NeuroPrime: a Pythonic framework for the priming of brain states in self-regulation protocols

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***Abstract*— Due to the recent pandemic and a general boom in technology, we are facing more and more threats of isolation, depression, fear, overload of information, between others. In turn, these affect our Self, psychologically and physically. Therefore, new tools are required to assist the regulation of this unregulated Self to a more personalized, optimal and healthy Self. As such, we developed a Pythonic open-source human-computer framework for assisted priming of subjects to "optimally" self-regulate their Neurofeedback (NF) with external stimulation, like guided mindfulness. For this, we did a three-part study in which: 1) we defined the foundations of the framework and its design for priming subjects to self-regulate their NF, 2) developed an open-source version of the framework in Python, NeuroPrime, for utility, expandability and reusability, and 3) we tested the framework in neurofeedback priming versus no-priming conditions. NeuroPrime is a research toolbox developed for the simple and fast integration of advanced online closed-loop applications. More specifically, it was validated and tuned for the research of priming brain states in an EEG neurofeedback setup. In this paper, we will explain the key aspects of the priming framework, the NeuroPrime software developed, the design decisions and demonstrate/validate the use of our toolbox by presenting use cases of priming brain states during a neurofeedback setup.**

Keywords— Self-regulation, assisted neurofeedback, neurostimulation, mindfulness, open-source BCI, machine learning.

I. Introduction

Self-regulatory (SR) techniques of mental states are widely used in the clinical, professional, athletic and gaming fields, whether for therapeutic, performance or entertainment reasons. They include imagery training, music regulation, breathing, meditation, amongst others [1]–[3]. With the advancement of technologies, mechanistic approaches are increasing, such as the case of brain-machine interfaces (BCI) that utilize our ability to learn how to self-regulate brain states when provided with corrective feedback training [4]–[6]. This type of training is defined as neurofeedback training (NFT).

It has been previously hypothesized that an "optimal" self-regulation state is necessary to achieve greater performance in voluntary modulating Neurofeedback. In this state, the learner should be more: engaged; focused (mental focus); undistracted; mindful of the experiment. Reversely, the learner should avoid: self-related thinking (self-monitoring); ruminating; distracting and task-unrelated thoughts; irrelevant associations between internal states and external reward (doubts, questioning, evaluation of progress); mind wandering [7]–[9]. Additionally, current electrophysiological (EEG) literature relates the previous states with electrophysiological up-regulation of alpha rhythm or/and sensory-motor rhythm (SMR), but also with desynchronization of surrounding bands [1], [3], [10]–[13]. Based on these studies, we hypothesized that it would be possible to develop a "Neurofeedback assisted self-regulation BCI" that combined the technical, behavioral, psychological, emotional, and electrophysiological components of EEG BCIs, NFT and SR in a single framework. For this, we performed a three-part study, that will be further developed in this paper, in which: 1) we defined the foundations of the framework and its design for priming subjects to self-regulate their NF, 2) developed NeuroPrime, an open-source version of the framework in Python for utility, expandability and reusability, and 3) we tested and validated the framework in different designs.

A. Related work

In the last decade, Python has gained big traction in the scientific community, providing a multi-purpose language that is powerful, versatile, open-source and is easily programmable, competing directly with Matlab. NeuroPrime is a research toolbox developed for the simple and fast integration of advanced online closed-loop applications. As such, simplicity and reusability are the foundation of the NeuroPrime package, as is intended to be an open-source project to be used by the neuroscience community. It is also intended to be a BCI hub that evolves with a synthesis of the best packages the python community has to offer in terms of signal processing, signal presentation and signal acquisition. Therefore, one of the requirements is an easy and simple structure to update and connect new packages within the same simple design.

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NeuroPrime provides a complete BCI structure in Python. Currently, a great BCI Python toolbox exists like the combination of wyrm[14], mushu[15] and pyff[16] (that will be further discussed), NeuroPype (Intheon, San Diego, CA) and Neurodecode [17]. However, these tools have their structure and design complexities, demanding a learning curve. To meet the framework requirements and develop a research-friendly toolbox, the packages should be wrapped/encapsulated in a single BCI design and tuned to research the priming of brain states.

