



Synchronization in Dynamical Systems from the Bifurcation Theory Point of View

Doctoral Thesis Defence

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February 4, 2026

Outline

Motivation

Focal epilepsy and VHFOs

VHFOs/UFOs – questions and objectives

Interneuron model

Two coupled INs

Neuronal network of coupled INs

Conclusion

Readers' Questions

Assoc. Prof. Ing. Luděk Berec, Dr.

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Focal epilepsy and VHFOs/UFOs

- **Synchronization** of large neuronal populations \rightsquigarrow recurrent spontaneous seizures
- Modeling via a population of coupled neurons/neural masses
- **HFOs**: 80–600 Hz, **VHFOs**: 600–2 000 Hz, **UFOs**: above 2 000 Hz
- Possible (physiological) frequencies: at most \sim 600 Hz

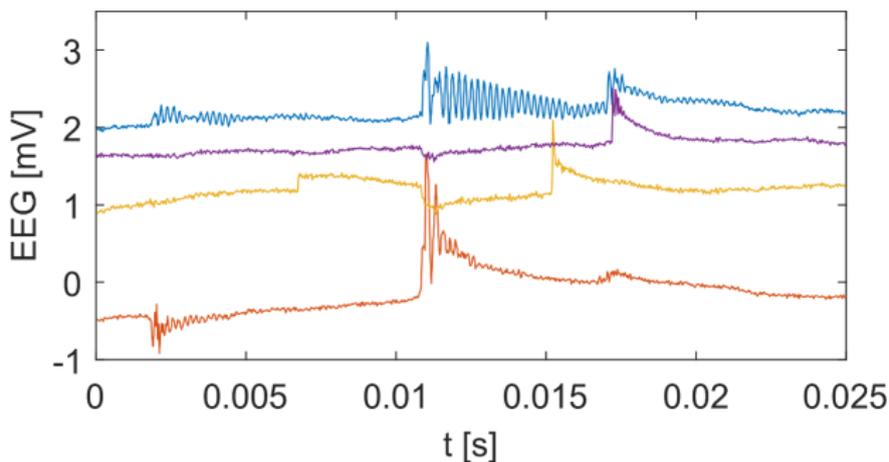


Figure: An example of real UFOs

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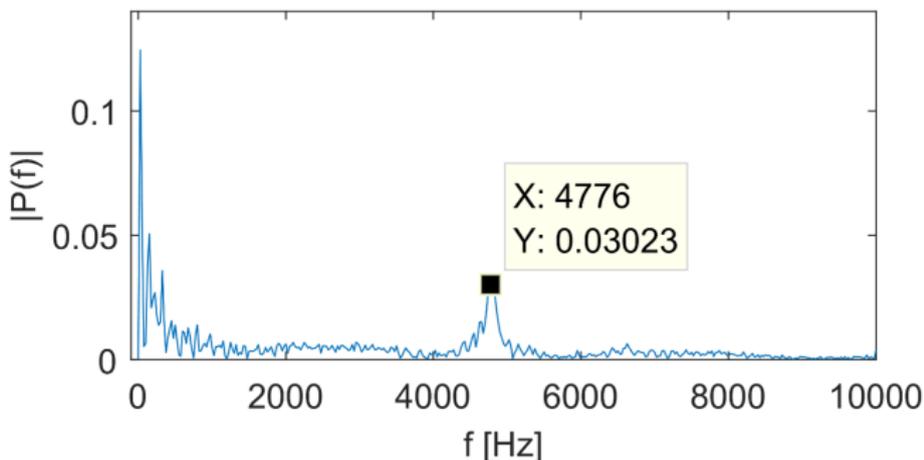


Figure: A periodogram of the signal with real UFOs

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VHFOS – questions and objectives

Overall (medical) objective

- HFOs – biomarker, maybe physiological, VHFOS/UFOs – new biomarker, non-physiological
- Possible explanation of VHFOS/UFOs emergence leading to a deeper understanding of electrical events in the human brain

Mathematical objectives

- Can we simulate such VHFOS/UFOs using models of neuronal networks?
- Which phenomenon is behind the emergence of VHFOS/UFOs?

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Interneuron model (IN)

- Model equations:¹

$$\left\{ \begin{array}{l} C \frac{d}{dt} V = I_{ext} - \overbrace{\bar{g}_L (V - V_L)}^{I_L} - \overbrace{\bar{g}_{Na} m_\infty^3(V) h (V - V_{Na})}^{I_{Na}} - \overbrace{\bar{g}_K n^4 (V - V_K)}^{I_K} \\ \frac{d}{dt} h = \frac{h_\infty(V) - h}{\tau_h(V)} \quad \frac{d}{dt} n = \frac{n_\infty(V) - n}{\tau_n(V)} \end{array} \right.$$

- Steady-state functions and time functions:

- Na²⁺-channel: $m_\infty(V) = (1 + \exp[-0.08(V + 26)])^{-1}$

$$h_\infty(V) = (1 + \exp[0.13(V + 38)])^{-1}$$

$$\tau_h(V) = 0.6(1 + \exp[-0.12(V + 67)])^{-1}$$

- K⁺-channel: $n_\infty(V) = (1 + \exp[-0.045(V + 10)])^{-1}$

$$\tau_n(V) = 0.5 + 2(1 + \exp[0.045(V - 50)])^{-1}$$

¹White, J. et al. (1998). Synchronization and oscillatory dynamics in heterogeneous, mutually inhibited neurons.

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- Typical parameter values for a hippocampal interneuron:
 - Capacitance: $C = 1$ [$\mu\text{F}/\text{cm}^2$]
 - Externally applied current: $I_{ext} \in [-2, 27]$ [$\mu\text{A}/\text{cm}^2$]
 - Maximum conductances: $\bar{g}_L = 0.1$, $\bar{g}_{Na} = 30$, $\bar{g}_K = 20$ [mS/cm^2]
 - Equilibrium potentials: $V_L = -60$, $V_{Na} = 45$, $V_K = -80$ [mV]
- Crucial role in the synchronization of hippocampal neuronal activity

¹White, J. et al. (1998). Synchronization and oscillatory dynamics in heterogeneous, mutually inhibited neurons.

