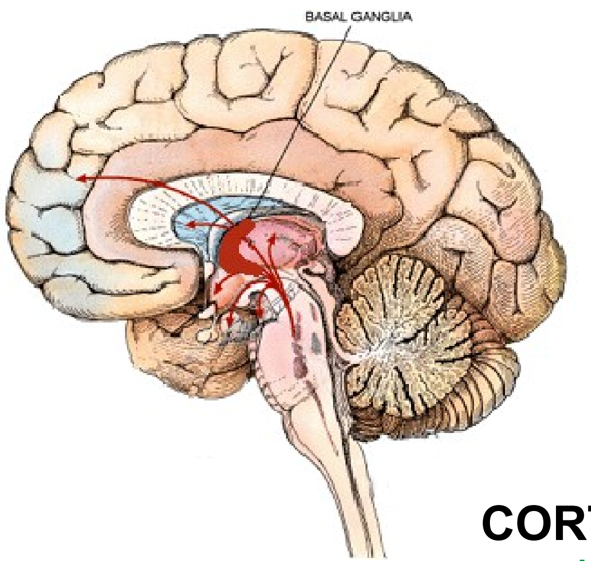
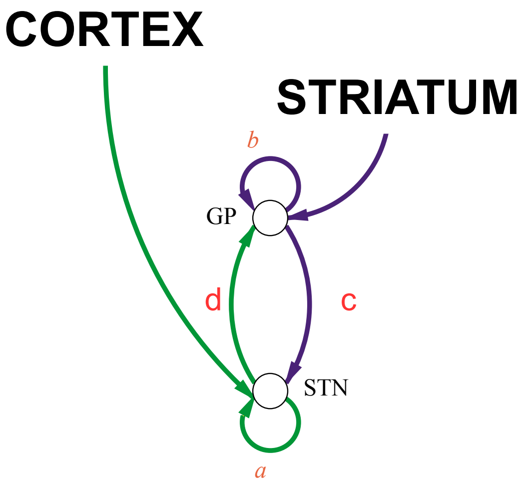
Controlling tremor in Parkinson's disease

Alessandro Sanzeni
Celani A., Tiana G., Vergassola M.

Parkinson's disease causes abnormal neuronal activity and hence tremor





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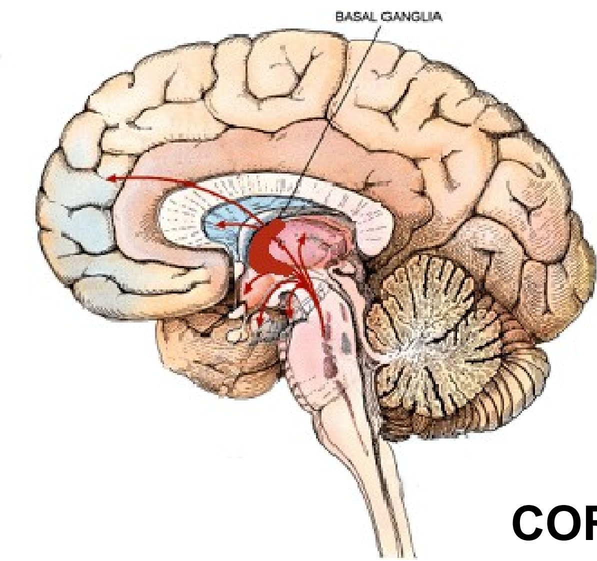

