Supplementary Information

Title: Electrophysiological Variability of GPe Neurons via Hodgkin-Huxley Modeling: Correlation between Leak and HCN Channels.

Authors:
Matheus Phellipe Brasil de Sousa,
Gabriel Moreno Cunha,
Gabrielle Tavares,
Gilberto Corso,
Karina Possa Abrahao,
*Gustavo Zampier Dos Santos Lima.

Table of electrophysiological features (empirical)

	Ark	Proto	Reference
Feature	$[Q_1; Q_2; Q_3]$	$[Q_1; Q_2; Q_3]$	
Firing (Hz)	[8; 10; 18]	[35; 53; 80]	[2, 6, 7, 8, 1]
Sag (mV)	[-50; -43; -25]	[-11; -9; -5]	[2, 6, 7, 8, 1]
Sag ratio	[1.28; 1.35; 1.46]	[1.05; 1.1; 1.13]	[2, 6, 7]
Trough (mV)	[-140; -150;-175]	[-85; -95; 102]	[2, 6, 7]
NaP	Low	High	[6, 7]
Kv2	Low	High	[6, 7]
HCN	Low	High	[6, 7, 3]

Tabela 1: **Electrophysiological Experimental Data.** The values of $[Q_1; Q_2; Q_3]$ represent the quartiles: Q_1 = first quartile, Q_2 = median, and Q_3 = third quartile.

Parameters tables

Ionic channel	Conductance density (mS/cm^2)	Reference
NaP	0.1; 0.5; 1.0; 2.0	[5, 4]
Kv2	0.1; 1.0; 10.0	[5, 4]
HCN	0.04; 0.20; 1.00; 5.00	[5, 4]
leak	0.07; 0.10; 0.30	[5, 4]

Tabela 2: **Electrophysiological Parameters Used in Computational Simulations (Hodgkin-Huxley Type Model).**

Parameter	Ark	Proto
C_m	$1\mu F/cm^2$	$1\mu F/cm^2$
g_{NaP}	$0.2mS/cm^2$	$2.0mS/cm^2$
g_{NaF}	$100mS/cm^2$	$100mS/cm^2$
g_{Kv2}	$0.1mS/cm^2$	$2.0mS/cm^2$
g_{Kv3}	$32mS/cm^2$	$32mS/cm^2$
g_{CaH}	$0.4mS/cm^2$	$0.4mS/cm^2$
g_{SK}	$0.2mS/cm^2$	$0.2mS/cm^2$
g_{HCNf}	-	0
g_{HCNs}	0	-
g_l	-	-
E_{Na}	50mV	50mV
E_K	-90mV	-90mV
E_l	-60mV	-60mV
E_{Ca}	130mV	130mV
E_{Cat}	-30mV	-30mV
γ	$30000cm^{-1}$	$30000cm^{-1}$
F	96485 sA/mol	96485 sA/mol
Z	2	2
K_{Ca}	0.4ms	0.4ms
Ca_{i0}	$0.01\mu M$	$0.01\mu M$
H_{coeff}	4.6	4.6
C_{50}	$0.35\mu M$	$0.35\mu M$
$[Ca^{2+}]_{sat}$	$5\mu M$	$5\mu M$
τ^0 (SK channel)	4ms	4ms
τ^1 (SK channel)	76ms	76ms

Tabela 3: **Parameters used.** Cells shaded in gray indicate parameters that differ between FoxP2 and PV neurons. The dash -"indicates that the parameter was varied over a specific range.

Tabela 4: Parameters of the ionic channel kinetics

Ionic channel	Parameter	Value
NaF	θ_m, k_m	-39, 5.0
	τ_m^0, τ_m^1	0.028, 0.028
	θ_h, k_h	-48, -2.8
	τ_h^0, τ_h^1	0.25, 4.0
	ϕ_h, σ_h^0, σ_h^1	-43, 10, -5.0
	θ_s, k_s, $s_{\min}$	-40, -5.4, 0.15
	ϕ_s, σ_s^0, σ_s^1	40, 18.3, -1.0
NaP	θ_m, k_m	-57.7, 5.7
	τ_m^0, τ_m^1	0.03, 0.016
	θ_h, k_h	-42.6, 14.4, -14.4
	ϕ_h, k_h, $h_{\min}$	-57, 4.0, 0.154
	τ_h^0, τ_h^1	10, 17
	ϕ_h, σ_h^0, σ_h^1	-34, 26, -31.9
	A_s^α, B_s^α	$-2.88\text{e}{-6}$, $-4.9\text{e}{-5}$
	K_s^α	4.63
	A_s^β, B_s^β	$6.94\text{e}{-6}$, $4.47\text{e}{-4}$
	K_s^β	-2.63
Kv2	θ_m, k_m	-33.2, 9.1
	τ_m^0, τ_m^1	0.1, 3.0
	ϕ_m, σ_m^0, σ_m^1	-33.2, 21.7, -19.3
	θ_h, k_h, $h_{\min}$	-20, 1.0, 0.02
	τ_h^0, τ_h^1	3400, 3400
Kv3	θ_m, k_m	-26, 7.8
	τ_m^0, τ_m^1	0.1, 14
	ϕ_m, σ_m^0, σ_m^1	-10, 10, 10
	θ_h, k_h, $h_{\min}$	-70, 33
	ϕ_h, σ_h^0, σ_h^1	0, 10, -10
CaH	θ_m, k_m	-20, 7.0
HCNf	θ_m, k_m	-76.4, -2.3
	τ_m^0, τ_m^1	500, 800
	ϕ_m	-76.4
	σ_m^0, σ_m^1	6.56, -7.48
HCNs	θ_m, k_m	-76.4, -3.3
	τ_m^0, τ_m^1	5000, 7000
	ϕ_m	-76.4
	σ_m^0, σ_m^1	6.56, -7.48