Types of dynamics

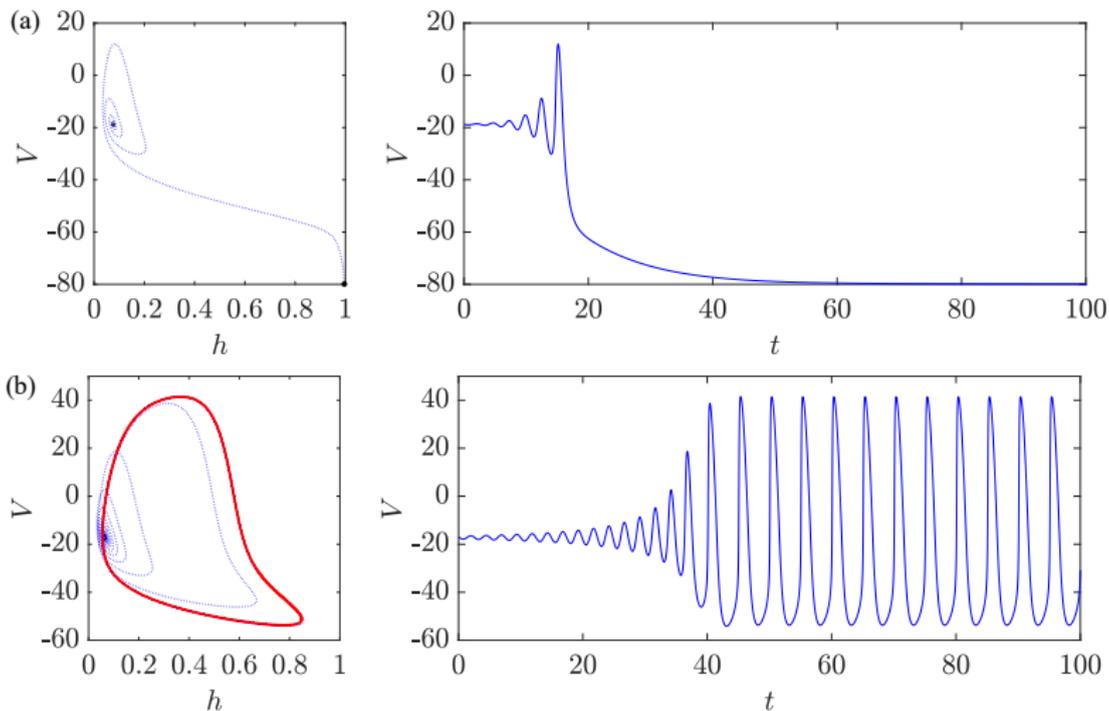


Figure: Orbits tending to (a) a stable equilibrium (resting state) for $I_{ext} = -2$ and (b) a limit cycle (spiking dynamics) for $I_{ext} = 8$

Model dynamics w.r.t. I_{ext}

- Variation of I_{ext} can switch the model dynamics
- **Rest./overstim. state** (EPs), **spiking dynamics** (min & max of LCs)
- – stable, - - unstable

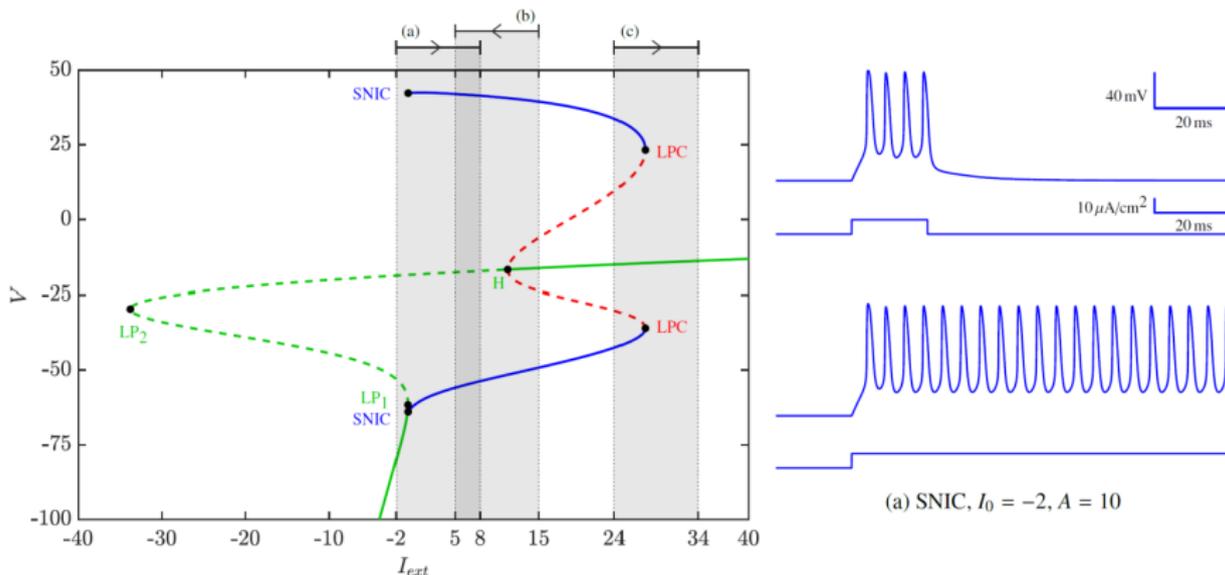


Figure: A bifurcation diagram of V w.r.t. I_{ext} , along with the stimuli ranges

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Types of dynamics (w.r.t. C_1 and ε)

- In-phase synchrony (IPS)
- Quasiperiodic behavior (QB)
- Anti-phase synchrony (APS)
- Quasiperiodic anti-phase synchrony (QAPS)
- Resting (RS) or overstimulated state (OS)
- Subthreshold oscillation (STO)

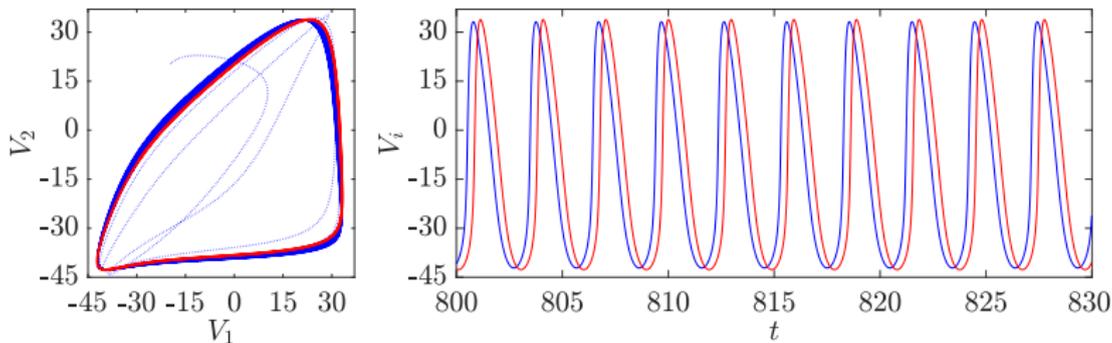


Figure: An orbit tending to the IPS for $C_1 = 0.99$, $\varepsilon = 0.04$

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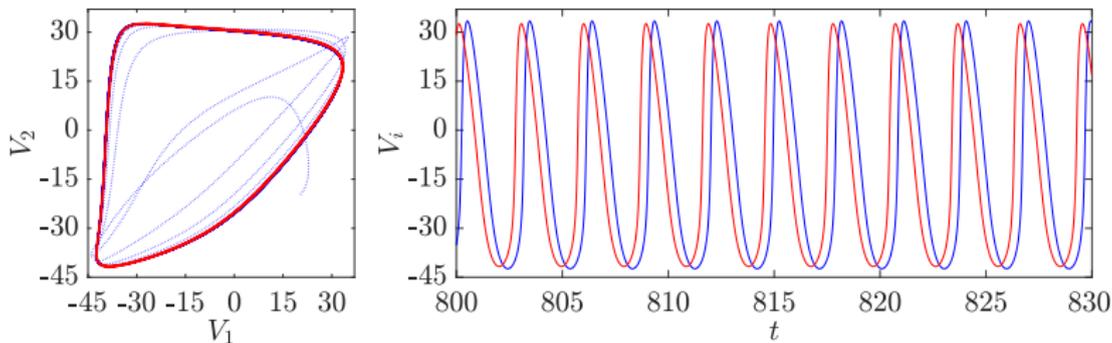


Figure: An orbit tending to the IPS for $C_1 = 1.01$, $\varepsilon = 0.04$

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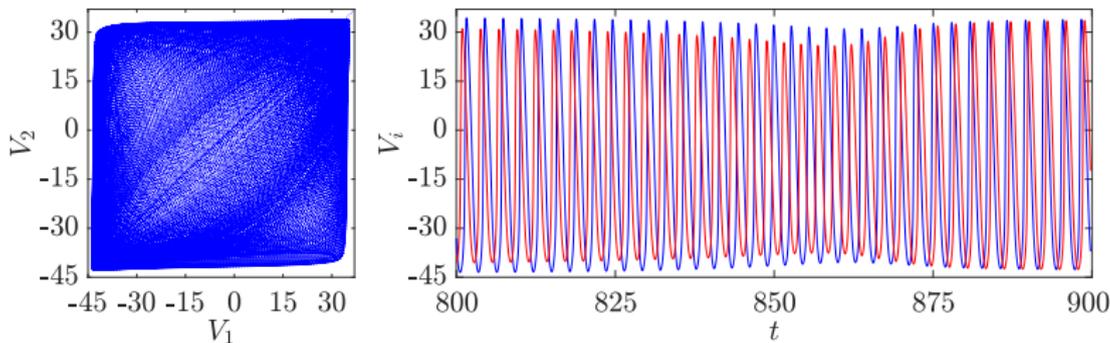


