Long-term desynchronization with Coordinated Reset in models with synaptic and structural plasticity

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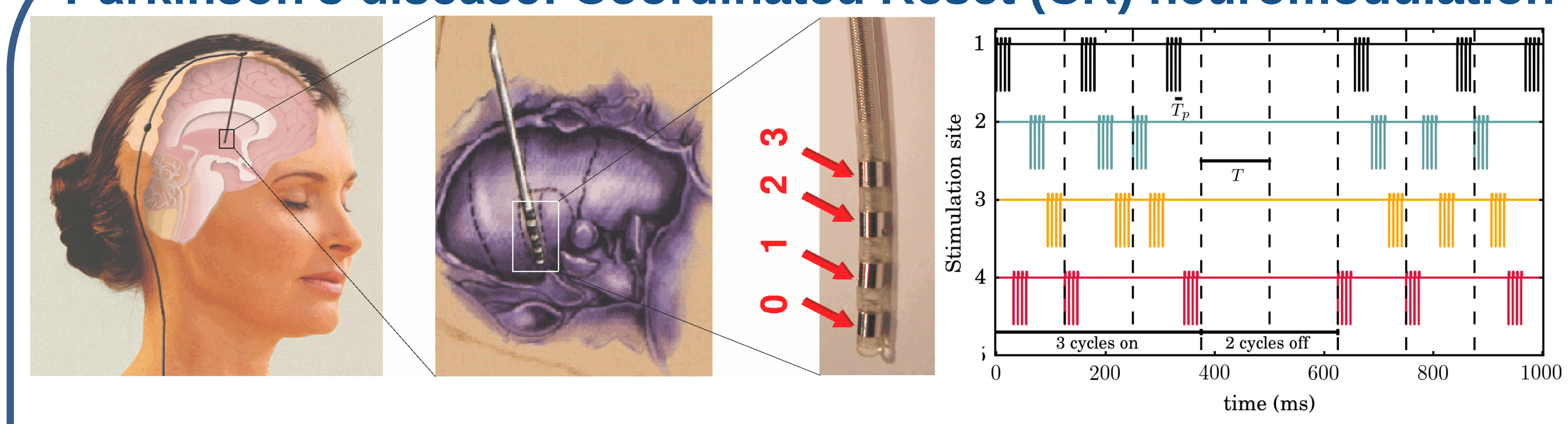
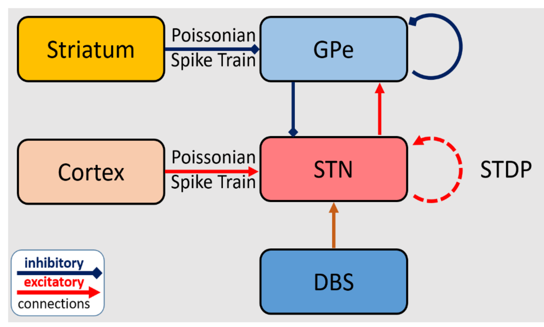
Parkinson's disease: Coordinated Reset (CR) neuromodulation

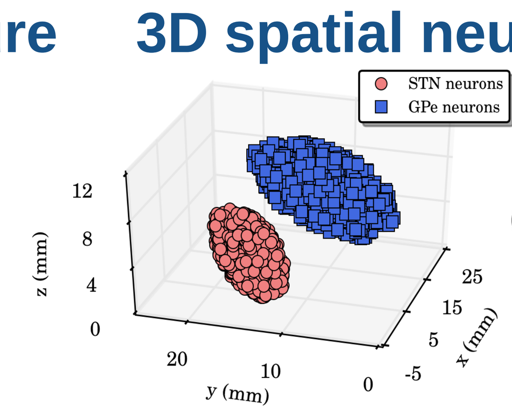


- Specifically designed to counteract abnormal neuronal synchronization (e.g. in Parkinson's disease) [1-4].
- Unitilizes spatio-temporally coordinated short electrical pulse trains of high-frequency deep brain stimulation (DBS).
- Administered via multi-contact depth electrodes implanted e.g. in the subthalamic nucleus (STN).