B. Paper structure

The paper is structured into four parts. The *NeuroPrime overview,* a brief description of the toolbox. The *Framework foundations* section, where we define the theoretical foundations of the priming framework propelling the development of NeuroPrime. The *Framework design* section, that builds upon the theoretical foundations to establish our framework. Finally, the *Framework & toolbox validation,* where we tested the framework in two different temporal experiment designs.

II. NeuroPrime overview

NeuroPrime was built from the ground up on Python and is free- and open-source software licensed under the terms of the GNU General Public License. This was achieved by synthesizing and using the best parts, we extensively tested, from specific BCI and EEG modules, for signal acquisition, signal processing/classification and signal presentation (diagram in Fig. 1). Signal Acquisition: pycorder (Brain Products, Gilching, Germany), pylsl/lab streaming layer [18], and mushu [15]. Signal processing/classification: wyrm [14] and mne [19]. Signal presentation: pyff [16] and psychopy [20]. Additionally, some other important scientific packages, pandas for managing data, matplotlib for graphs, numpy for arrays, scipy for specific algorithms, pygatt for bluetooth connectivity with GSR and HR sensors, and also pyqtgraph for real-time graphical interfaces. This framework was built, following the necessity for further expandability, utility, and reusability from the neuroscience community. Python has great modules in machine learning that could help optimize and automate the paradigm of priming subjects in future experiments. Also, the code is ready to use with any EEG amplifier that can connect with the lab streaming layer (LSL) [18]. The name chosen for the package was NeuroPrime, a combination of neuromodulation and priming.

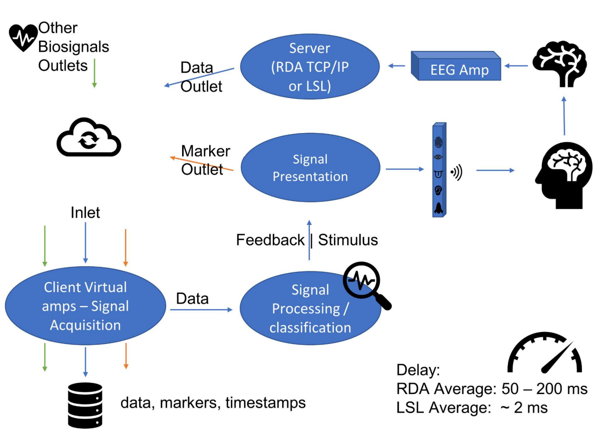

Fig. 1 – NeuroPrime. Online closed loop BCI Python framework. It is comprised of 3 main parts: signal acquisition, signal processing and signal presentation.

An in-depth toolbox overview is located online at the NeuroPrime repository [21]. In the *"TOOLBOX_ARCHITECTURE.pdf"* file we included the design of the NeuroPrime toolbox: the packages, the data structure, an overview of the functions, how to perform online and simulated online experiments, offline signal analysis and some means of quality assurance we have undertaken. Also, we go deeper into the Pythonic structure of each of the parts that constitute the software and how to use them (signal acquisition; signal presentation; signal processing & classification).

In the next sections, we will go deeper into the framework supporting NeuroPrime: its theory, its contributions and its value for NF applications.

III. Framework foundations

There are different attempts to explain how technical, psychological, and physiological mechanisms interact to produce self-regulation of NF. From crossing NF learning with theories, like control theory, dynamical system theory, multi-stage learning theory, instructions design theories [4], [7], [8], [22]–[25], to theories explaining the phenomenon of BCI/NFT illiteracy [26]–[28], the learning ability assessment and measuring learning of self-regulation [29]–[31] and theories that try to demystify self-control of brain ability [7], [8], [28]. We selected some of those theories to be the building blocks of our framework model: (1) Control-theory, (2) Multi-stage NF learning theory, (3) dynamical-systems theory [4], [24], [25], (4) dual-process theory [8], (5) epistemology [32] and instruction design [23]. From these, we get a good foothold of what our NF learning framework can entail. In Fig. 2 we put all the building blocks together, so the reader gets a full picture.

The Learner can be considered a dynamic system with an uncertain number of free parameters, a gray box model, a highly complex system. This system internal "optimal" set point is when the target is reached after several runs. Our research aims at supporting the user to get into this optimal state, by trying to find what can be gained by forming a human-computer hybrid for control of brain activity.

