

# Non-Invasive Stimulation Strategies for Seizure Delay Using the Epileptor Model in TVB

**Abstract**—Epilepsy, a debilitating neurological disorder affecting millions worldwide, is characterized by abnormal brain activity resulting in seizures. Though pharmacological and surgical interventions exist, these treatments fail to cure a significant number of patients. Recently, non-invasive brain stimulation has emerged as a promising approach for seizure suppression, yet there lacks certainty in the mechanics of underlying mechanisms and optimal parameters. This study employs a modified version of the The Virtual Brain (TVB) Epileptor Resting State (ERS) model to simulate the onset and possible suppression or delay of a seizure-like activity onset (SLAO) event by varying parameters of a modified stimulus model. Among the 243 simulations conducted, 95.1% resulted in a delay of SLA onset, with a mean delay of 2,546.26 ms (standard deviation: 1,064.17 ms). Notably, higher amplitude stimulations were more effective in delaying SLA onset. These findings suggest that specific stimulation parameters can modulate seizure dynamics, potentially offering therapeutic avenues for seizure management.

**Keywords**—stimulation, epilepsy, seizure, epileptor

## I. INTRODUCTION

Epilepsy is a neurological disorder characterized by recurrent seizure events, affecting over 60 million individuals worldwide, with about one-third of patients being resistant to pharmacological treatments (Scholly et al., 2022). Surgical interventions, such as resection of the epileptogenic zone, have shown variable success rates, highlighting the needs for alternative therapeutic solutions (Ozturk-Sonmez et al., 2022). Recent stimulation techniques, including deep brain stimulation (DBS) and responsive nerve stimulation, as potential alternatives to traditional treatments (Zhang et al., 2023). However, stimulation parameters that yield maximum therapeutic efficacy are found by trial and error, which delays the benefits stimulation, the challenge remains in rapidly identifying optimal stimulation parameters that maximize therapeutic efficacy in a patient-specific manner.

The Virtual Epileptic Patient (VEP) model has emerged as a powerful tool for simulating and understanding the dynamics of epilepsy (Matiasek et al., 2015). This model allows for the integration of patient-specific data to model epileptic activity and assess the impact of various stimulation strategies. Additionally, the taxonomy of seizure dynamotypes has provided insights into the classification of seizure-like events, emphasizing the importance of understanding the underlying mechanisms that contribute to their propagation (Saggio et al., 2020). Despite these advancements, there exists a notable gap in the literature regarding seizure modeling and the effects of stimulation on their dynamics.

This study employs the TVB Epileptor Resting State model to investigate the temporal effects of electrical stimulation on the onset of SLA events. By systematically varying stimulation waveform parameters, we identified parameter combinations that effectively delay or suppress the onset of SLA events. These findings contribute to a deeper understanding of the complex interactions between stimulation parameters and seizure-like dynamics, allowing for pathways to more personalized and effective therapeutic outcomes.

## II. METHODOLOGY

### A. Model Setup and Modification

The study employs The Virtual Brain (TVB) platform's Epileptor Resting State (ERS) model to stimulate large scale dynamics of seizure-like activity using neuron mass models that capture general seizure dynamics (Jirsa et al. 2014 ). The model was then modified to integrate compatibility with external electrical stimulation and state variable tracking, enabling exploration of parameter combinations that lead to delaying SLA onset maximally.

The ERS model is particularly suited for this study because of its ability to model both normal brain activity and seizures with the same set of differential equations.

$$\dot{x}_1 = y_1 - f_1(x_1, x_2) - z + I_{ext} \quad (1)$$

$$f_1(x_1, x_2) = \begin{cases} ax_1^3 - bx_1^2, & \text{if } x_1 < 0, \\ -(m - x_2 + 0.6(z - 4)^2)x_1, & \text{if } x_1 \geq 0. \end{cases} \quad (2)$$

The ERS model is composed of a set of coupled differential equations that describe the relationship between fast and slow dynamics in neuronal activity. The function (2) models transitions between normal and pathological brain states, enabling the study of seizure-like activity (SLA). Electrical stimulation is modeled (1) as an external input  $I_{ext}$  to allow for experimentation of various stimulation waveform parameters. The stimulation interacts with the dynamics of the system, potentially stabilizing or destabilizing the trajectory of state variables depending on its amplitude, frequency, and timing. The model was set up to produce neural activity within physiologically plausible bounds. In the TVB full-brain structural connectivity matrix, node 40, corresponding to the hippocampus, was chosen and its epileptogenicity parameter set to a value of  $-2.601$  to simulate seizure activity. State variables were bounded between  $-2.0$  and  $2.0$  mV to simulate realistic electrical activity in cortical regions. Integration time steps of  $0.1$  ms were chosen to capture fine temporal details throughout a simulated 7-second window.

