UNIVERSITY OF TWENTE.

DYNAMICS OF THE BASAL GANGLIA

NDNS 13-16 APRIL 2010

STEPHAN VAN GILS

APPLIED ANALYSIS AND MATHEMATICAL PHYSICS @ UT

PARKINSON'S DISEASE

Symptoms:

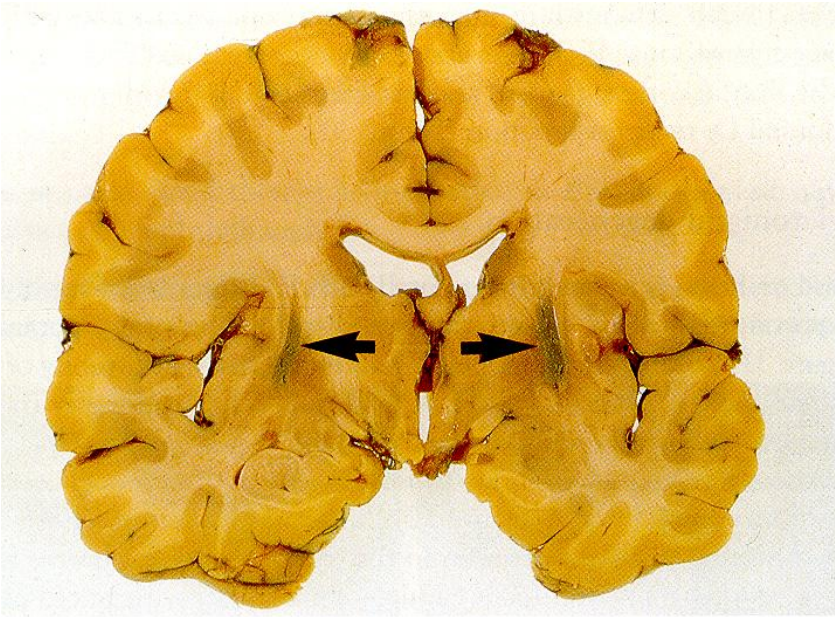
tremor

rigidity

slowness of movement

Parkinson’s disease

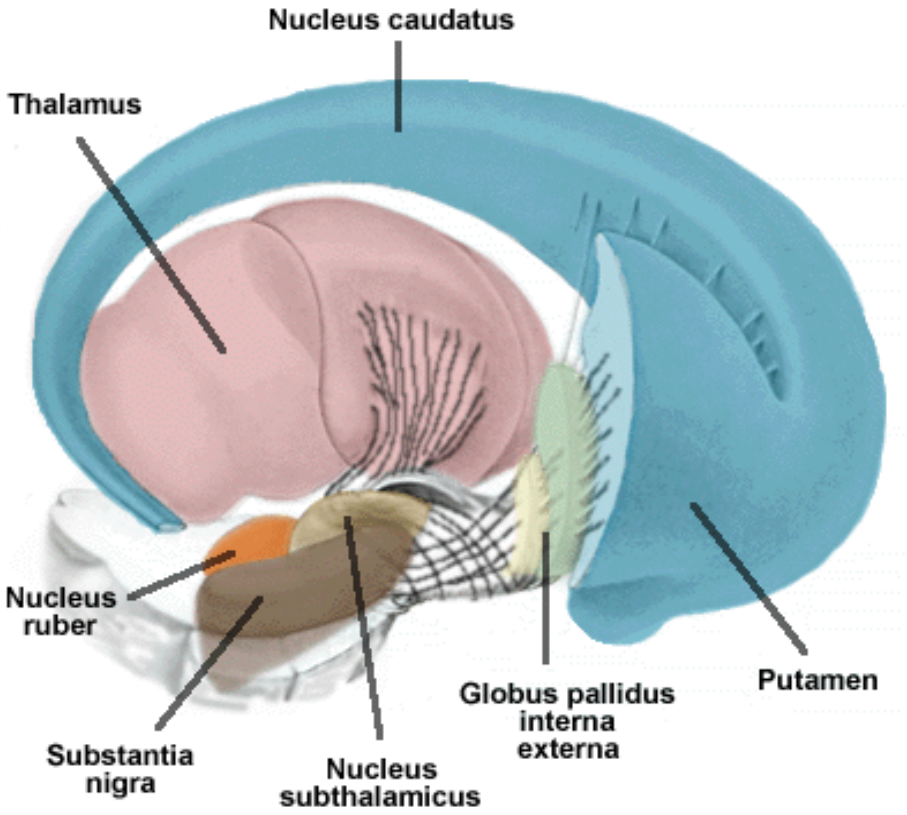
Degeneration of substantia nigra causing a depletion of dopamine in the striatum



BASAL GANGLIA

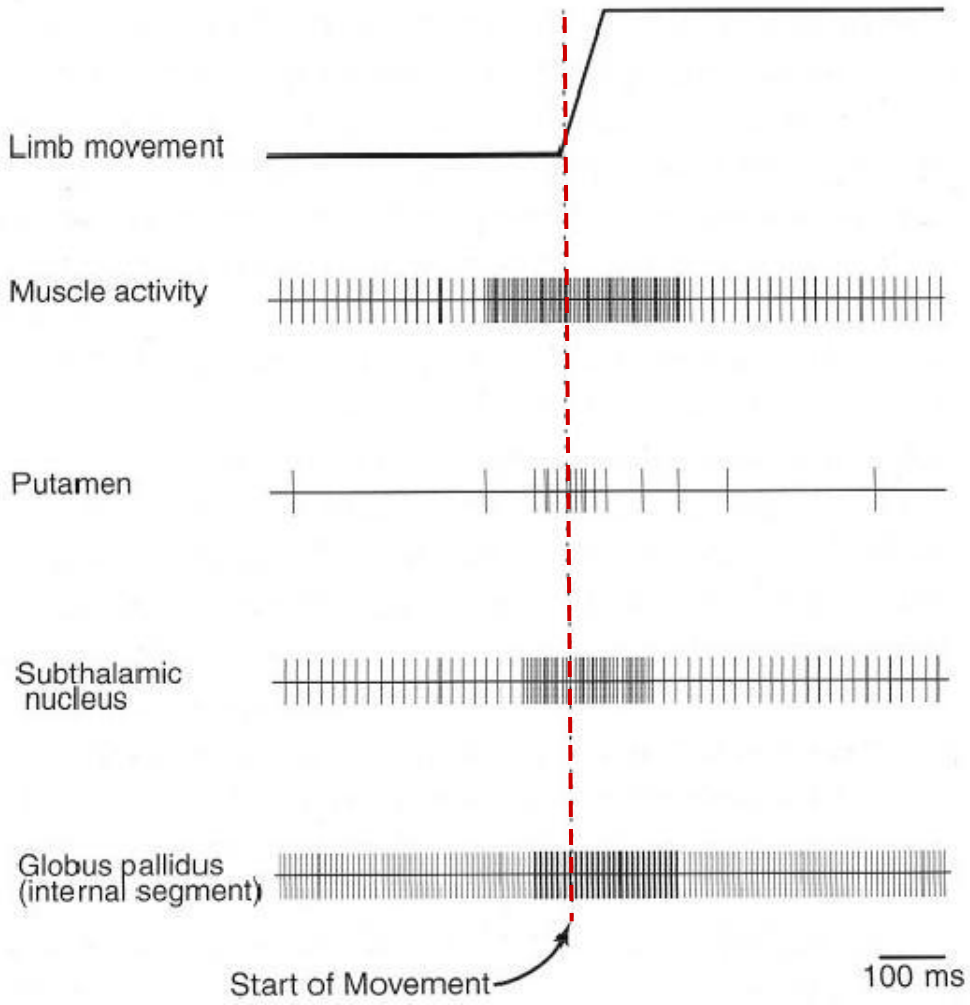
Five extensively interconnected nuclei:

- Striatum (caudate nucleus, putamen)
- Globus Pallidus
- Substantia Nigra
- Subthalamic nucleus



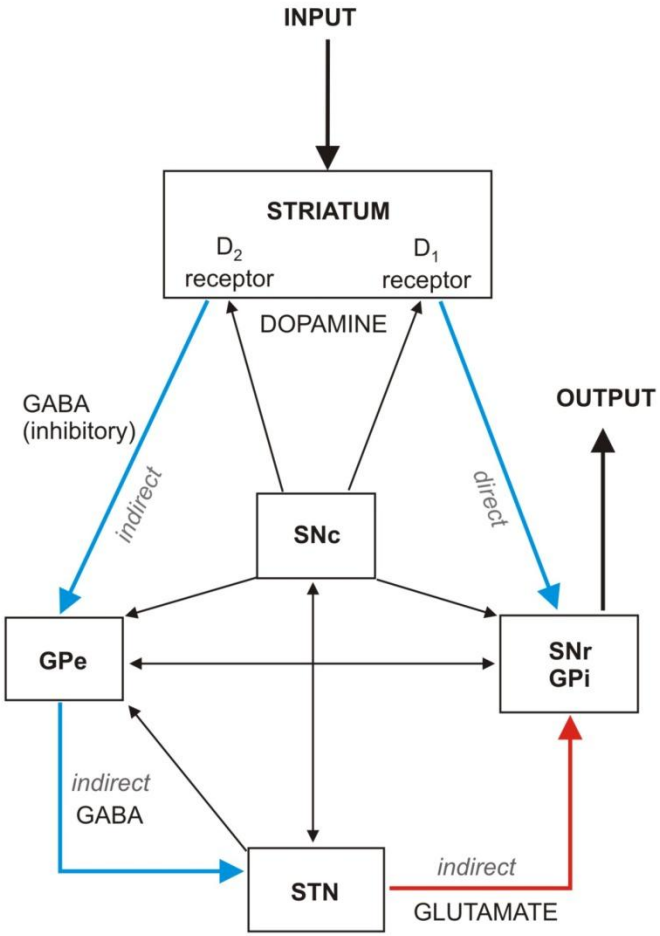
Role of Basal Ganglia

- The majority of neurons is activated before the onset of movement, but after agonist muscle activity.
- BG is unlikely to be involved in initiation of movement.
- *Likely roles*: facilitation, gating or scaling of cortically initiated movement.