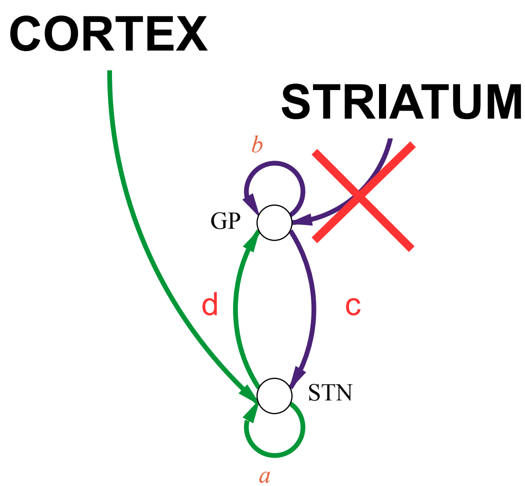

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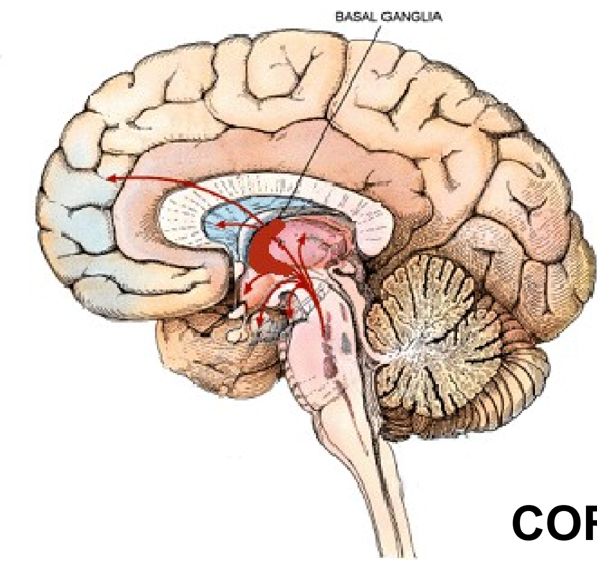
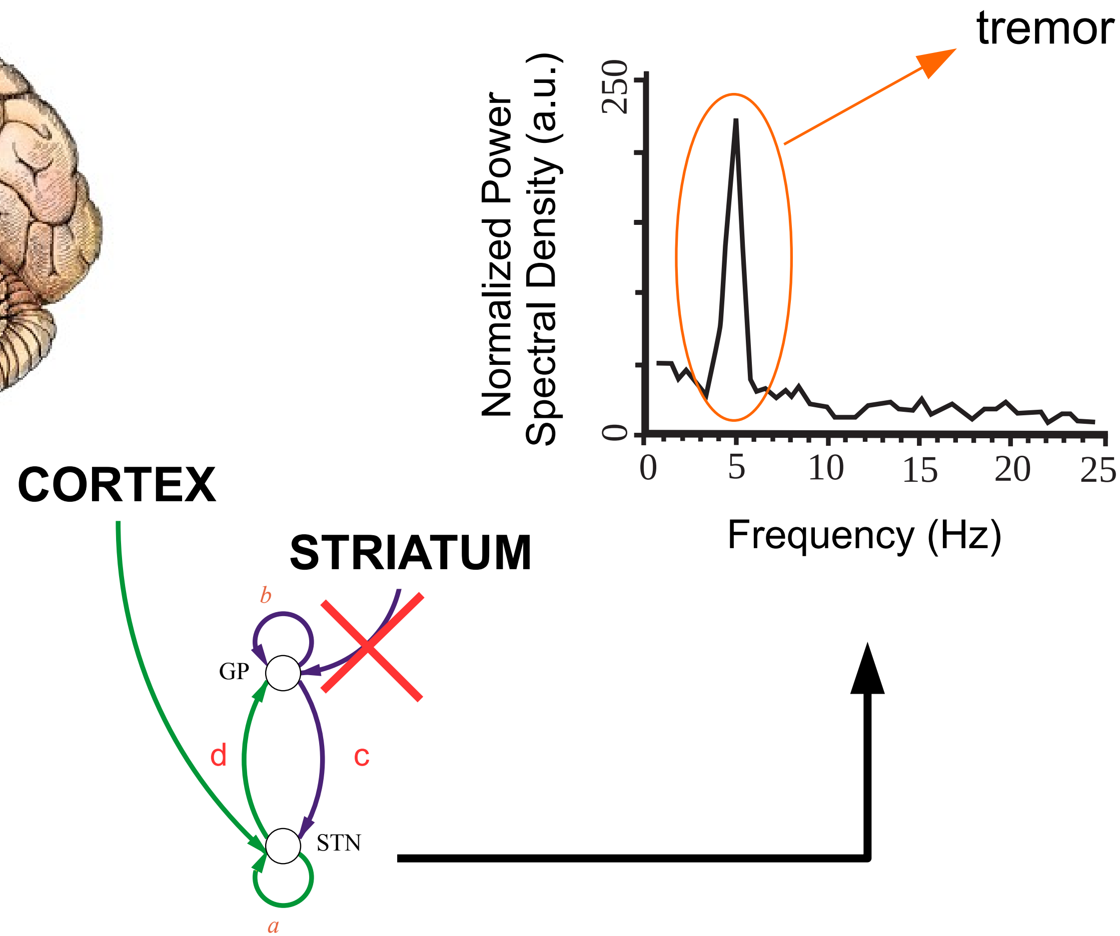
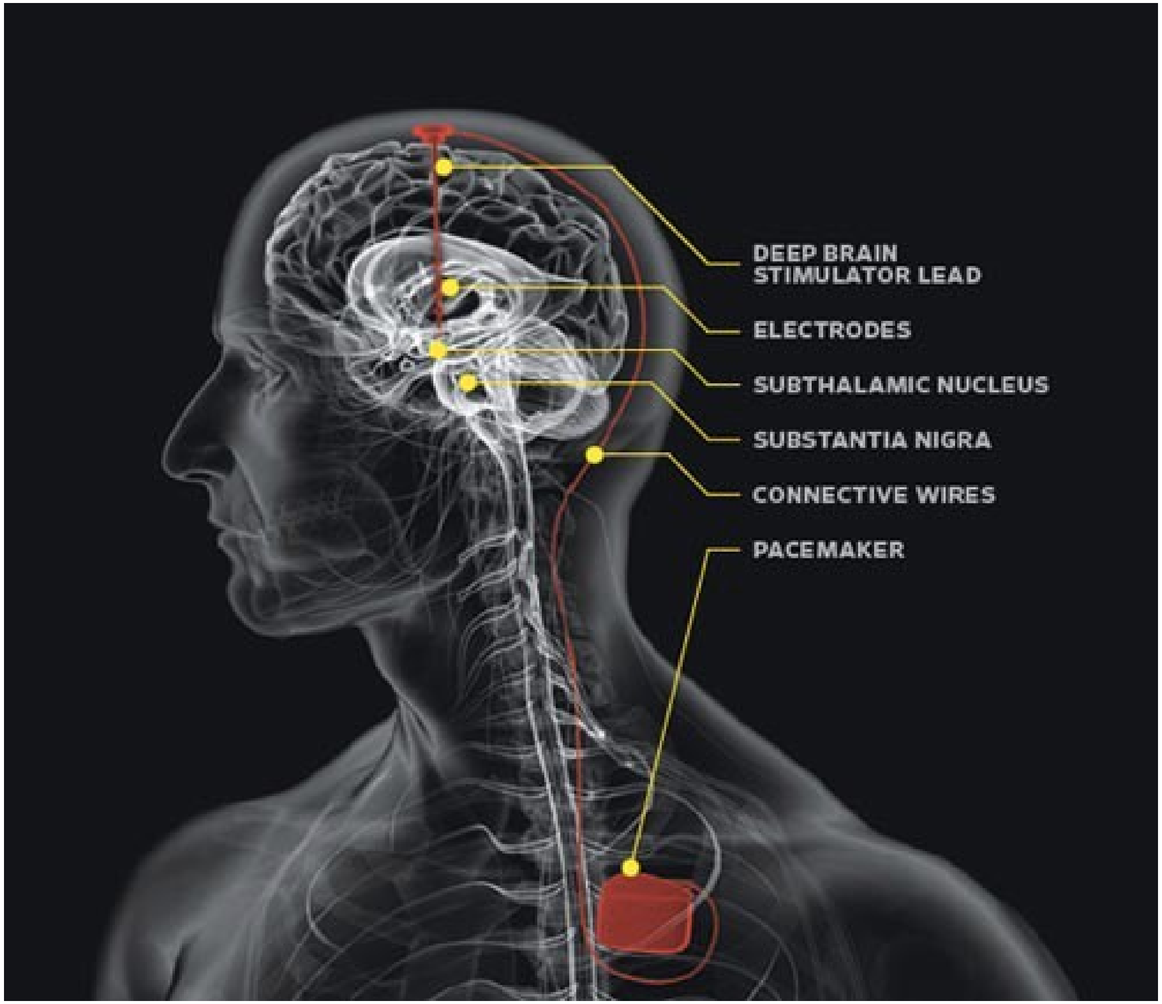
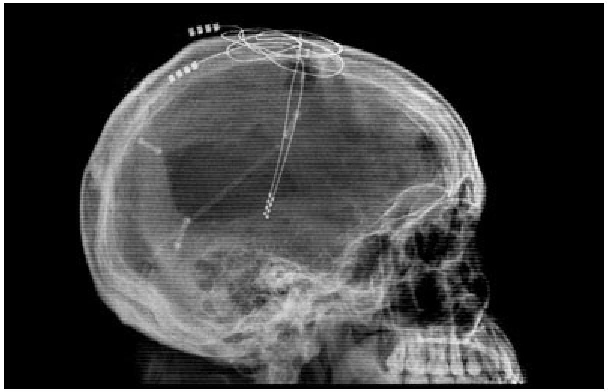


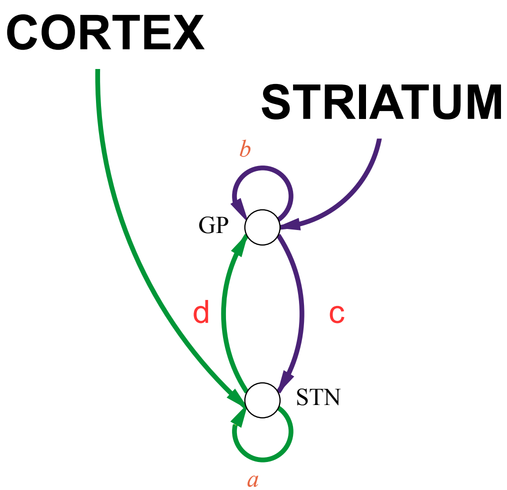


Tremor is reduced by high frequency external stimulation (DBS)

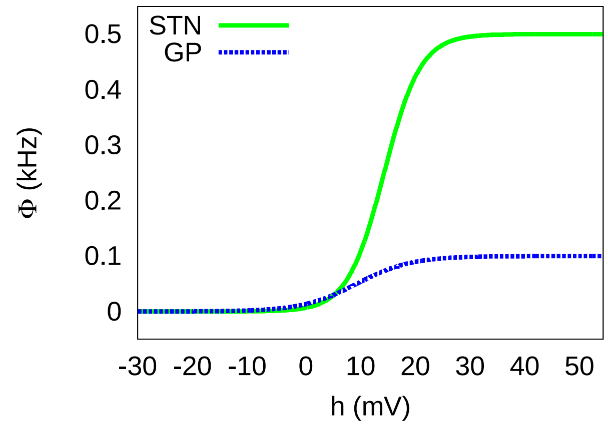




Effective two-neuron model



Single neuron response function



$$\begin{cases} \tau^{STN}\frac{\mathrm{d}h_{STN}}{\mathrm{d}t} = -h_{STN} + a\phi_{STN}\left(h_{STN}\right) - c\phi_{GP}\left(h_{GP}\right) + I^{CTX} \\ \tau^{GP}\frac{\mathrm{d}h_{GP}}{\mathrm{d}t} = -h_{GP} + d\phi_{STN}\left(h_{STN}\right) - b\phi_{GP}\left(h_{GP}\right) + I^{STR} \end{cases}$$