### B. Control Simulation

A baseline control simulation, without any stimulation, was conducted to determine the default SLA onset. Event onsets are detected when the SEEG signal crosses below a threshold of  $-1.8$  mV. Visible in the control simulation are two SLA events. The first event was monitored and its delay in correspondence to various stimulation parameters were measured.

### C. Simulation and Stimulation Parameters

Virtual stimulation was delivered at fixed time points using a stimulation waveform composed by monophasic square pulses. A comprehensive parameter sweep was performed varying the following parameters:

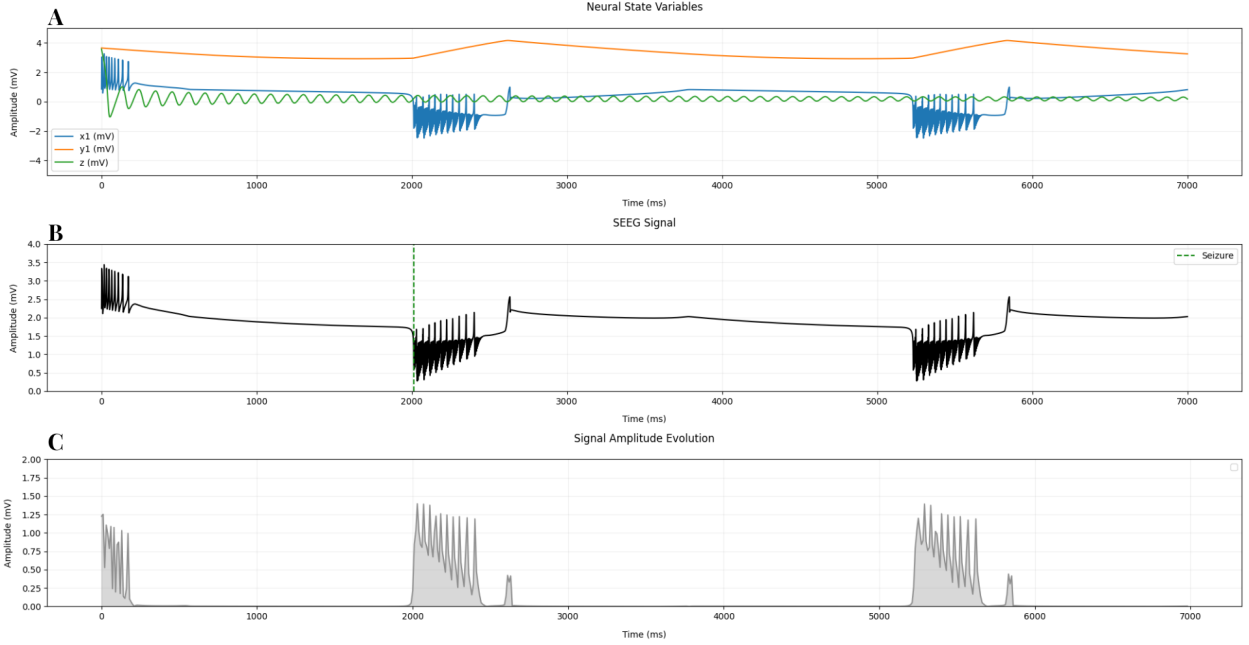


Figure 1. A: State Variables  $x_1$ ,  $x_2$ , and  $z$  in microVolts are shown in relation to time. There is a noticeable SLA onset around  $t_1 = 2000$  ms and a second one at around  $t_2 = 5300$  ms. Onset  $t_1$  represents the value of the control simulation onset. B: SEEG signal (mV) of the combined state variables over time. C: Absolute value (mV) of the signal amplitude over time.