Neural network structure

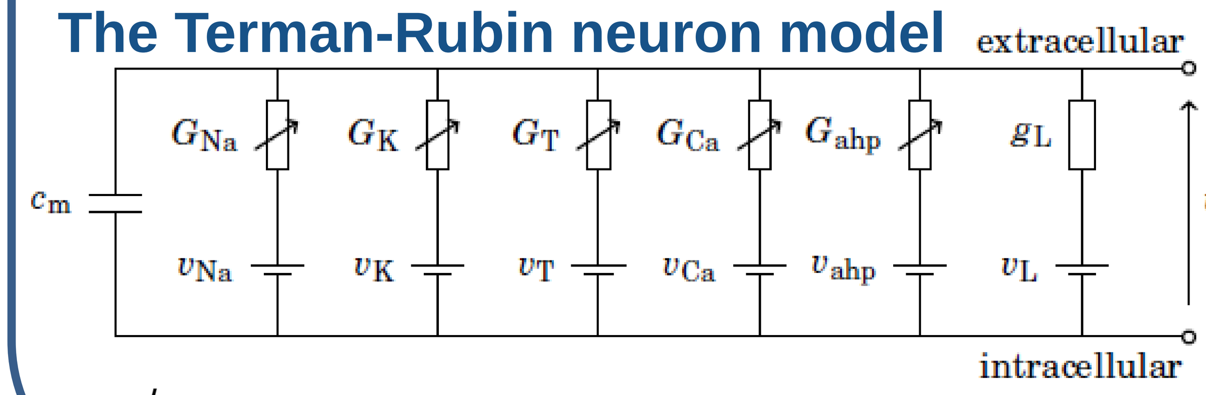


3D spatial neuron configuration



Coordinates → MRI before DBS surgery (left-brain hemisphere)

The Terman-Rubin neuron model



Ionic currents:

$$I_{\mathrm{L}} = g_{\mathrm{L}}\left[v - v_{\mathrm{L}}\right]$$

$$I_{\mathrm{K}} = g_{\mathrm{K}} n^4 \left[v - v_{\mathrm{K}}\right]$$

$$I_{\mathrm{Na}} = g_{\mathrm{Na}} m_\infty^3(v)\, h \left[v - v_{\mathrm{Na}}\right]$$

$$I_{\mathrm{T}} = g_{\mathrm{T}} a_\infty^3(v)\, b_\infty^2(v) \left[v - v_{\mathrm{Ca}}\right]$$

$$I_{\mathrm{T}} = g_{\mathrm{T}} a_\infty^3(v)\, r \left[v - v_{\mathrm{Ca}}\right]$$

$$I_{\mathrm{Ca}} = g_{\mathrm{Ca}} s_\infty^2(v)\, h \left[v - v_{\mathrm{Ca}}\right]$$

$$I_{\mathrm{ahp}} = g_{\mathrm{ahp}}\left[v - v_{\mathrm{K}}\right] \frac{[\mathrm{Ca}]}{[\mathrm{Ca}] + k_1}$$

$$\frac{d[\mathrm{Ca}]}{dt} = \Gamma\left(-I_{\mathrm{Ca}} - I_{\mathrm{T}} - k_{\mathrm{Ca}}[\mathrm{Ca}]\right)$$