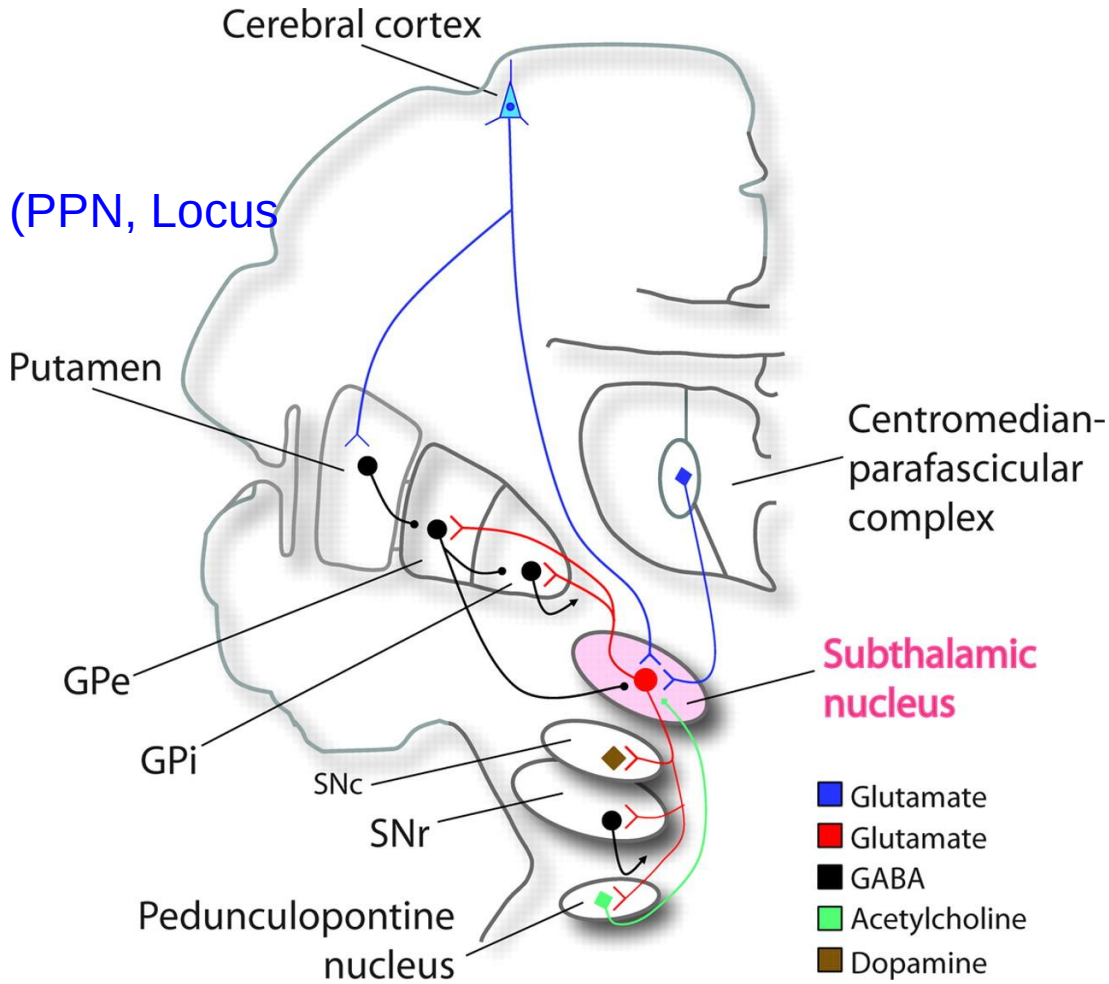
BASAL GANGLIA PATHWAYS

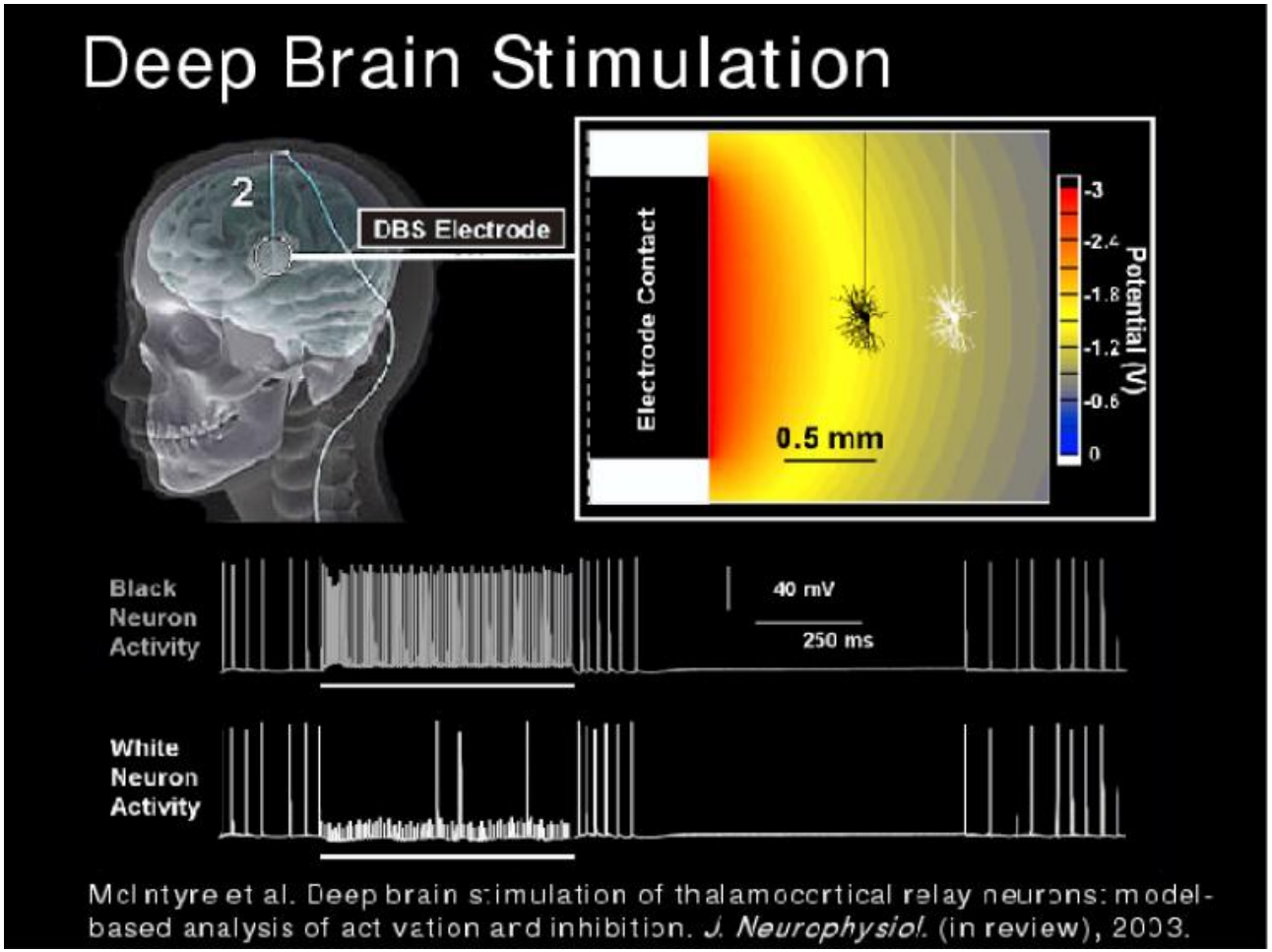
- Direct pathway
- Indirect pathway



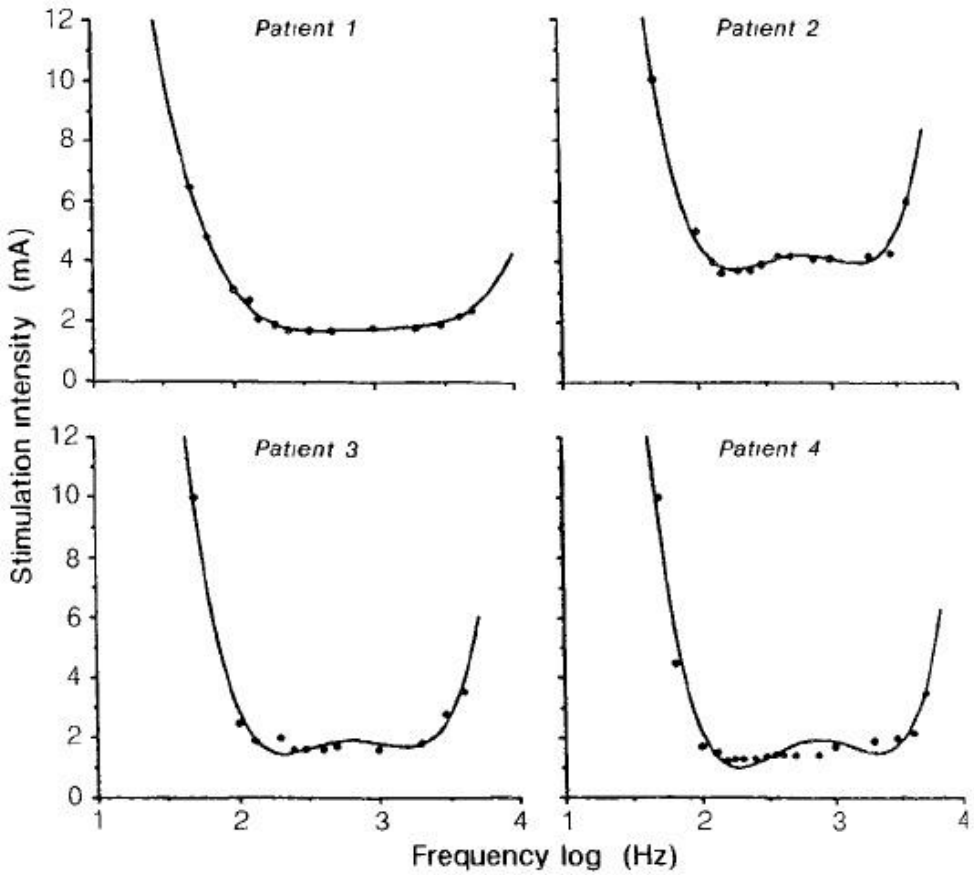
Parkinsons's disease

- Lewy bodies
- degeneration of other nuclei (PPN, Locus Coeruleus)

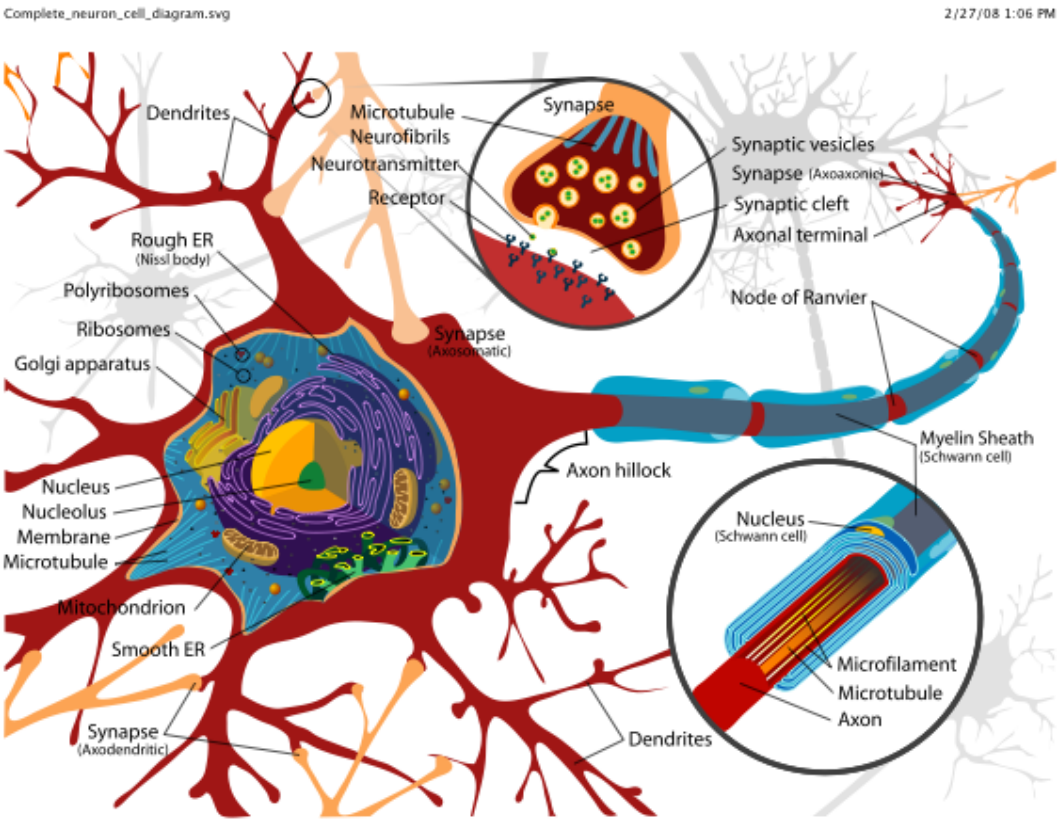



Deep Brain Stimulation
2
DBS Electrode
Electrode Contact
0.5 mm
Potential (V)
-3
-2.4
-1.8
-1.2
-0.6
0
Black Neuron Activity
40 mV
250 ms
White Neuron Activity
McIntyre et al. Deep brain stimulation of thalamocortical relay neurons: model-based analysis of activation and inhibition. J. Neurophysiol. (in review), 2003.

BENABID CURVE



NEURON CELL


Complete_neuron_cell_diagram.svg
2/27/08 1:06 PM
Dendrites
Microtubule