Parameter	Value		
Stimulation Onset (ms)	1000	1500	2000
Stimulation Amplitude (mV)	2.0	5.0	7.5
Stimulation Frequency (Hz)	50	150	250
Pulse Width (ms)	5.0	25.0	45.0
Stimulation Durations (ms)	250	500	750

Table 1. Parameter values included in the parameter sweep. Values were selected from a larger set of experimented values with even increments.

#### D. SLAO Detection and Stimulation Effect Analysis

Each simulation assessed the time of seizure-like activity onset and whether the stimulation effectively delayed or suppressed the seizure compared to a control scenario with no stimulation. After stimulation, SEEG signals were monitored for threshold crossing below (-1.8 mV) to mark the SLA onset. The delay as a result of the stimulation was measured and compared to the control (no stimulation) simulation. Additionally, total charge (in  $\mu\text{C}$ ) delivered during stimulation was calculated by integrating the stimulus waveform over time (2), specifically, (3).

$$Q = \int_{t_1}^{t_2} I(t) dt \quad (2)$$

$$Q = A \times \tau \times \frac{D}{T} \quad (3)$$

$Q$  ( $\mu\text{C}$ ) is calculated using stimulation parameters, where  $A$  (mV) is the stimulation amplitude,  $\tau$  is the pulse width (ms),  $D$  is the stimulation duration (ms), and  $T$  (ms) is the period interval.

All analysis and simulations were done with custom Python scripts.

### III. RESULTS

The results revealed a diverse range of effects resulting from the various stimulation parameters. Among the 243 simulations conducted, 12 (4.9%) resulted in an advancement of the SLA event, while the remaining 231 (95.1%) led to a delay in SLA onset. The delays had a mean of 2,546.26 ms, a median of 2,541.30 ms, and a standard deviation of 1,064.17 ms. Notably, none of the tested parameters succeeded in suppressing SLA within the 7-second observation

Statistic	Value
SLAO Advancements	12 (4.9%)
SLAO Delays	231 (95.1%)
Mean Delay	2546.26 ms
Median Delay	2541.30 ms
Standard Deviation	1064.17 ms
Minimum Delay	-763.30 ms
Maximum Delay	4314.40 ms

Table 2. Simulation statistics including percentage anticipated, percentage delayed, mean, median, standard deviation, minimum, and maximum (ms).

### IV. DISCUSSION

This research provides insight into the dynamics and complexity involved in using electrical stimulation to modulate epileptic brain activity. Specifically, because it only involved one node and a 7-second timeframe, this study highlights the granular complexity and variability of a neural mass model in such a small-scale environment. The observed