HH-GPe code

Main code (.m)

```
%% HH-GPe model
% Created by Matheus Phellipe Brasil de Sousa
```

```
% UFRN- Natal

clear all

t0 = 0; %initial time (ms)
tf = 2000; %final time (ms)
passo =0.01; %time step
tempo = t0:passo:tf; %total time of simulation

%%---------PV (proto neuron) ------------
eqns=['dv/dt= I(t)+@current/Cm +@rr; Cm=1.0; v(0)=-45;' ...
'{iNaFgpe,iNaPgpe,ikv3gpe,fujita_iLeak,iCaHgpe,CalciumDyn,iSKgpe,ikv2gpe,iHCNgpe1,
    iHCNgpe4,noise_mech};' ...
'ton=500; toff=1500; Iapp=-5 ; I(t) = Iapp*(t>ton&t<toff);' ...
'g_NaP = 2.0;g_NaF = 100.;g_l = 0.3;g_CaH = 0.4;g_SK =0.2;g_kv3=36;g_kv2=0.1;g_HCN1
    =0.05;g_HCN4=0.1;'];

tic
Data5=dsSimulate(eqns,'tspan',[t0 tf],'dt',passo);
toc
```

Mechanism (.mech)

Persist sodium current

```
%Persist sodium current NaP for GPe neurons (Fujita 2012)

g_NaP = 2.; % mS/cm2, maximal conductance
E_Na = 35; % mV, sodium reversal potential

% Kinetics parameters NaP
q_m_NaP = -57.7; k_m_NaP = 5.7;
t0_m_NaP = 0.03; t1_m_NaP = 0.146;
fm_NaP = -42.6; s0_m_NaP = 14.4; s1_m_NaP = -14.4;
q_h_NaP = -57; k_h_NaP = -4; h_min_NaP = 0.154;
t0_h_NaP = 10; t1_h_NaP = 17;
fh_NaP = -34; s0_h_NaP = 26; s1_h_NaP = -31.9;
q_s_NaP = -10; k_s_NaP = -4.9;
A_alpha_s_NaP = -2.88e-6; B_alpha_s_NaP = -4.9e-5; K_alpha_s_NaP = 4.63;
A_beta_s_NaP = 6.94e-6; B_beta_s_NaP = 4.47e-4; K_beta_s_NaP = -2.63;

hnascale=1;
IC_noise=0;

% Functions

m_inf_NaP(X)=1./(1 + exp((q_m_NaP - X)./k_m_NaP));
h_inf_NaP(X)=1./(1 + exp((q_h_NaP - X)./k_h_NaP));
s_inf_NaP(X) = 1./(1 + exp((q_s_NaP - X)./k_s_NaP));


tau_m_NaP(X) = t0_m_NaP + (t1_m_NaP - t0_m_NaP)./(exp((fm_NaP-X)./s0_m_NaP) + exp((
    fm_NaP-X)./s1_m_NaP));
tau_h_NaP(X) = t0_h_NaP + (t1_h_NaP - t0_h_NaP)./(exp((fh_NaP-v)./s0_h_NaP) + exp((
    fh_NaP-v)./s1_h_NaP));