Neurofibrils
Neurotransmitter
Receptor
Synapse
Synaptic vesicles
Synapse (Axoaxonic)
Synaptic cleft
Axonal terminal
Rough ER
(Nissl body)
Polyribosomes
Ribosomes
Golgi apparatus
Synapse
(Axosomatic)
Node of Ranvier
Myelin Sheath
(Schwann cell)
Axon hillock
Nucleus
Nucleolus
Membrane
Microtubule
Mitochondrion
Smooth ER
Synapse
(Axodendritic)
Nucleus
(Schwann cell)
Microfilament
Microtubule
Axon
Dendrites

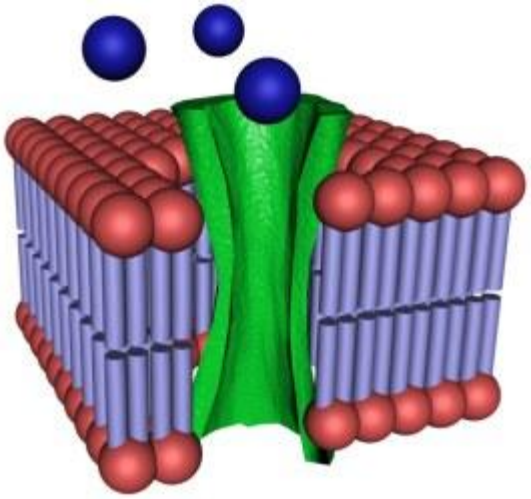
STN conductance-based models

$$C_m \frac{dV_m}{dt} = -I_{leak} - I_K - I_{Na} - I_T - I_{Ca} - I_{AHP}$$

Source: Terman, Rubin (2002/2004)

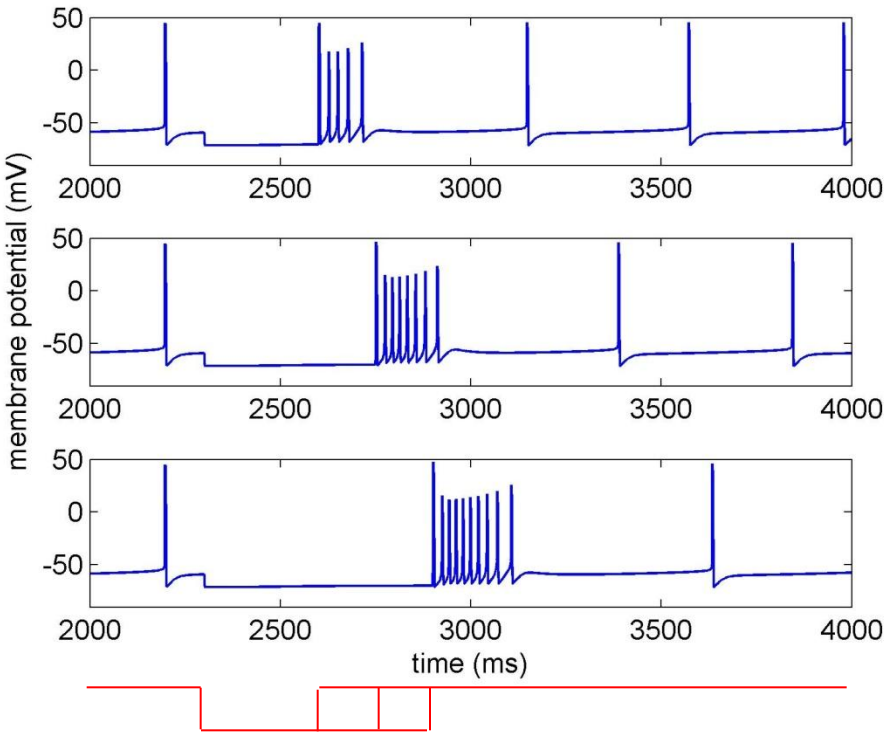
$$C_m \frac{dV_m}{dt} = -I_{leak} - I_K - I_{Na} - I_T - I_L - I_{Ca-K} - I_A$$

Source: Otsuka et al. (2003)