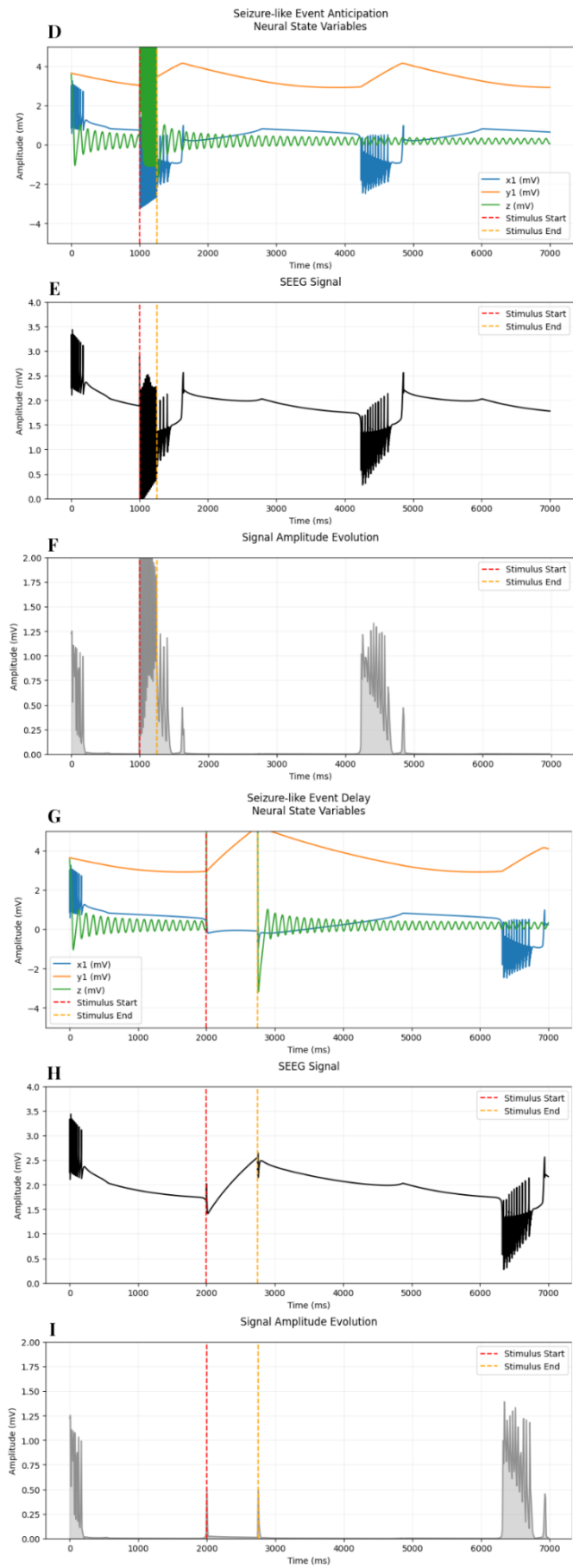


Figure 2. D: Neural state variables for SLAO anticipation. Variables  $x_1$ ,  $y_1$ , and  $z$  in microVolts over time, with stimulus timing marked. E: Neural state variables for seizure-like event delay. Variables  $x_1$ ,  $y_1$ , and  $z$  in microVolts over time, with stimulus timing marked. F: SEEG signal for seizure-like event anticipation, showing amplitude over time with stimulus markers. G, H, I are similar graphs but for SLAO with a delay.

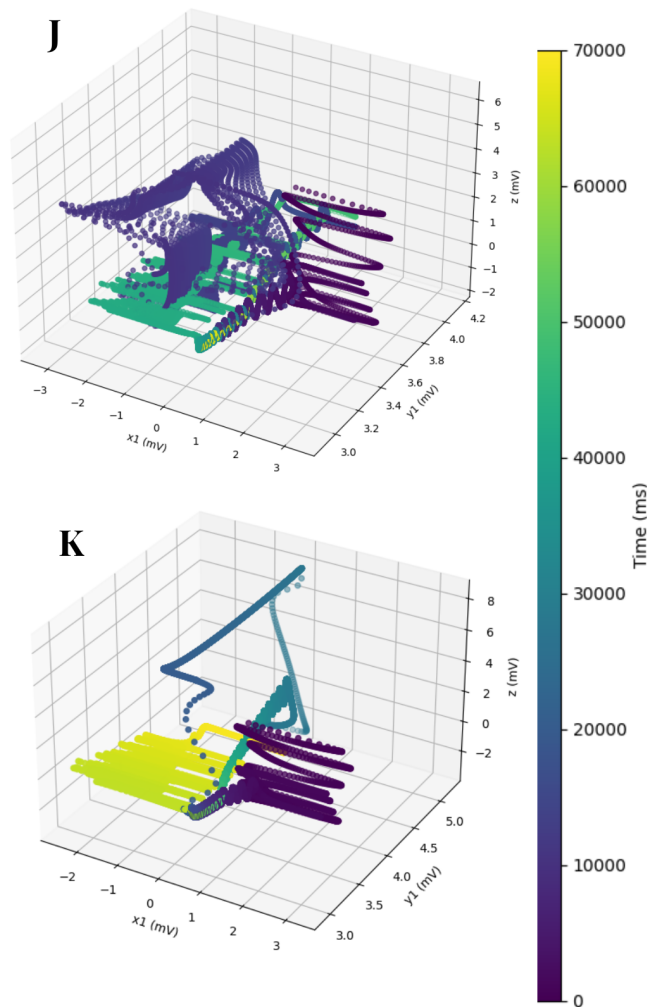


Figure 3. J: 3D state space of seizure-like event anticipation, showing variables  $x_1$ ,  $y_1$ , and  $z$  in microVolts. Time progression is indicated by color. K: 3D state space of seizure-like event delay, with variables  $x_1$ ,  $y_1$ , and  $z$  in microVolts. Time is represented by color range shown on the left.

delays suggest that it is possible that electrical stimulation can modulate the timing of seizure onset—potentially providing a window for therapeutic intervention before the onset occurs.