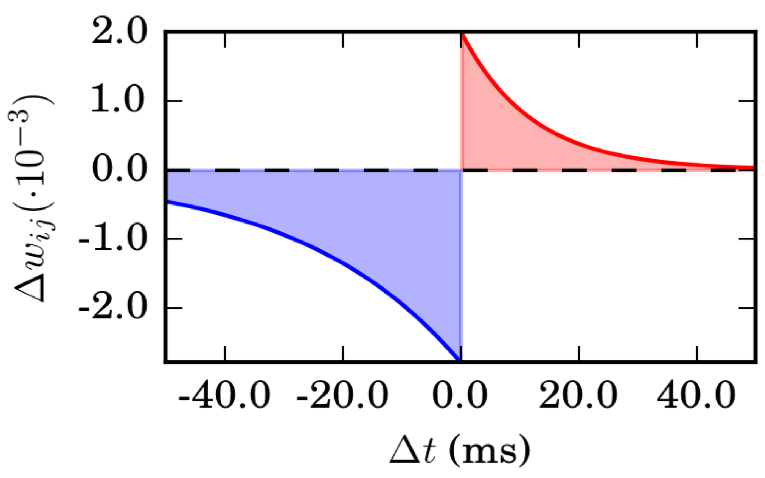
$$c_{\mathrm{m}} \frac{dv}{dt} = -I_{\mathrm{L}} - I_{\mathrm{K}} - I_{\mathrm{Na}} - I_{\mathrm{T}} - I_{\mathrm{Ca}} - I_{\mathrm{ahp}} - I_{\mathrm{syn}} + I_{\mathrm{stim}} + I_{\mathrm{noise}}$$

(see [6,7])

Spike timing-dependent plasticity (STDP) rule - STN neurons

- We employ the following rule STDP [5]:

$$\Delta w_{ij}(\Delta t) = \begin{cases} \lambda e^{-\frac{|\Delta t|}{\tau_+}}, & \Delta t > 0 \\ \lambda \alpha e^{-\frac{|\Delta t|}{\tau_-}}, & \Delta t \le 0 \end{cases}$$



- We restrict the synaptic weights w_{ij}^{ss} (within the STN neurons) on the interval, avoiding in this way a non-physiological unbounded increase or decrease.
- The (de)synchronized dynamics are stable with the above rule and parameter values resulting in multistability.

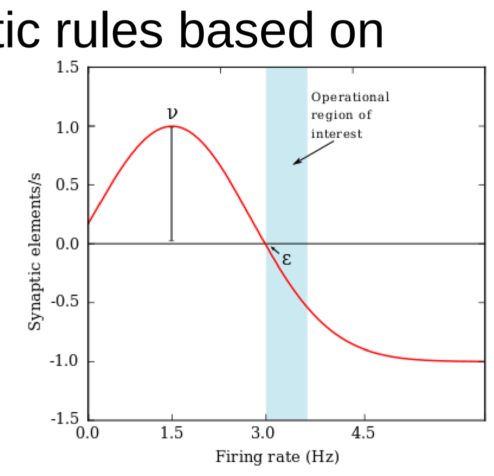
Structural plasticity (SP) - STN neurons

- Physical creation/deletion of synapses (during brain development, learning and recovery after lesions). Synaptic elements (axonal boutons and dendritic spines) grow and recede following homeostatic rules based on the mean electrical activity of the neuron [8]:

$$\frac{d\mathrm{FR}}{dt} = \begin{cases} -\frac{\mathrm{FR}(t)}{\tau_{\mathrm{SP}}} + \beta, & \text{if the neuron fires} \\ -\frac{\mathrm{FR}(t)}{\tau_{\mathrm{SP}}}, & \text{otherwise} \end{cases}$$

