of the feedback.

5. Using ILF neurofeedback to train the conductor of the brainwave symphony

Despite an attempt to present this information fairly and objectively, my personal bias for ILF neurofeedback is likely obvious. The way I describe ILF neurofeedback to my clients nowadays is to consider the brain like an orchestra and the brainwaves like a symphony, which, of course, is not my own original analogy [66]. Each brainwave is like the music playing from each section of the orchestra, such as the winds, brass, strings, or percussion sections. You can train each section separately, but, due to the nature of systems, by training - and possibly changing - one section, the other sections will also likely be perturbed in some way that may not be readily discernable or beneficial. Alternatively, you can train the conductor, which, in this analogy, is the ISO or ILF. Thus, when you train the ILF, you train the entire symphony of brainwaves, which continue to play together, but with greater harmony after neurofeedback training.

6. Conclusions

The future of neurofeedback depends on the diverse field of methods coming together and defining the mechanism(s) of action of neurofeedback that can be

applied to all methods. Detailed mechanisms of action are likely different for the different methods, but their fundamental processes should not contradict each other. Not only will this help advance the field, but it will also help potential clients to understand how all neurofeedback works in general, then they can choose which methodology works best for them based on the specific characteristics of that method. A two-part mechanism of action is presented here, one that is general for all forms of biofeedback, and one that is more specific to neurofeedback, yet still general enough to be applicable to each specific method. Hopefully, other neurofeedback practitioners and researchers will consider these hypotheses, possibly further developing them and testing them through well-designed research studies. As the field and use of neurofeedback grows, these mechanistic models can be further refined to fit all methodologies and conditions.

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Conflict of interest

The author declares no conflicts of interest.

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