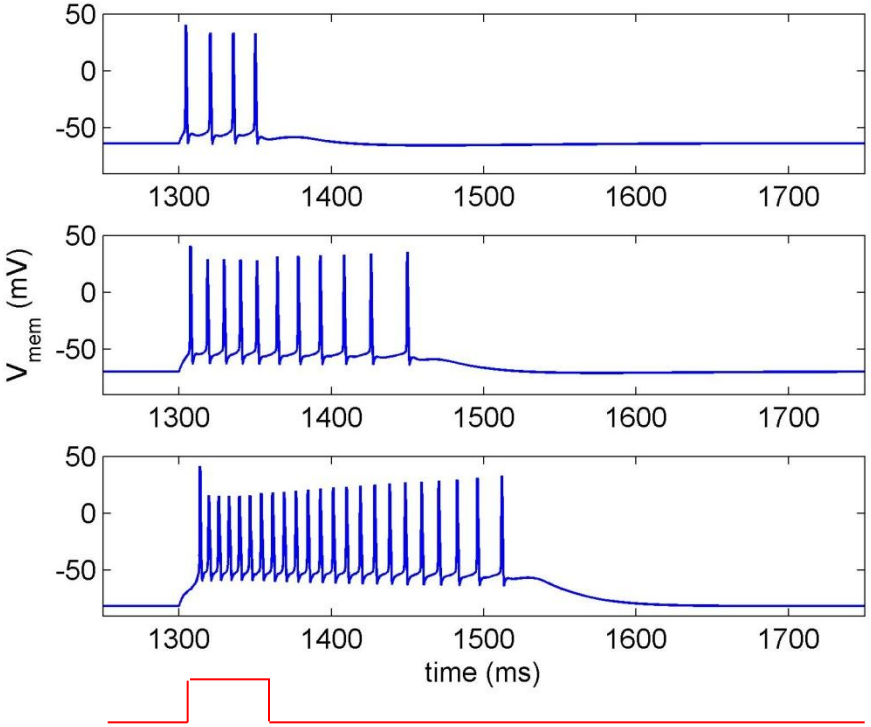
STN bursting activity – plateau potential

Terman, Rubin (2002/2004)



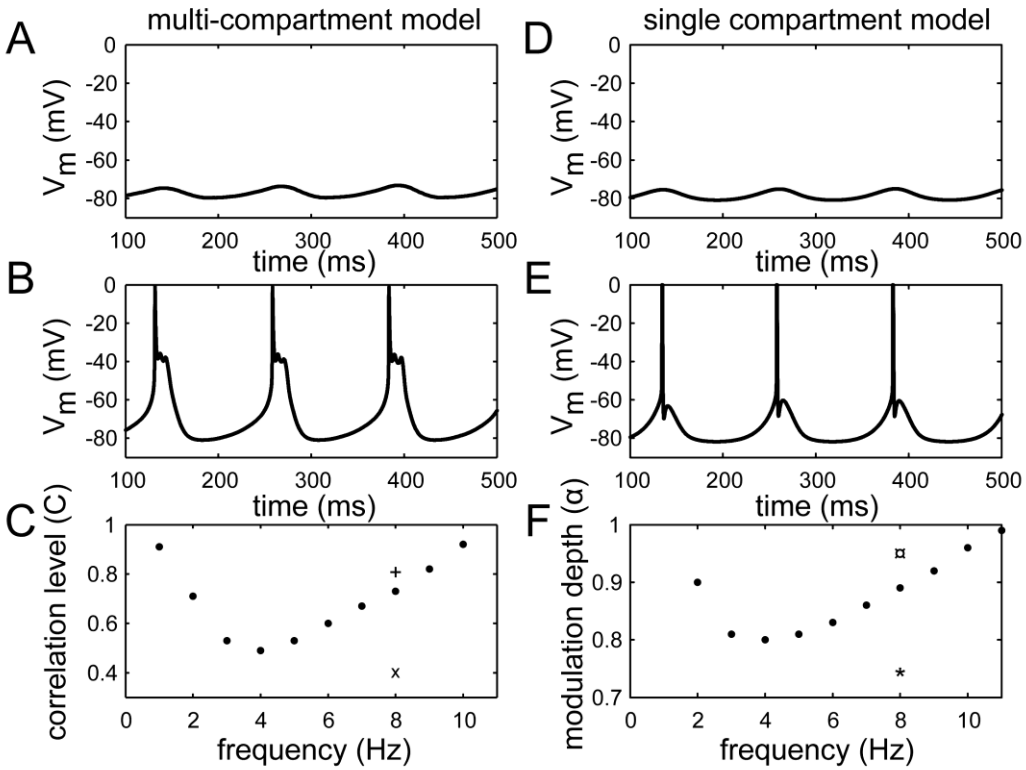
hyperpolarizing input -25 pA/μm^2 with different durations

Otsuka et al. (2003)



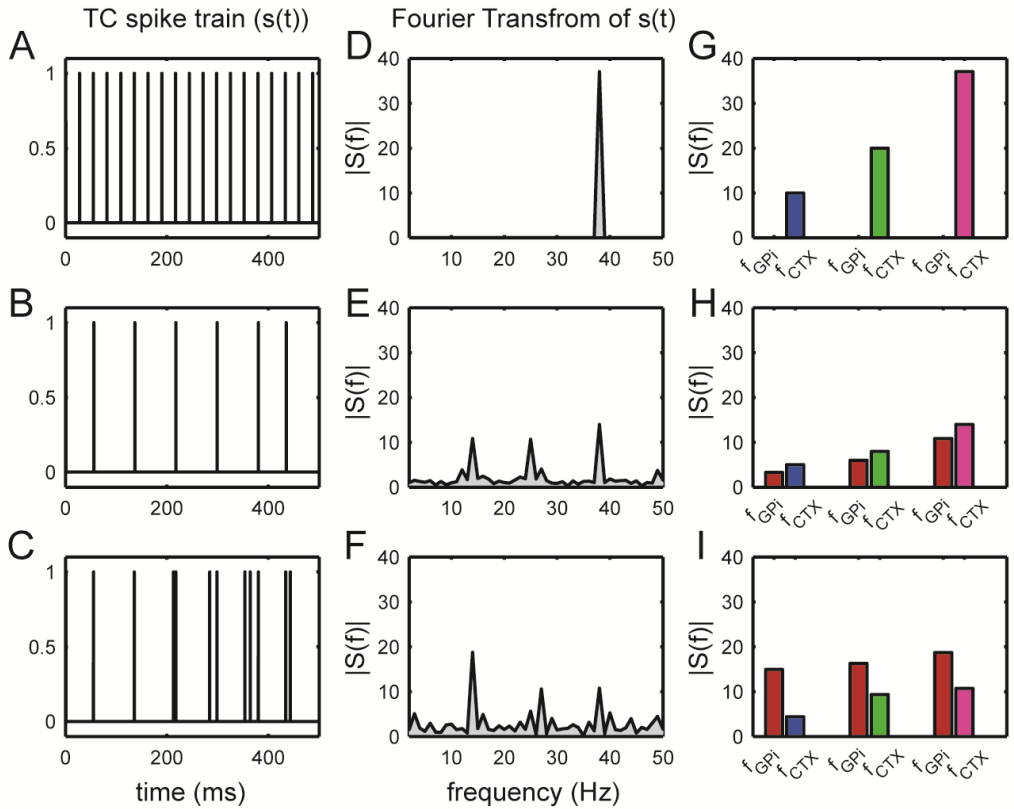
depolarizing input 5 μA/cm^2 at different hyperpolarized states

SELECTIVE RESPONSE OF THALAMOCORTICAL CELL



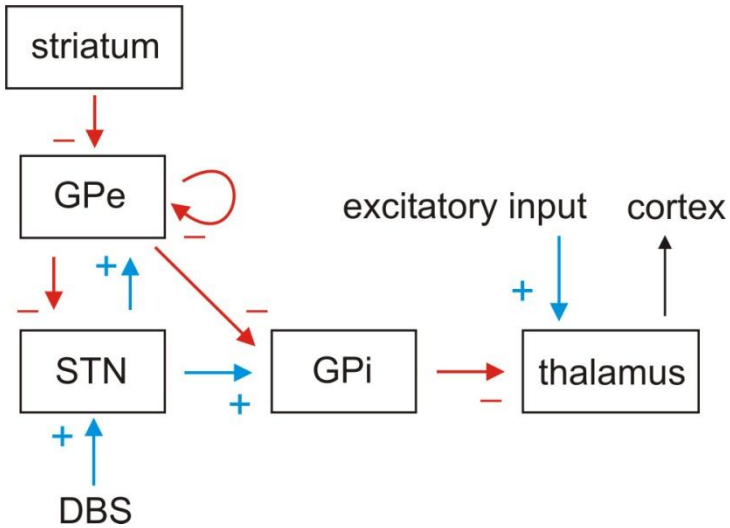
Frequency selectivity of a thalamocortical relay neuron during Parkinson's disease and Deep stimulation: a computational study. European Journal of Neuroscience. Hayriye Cagnan e.a. (2009)

RELAY FUNCTIONALITY OF TC NEURON

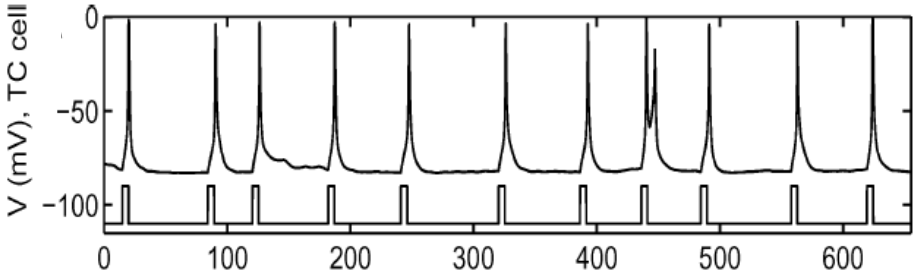


STN DBS – restoring TC relay function?

Rubin & Terman (2004)



normal



STN DBS – restoring TC relay function?