Figure: A quasiperiodic orbit for $C_1 = 0.95$, $\varepsilon = 0.04$

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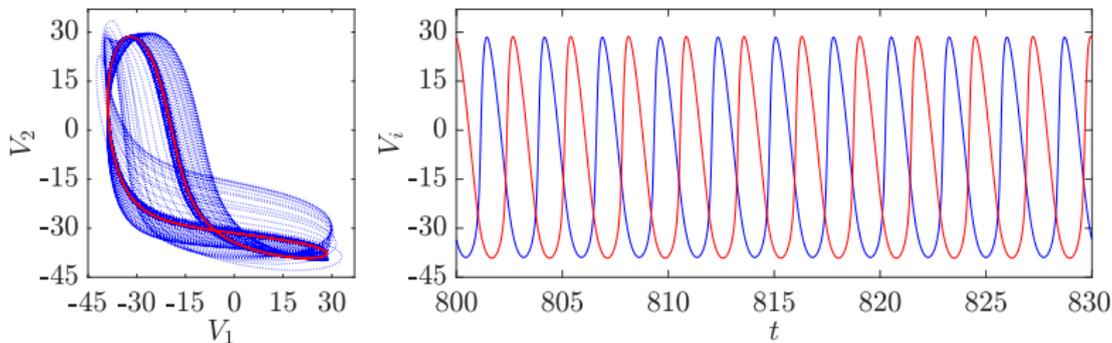


Figure: An orbit tending to the APS for $C_1 = 0.99$, $\varepsilon = 0.035$

Types of dynamics (w.r.t. C_1 and ε)

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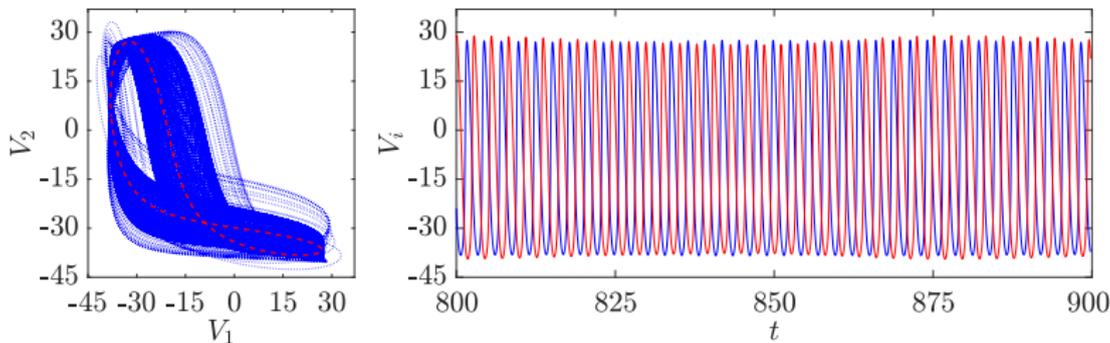


Figure: A quasiperiodic orbit on an invariant anti-phase torus (QAPS) near the unstable APS for $C_1 = 0.99$, $\varepsilon = 0.04$

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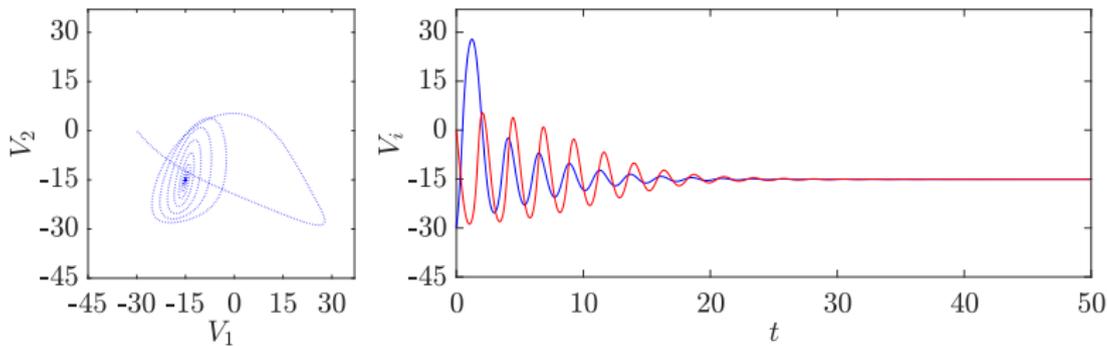


Figure: An orbit tending to the RS for $C_1 = 0.99$, $\varepsilon = 0.04$

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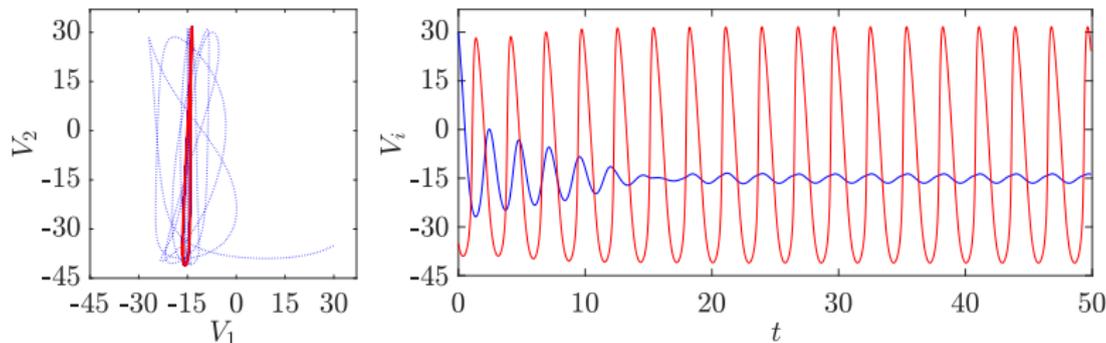


Figure: An orbit tending to a limit cycle representing the STO of the first neuron for $C_1 = 0.99$, $\varepsilon = 0.04$

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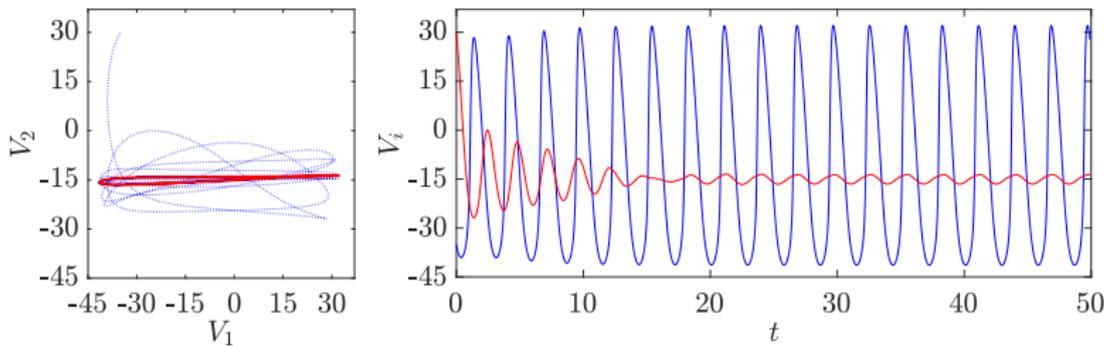


Figure: An orbit tending to a limit cycle representing the STO of the second neuron for $C_1 = 0.99$, $\varepsilon = 0.04$