Our framework intends to reset "for a few moments" some self-related thinking (trying states), by focusing the attention to present sensations (sensing states) and trying to: 1) lower the switching cost of state transitions throughout NFT, this initially minimizes the cognitive demand on the users during training, and hence the risk to frustrate and demotivate them; 2) drive a specific trajectory of brain states, that is closer to the NF target state.

If the NF system essentially augments the sensory repertoire, allowing the brain to ''sense" the neuroelectrical patterns and thus make them amenable to control in a homeostatic manner. This approach supports the NF to enlarge the cerebral sensorium, through implicitly "outsource" sensory-feedback processing to extrinsic neurostimulation, using the computer as a virtual machine controller of the system, capitalizing in its superior sensing accuracy and temporal resolution. Thus, the hypothesis that external stimuli can prime & scaffold self-regulation of NF can be assessed [4], [24], [25].

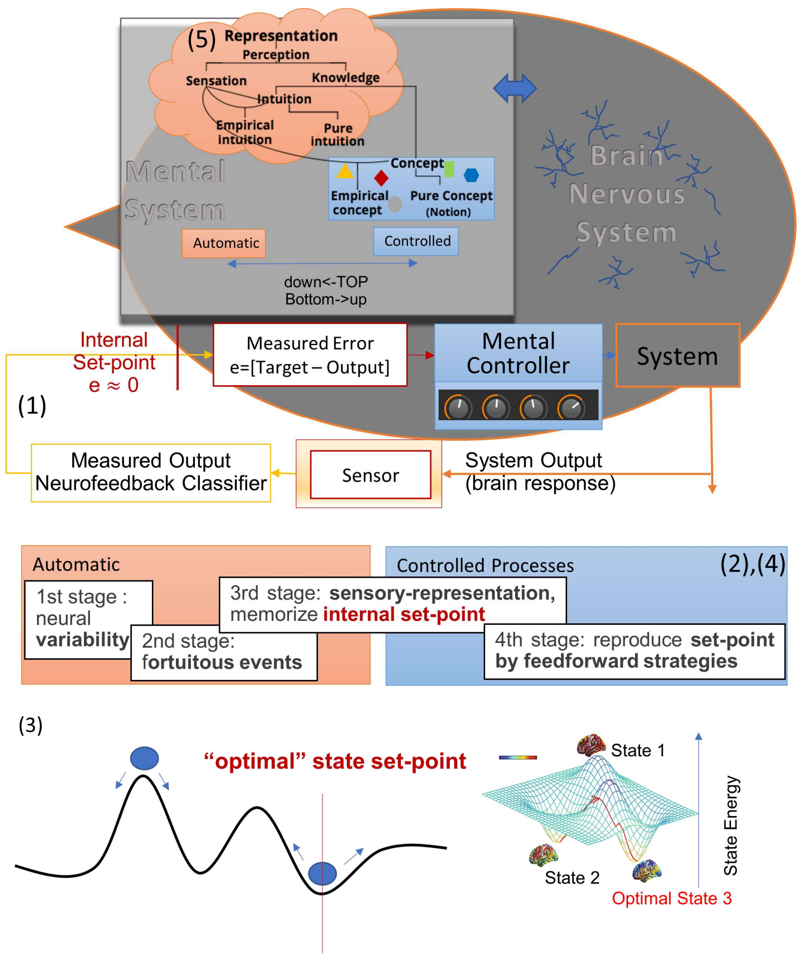

Fig. 2 - Neurofeedback Learning Model. Control-theory (1), Multi-stage Neurofeedback learning theory (2), dynamical-systems theory (3) based on [25], dual-process theory (4), epistemology (5).

From a multi-stage point of view, we will try to lower the transition cost to reach the internal set point. Trying to start from an optimal variability state, where the user has more fortuitous events above the threshold [4], [24].

Literature uses dynamical systems theory to argue that NF functions to bring a disordered brain into a regime where there is maximal information transfer (near criticality), which in turn explains the benefits on cognitive and creative abilities of NFT [1], [3], [4], [24], [25]. We hypothesize that the framework can support these transitions (automation and personalization) and facilitate the transition between automatic to controlled mental processes of attention, enabling the user to reach a state in which self-regulation of brain activity is facilitated. In this way, trying to facilitate the brain control state transitions with the help of external eliciting state transitions using non-invasive neurostimulation.