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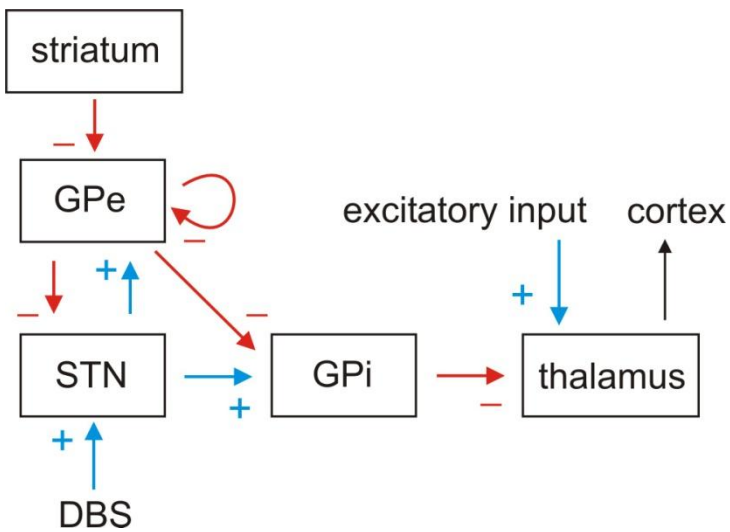
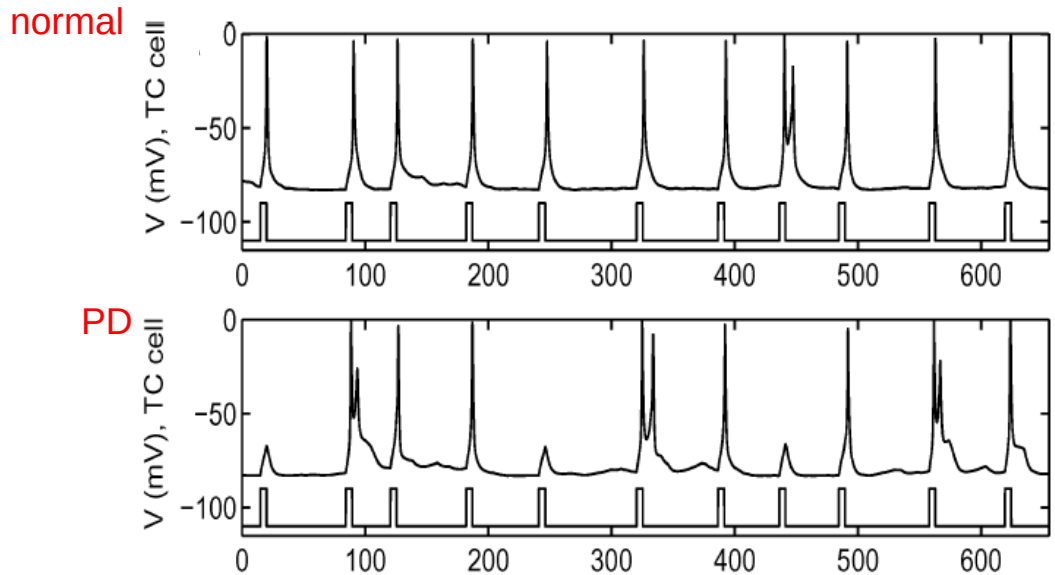
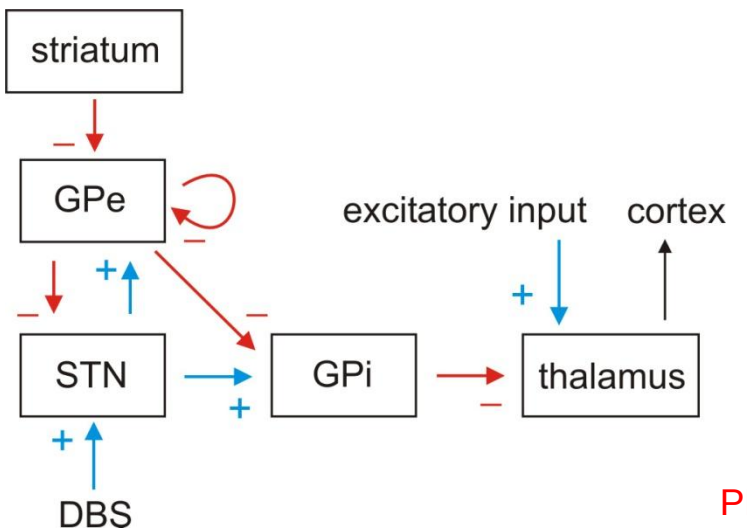


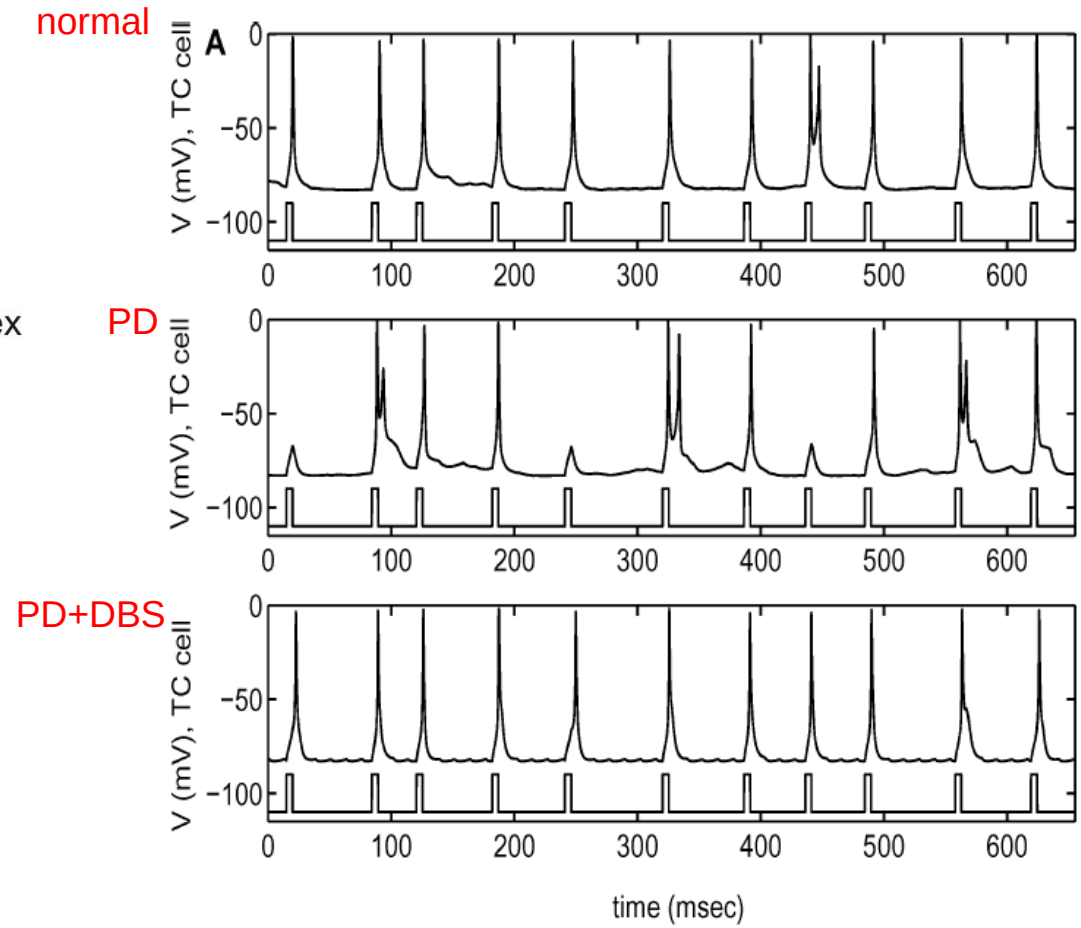


- increased striatal input
- decreased inter-pallidal inhibition

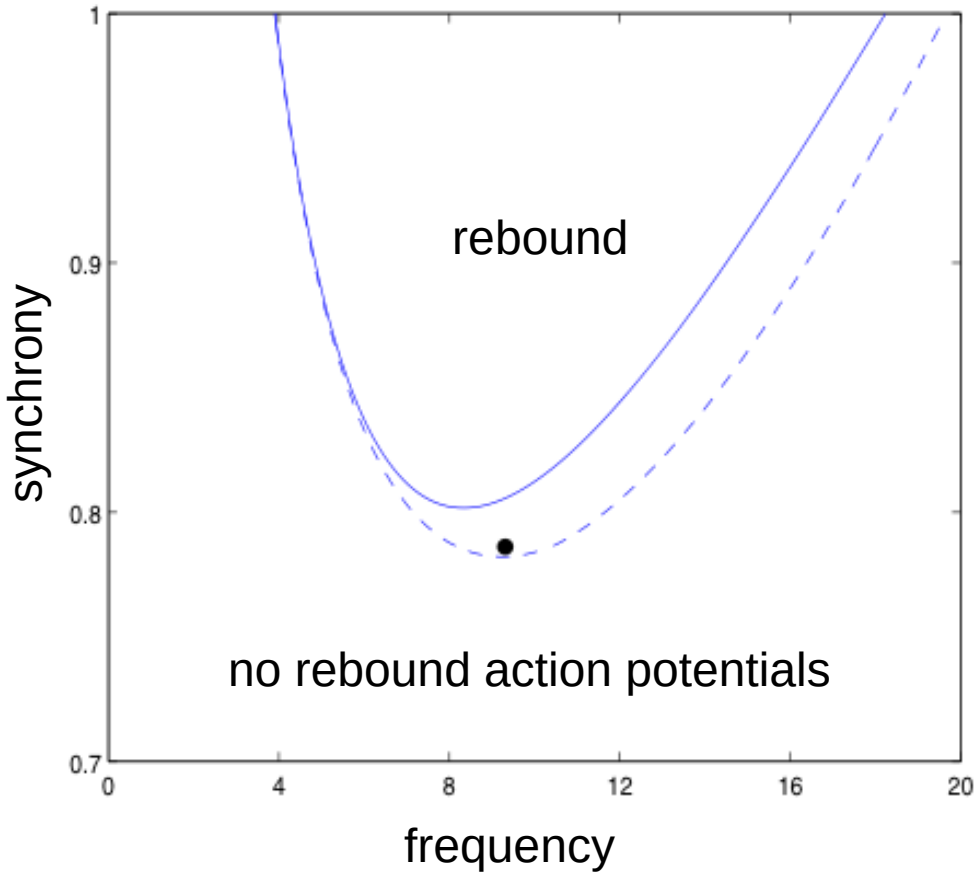
STN DBS – restoring TC relay function?