Gillies A, Willshaw D, Li Z. Subthalamic–pallidal interactions are critical in determining normal and abnormal functioning of the basal ganglia. Proc Roy Soc Lond – B Biol Sci. 2002;269:545–551

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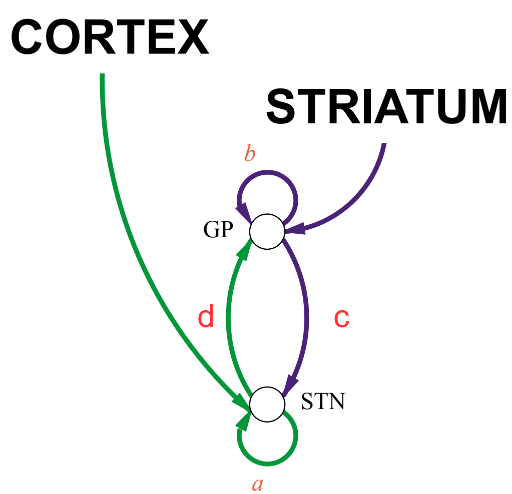

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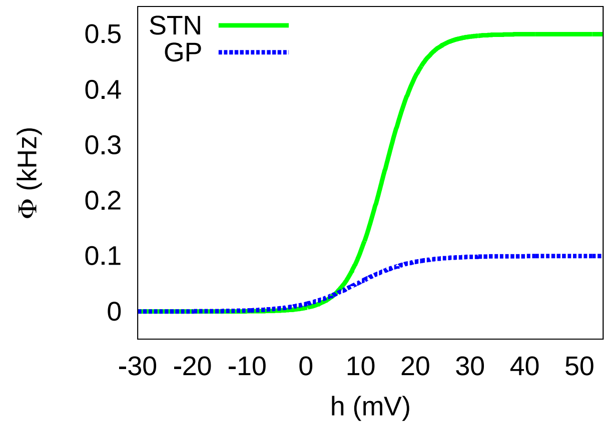

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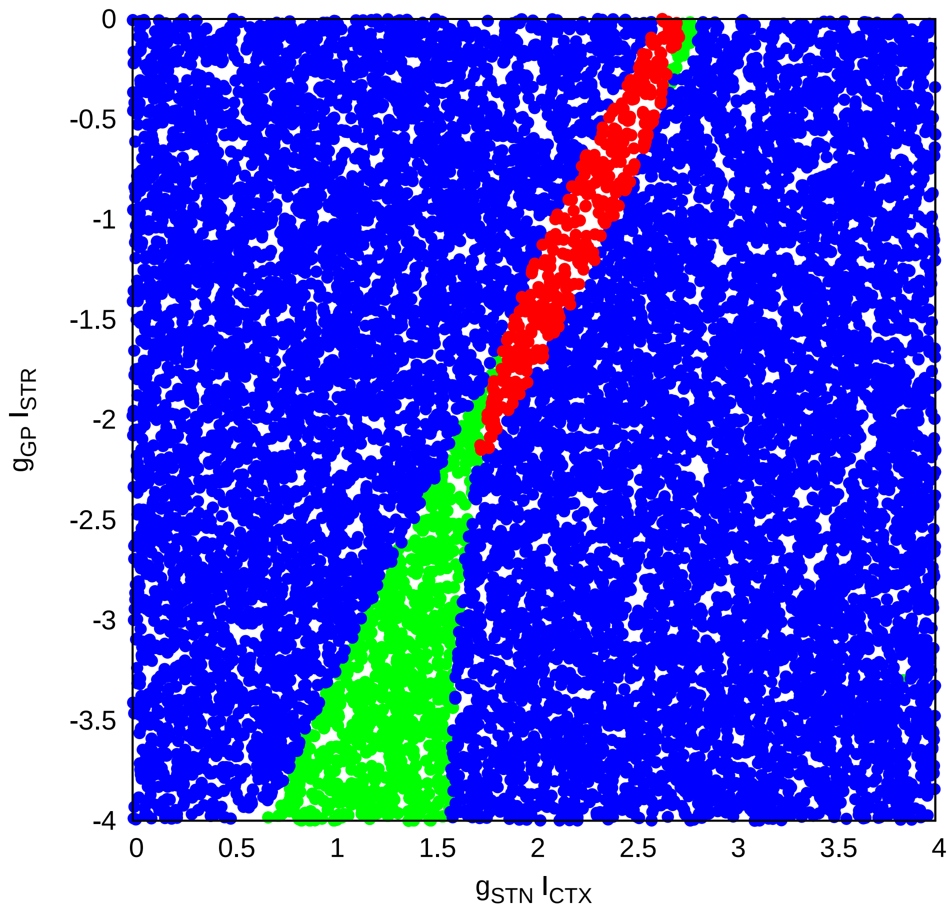
Stability of the system