However, the high variability in resultant delay across parameters suggest that working with electrical stimulation can be both beneficial and harmful to patient outcomes, and there still lies uncertainty in the ability of stimulation to effectively delay a seizure in a clinical setting. Additionally, the lack of complete suppression indicates the need for further parameter optimization and possibly alternative stimulation strategies. Overall, in analyzing small-scale dynamics of a neural mass model, this study provides insight into the complexity involved in future epilepsy solutions.

Several limitations must be acknowledged: (1) The Epileptor Resting State model, at a single node, may not capture all the intricacies of real-world human epileptic activity. (2) Though initially refined from a larger range, the chosen parameter ranges may not encompass the optimal settings required for seizure suppression. (3) A 7-second

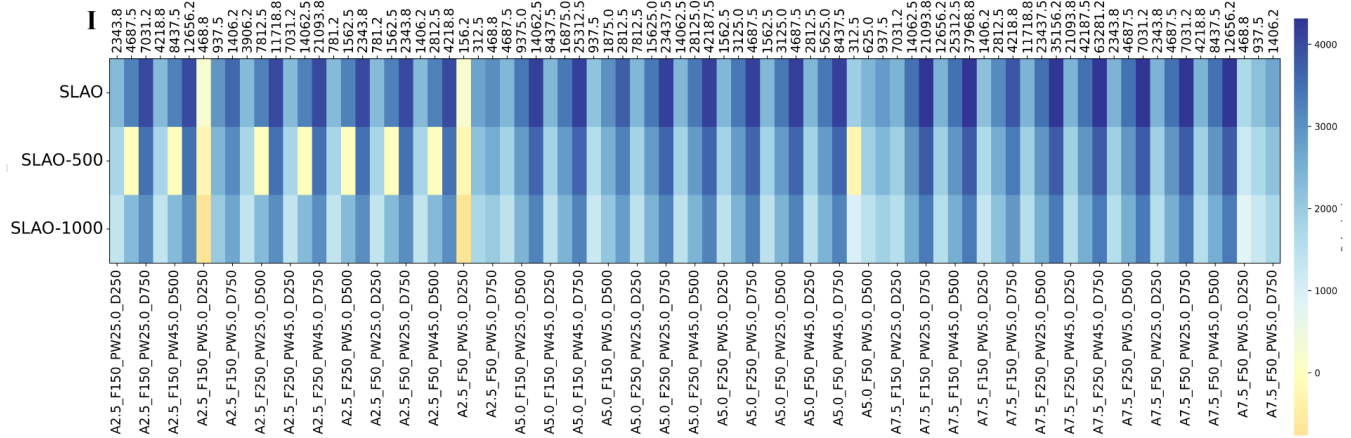


Figure 4. I: Heatmap visualization of stimulation parameter effects on seizure-like activity (SLA) delay. The x-axis shows parameter combinations of amplitude (A, mV), frequency (F, Hz), pulse width (PW, ms), and duration (D, ms). The y-axis indicates timing relative to SLA onset (SLAO), with incremented onsets relative to the control simulation onset. Total charge ( $\mu\text{C}$ ) for each parameter combination is shown at the top. Color intensity represents delay magnitude (ms), with darker blue indicating longer delays and yellow showing negative delays (anticipation).

observation window may not fully capture long-term seizure dynamics.

To address these, future studies should consider expanding the parameter space, incorporating adaptive stimulation strategies that respond to real-time neural activity, and creating more realistic scenarios with more nodes and a larger time frame.

## V. CONCLUSION

This study investigated electrical stimulation as a means of seizure dynamics control using a specially adapted Epileptor model in The Virtual Brain. Through a systematic parameter sweep of 243 simulations, a range of effects on the timing of seizure onset was observed but did not completely suppress seizures within 7-seconds. This study demonstrates the complex relation between the stimulation parameters and epileptic activity that provides insight into personalized and preventative epilepsy treatment.

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