Frequency of the IPSs and APS w.r.t. C_1

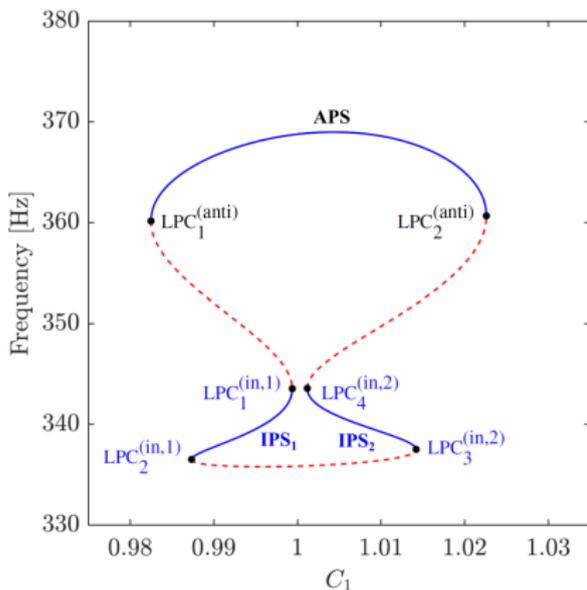
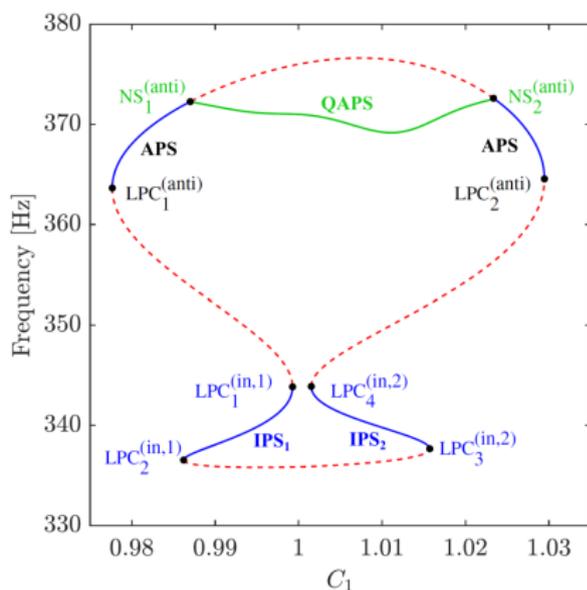
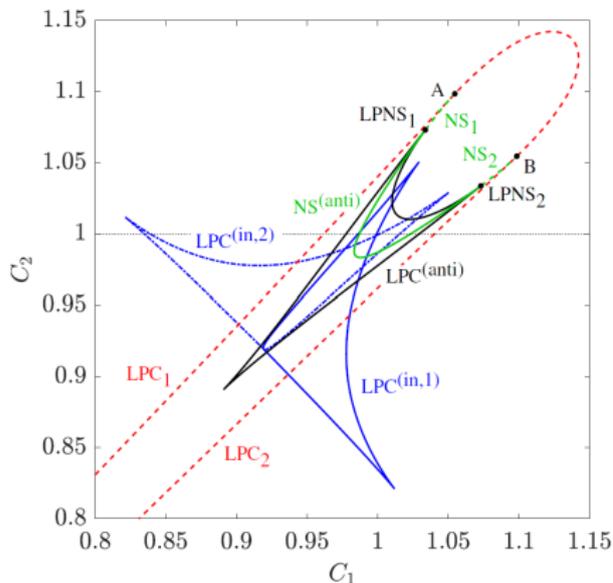
(a) $\varepsilon = 0.035$ (b) $\varepsilon = 0.04$

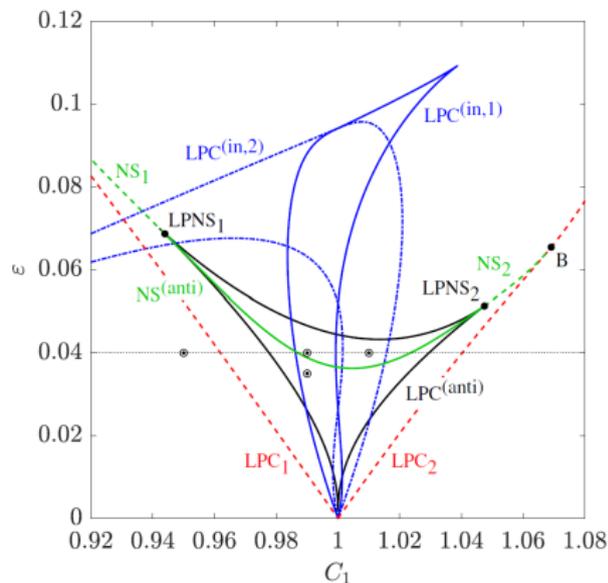
Figure: Frequency of the IPSs, APS (and QAPS) w.r.t. C_1 , while $C_2 = 1$ is fixed