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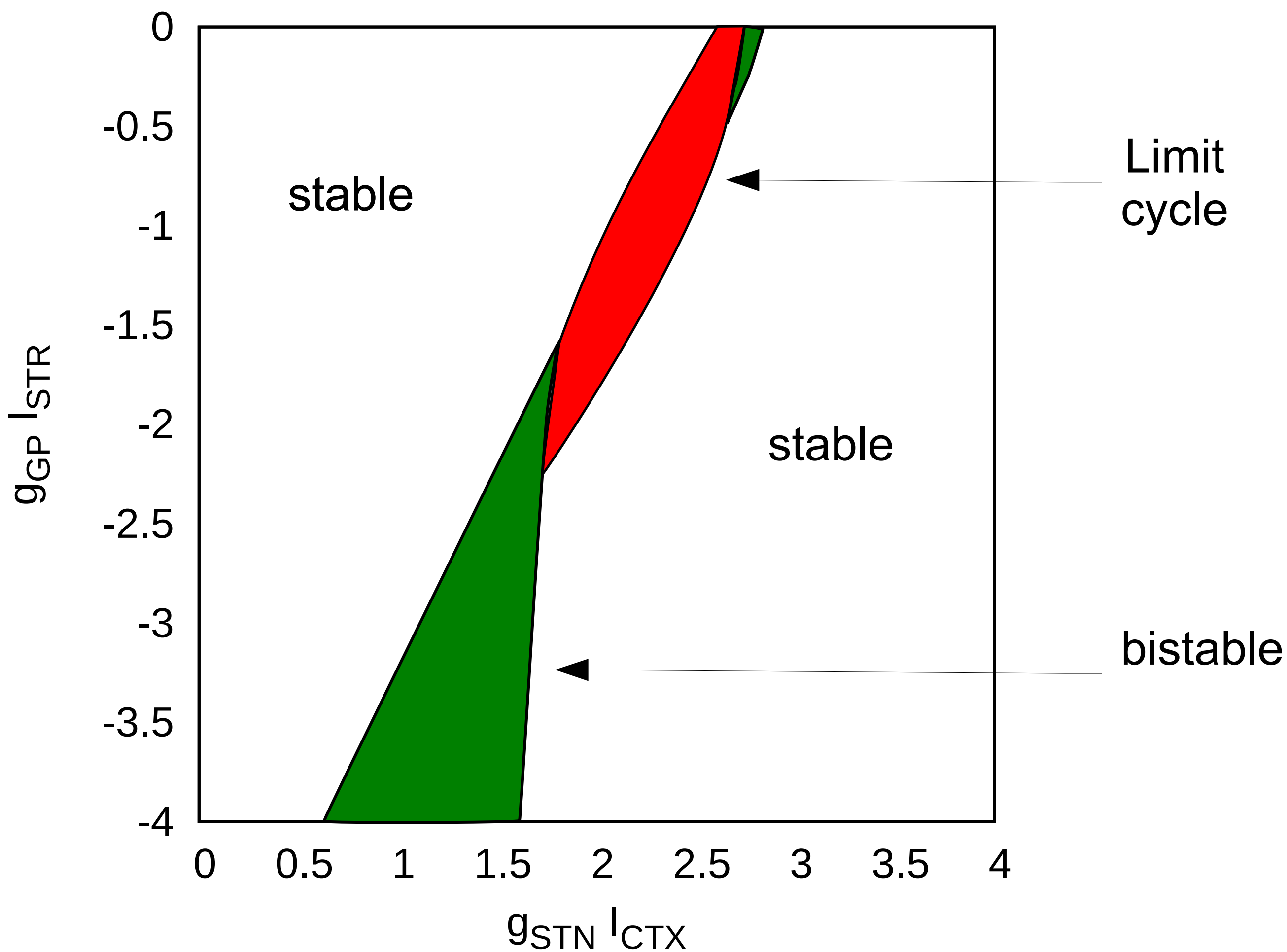
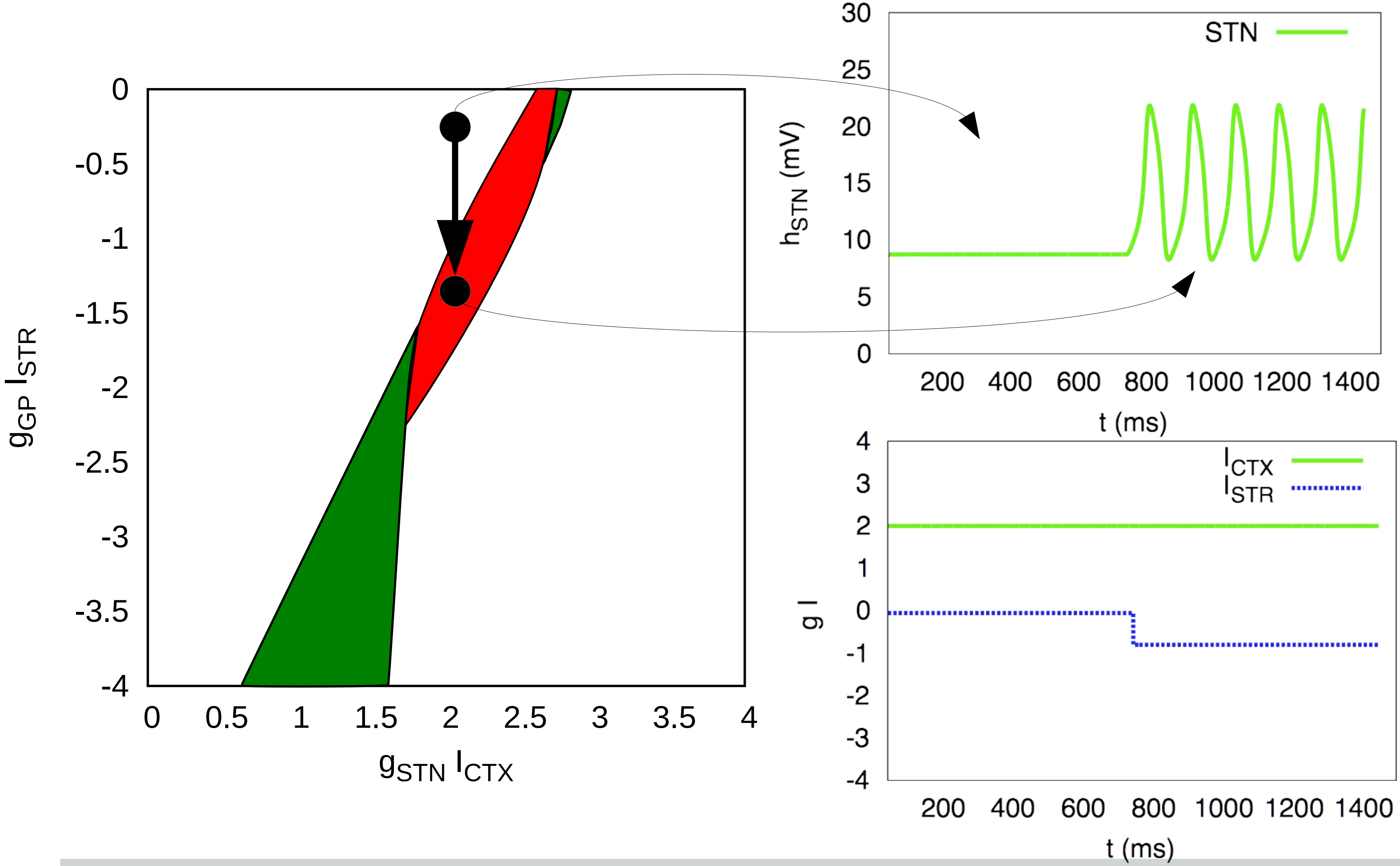


