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Letter to the Editor

Toward a biomimetic neurostimulation taxonomy: Distinguishing replay approaches from engineered transcranial endogenous current stimulation

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Dear Editor,

We thank Tecchio et al. (2026). for their response to our recent introduction of transcranial endogenous current stimulation (tECS) (Stein et al., 2026), and we agree that their earlier work on transcranial individual neurodynamics stimulation (tIDS) (Cottone et al., 2018) is an important contribution, alongside (Gebodh et al., 2019; Poltorak, 2021) in the broader development of biomimetic neurostimulation. However, their response implies that tECS follows directly from, or is largely encompassed by, the earlier tIDS framework. While the two approaches share the use of EEG-derived signals, they perform fundamentally different operations on the EEG-derived signal prior to delivery. This distinction has direct consequences for how biomimetic neurostimulation should be classified and advanced.

tECS was introduced as a biomimetic neurostimulation framework in which an individual's EEG is used to generate a stimulation waveform that is then *parametrically engineered* prior to delivery as a neuromodulation intervention, with the explicit goal of perturbing a predefined neurophysiological feature. The principle traces directly to *in vitro* cortical slice electrophysiology findings that endogenous electric fields entrain ongoing cortical activity when re-applied to a cortical slice (Fröhlich & McCormick, 2010). In Stein et al. (2026), the neural feature targeted by tECS was the 1/f aperiodic exponent of the EEG power spectrum, selected as a putative macroscopic marker of excitation-inhibition balance (Hacker et al., 2025). Resting-state high-density EEG was decomposed using FOOOF (Donoghue, 2024), the aperiodic exponent was reduced by 50% (as a proxy for increased cortical excitation (Guirguis et al., 2025), the original phase spectrum and oscillatory residuals were preserved and reintegrated, and the resulting waveform was reconstructed in the time domain, scaled, and clipped before being delivered over five consecutive days. Critically, target engagement was assessed via change in the same EEG feature that had been mathematically manipulated in the delivered tECS waveform.

This is a fundamentally different operation from that performed in tIDS. In tIDS, region-specific neurodynamics are extracted from EEG via Functional Source Separation and replayed as stimulation, without deliberate modification of the signal's structure prior to redelivery. In tECS, individual EEG serves as the starting material for targeted signal engineering, in which a specified physiological feature is mathematically perturbed while substantial native structure is preserved. This is not a semantic distinction; it is the difference between physiology-aligned replay and mechanistically engineered perturbation. This marks a significant contrast between the two approaches, perhaps best illustrated by an analogy from medicine: tIDS is similar to an autologous blood donation, whereas tECS is more akin to extracting specific immune cells from an individual patient, modulating them with a targeted modification to increase therapeutic efficacy for a known mechanism, and resupplying them to the patient for personalized treatment. Here, biological compatibility is preserved, but the therapeutic action arises from the deliberate modification.

This operational distinction resolves a misunderstanding in the Tecchio et al. reply, which states that *"tECS focuses on the spectral properties of EEG signals, [while] tIDS emphasized preserving the full temporal structure of ongoing activity patterns."* The aperiodic manipulation in tECS is implemented within the spectral decomposition, but the original phase spectrum is retained, oscillatory residuals are preserved and reintegrated, and the waveform is reconstructed in the time domain via inverse FFT before amplitude scaling and clipping. The delivered tECS waveforms remained highly correlated with the original EEG in the time domain ($r = 0.92–0.94$; (Stein et al., 2026), Table S2)), while implementing the intended broadband aperiodic change. Thus, the relevant distinction is not "spectral" versus "temporal," but replay of neural activity (tIDS) versus engineering of an endogenous waveform to perturb a specified physiological feature while preserving substantial native structure (tECS).

To reconcile and integrate the work from the Tecchio group and other literature in this emerging field, we establish an initial taxonomy, termed biomimetic neurostimulation (Fig. 1), defined as brain-derived stimulation modalities in which neurophysiological signals are used as the stimulation paradigm, moving beyond synthetic waveforms that capture only narrow features of neural activity toward interventions informed by richer endogenous signal structure. Within this framework, we distinguish at least two mechanistically distinct stimulation classes. The first is replay endogenous stimulation, in which recorded neural

