MODELING THE EFFECT OF NEUROTRANSMITTER: EFFECT OF DOPAMINE ON MEDIUM SPINY NEURON

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5 June 2013
**Striatum and Basal Ganglia Circuits**

Basal Ganglia (BG) circuit

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1 Squire, L et al., Fundamental Neuroscience, Elsevier, 2008
Parkinson (PD), Deep Brain Stimulation (DBS)

2

2 J. Eric Ahlskog, The Parkinson’s Disease Treatment Book, Oxford University Press, 2005
Neuron Models

Hodgkin-Huxley equation

\[ C_m \dot{v_m} = I - I_K - I_{Na} - I_L \]
\[ \dot{n} = \alpha_n(v_m)(1 - n) - (\beta_n(v_m)n) \]
\[ \dot{m} = \alpha_m(v_m)(1 - m) - (\beta_m(v_m)m) \]
\[ \dot{h} = \alpha_h(v_m)(1 - h) - (\beta_h(v_m)h) \]

Current Equations

\[ I_K = g_K n^4(v_m - E_K) \]
\[ I_{Na} = g_{Na} m^3 h(v_m - E_{Na}) \]
\[ I_L = g_L(v_m - E_L) \]

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3E.M. Izhikevich, Dynamical Systems in Neuroscience, MIT, 2007
Neuron Behaviours

4 E.M. Izhikevich, Dynamical Systems in Neuroscience, MIT, 2007
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Neuron Behaviours

E.M. Izhikevich, Which model to use for Cortical spiking neurons?, IEEE, 2004
Ion currents that can be added to the HH model:

Na Currents:
Noninactivating Na current:

\[ I_{Nap} = g_{Nap} \cdot m \cdot (v_m - E_{Na}) \]
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Ca Currents:
T type Ca current

\[ I_{T_{Ca}} = g_{T_{Ca}} s_{\infty}(v_m)(v_m - E_{Ca}) \]
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Ca Currents:

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\[ I_{T_{Ca}} = g_{T_{Ca}} s_{\infty}(v_m)(v_m - E_{Ca}) \]
Ion currents that can be added to the HH model:
Ca Currents:
L type Ca current .

\[
I_{Ca} = \frac{g_{Ca} \cdot m_{Ca}^2 \cdot v_m \cdot \frac{z^2 \cdot F^2}{R \cdot T} \cdot ([Ca^{2+}]_e \cdot e^{-v_m \cdot \frac{z \cdot F}{R \cdot T}} - [Ca^{2+}]_i)}{1 - e^{-v_m \frac{z \cdot F}{R \cdot T}}}
\]
Ion currents that can be added to the HH model:

Ca Currents:
L type Ca current.

\[
I_{LCa} = \frac{g_{LCa} \cdot m_{LCa}^2 \cdot v_m \cdot z^2 \cdot F^2}{R \cdot T} \cdot \left( [Ca^{2+}]_e \cdot e^{-v_m \cdot \frac{z\cdot F}{R \cdot T}} - [Ca^{2+}]_i \right) \frac{1 - e^{-v_m \cdot \frac{z\cdot F}{R \cdot T}}}{1 - e^{-v_m \cdot \frac{z\cdot F}{R \cdot T}}}
\]

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Fast Slow Inactive K current

\[ I_{Kv1} = g_{Kv1} \cdot n^2 \cdot h \cdot (v_m - E_K) \]
Ion currents that can be added to the HH model:

**K Currents:**

Fast Slow Inactive K current

\[ I_{Kv1} = g_{Kv1} \cdot n^2 \cdot h \cdot (v_m - E_K) \]
Ion currents that can be added to the HH model:
K Currents:
After Hyperpolarization Current:

\[ I_{AHP} = g_{AHP}(v_m - E_K) \cdot \frac{[Ca^{2+}]_i}{[Ca^{2+}]_i + k_I} \]
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K Currents:
After Hyperpolarization Current.

\[ I_{AHP} = g_{AHP} (v_m - E_K) \cdot \frac{[Ca^{2+}]_i}{[Ca^{2+}]_i + k_l} \]
Medium Spiny Neuron (MSN) Model

\[ C_m \dot{v}_m = I - I_K - I_{Na} - I_L - I_{L_{Ca}} - I_{Kv1} - I_{T_{Ca}} - I_{AHP} \]
Medium Spiny Neuron (MSN) Model

\[ C_m \dot{v}_m = I - I_K - I_{Na} - I_L - I_{L_{Ca}} - I_{Kv1} - I_{T_{Ca}} - I_{AHP} \]
Medium Spiny Neuron (MSN) Model

\[ C_m \frac{\partial v_m}{\partial t} = I - I_K - I_{Na} - I_L - I_{L_{Ca}} - I_{Kv1} - I_{T_{Ca}} - I_{AHP} \]
Medium Spiny Neuron (MSN) Model

\[ C_m \dot{v}_m = I - I_K - I_{Na} - I_L - I_{L_{Ca}} - I_{Kv1} - I_{T_{Ca}} - I_{AHP} \]

\[ I_{Kv1} = g_{Kv1} \cdot n^2 \cdot h \cdot (v_m - E_K) \]