- Presence of **bistability** for a relatively wide range of C_1

Arnold tongues in (C_1, C_2) and (C_1, ε) -planes



(a) $\varepsilon = 0.04$

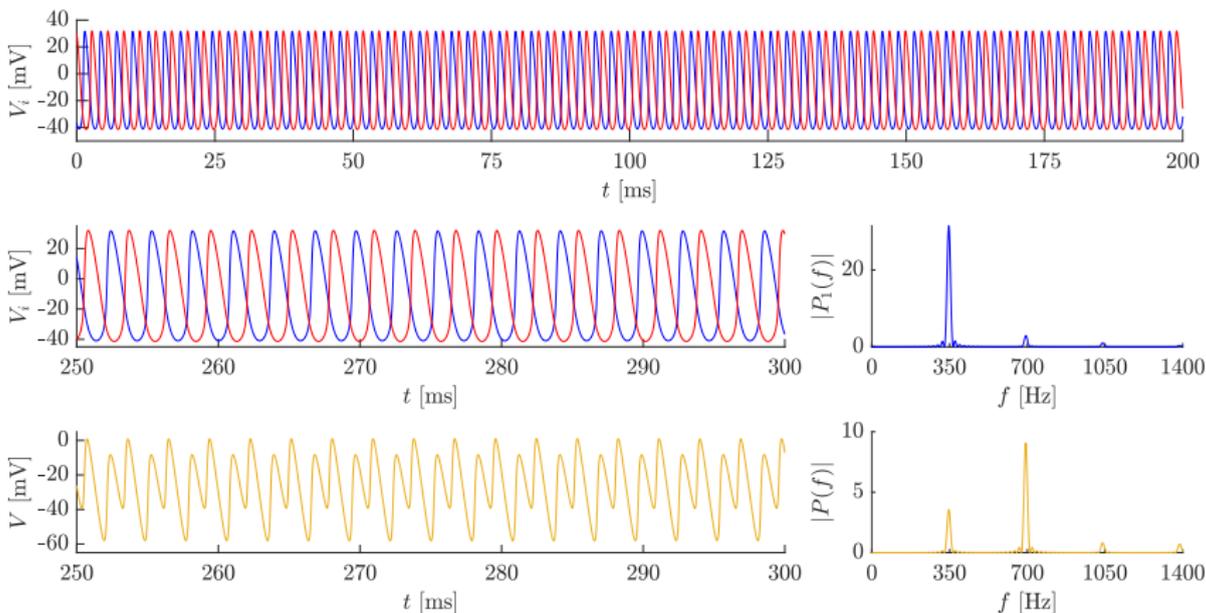


(b) $C_2 = 1$

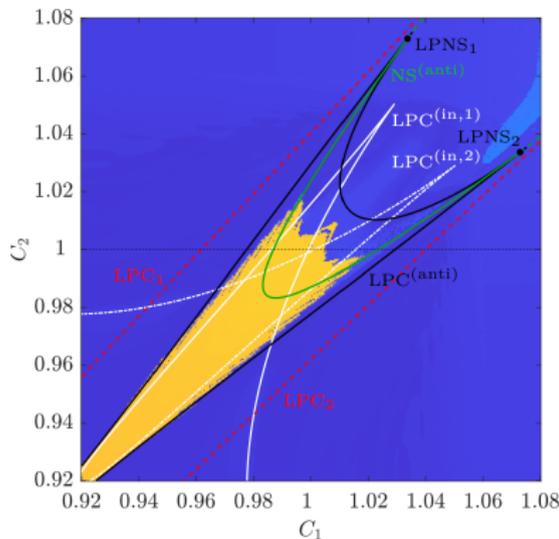
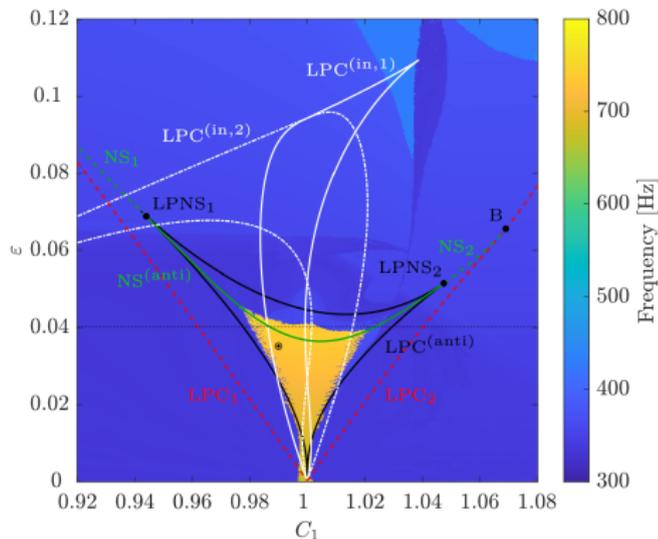
- **Blue/black** lines – LPC for two symmetrical **IPs** and one **APS**
- **Red** dashed line – LPC for two unstable periodic solutions
- **Green** line – NS bifurcation of the APS

Modeling EEG signal

- Real EEG signals (LFP) – local electrical events
- Combined signal: $V = \sum_{i=1}^N V_i$

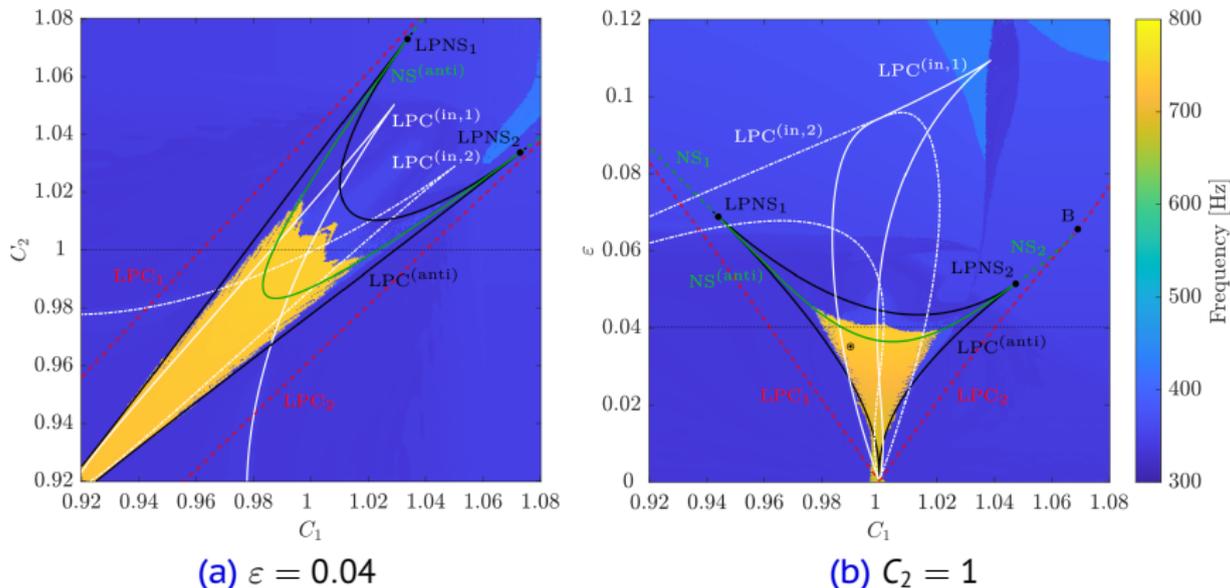


Doubled dominant frequency in $V = V_1 + V_2$

(a) $\varepsilon = 0.04$ (b) $C_2 = 1$

- White/black lines – LPC for two symmetrical IPSs and one APS
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Doubled dominant frequency in $V = V_1 + V_2$



- Background color – the **dominant** frequency in the summed signal $V = V_1 + V_2$
- ICs – near the APS (if applicable)

Variation of I_{ext} can switch the dynamics: RS \leftrightarrow IPS

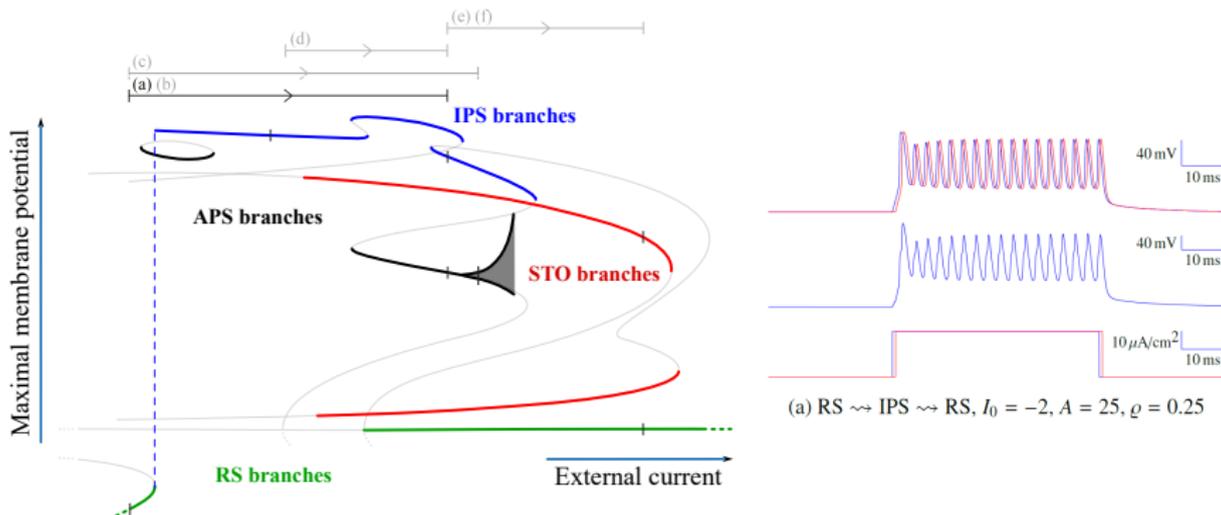


Figure: A simplified scheme of the bifurcation diagram w.r.t. I_{ext} , along with the stimuli ranges

- I_0 – baseline current
- A – amplitude
- ϱ – relative propagation delay for the second neuron