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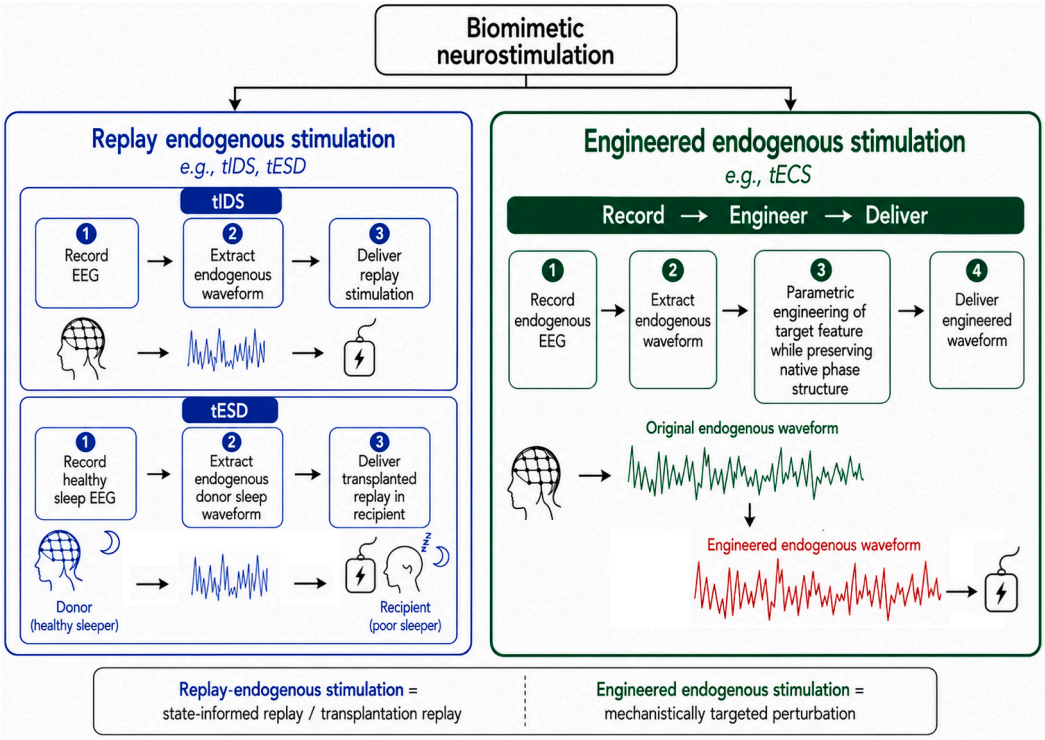

Fig. 1. Taxonomy of biomimetic neurostimulation. Two distinct stimulation approaches are delineated, specifically, replay endogenous stimulation (i.e., tIDS, tESD) in which neural activity is replayed as stimulation, vs. engineered endogenous stimulation (tECS) in which neural activity is parametrically engineered to target and modulate specific mechanistic features of neural activity. tECS, transcranial endogenous current stimulation; tIDS, transcranial individual neurodynamics stimulation; tESD, transcranial endogenous sleep derived stimulation.

dynamics are re-presented to the brain. This includes tIDS and prior brain-state "transplantation" work in sleep, in which a recorded donor brain state is replayed in a recipient, termed transcranial endogenous sleep-derived (tESD) stimulation (Gebodh et al., 2019). A second, distinct class is engineered endogenous stimulation, in which a physiologically derived waveform is deliberately modified prior to delivery in order to perturb a defined target while preserving key endogenous phase structure (as in tECS). Indeed, tECS is not limited to aperiodic exponent manipulations, but rather represents a broader platform for engineering endogenous waveforms to perturb defined neurophysiological targets. Specifically, the tECS framework creates a principled basis for engineering additional endogenous waveform features beyond the aperiodic exponent, including oscillatory, cross-frequency, and other temporally structured components, and for testing these manipulations mechanistically across non-invasive, invasive, and animal models.

This taxonomic distinction is important because the two classes of stimulation involve fundamentally different mechanisms. Replay approaches test whether re-presenting native neural dynamics to the brain yields stronger or more physiologically congruent effects than synthetic stimulation (such as transcranial alternating current stimulation or tACS). Conversely, engineered endogenous approaches test whether deliberate manipulation of a biomimetic waveform can drive predictable change in a specified neural feature. This follows our earlier work demonstrating that tuning synthetic sine waveforms in tACS to endogenous features such as peak frequencies has stronger entrainment effects, following the Arnold tongue principle (Ali et al., 2013). Clearer differentiation between replay and engineered tECS approaches will therefore help the field develop more precise language, compare methods more rigorously, and support the next generation of personalized biomimetic neurostimulation.

Sincerely,

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Declaration of generative AI and AI-assisted technologies in the manuscript preparation process.

During the preparation of this work the authors used ChatGPT in order to improve readability of originally drafted text. ChatGPT was not used to synthesize original content. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

Declaration of competing interest

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