Parkinson's disease as a Hopf bifurcation



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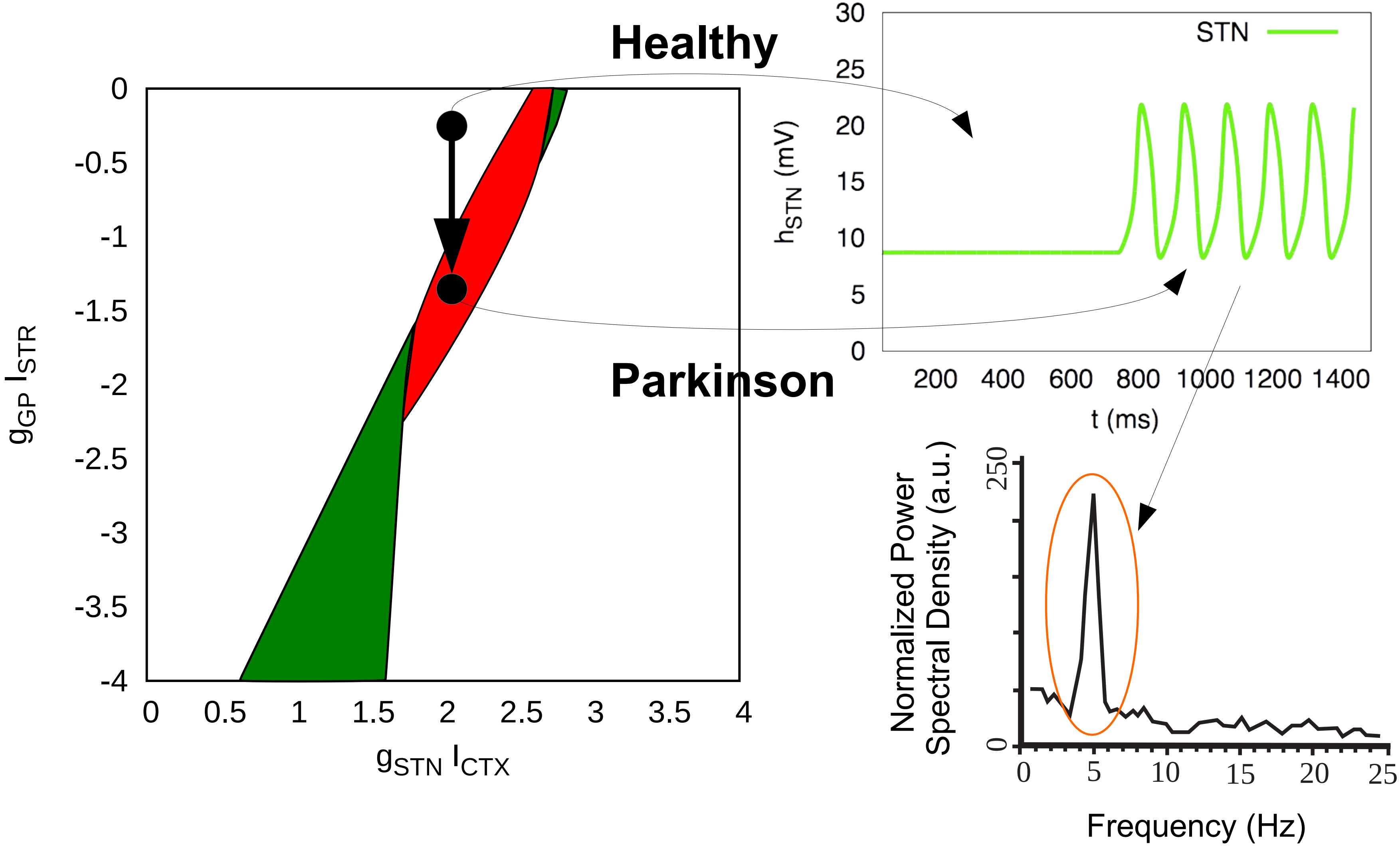
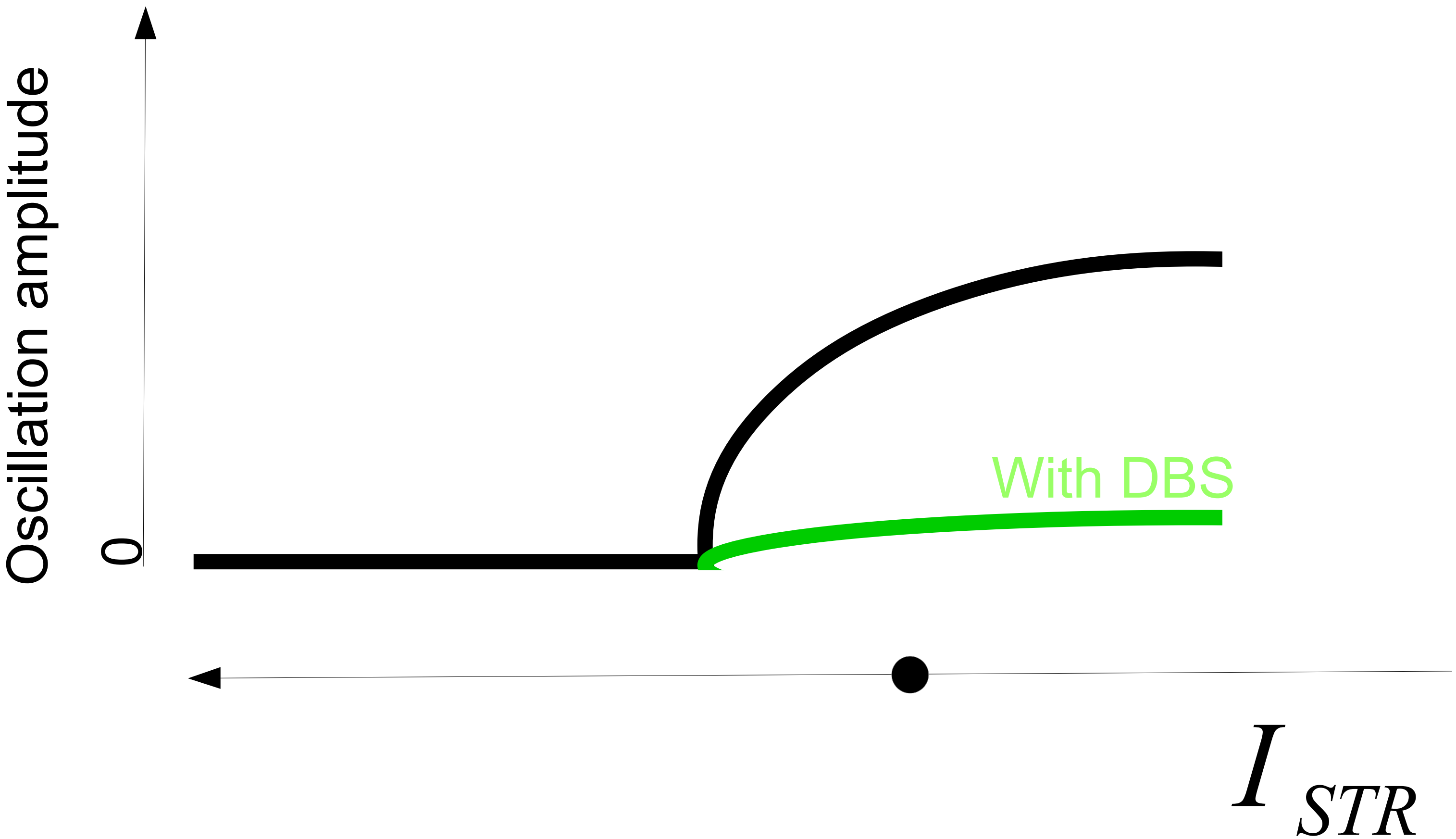


DBS decreases the amplitude of oscillations



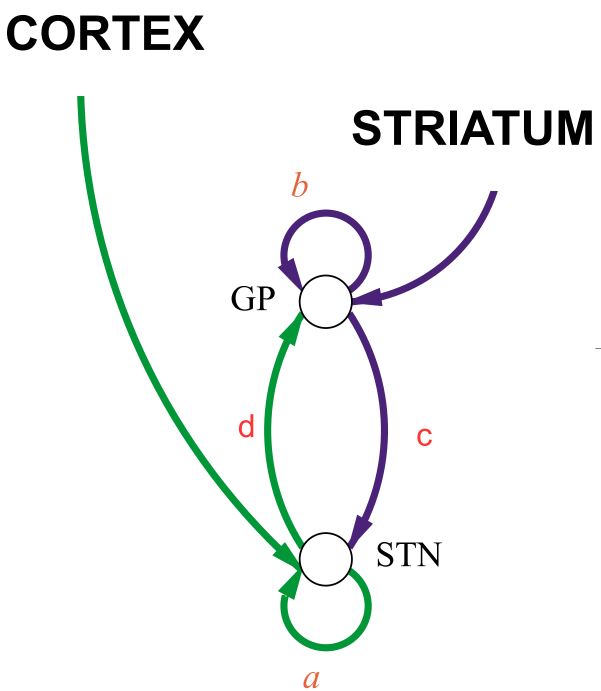
MODOLO, J.; HENRY, Jacques; BEUTER, A. Dynamics of the subthalamo-pallidal complex in Parkinson’s disease during deep brain stimulation. Journal of biological physics, 2008, 34.3-4: 251-266.

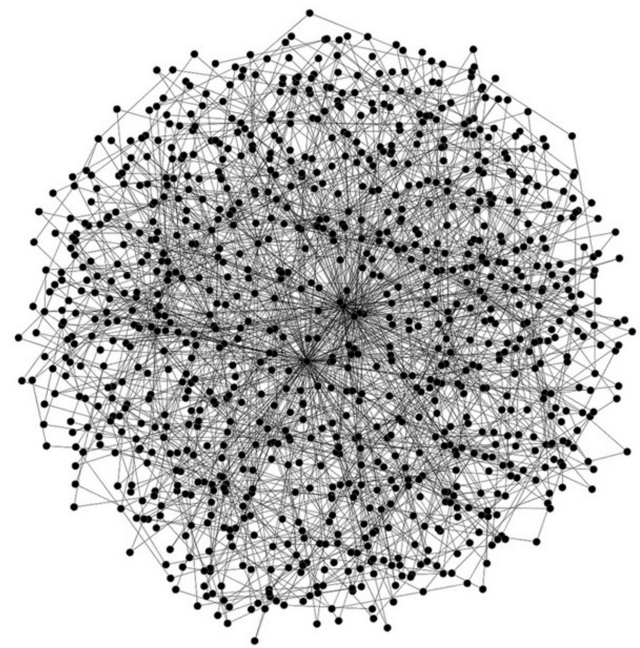
Open questions

- Microscopical foundations of the effective two-neuron model
- Control system that prevents the Hopf bifurcation