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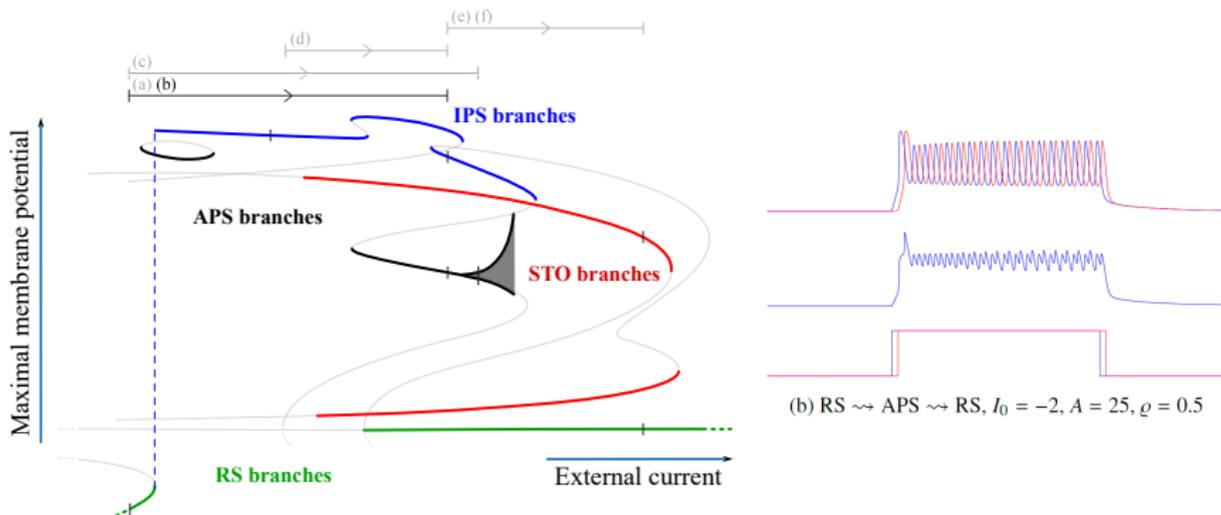


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80 coupled INs – simulation setting (1)

- $N = 80$ INs, $\mathcal{P}_1 = \{1, \dots, 40\}$, $\mathcal{P}_2 = \{41, \dots, 80\}$
- $C_i \sim TN(1, 0.03^2, 0.91, 1.09)$, $i \in \mathcal{P}_1 \cup \mathcal{P}_2$
- Symmetrical gap-junctional coupling

$$\varepsilon_{ij} = \begin{cases} 0, & i = j, \\ 0.01, & (i, j) \in \mathcal{P}_1 \times \mathcal{P}_1 \cup \mathcal{P}_2 \times \mathcal{P}_2, \quad i \neq j, \\ 0.001, & \text{otherwise} \end{cases}$$

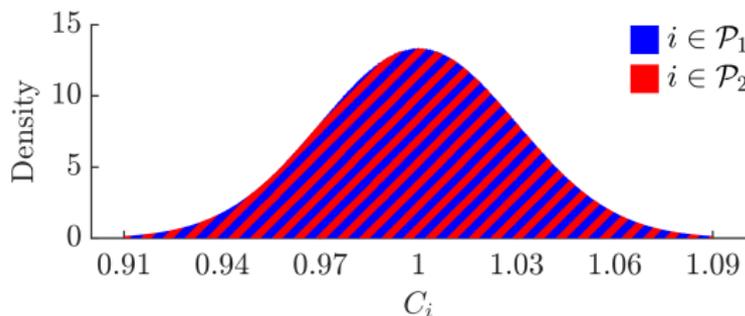


Figure: Capacitances

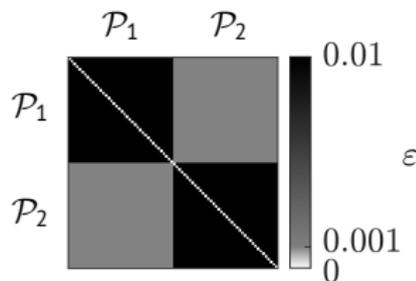


Figure: Coupling

80 coupled INs – simulation setting (2)

- Equal ICs near the collective resting state for $I_{ext} = -2$
- Random input

$$I_{ext,i}(t) = \underbrace{-2 + p_i(t)}_{deter.} + \underbrace{\xi_i(t)}_{stoch.}, \quad \xi_i(t) \stackrel{ind}{\sim} N(0, 1^2), \quad i \in \mathcal{P}_1 \cup \mathcal{P}_2$$