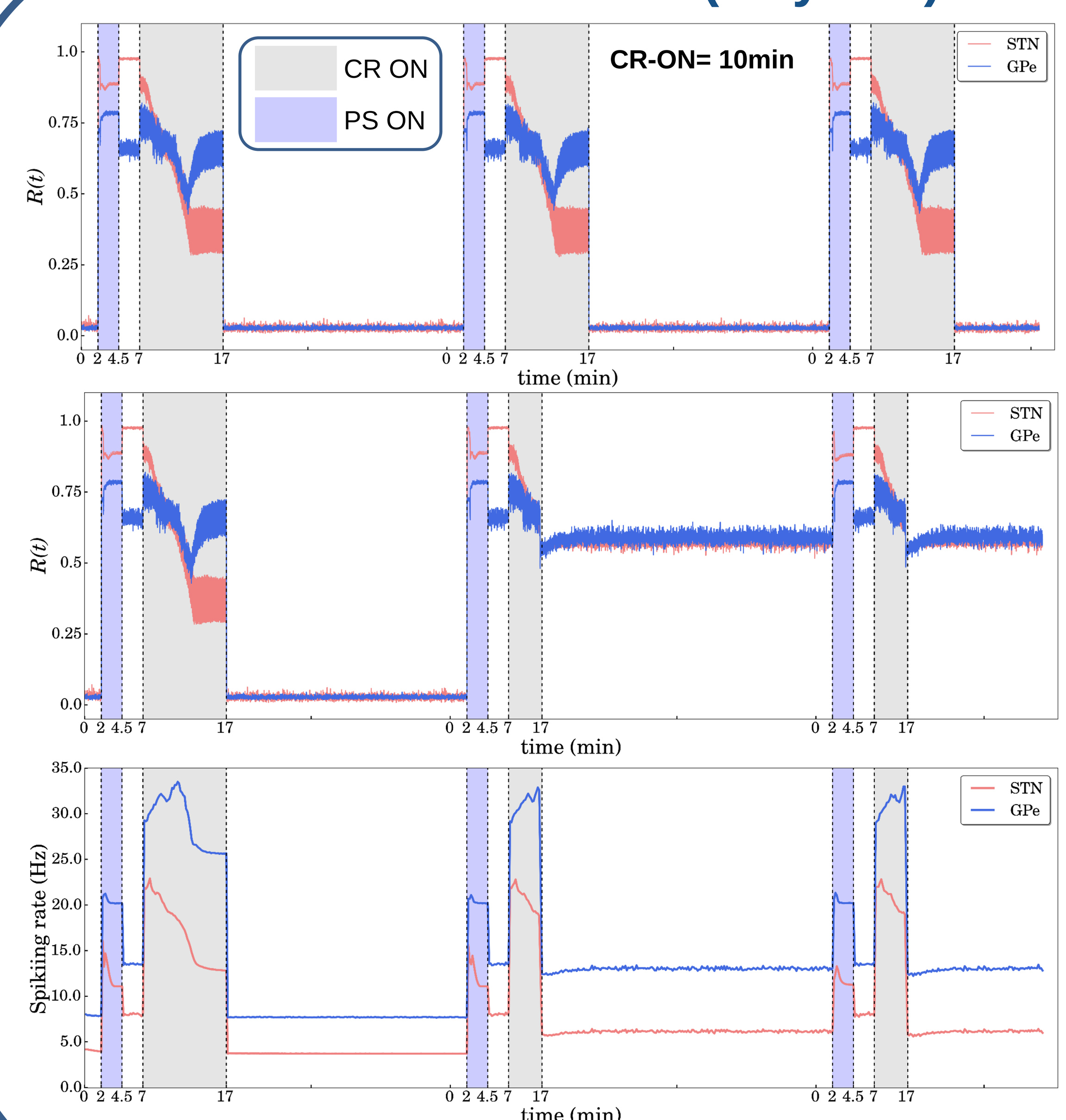
with a Gaussian growth rate [9]:

$$\frac{dz}{dt} = \nu\left[2e^{\left(\frac{Ca(t)-\xi}{\zeta}\right)^2} - 1\right], \text{ where } \zeta = \frac{\varepsilon - \eta}{2\sqrt{\ln 2}}, \xi = (\varepsilon + \eta)/2.$$