Rubin & Terman (2004)

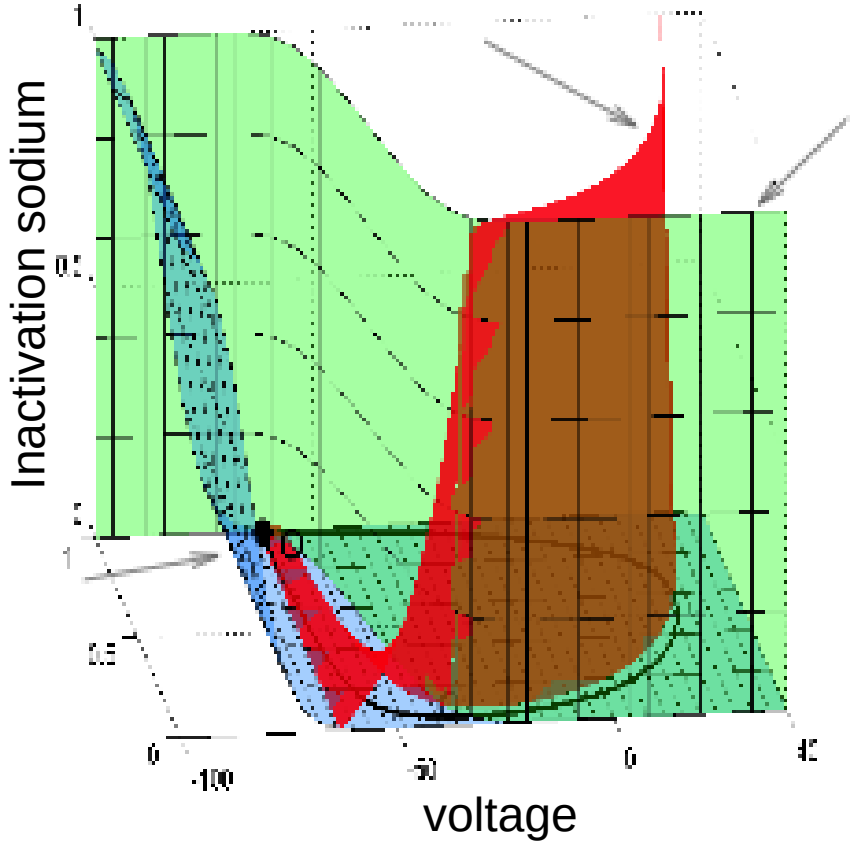




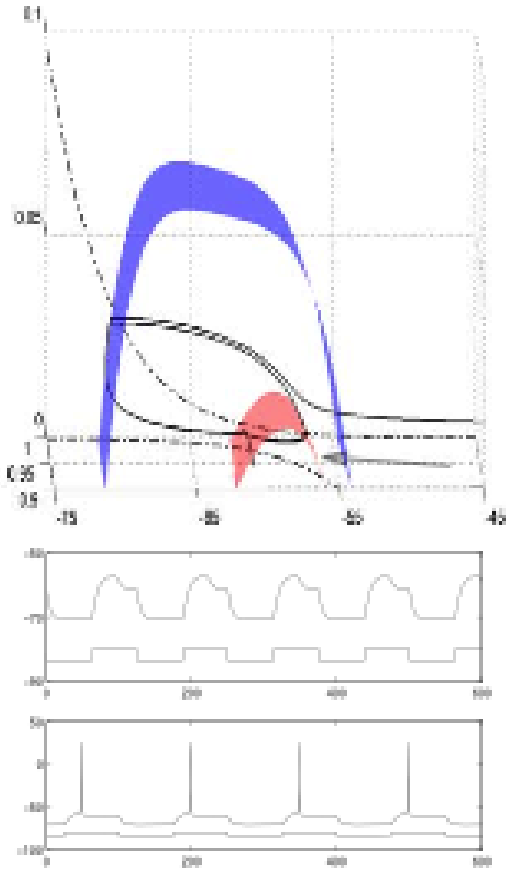
FREQUENCY SELECTIVITY IN 3D MODEL



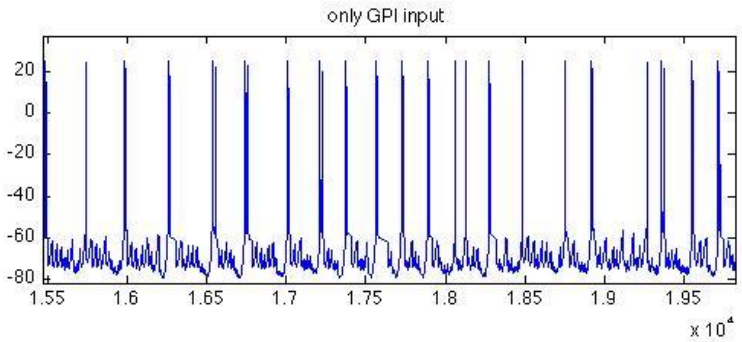
DYNAMICS OF REBOUNDS

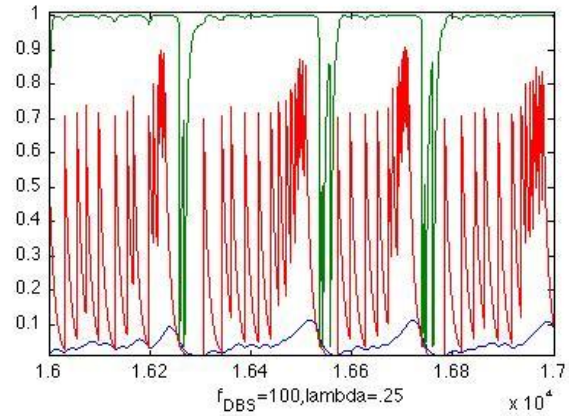


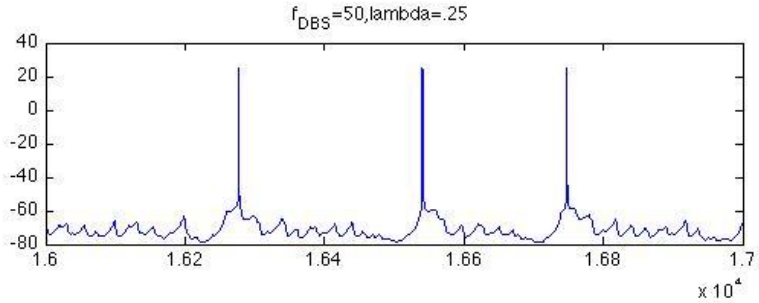
PARKINSON REBOUND

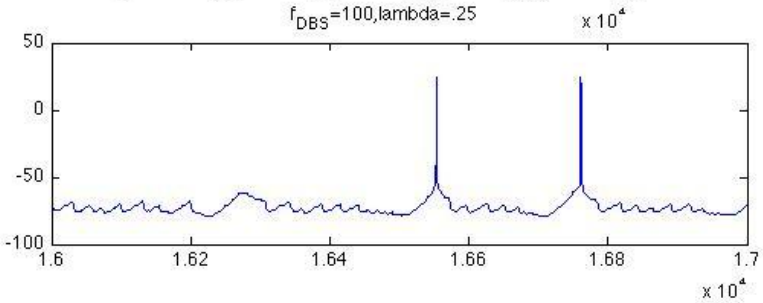


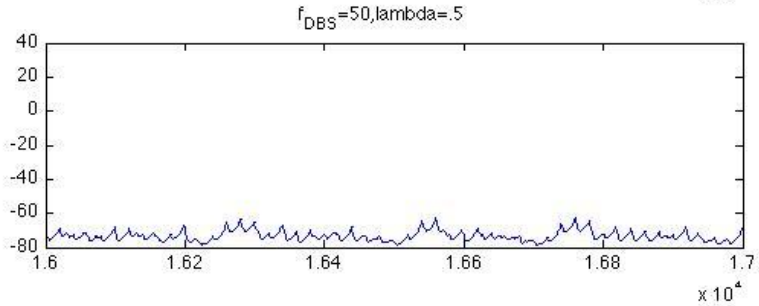
REAL GPI DATA TO MODEL TC INPUT

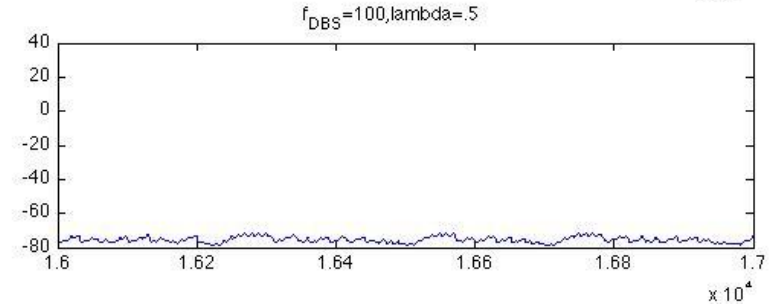




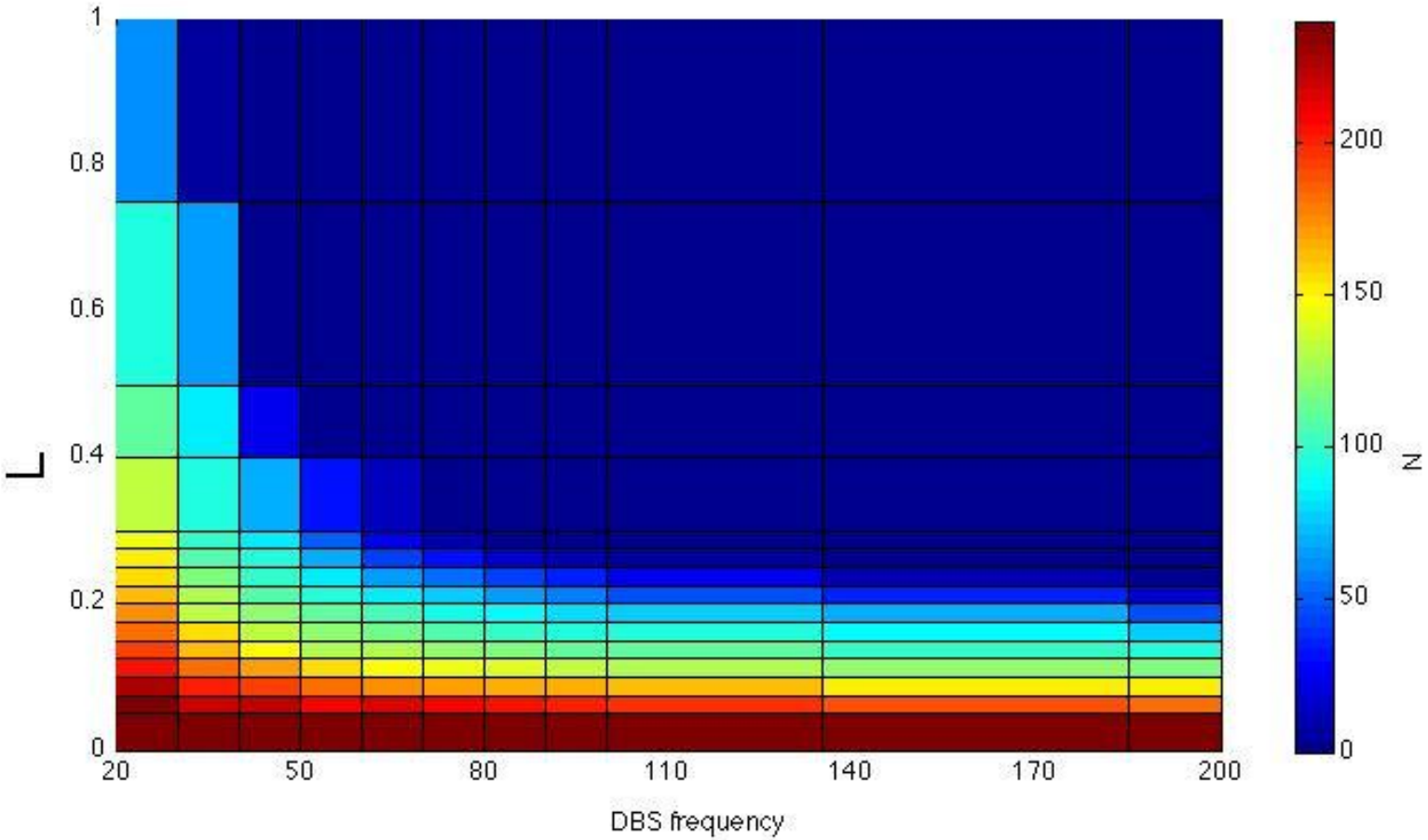