Microscopical derivation of the effective two-neuron model

Many-body model





$$\tau_i \frac{\mathrm{d}h_i}{\mathrm{d}t} = -h_i + \sum_{k=1}^{N} R_{ik}\phi_k\left(h_k\right) + I_i + \eta_i$$

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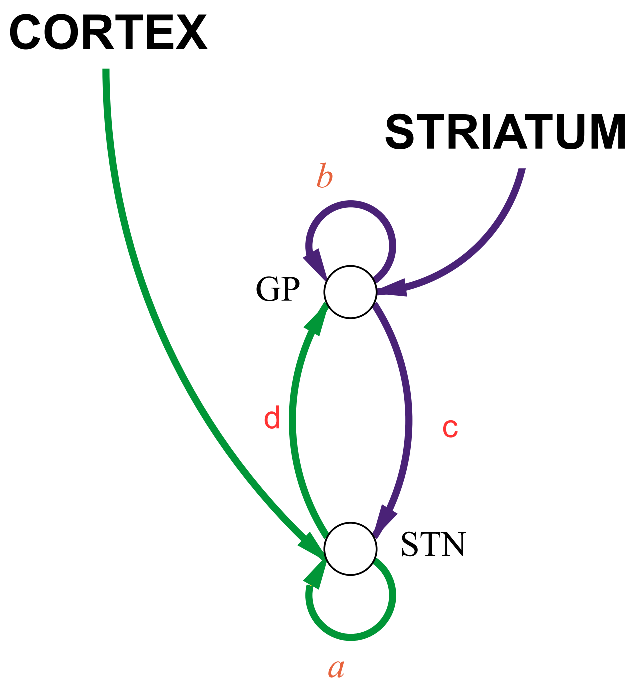


$$< \eta_i(t)\eta_j(t') >_\eta = \Omega_i \delta_{ij}\delta(t-t')$$

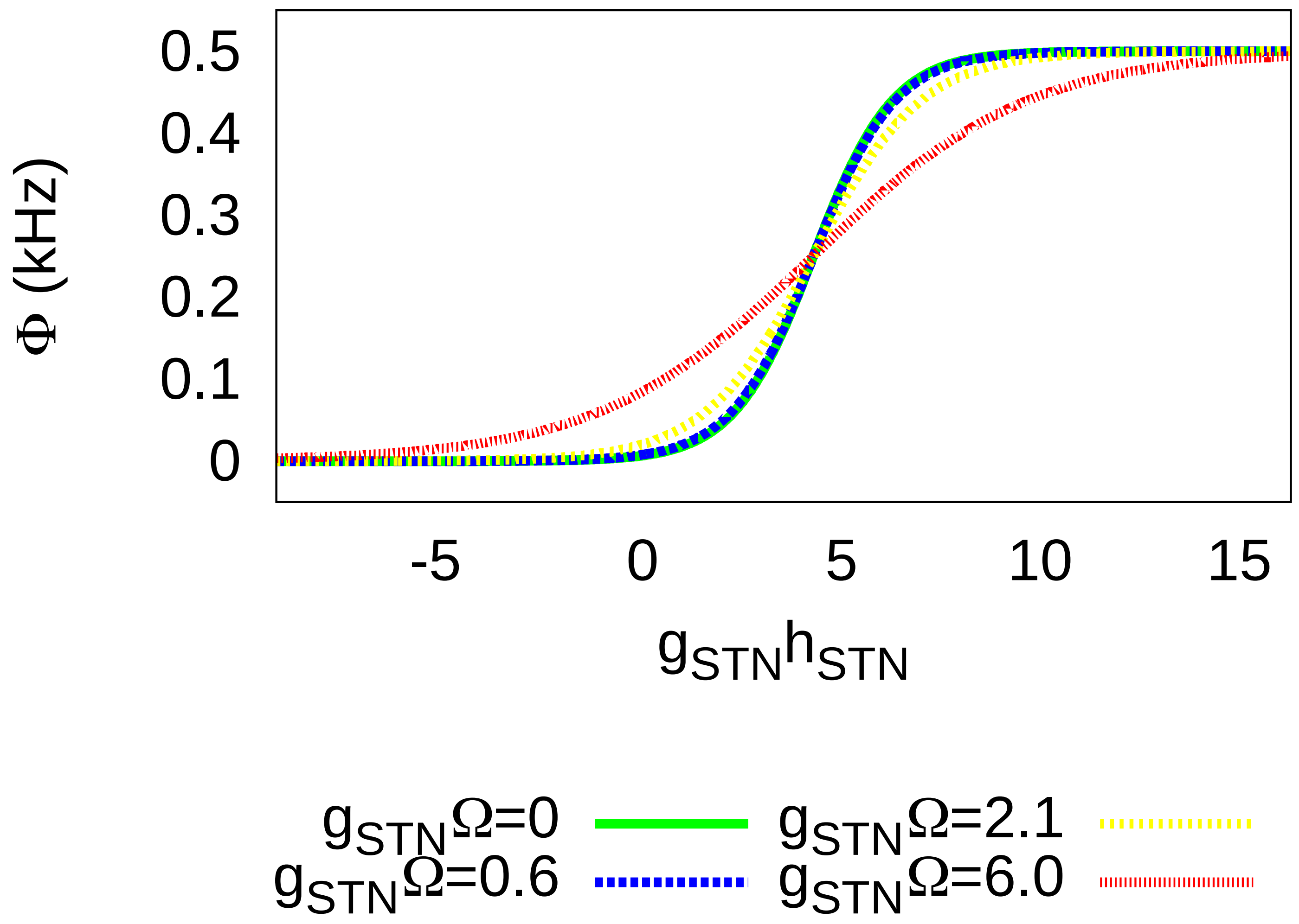
$$R = \left(\begin{array}{c|c} \begin{pmatrix} d_{11} & d_{12} & \dots \\ d_{21} & d_{22} & \dots \\ \dots & \dots & \dots \end{pmatrix} & \begin{pmatrix} b_{11} & b_{12} & \dots \\ b_{21} & b_{22} & \dots \\ \dots & \dots & \dots \end{pmatrix} \\ \hline \begin{pmatrix} a_{11} & a_{12} & \dots \\ a_{21} & a_{22} & \dots \\ \dots & \dots & \dots \end{pmatrix} & \begin{pmatrix} c_{11} & c_{12} & \dots \\ c_{21} & c_{22} & \dots \\ \dots & \dots & \dots \end{pmatrix} \end{array} \right)$$

$$\left[R_{ik}\right] = \mu_{ik}$$
$$\left[R_{ik}R_{ln}\right] - \left[R_{ik}\right]\left[R_{ln}\right] = \delta_{ik}\delta_{kn}\sigma_{ik}^2$$