\[ I_{L_{Ca}} = \frac{g_{L_{Ca}} \cdot m_{L_{Ca}}^2 \cdot v_m \cdot \frac{z^2 \cdot F^2}{R \cdot T} \cdot ([Ca^{2+}]_e \cdot e^{-v_m \cdot \frac{z \cdot F}{R \cdot T}} - [Ca^{2+}]_i)}{1 - e^{-v_m \cdot \frac{z \cdot F}{R \cdot T}}} \]

\[ I_{T_{Ca}} = g_{T_{Ca}} \cdot s_{\infty} (v_m) \cdot (v_m - E_{Ca}) \]

\[ I_{AHP} = g_{AHP} \cdot (v_m - E_K) \cdot \frac{[Ca^{2+}]_i}{[Ca^{2+}]_i + k_l} \]

\[ m_{L_{Ca}} = \left( m_{L_{Ca}}(V) - m_{L_{Ca}} \right) / \tau_{L_{Ca}}(V) \]

\[ [Ca^{2+}]_i = \epsilon \cdot (\sum I_{Ca} - k_{Ca} \cdot [Ca^{2+}]_i) \]
Medium Spiny Neuron (MSN) Model
Dopamine effect

Neurotransmitter

http://www.fmhs.uaeu.ac.ae/wlammersteach/Introduction to PathoPhysiology/Lect3/Chemical_Synaps.html

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Dopamine effect

Houk et al. (2002):

\[-C_m \frac{dv_m}{dt} = \gamma(I_{IRK} + I_{L_{Ca}}) + I_{ORK} + I_I + I_s\]

$I_{IRK}$: Inward rectifying Potassium current
$I_{ORK}$: Outward rectifying Potassium current

Guthrie et al (2009):

\[-C_m \frac{dv_m}{dt} = D_{Tonic}(I_{Kir} + I_{L_{Ca}}) + I_{Ksi} + I_{Krp} + I_L + I_s\]

$I_{Kir}$: inwardly rectifying Potassium current
$I_{Ksi}$: slowly inactivating A-type Potassium current
$I_{Krp}$: non-inactivating Potassium current

$\gamma$ and $D_{Tonic}$ parameters changes dynamic behaviour.
Bifurcations

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6 E.M. Izhikevich, Dynamical Systems in Neuroscience, MIT, 2007
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Modeling Dopamine Effect

The first model $C_m \frac{dv_m}{dt} = I - I_K - I_{Na} - I_L - Dop \cdot (I_{L_{Ca}} + I_{Kv1}) - I_{T_{Ca}} - I_{AHP}$
Modeling Dopamine Effect

The first model \( C_m \dot{v}_m = I - I_K - I_{Na} - I_L - Dop \cdot (I_{L_{Ca}} + I_{Kv1}) - I_{T_{Ca}} - I_{AHP} \)
Modeling Dopamine Effect

The second model:

\[ C_m \dot{v}_m = I - I_K - I_{Na} - I_L - I_{LCa} - I_{Kv1} - I_{Ca} - I_{AHP} \]
Modeling Dopamine Effect

The second model;

\[ C_m \frac{\dot{v}_m}{I} = I - I_K - I_{Na} - I_L - I_{La} - I_{KV1} - I_{Ca} - I_{AHP} \]

Currents;

\[ I_{Na} = (g_{Na} + g_{DNa})m^3h(v_m - E_{Na}) \]

\[ I_{KV1} = (g_K + g_{DK})n^2h(v_m - E_K) \]

\[ I_{La} = (g_{La} + g_{DLa})m^{2}_La \frac{\nu_m z^2 F^2}{RT} \frac{[Ca^{2+}]_e e^{-\nu_m z F RT}}{1 - e^{-\nu_m z F RT}} \]
Results

Bifurcation diagrams of model with parameter $g_{DNa}$.  

![Bifurcation Diagram](image_url)
Results

Bifurcation diagrams of model with parameter $g_{D_{Na}}$. 
Results

Bifurcation diagrams of model with parameter $g_{D_{Na}}$. 
Results

Bifurcation diagrams of model with parameter $g_{D_{Na}}$. 

![Bifurcation Diagrams](image1)

![Bifurcation Diagrams](image2)

![Bifurcation Diagrams](image3)
Results

Bifurcation diagrams of model with parameter $g_{D_K}$. 
Results

Bifurcation diagrams of model with parameter $g_{D_K}$. 
Results

Bifurcation diagrams of model with parameter $g_{D_K}$ iletkenliğine göre dallanma diyagramı.
Results

Bifurcation diagrams of model with parameter $g_{D_{Na}}$.

Bifurcation diagrams of model with parameter $g_{D_{K}}$.
Results

Bifurcation diagrams of model with parameter $g_{D_{L_{Ca}}}$.
Results

Bifurcation diagrams of model with parameter $g_{D,LCa}$. 
Results

Bifurcation diagrams of model with parameter $g_{D_{LCa}}$.
Results

Bifurcation diagrams of model with parameter $g_{DNa}$.

Bifurcation diagrams of model with parameter $g_{DK}$.

Bifurcation diagrams of model with parameter $g_{DLCa}$.
Results

investigate HH model and Ion currents that can be added to the HH model.
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obtain meaningful of MSN model.
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modeling DA effect two different approaches.
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modeling DA effect, using dynamical systems and bifucation analysis tools.
References


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Harlow, J.M., 1868. Recovery from the passage of an iron bar through the head, Publications of the Massachusetts Medical Society, 2, 327–347.


Thank you for your attention.