```

```
alpha(X) = (A_alpha_s_NaP*X + B_alpha_s_NaP)./(1 - exp((X + (B_alpha_s_NaP./A_alpha_s_NaP))./K_alpha_s_NaP));
beta(X) = (A_beta_s_NaP*X + B_beta_s_NaP)./(1 - exp((X + (B_beta_s_NaP./A_beta_s_NaP))./K_beta_s_NaP));

tau_s_NaP(X) = 1./(alpha(X)+beta(X));


INaP_Gpe(X,m,h,s) = g_NaP.*m.^3.*h.*s.*(X-E_Na)

% ODEs and ICs

m'=((m_inf_NaP(X) - m)./tau_m_NaP(X))
h'=((h_inf_NaP(X) - h)./tau_h_NaP(X))
s'=((s_inf_NaP(X) - s)./tau_s_NaP(X))

m(0)=m_inf_NaP(-65)+IC_noise.*rand(1,Npop)
h(0)=h_inf_NaP(-65)+IC_noise.*rand(1,Npop)
s(0)=s_inf_NaP(-65)+IC_noise.*rand(1,Npop)

% Linkers
@current += -INaP_Gpe(X,m,h,s)
```

Fast sodium current

```
%Fast sodium current NaF for GPe neurons (Fujita 2012)

g_NaF = 50; % mS/cm2, maximal conductance
E_Na = 33; % mV, sodium reversal potential


% Kinetics parameters NaF
q_m_NaF =-39; k_m_NaF = 5;
t0_m_NaF = 0.028; t1_m_NaF = 0.028;
q_h_NaF = -48; k_h_NaF = -2.8;
t0_h_NaF = 0.25; t1_h_NaF = 4;
fh_NaF = -43; s0_h_NaF = 10; s1_h_NaF = -5.0;
q_s_NaF =-40; k_s_NaF = -5.4; s_min_NaF = 0.15;
t0_s_NaF = 10; t1_s_NaF = 1000;
fs_NaF = -40; s0_s_NaF = 18.3; s1_s_NaF = -10;

hnascale=1;
IC_noise=0;

% Functions

m_inf_NaF(X)=1./(1 + exp((q_m_NaF - X)./k_m_NaF))
h_inf_NaF(X)=1./(1 + exp((q_h_NaF - X)./k_h_NaF))
s_inf_NaF(X)=s_min_NaF + (1 - s_min_NaF)./(1 + exp((q_s_NaF - X)./k_s_NaF))

tau_m_NaF(X)=t0_m_NaF
tau_h_NaF(X)=t0_h_NaF + (t1_h_NaF - t0_h_NaF)./(exp((fh_NaF-X)./s0_h_NaF) + exp((fh_NaF-X)./s1_h_NaF))
tau_s_NaF(X)=t0_s_NaF + (t1_s_NaF - t0_s_NaF)./(exp((fs_NaF-X)./s0_s_NaF) + exp((fs_NaF-X)./s1_s_NaF))

INaF_Gpe(X,m,h,s) = g_NaF.*m.^3.*h.*s.*(X-E_Na)
```

```

% ODEs and ICs

m'=((m_inf_NaF(X) - m)./tau_m_NaF(X))
h'=((h_inf_NaF(X) - h)./tau_h_NaF(X))
s'=((s_inf_NaF(X) - s)./tau_s_NaF(X))

m(0)=m_inf_NaF(-65)+IC_noise.*rand(1,Npop)
h(0)=h_inf_NaF(-65)+IC_noise.*rand(1,Npop)
s(0)=s_inf_NaF(-65)+IC_noise.*rand(1,Npop)

% Linkers
@current += -INaF_Gpe(X,m,h,s)
```

Kv2 current

```
%slow delayed rectifier potassium current kv2 for GPe neurons (Fujita 2012)

% Parameters
%g_kv2 = 0.1;
E_K = -90; % Reversal potential for K, mV
IC_noise=0;

%q_m_Kv2 = -33.2; k_m_Kv2 = 9.1;
q_m_Kv2 = -33.2; k_m_Kv2 = 6.1;
t0_m_Kv2 = 0.1; t1_m_Kv2 = 3.0;
fm_Kv2 = -33.2; s0_m_Kv2 = 21.7; s1_m_Kv2 = -13.9;
q_h_Kv2 = -20; k_h_Kv2 = -10; h_min_Kv2 = 0.2;
%t0_h_Kv2 = 3400; t1_h_Kv2 = 3400;
t0_h_Kv2 = 1000; t1_h_Kv2 = 3400;

% Functions
m_inf_kv2(X) = 1./(1 + exp((q_m_Kv2 - X)./k_m_Kv2));
h_inf_kv2(X) = h_min_Kv2 + (1 - h_min_Kv2)./(1 + exp((q_h_Kv2 - X)./k_h_Kv2));

tau_m_kv2(X) = t0_m_Kv2 + (t1_m_Kv2 - t0_m_Kv2)./(exp((fm_Kv2-X)./s0_m_Kv2) + exp((
    fm_Kv2-X)./s1_m_Kv2));
tau_h_kv2(X) = t0_h_Kv2;

I_kv2(X,m,h) = g_kv2*m.^4*h.*(X-E_K)

% ODEs and ICs

m'=((m_inf_kv2(X) - m)./tau_m_kv2(X))
h'=((h_inf_kv2(X) - h)./tau_h_kv2(X))

m(0)=m_inf_kv2(-65)+IC_noise.*rand(1,Npop)
h(0)=h_inf_kv2(-65)+IC_noise.*rand(1,Npop)

% Linkers
@current += -I_kv2(X,m,h)
```