The hypothesis that stems from this interpretation is that NF-assisted control could prove more effective compared to an unassisted human operator.

IV. Framework Design

NF as a closed-loop system (i.e., brain activity is continuously fed back to the neural system) can be applied as an experimental method to investigate the causal character of specific neural events (such as brain oscillations) within cognition and behavior. This procedure is defined as brain-state dependent stimulation (BSDS) [6], [33], [34]. NFT closed-loop design can be divided into three parts, as depicted in Fig. 3: signal presentation (SP), signal acquisition (SA), signal processing and classification (SPC). SP deals with the GUI used to present the NF (stimuli and feedback modality, feedback presentation and timing). SA deals with the acquisition of the signal from the learner, the data structure and storage. While SPC uses the data acquired for online data preprocessing, online feature extraction and online feedback generation.

Our priming framework training design follows the BSDS experimental method to investigate the functional role of certain target oscillations (brain states). It is envisioned as a closed-loop stimulator, meaning that the stimulus is updated by the brain states of the participants, as can be found in Fig. 4.

A. Signal presentation

The signal presentation will support explicit NFT with stimuli targeting implicit neural responses. Temporally, the stimuli can be presented before, after, or during NFT. In this paper, the research concerns the before, the priming.

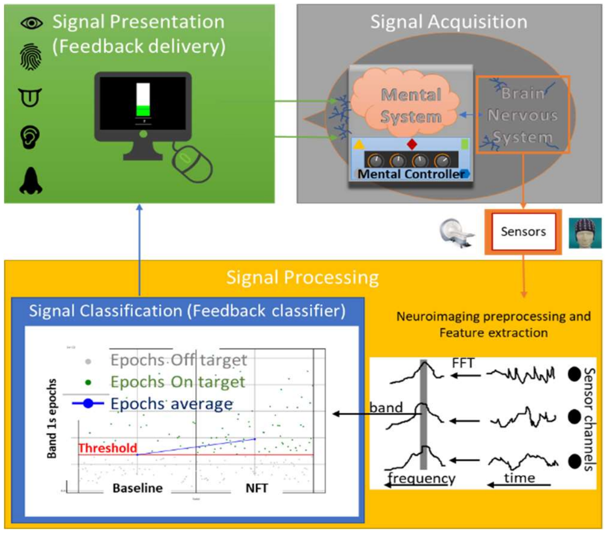

Fig. 3 – Neurofeedback training design diagram. The NFT is divided in: signal presentation, the feedback delivery interface; signal acquisition, the data; signal processing and classification, the feedback feature extraction and classifier.

B. Signal acquisition

NF plus the neurophenomenological target (described in the next section *signal processing*), offer a new way to relate the phenomenological structure of subjective experience with a real-time objective characterization of large-scale neural operations continuously throughout the experiment. Other biodevices can also be added for more precise signal acquisition and classification, but also as complementary biofeedback [35]. The possibilities are endless, but for instance, body biomarkers like galvanic skin response (GSR), heart rate (HR), and facial expressions (through video recording and machine learning) can provide the big data needed to push this framework classification forward [36], [37].

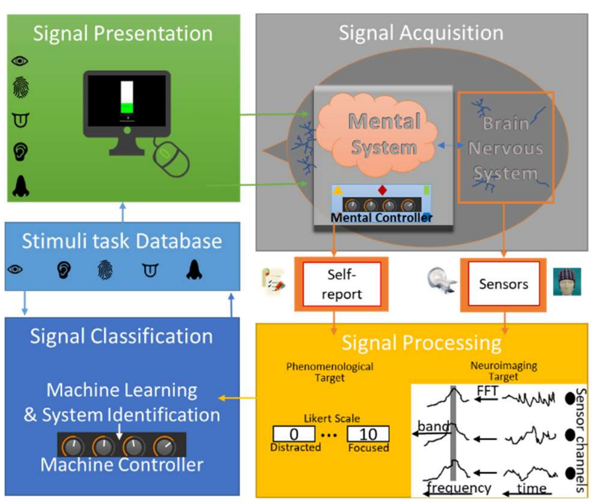

Fig. 4 - Framework design diagram. The framework has a similar division to NFT: signal presentation, the feedback and stimulus presentation; signal acquisition, the data; signal processing, phenomenological and neuroimaging feature extraction; signal classification, the machine learning controller decoding and classify mental states; stimuli task database, the database with the stimulus categories to be presented to the user.