with time-distributed stimuli given by

$$q_i \sim TN(0, 0.2^2, -0.6, 0.6), \quad i \in \mathcal{P}_1,$$

$$q_i \sim TN(r, 0.2^2, r - 0.6, r + 0.6), \quad i \in \mathcal{P}_2$$

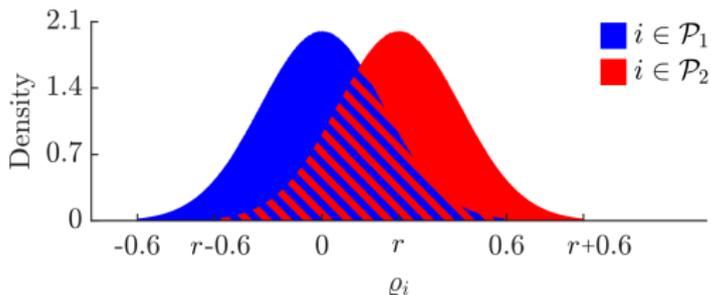
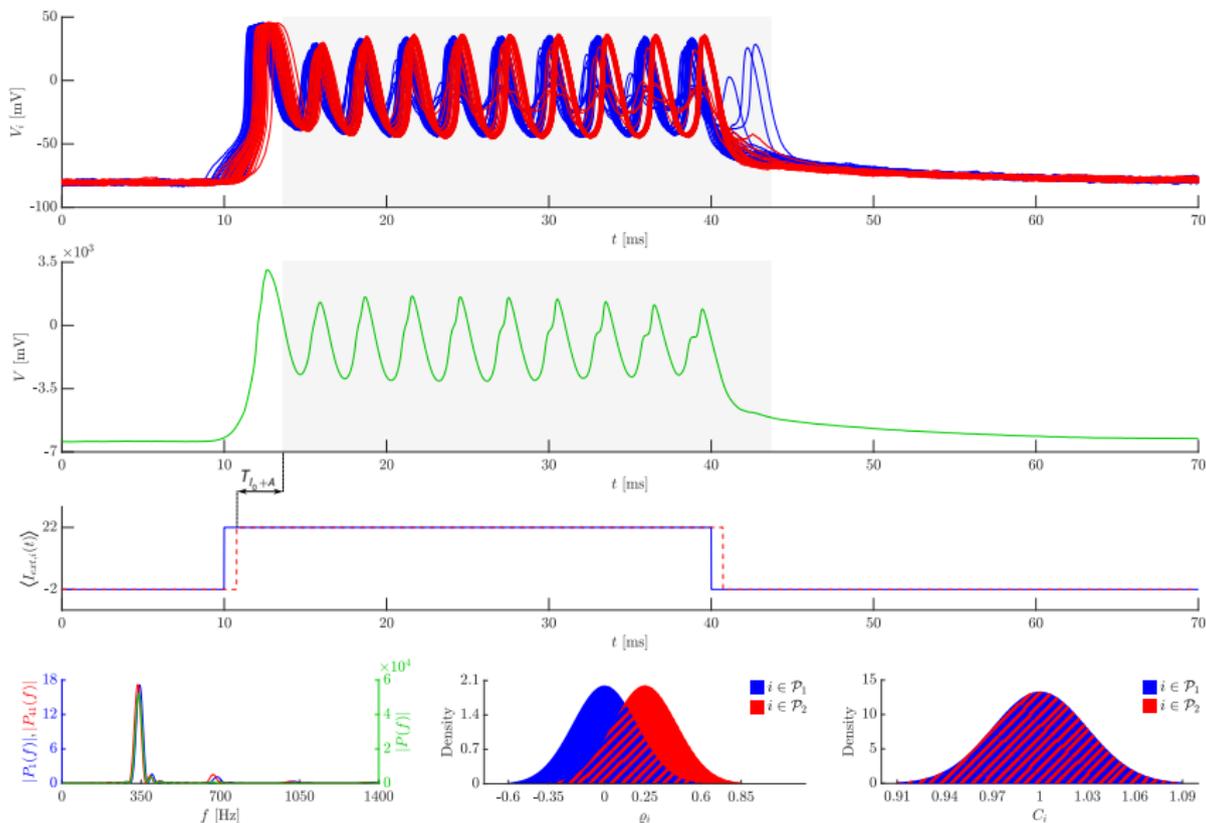
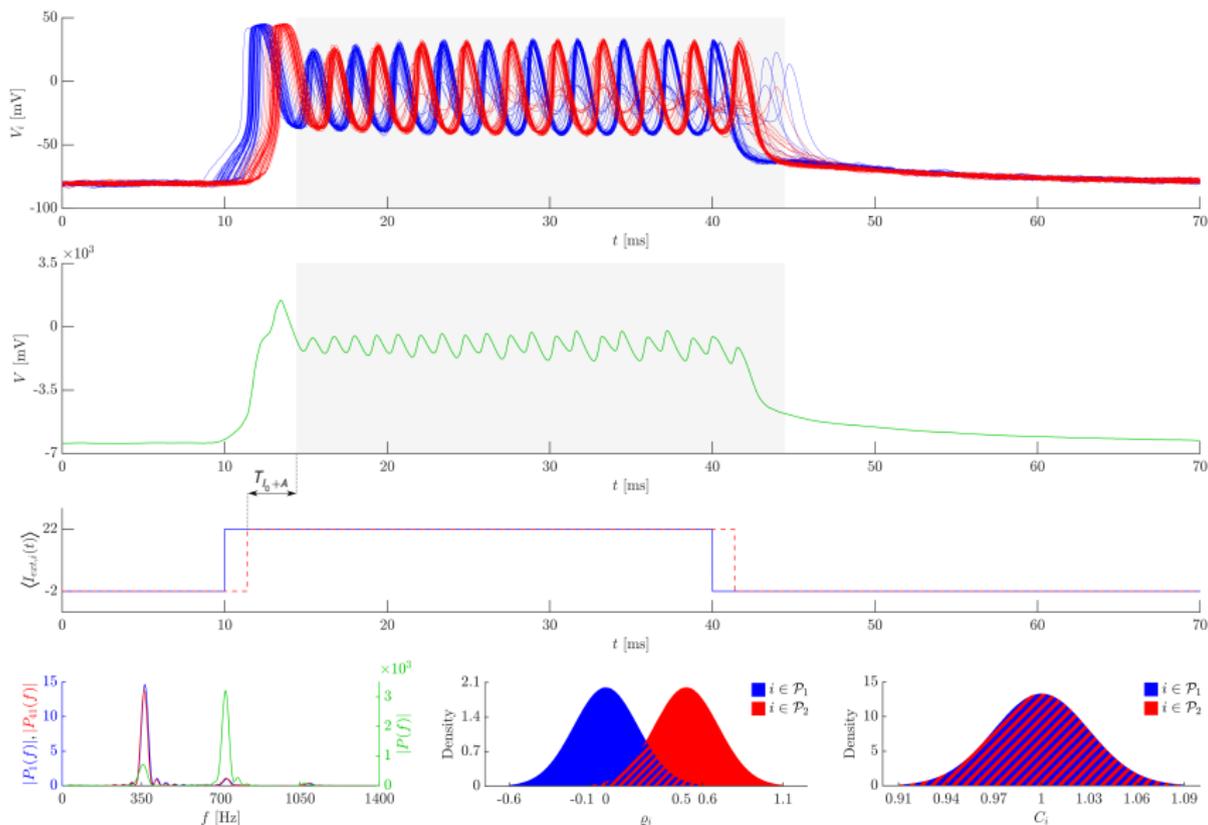


Figure: Relative delay

Collective in-phase behavior for $r = 0.25$



Collective anti-phase behavior for $r = 0.5$



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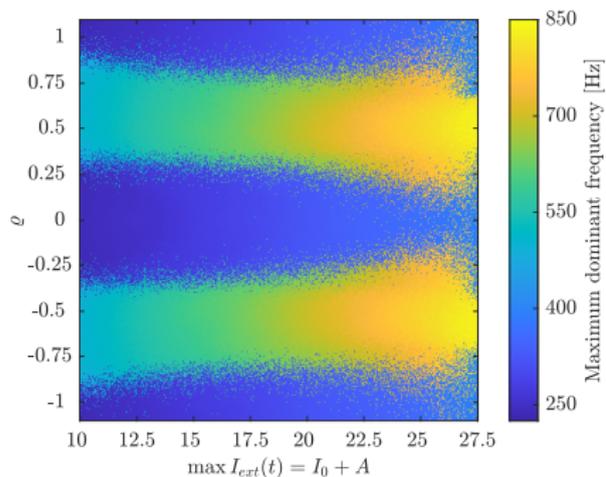
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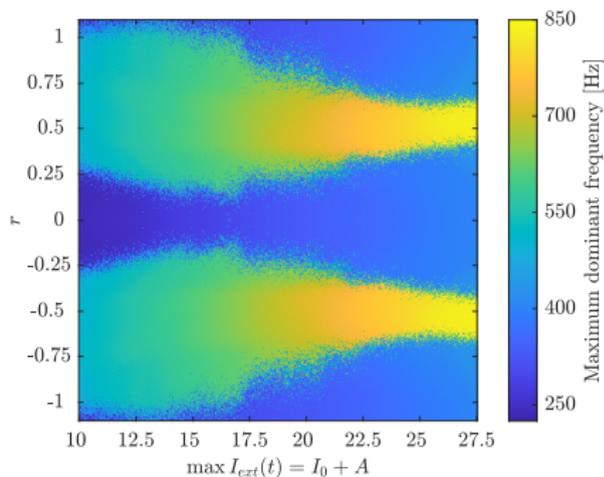
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Comparison of small- and large-scale networks

- Evoked neuronal response within 30 ms after the stimulus onset



(a) 2 coupled INs

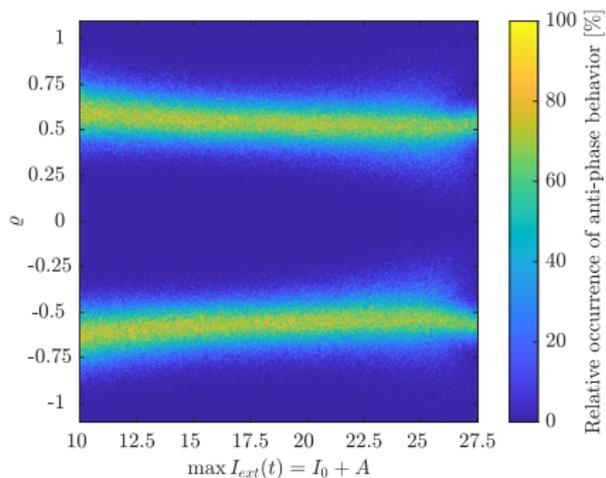


(b) 2×40 coupled INs

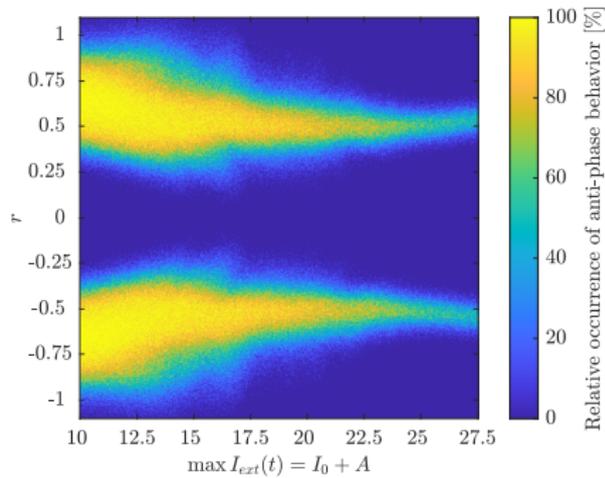
Figure: The **maximum dominant frequency** in the summed signal V