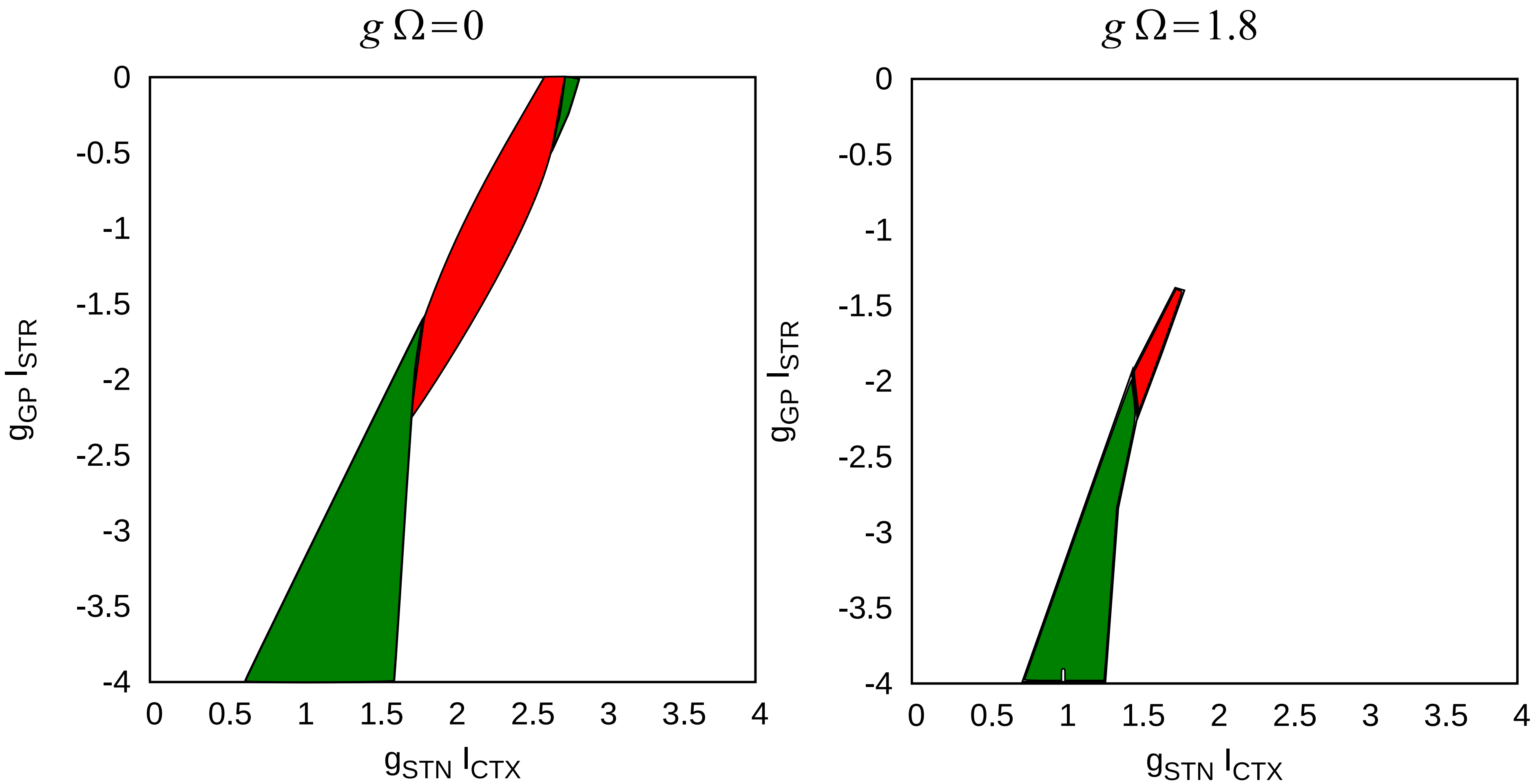
$$N \to \infty$$

$$\begin{cases} \tau^{STN}\frac{\mathrm{d}\bar{h}_{STN}}{\mathrm{d}t} = -\bar{h}_{STN} + a\tilde{\phi}_{STN}\left(\bar{h}_{STN}\right) - c\tilde{\phi}_{GP}\left(\bar{h}_{GP}\right) + I^{CTX} \\ \tau^{GP}\frac{\mathrm{d}\bar{h}_{GP}}{\mathrm{d}t} = -\bar{h}_{GP} + d\tilde{\phi}_{STN}\left(\bar{h}_{STN}\right) - b\tilde{\phi}\left(\bar{h}_{GP}\right) + I^{STR} \end{cases}$$

Renormalization of the response function

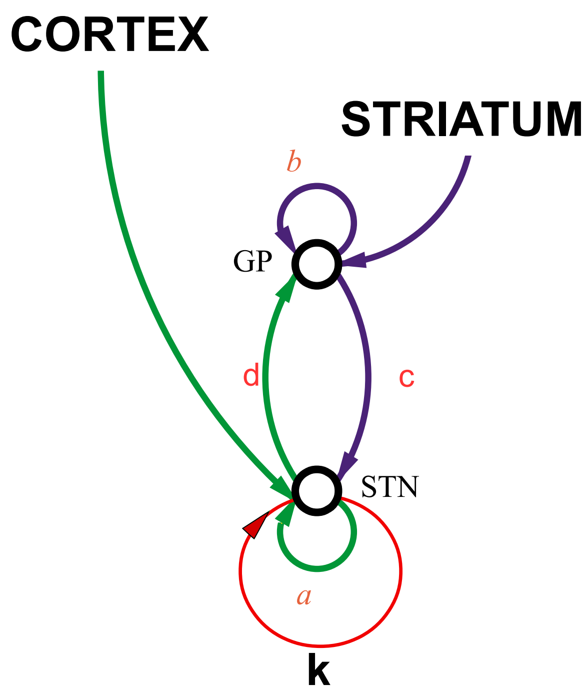


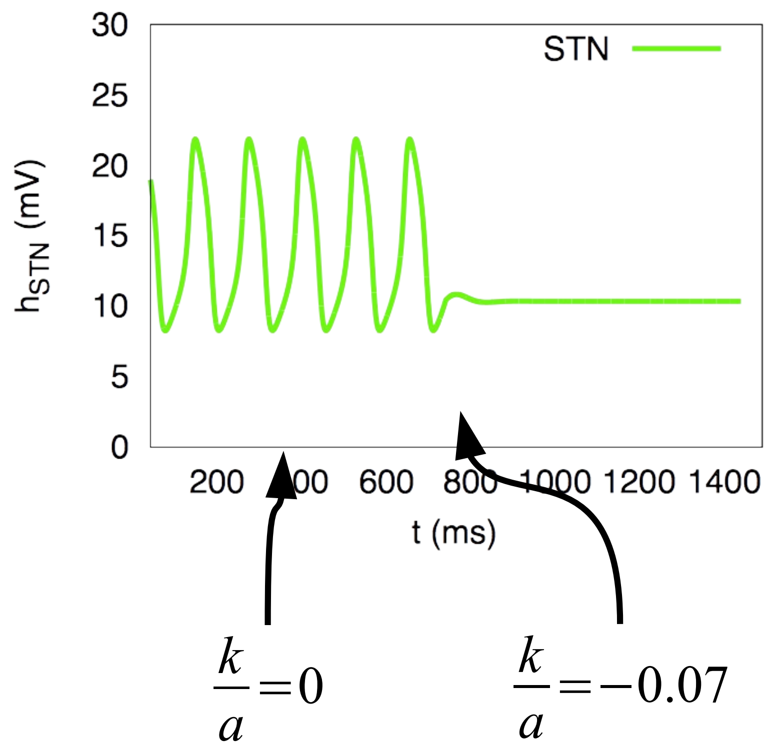
The stability of the system depends on the noise variance