C. Signal processing

1) Neuroimaging targets

As we already described, current EEG literature relates the "optimal" state with up-regulation of alpha rhythm or/and SMR (both linked to attentional processes), but also with desynchronization of surrounding bands. An example of this is shown by van Lutterveld et al. 2016 [13], who found that amplitude reduction in gamma-frequency range within the posterior cortex (posterior cingulate) associated with the experience of effortless awareness, and correlated effects were also observed within the alpha frequency range, among others.

2) Phenomenological targets

Exploring the phenomenological experience is an important complementary mechanism to understand the NF data. The challenge is how to transform the qualitative data into factual quantitative data. Davelaar et al. [9], [24] have experimented with guided reports through interviews, while others like Garrison et al. [38] used self-reports (e.g., "on a scale from zero to ten how did you feel during the task?" 0 = distracted; 10 = focused).

Phenomenological analyses have established that different NF protocols are related to different subjective experiences [39], and that differences in learning success may in part be due to differences in subjective experiences [9], [24].

D. Signal classification & stimulus database

We approached the problem through a framework that should learn how to guide the user to an attentive mental state using a sequence of stimuli (simple or/and complex). It is based on NF learning theories, intra-individual differences, system identification and machine learning. Additionally, our theoretical framework should follow an Adaptive Design Optimization approach (ADO) [40]. In the paper, Sanchez et al., show the benefits of adaptive real-time (online) approaches and the contrasts with classical (offline) approaches. In contrast with linear offline approaches (experimental design, followed by data analysis and hypothesis testing), the adaptive approach operates in real-time and proceeds with design optimization, data acquisition and analysis at each experimental stage or trial. The online approach enables hypothesis testing to be optimized at the individual level by adapting the experimental design based on past observations. This is the general principle of ADO, which can be extended to advanced computational models of electrophysiological responses thanks to brain-computer interface (BCI) technology, to optimize experimental conclusions.

Instead of a white-box system based on first principles (e.g. Newtonian principles) - such models are overly complex, and possibly even impossible at the moment, due to the complex nature of many mental systems and processes - a much more common approach is to start from measurements of the behavior of the system and the external influences (inputs to the system), and then try to determine a mathematical relation between them without going into the details of what is happening inside the system. This approach is called system identification. Systems theory identification and reinforcement learning (neural network approach) will try to emulate the learner mental controller (i.e. the subject that tries to learn to voluntary self-regulate brain activity through mental strategies) assisting and outsourcing the identification of mental strategies to the next best external stimulus (external instructional strategies) for optimal NF self-regulation [4], [41], [42]. These interactions are represented in the diagram in Fig. 5.

Due to the workload of implementing this theoretical framework (see Fig. 5), a "divide and conquer" strategy was followed. (1) Develop Open-source software (NeuroPrime) for simple and fast integration of advanced closed-loop applications. (2) Answer the question: Does priming with external stimulation affects the self-regulation of NF? This can be further divided into four main questions. Targets, which mental/brain states can be optimal for learning self-regulation of brain activity? Stimulus, how can we non-invasively stimulate the aforementioned states? Measurements, how can we measure the target performance (learning and behavioral outcomes) of each individual? Framework experimental temporal Design, what is the best temporal design to implement the framework? (3) Automate the framework and optimize priming personalization: adapt convolutional neural networks to learn (e.g., using transfer learning) the sequence of stimulus that leads momentarily the subject towards the desired "optimal" state. Particularly, the aims of this paper are task (1) and use task (2) as a means of framework validation.

E. Framework simplification

NeuroPrime architecture is prepared for the personalized machine learning priming with an ADO approach. However, following the "divide and conquer" strategy, we need to validate the framework by demonstrating that priming can affect the learning to voluntary self-regulate brain activity and by consequence NFT performance. The simplest way is to find a priming technique that leads the person closer to the previously defined "optimal" state. One of the techniques that have similar priming targets as NFT is mindfulness meditation (MM) of focused attention forms. Mindfulness effects involve general and large-scale brain networks [2], as does the NFT [12], because they involve multiple aspects of mental function that use multiple complex interactive networks in the brain, e.g. stroke patients get better accuracy in controlling BCIs