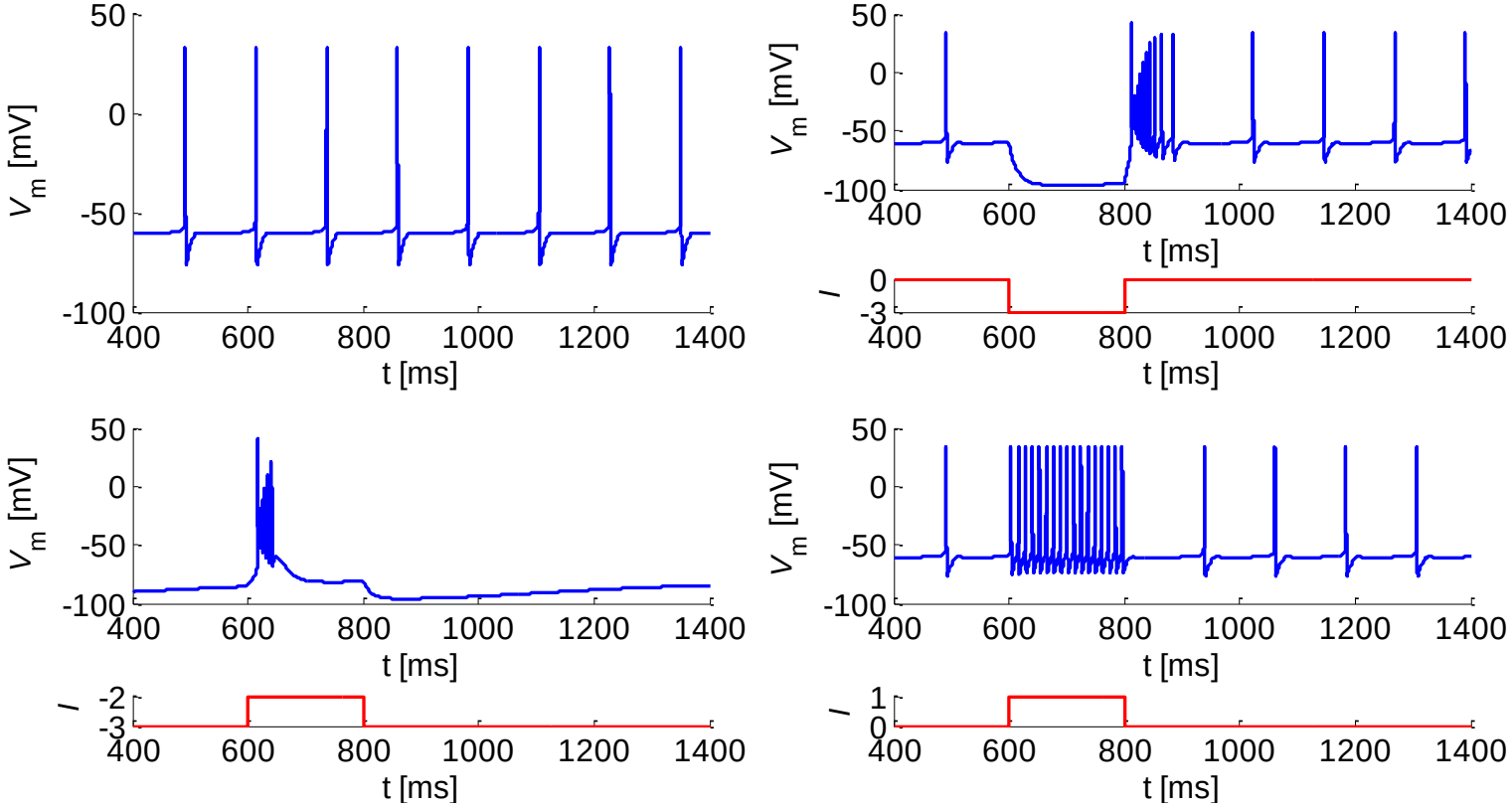




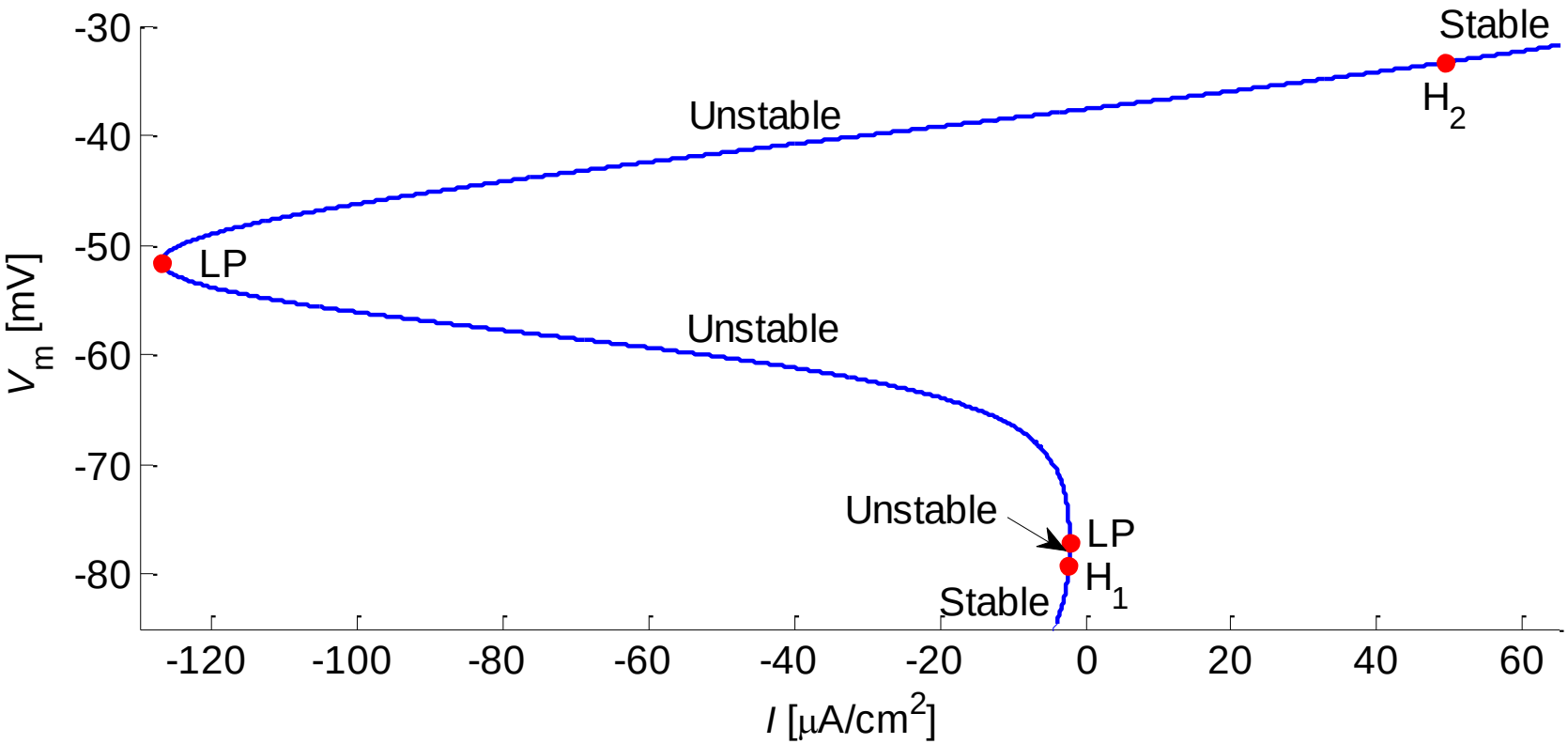
REBOUND SUPPRESSION (REAL DATA)



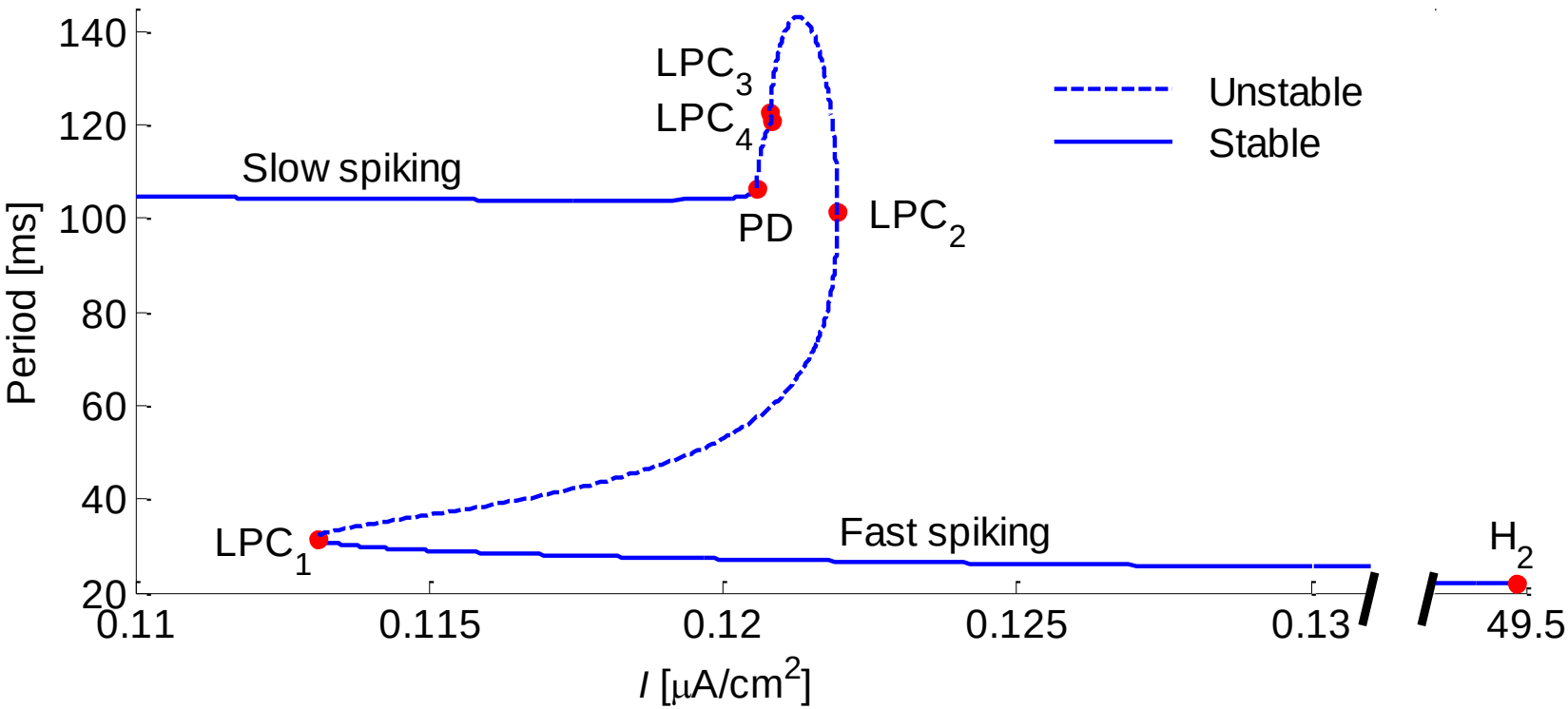
PPN TYPE I CELL



BIFURCATION ANALYSIS



CONTINUATION OF LIMIT CYCLES

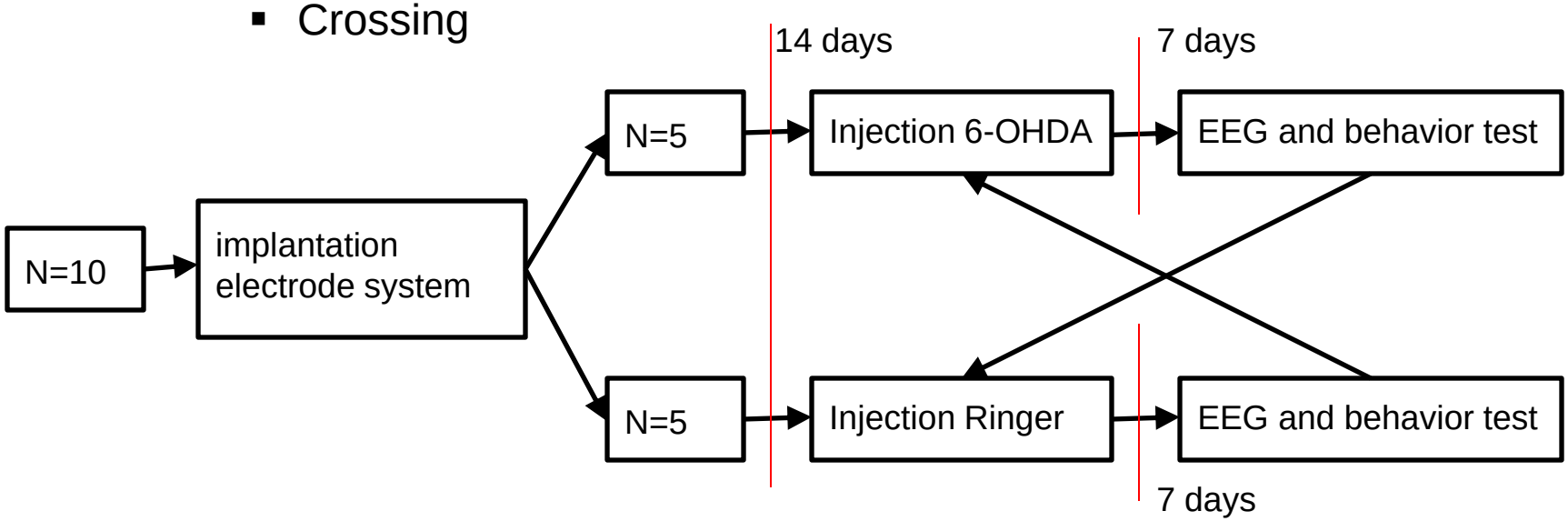


ANIMAL MODEL

- Study an animal model of Parkinson’s disease: Unilateral 6-OHDA lesioned rat
- Determine changes in functional connectivity bases on local field potentials
- Determine connectivity in network model of the Basal ganglia including PPN
- Effect of STN-DBS and/or PPN-DBS
- In cooperation with Radboud Universiteit Nijmegen

EXPERIMENTAL DESIGN

- 10 adult male Wistar rats (300-450 gram)
- 5 rats receive an unilateral 6-OHDA lesion and 5 rats receive an unilateral Ringer lesion
- 7 days post-lesion EEG recording and behavior test
- Crossing



PEOPLE INVOLVED

Marcel Lourens (BrainGain)

Hayriye Cagnan (Philips)

Lo Bour (AMC)

Gyles van Luijtelaar (RUN)

Ciska Heida (UT)

Hil Meijer (UT)

SPIKE SORTING