Control system

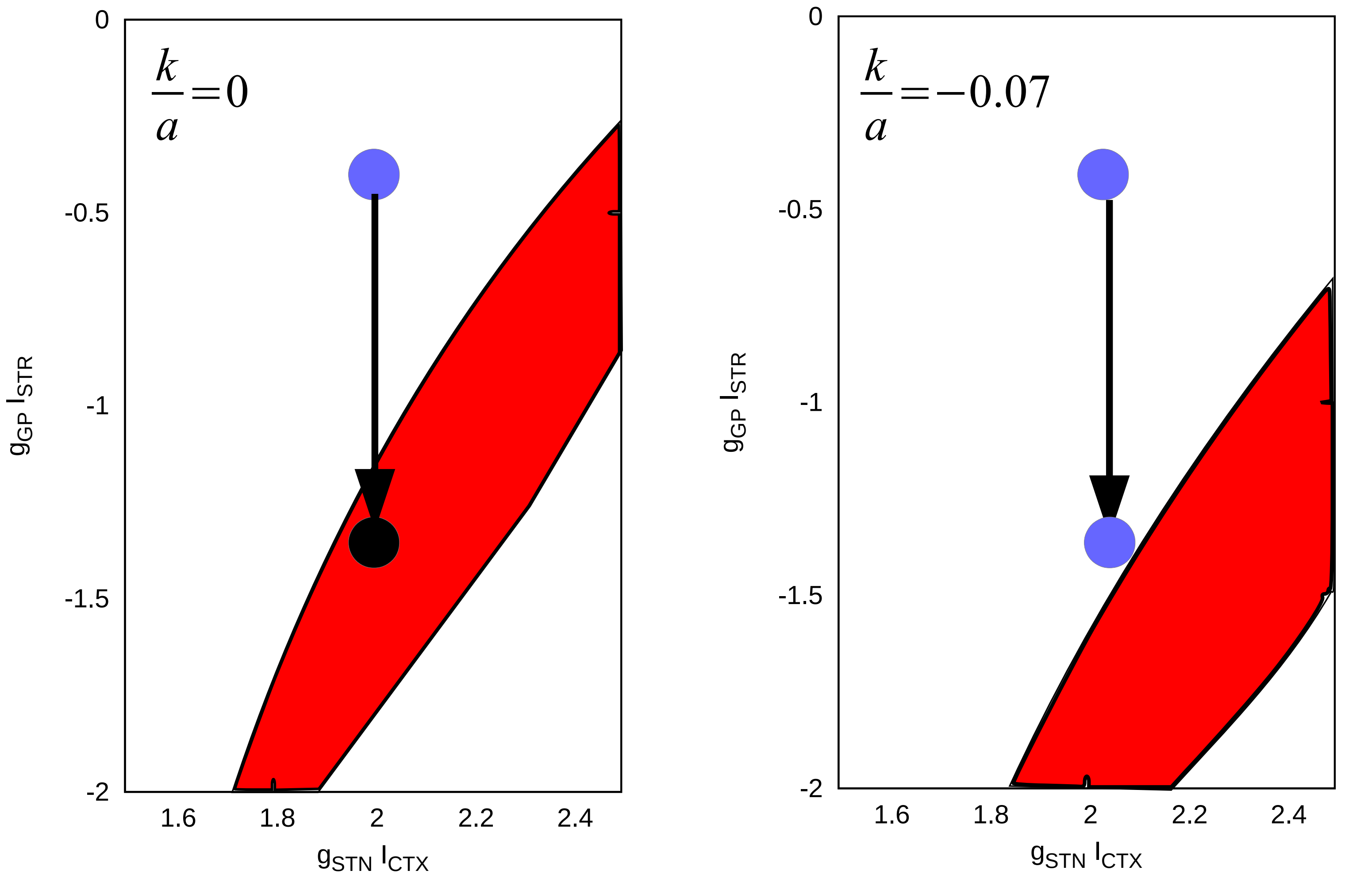
A feedback system prevents the Hopf bifurcation





$$
\begin{cases}
\tau^{STN}\frac{\mathrm{d}\bar{h}_{STN}}{\mathrm{d}t} = -\bar{h}_{STN} + a\tilde{\phi}_{STN}\left(\bar{h}_{STN}\right) - c\tilde{\phi}_{GP}\left(\bar{h}_{GP}\right) + I^{CTX} + k\tilde{\phi}_{STN}\left(\bar{h}_{STN}\right) \\
\tau^{GP}\frac{\mathrm{d}\bar{h}_{GP}}{\mathrm{d}t} = -\bar{h}_{GP} + d\tilde{\phi}_{STN}\left(\bar{h}_{STN}\right) - b\tilde{\phi}_{GP}\left(\bar{h}_{GP}\right) + I^{STR}
\end{cases}
$$

Modification of the stability diagram due to the control term



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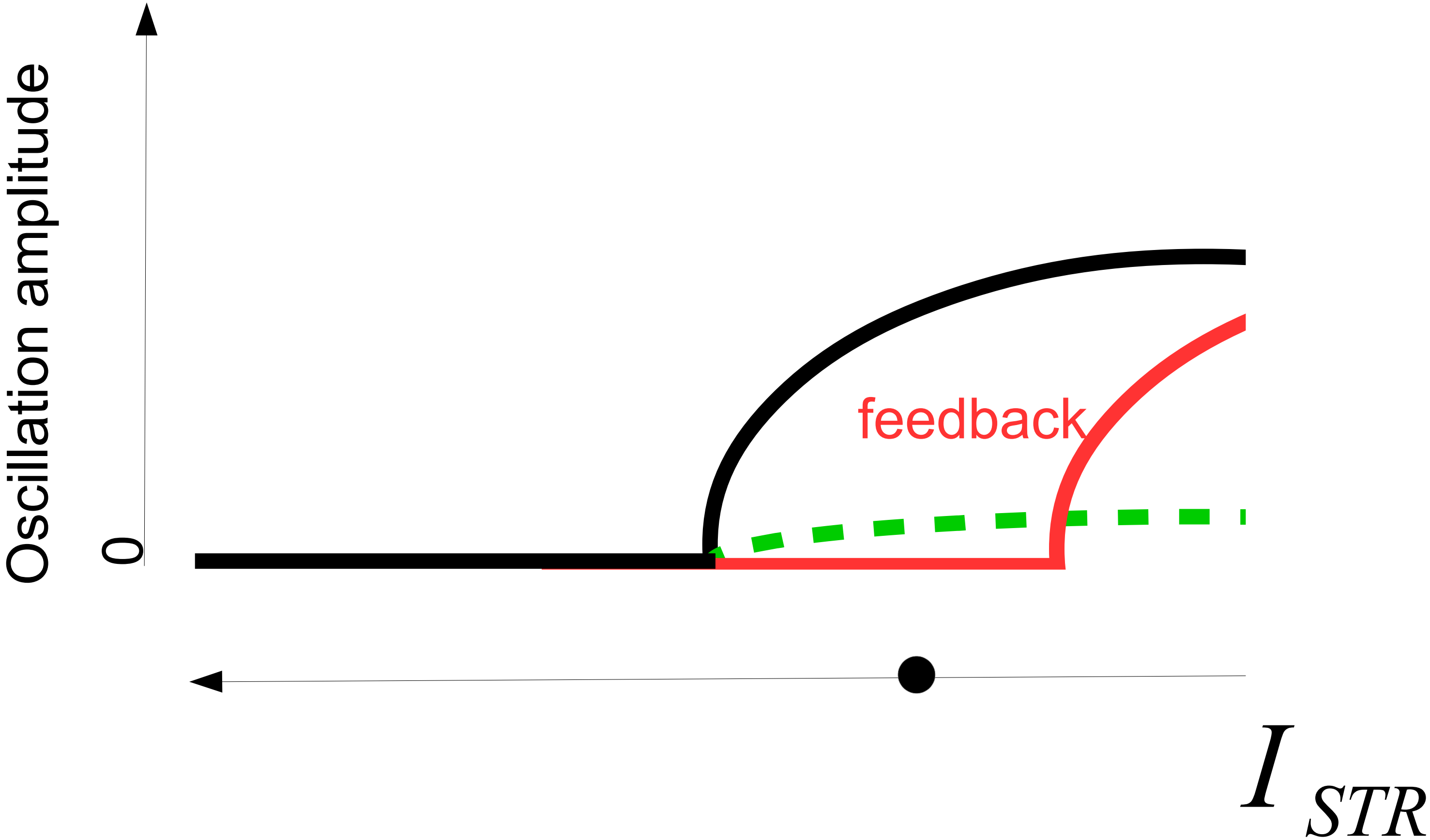

Bistable region