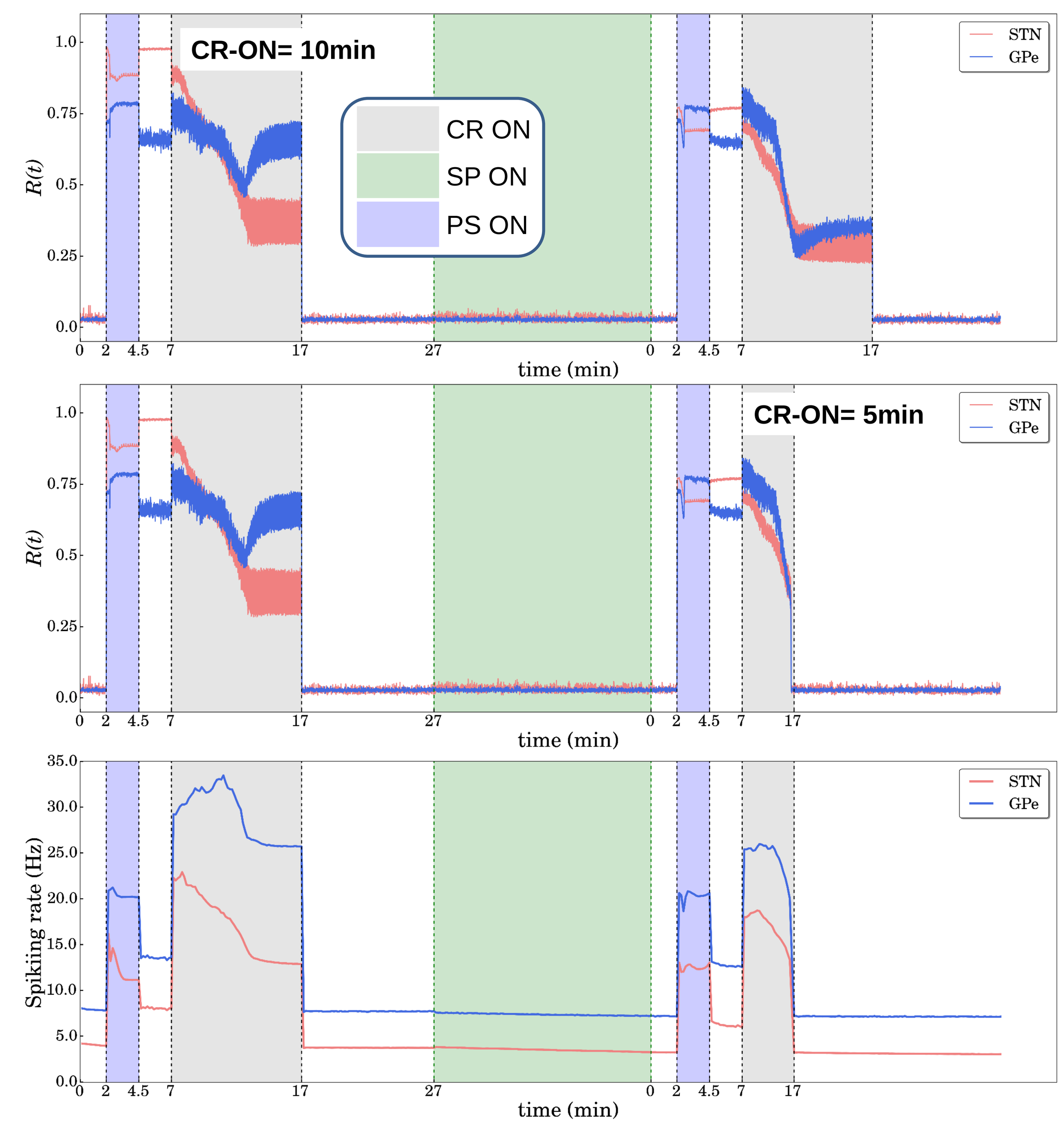


- Global connectivity is updated on a much slower timescale than changes in electrical activity.