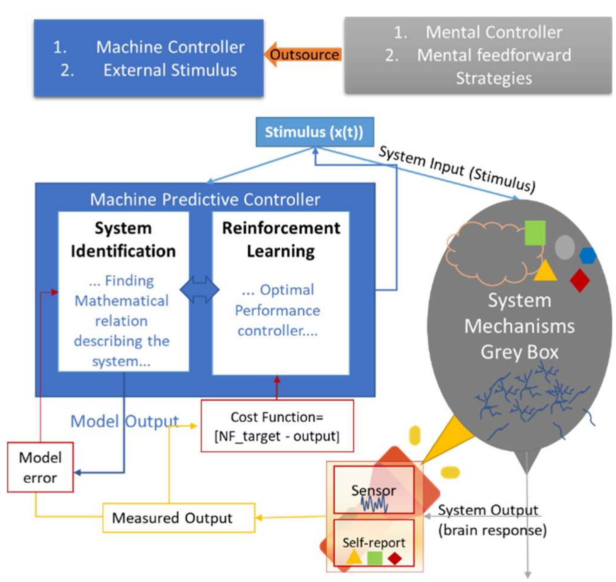

Fig. 5 - Framework Theoretical Design. Systems theory identification and reinforcement learning emulate the learner mental controller assisting and outsourcing the identification of mental strategies to the next best external stimulus for optimal Neurofeedback self-regulation.

[43]. Additionally, EEG reports show similar correlates of up-regulation of alpha with mindfulness practice [44]–[48], and up-regulation of SMR with spiritual practice [12].

Mindfulness training causes neuroplastic changes in the structure and function of brain regions involved in the regulation of attention, emotion, and self-awareness. In NFT, a hypothesized "optimal" mental/brain state should be reached for optimal self-regulation of brain activity. For that, irrelevant mental processes should be decreased, and relevant mental processes should be intensified, basically [2], [8]: evaluative self-referential processes should decrease; awareness of present-moment with non-judgmental attention (acceptance) should increase; a shift in self-referential processing (affective, subjective) towards a more self-detached and objective analysis of interoceptive and exteroceptive sensory events (greater awareness, meta-awareness) should also increase.

V. Experimental Design & Validation

The temporal design is also one of the key players of the framework and needs validation. As such, the theoretical framework was translated into an experimental session design and implemented. We implemented two experiments and the framework - theory, hardware and software - evolved along with these two experiments (Experiment 1 [49] and experiment 2 to be published elsewhere). In this section, we discuss the basis of their experimental design and the steps to follow to reproduce the framework.

As already discussed, the experimental design is based on a closed-loop BSDS design and a simple NFT protocol [6] to test the question: does mindfulness, focused attention to stimuli, has a role in NF SR? The methodology of a BSDS is to substitute the NFT learner (explicit NF), who is actively engaged and adapting strategies to alter the brain activity in the intended direction, with a stimulator device (implicit NF), who is adapted online to present an experimental stimulus [6]. Hence, our framework for studying brain states and stimuli that complement the NFT for a better SR performance uses the two methodologies together for a loop of implicit and explicit training. The reason being that priming implicitly the target brain state can help explicitly control it. However, instead of adapting online the stimulus, we started by testing two MM stimuli (breathing and imagery of a calm place, please refer to [49]) to demonstrate that priming can indeed affect the learning to voluntary self-regulate brain activity and by consequence NFT performance and to verify the necessity of using a closed-loop machine learning BSDS framework.

A single-session design is enough to investigate specific features of oscillations and their association with behavioral performance, between and within groups (e.g., comparison of behavioral effects when MM stimulus is presented versus a rest task) [6]. Whereas most intervention studies of the effects of MM and NFT involve multiple sessions taking place over several weeks, an emerging trend in literature has investigated the subjective (phenomenological) and neural effects of brief, single-session interventions [9], [12], [48]. Gruzelier states that while one cannot anticipate durability of outcome enhancement following a single session, and concluding a null outcome about learning potential would be premature, single-session experiments have practical advantages in addressing some research questions and by recruiting larger groups of subjects which allows an increase in statistical power compared with the labor-intensive smaller-scale studies [1].