Comparison of small- and large-scale networks

- Evoked neuronal response within 30 ms after the stimulus onset
- Increasing the network size **enhances** the probability of achieving APB



(a) 2 coupled INs



(b) 2×40 coupled INs

Figure: The **relative occurrence** of the generated APB

VHFOs – possible mathematical explanation

Mathematical objectives

- Can we simulate such VHFOs/UFOs using models of neuronal networks?
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Possible answers

- **Weakened connections** between similar neuronal populations (near-identical neurons) can result in apparent VHFOs
- **Anti-phase** (phase-shift) **synchronization** of neuronal subpopulations (neuronal firing)

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Thank You for Your Attention!

References

Ševčík, J., & Příbylová, L. (2025). Cycle multistability and synchronization mechanisms in coupled interneurons: In-phase and anti-phase dynamics under current stimuli. *Applied Mathematics and Computation*, 503, 129500. doi: 10.1016/j.amc.2025.129500.

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(1) Monography × a commented collection of papers

- **Coherent restructuring** and **unification** of all results into a single, logically consistent narrative
- **Space to integrate additional results** that could not be included in journal articles
- Harmonized **heterogeneous publications** with different scopes, journals, and levels of my authorship contribution
- Eliminated **redundancy** and **overlap** in motivation, methodology, and model descriptions across papers
- **Conceptual** (not chronological) **organization of results**
- Unified findings within a **bifurcation-theoretic view of synchronization** (official thesis assignment), improving clarity and accessibility

(2) Author's contributions

- Published papers = **joint results** of the entire research team
↪ a strict separation of individual contributions non-trivial (see Section List of Published Works)
- I collaborated on **all results** included in the dissertation
- All results not previously published in journal articles are **entirely my own**
- My core contributions:
 - **numerical computations** and **simulations**,
 - **visualization** and **graphical presentation** of results,
 - **software (co-)development** (including complete code implementation or tuning/refactoring),
 - **writing** and **structuring** of the thesis text

(3) Broader context and relevance to epilepsy research

- Deeper understanding of **electrical events in the human brain**, possible **mechanisms underlying the onset of epilepsy seizures**
- **Potentials of UFOs**
 - More accurate **detection and localization** of epileptogenic zones (improved **surgical outcomes**)
- **Contribution of bifurcation diagrams**
 - **Systematic map** of dynamical regimes (DRs)
 - **Robustness** of DRs under small parameter perturbations
 - Reveal **transitions between DRs** as model parameters vary
 - Diagrams w.r.t. I_{ext} show **response** to:
 - fluctuating synaptic input,
 - information transfer from the surrounding network,
 - externally induced modulation (e.g., stimulation or pharmacological effects)
- Principled framework for **interpreting and predicting transitions** to epileptic activity

(4) Morris–Lecar (ML) × Interneuron (IN) model

- **Model type and biological interpretation**
 - Both are **conductance-based neuronal models**
 - ML: a **pyramidal cell**, IN: an **interneuron**
- **Single-cell dynamics**
 - Both are **class-I excitable models**
 - Similar bifurcation structure and **comparable dynamical repertoire** (resting state, spiking, overstimulated state)
 - Physiological firing ranges (ML: $\sim 0\text{--}60$ Hz, IN: $\sim 0\text{--}400$ Hz)
- **Network-level bifurcation structure**
 - The bifurcation structure of the **two-cell interneuronal system** is **significantly richer** than that of two ML neurons
 - APS in the ML system is **more robust** (longer hyperpolarization)
- **Role within the thesis**
 - Analysis started with the **ML**, further extended to the **IN**
 - **Non-model-specific nature** of the APS

(5) Declaration on the use of AI tools

Dissertation, page iv

*“Throughout the preparation of this dissertation, I used ChatGPT (OpenAI, 2024) as a supplementary writing and editing tool. It assisted in refining the clarity of formulations, improving stylistic consistency, and resolving various technical matters related to terminology and \LaTeX . **The tool was employed exclusively to support the presentation of ideas; it did not contribute to any of the scientific results, analyses, or conclusions presented herein.**”*

- Used primarily for individual sentences rather than entire paragraphs

Motivation

Focal epilepsy and VHFOs

VHFOs/UFOs – questions and objectives

Interneuron model

Two coupled INs

Neuronal network of coupled INs

Conclusion

Readers' Questions

Assoc. Prof. Ing. Luděk Berec, Dr.

Prof. RNDr. Marek Lampart, Ph.D.

(A.1) Solver tolerances and scale separation (ode45)

- Neuronal model exhibit **separated scales**:
 - membrane potential (V): $\mathcal{O}(10)$,
 - gating variables: $\mathcal{O}(10^{-1})$
- RelTol controls the **relative accuracy** of large-amplitude variables
 - RelTol = 10^{-3} allows $\mathcal{O}(10^{-2})$ accuracy for V ,
 - sufficient for capturing frequencies, phases, and bifurcation structure
- AbsTol protects **small-amplitude variables**
 - AbsTol = 10^{-6} prevents numerical suppression of gating dynamics,
 - ensures stability near equilibria and bifurcation boundaries
- **Large RelTol & small AbsTol** is thus **computationally efficient** (especially in grid simulations of systems with separated scales)
- **Adaptive time step** with **upper bound** MaxStep given by dt (IN)
 - Fixed choice dt = 0.01 (based on observed system dynamics)

(A.2) Stiffness and numerical issues

■ Time-domain simulations

- typically strongly separated time scales,
- explicit solvers (e.g. ode45) require **very small time steps**
- No stiffness-related issues for **IN2**
- Stiffness encountered for **ML2** and **vdP2**

■ Parameter continuation (MatCont)

- Near ill-conditioned points during continuation
- Numerical difficulties near **bifurcation points** or **sharp transitions**
- Typically suppressed by:
 - adaptive step size control,
 - adjustment of tolerances (RelTol, AbsTol),
 - refined discretization of limit cycles

(B.1 & B.2) Discontinuities: time-domain and continuation

■ Time-domain simulations

- ode45 assumes a **smooth RHS** \rightsquigarrow loss of accuracy or solver failure
 - Possible solution: **event handling** & **piecewise integration**
- **Euler–Maruyama scheme**:
 - natural inclusion of **noise** (stochastic simulations),
 - ability to handle **discontinuous forcing** (shocks, jumps),
 - lower order of accuracy,
 - requirement of sufficiently small time step dt

■ Parameter continuation (MatCont)

- Relies on derivatives and **Jacobian matrices**
- Requires a **smooth** (at least C^1) vector field
 - Discontinuities or switching mechanisms not admissible
 - Switches commonly handled by **regularization** (e.g. smooth sigmoid-type approximations)

(B.3) Lyapunov definition of chaos

- **Sensitivity to initial conditions**
- Quantified by a **positive maximal Lyapunov exponent** (MLE)

$$\lambda_{\max} > 0$$

- Nearby trajectories diverge **exponentially in time**

$$\|\delta\mathbf{x}(t)\| \approx e^{\lambda_{\max}t} \|\delta\mathbf{x}(0)\|$$

- Known as the **butterfly effect**:
 - arbitrarily small perturbations \rightsquigarrow large long-term differences,
 - limits long-term predictability of the system
- Standard, **operational definition** in numerical studies

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