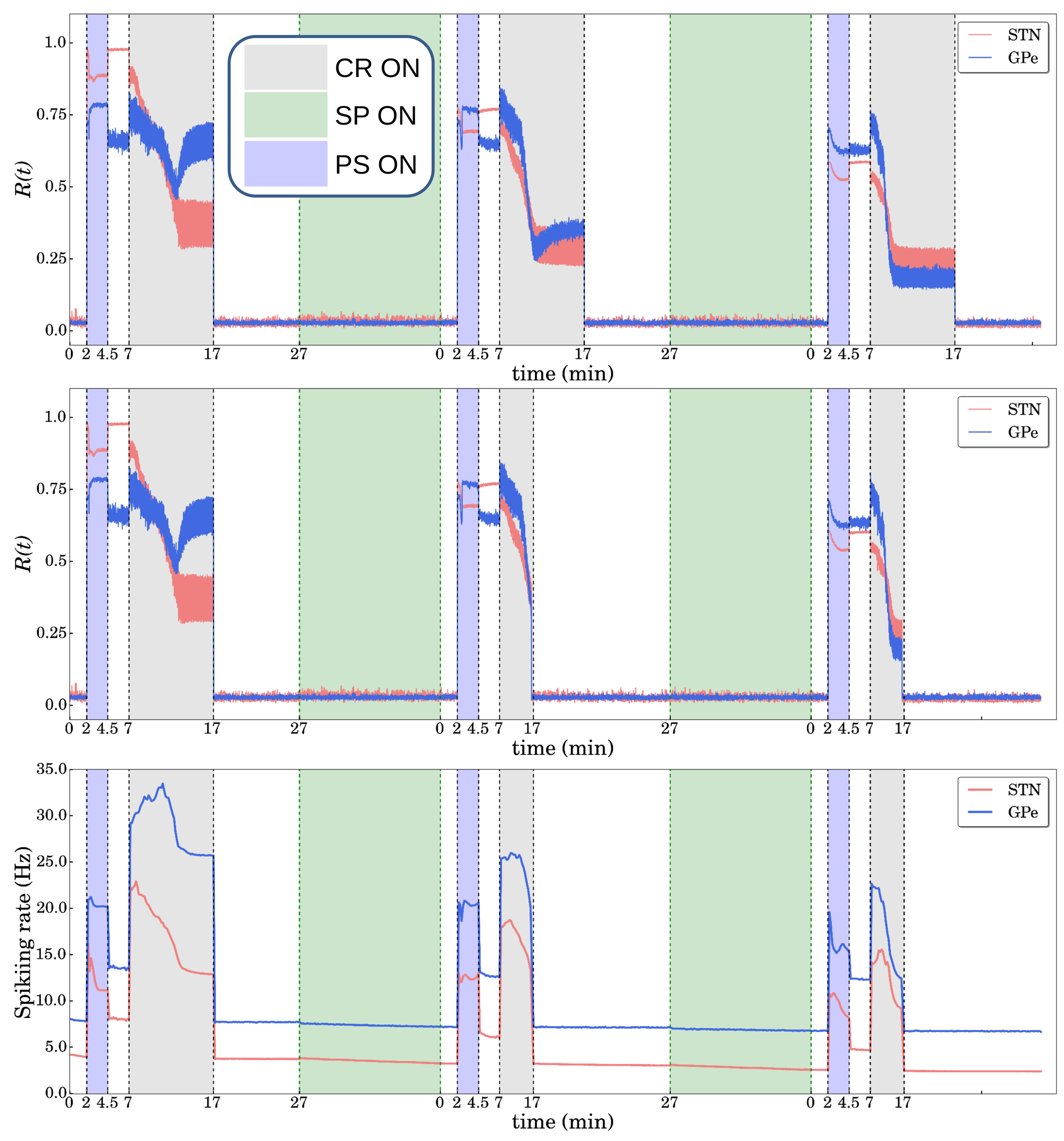
Simulation without SP (3 cycles)



Simulation with SP (2 cycles)



Simulation with SP (3 cycles)



Summary

- Degenerative diseases such as Parkinson's induce slow changes in brain networks, leading to deterioration of higher brain function and memory.
- Therapy and rehabilitation can employ structural plasticity to counteract maladaptive plastic changes and ultimately restore brain function.
- We designed, in NEST, a simulation protocol which allows us to combine fast (synaptic - STDP) and slow (structural - SP) connectivity changes, in order to study the long term effects of CR stimulation [10].
- Taking into account structural plasticity reveals memory-type effects of the network's treatment susceptibility.
- Periods of CR-induced desynchronization increase the susceptibility to desynchronizing stimulation in the event of an externally triggered relapse.
- Structural plasticity may enable to predict dosage-dependent phenomena relevant for clinical studies.

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