The single session was divided into short intervention blocks instead of one continuous block. This decision was made based on the following contextual hypothesis: naïve subjects probably need short tasks for more focused attention; naïve subjects need rest intervals between tasks; test immediate effects of priming in NF; blocks are important to evaluate the mindset/subjective experience (with state self-reports) during the different tasks on the session; enable randomization of tasks and conditions like eyes open/eyes closed. Also, this type of short block design probably has some limitations in the level of priming (attention control, emotional regulation, and self-awareness states) achieved per block, yet it seems adequate for naïve populations. Of note, when using a paradigm with eyes open and eyes closed one has to include not only visual but also auditory cues that signal the end of the task. So, each task has an auditory bell at the end, and if NFT is with eyes closed, then the visual feedback needs to be translated to audio.

Before the training session starts, the participant is verbally instructed with a GUI representation about how each task works (pre-Training instructions). They are essential to baseline all the subject knowledge, but also to prepare them for the experiment. Then, during the training session, the initial baseline threshold should be chosen, and one can make the threshold adaptive to the subject and change it accordingly (the change will depend on certain conditions). The last block serves as the outcome block for comparison with the first block. The differences between the CG and the experimental group (EG) reside in the use of priming tasks. While the CG is only primed with rest tasks (no-priming), the EG is primed with randomized mindfulness focused attention forms, breathing bodily sensations meditation, named "breathing mindfulness" (BM), and the imagery of calm place sensations meditation, named "imagery mindfulness" (IM). These external priming stimuli are pure instructional audio manipulations to lead the person from a subjective trying state to a more sensing state. These transitions can be referred to as belonging to the trying-sensing continuum discussed by Davelaar and colleagues [9].

These design choices culminated in two different experimental designs (Experiment 1 and 2, one can check their designs in the file *"TOOLBOX_ARCHITECTURE.pdf"* at NeuroPrime Toolbox [21]). They diverge in the temporal design and other attributes, but the main goal was to have short sequences of prime-NFT-rest. For the justification of the choice of attributes in the Experiment 1 design, please refer to the following publication [49]. Experiment 2 results are still in submission elsewhere, however, as an example of a complete BCI, the Experiment 2 pipeline can be found in the folder *"brain_interfaces"* in the NeuroPrime Toolbox [21].

VI. Limitations

The NF online experiments were developed in house using NeuroPrime [21]. Various tests were performed and proved consistency. Nonetheless, the two experiments discussed in this paper are the initial case studies for the present framework. This is an open-source framework, future studies from our and other research groups will allow further improvements. We invite groups to use the framework and help us improve it. Working with real-time decoding of EEG signals has multiple limitations such as noise and movement-related artifacts [50]. For example, small movements above the neck, such as eye blinks or muscle contractions can add artifacts to the signal. Attempts were made to prevent and detect such artifacts in real-time, however, a good calibration stage is recommended.

VII. Future work

For a final product, this framework still lacks refinement and personalization. To optimize self-regulation learning, future work will address the use of neural networks to learn (e.g. using reinforcement learning, deep learning for time series forecasting with long short-term memory networks, multilayer perceptron's, convolutional neural networks, between others) the sequence of stimuli that leads the subject towards the desired "optimal" state. The framework should adapt to the user own pace (even slow down user pace if needed) and regulate/control the user brain state according to the target.

One of the requirements was software that runs on all major operating systems. As such, NeuroPrime was developed and tested on Mac OS and Windows OS and depending on the hardware requirements it can run in all major OS that runs all the Python packages. Currently, the NeuroPrime package has a to-do list: parse the package completely from Python 2.7 to Python 3; documentation needs to be reviewed and simplified; variable nomenclature needs to be reviewed for standardization (e.g standardization of uppercase and lowercase); deprecated code should be removed and implementation of machine learning algorithms. In retrospect, this package is stable in the current version but should be continuously simplified, tested and updated to meet the criteria of new experiments.

VIII. Conclusion

Translating theory into application, NeuroPrime meets the requirements of the theoretical framework defined in this paper, enabling the research of priming subjects with stimulus before NFT, by providing simple tools to design BCI experiments concerning the problem. Furthermore, we discussed the experimental designs used to test NeuroPrime and how they helped in enhancing the toolbox and the value it brings to NFT protocols. Although the two designs are described in this paper, there are other ways to design a session with the priming attributes of our framework. We invite groups to use NeuroPrime in experiments and help us improve it.

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