Kv3 current

```
%fast delayed rectifier potassium current kv3 for GPe neurons (Fujita 2012)
```

```

% Parameters
g_kv3 = 10;
E_K = -90; % Reversal potential for K, mV
IC_noise=0;

q_m_Kv3 = -26; k_m_Kv3 = 7.8;
t0_m_Kv3 = 0.1; t1_m_Kv3 = 14;
fm_Kv3 = -26; s0_m_Kv3 = 13; s1_m_Kv3 = -12;
q_h_Kv3 = -20; k_h_Kv3 = -10; h_min_Kv3 = 0.6;
t0_h_Kv3 = 7.0; t1_h_Kv3 = 33;
fh_Kv3 = 0; s0_h_Kv3 = 10; s1_h_Kv3 = -10;

% Functions
m_inf_kv3(X) = 1./(1 + exp((q_m_Kv3 - X)./k_m_Kv3));
h_inf_kv3(X) = h_min_Kv3 + (1 - h_min_Kv3)./(1 + exp((q_h_Kv3 - X)/k_h_Kv3));

tau_m_kv3(X) = t0_m_Kv3 + (t1_m_Kv3 - t0_m_Kv3)./(exp((fm_Kv3-X)./s0_m_Kv3) + exp((
    fm_Kv3-X)./s1_m_Kv3));
tau_h_kv3(X) = t0_h_Kv3 + (t1_h_Kv3 - t0_h_Kv3)./(exp((fh_Kv3-X)./s0_h_Kv3) + exp((
    fh_Kv3-X)./s1_h_Kv3));

I_kv3(X,m,h) = g_kv3*m.^4*h.*(X-E_K)

% ODEs and ICs

m'=((m_inf_kv3(X) - m)./tau_m_kv3(X))
h'=((h_inf_kv3(X) - h)./tau_h_kv3(X))

m(0)=m_inf_kv3(-65)+IC_noise.*rand(1,Npop)
h(0)=h_inf_kv3(-65)+IC_noise.*rand(1,Npop)

% Linkers
@current += -I_kv3(X,m,h)
```

Leaking current

```
% Hodgkin-Huxley leak current

% Parameters
%g_l = 0.068      % mS/cm^2
E_l = -60;      % mV

% Current function
i_l(X) = -g_l*(X-E_l)

% Linker
@current += i_l(X)
```

SK current

```
%calcium dependent potassium current SK for GPe neurons (Fujita 2012)

% Parameters
g_SK = 0.4; %Sk conductance
```

```
c1 = 1000;
E_K = -90; % Reversal potential for Cat, mV
Hcoeff=4.6;
C50=0.35;
Ca_sat = 5;
Ca0 = 0.01;

IC_noise=0;

%functions

m_inf_SK(@Ca)= ((@Ca).^Hcoeff)./(((C50).^Hcoeff) + ((@Ca).^Hcoeff));

tau_SK(@Ca) = (76 - (72 * @Ca / Ca_sat)) * (@Ca < Ca_sat) + 4 * (@Ca >= Ca_sat);

I_SK(X,m) = g_SK*m*(X-E_K)

% ODEs and ICs
m'=((m_inf_SK(@Ca) - m)./tau_SK(@Ca))
m(0)=(Ca0)+IC_noise*rand(1,Npop)

% Linkers
@current += -I_SK(X,m)
```

Calcium dynamics

```
%Calcium dynamics by Fujita (2012) approach

%parameters
c1 = 1000;
gamma = 30000 %ratio of surface area to volume (cm^-1)
Z = 2; %valence of Ca^+2
F = 96485   % ms*A/mmol, Faraday constant
Kca = 0.4 % Ca^2+ removal rate (ms)
Ca0 = 0.01; %  baseline of Ca^2+ (uM)
a = gamma./(Z*F);
IC_noise=0

% ODEs
Ca' = -a*@I_CaH - Kca*(Ca - Ca0)
Ca(0) = Ca0+IC_noise.*rand(1,Npop)

% Interface
@Ca += Ca
```

Calcium current

```
%comprises high-voltageactivated calcium currents CaH for GPe neurons (Fujita 2012)

% Parameters
%g_CaH = 0.3;
E_Ca = 130; % Reversal potential for Ca, mV
IC_noise=0;

q_m_CaH = -20; k_m_CaH = 7;
```

```
t0_m_CaH = 0.2; t1_m_CaH = 0.2;

% Functions

m_inf_CaH(X) = 1./(1 + exp((q_m_CaH - X)./k_m_CaH));

tau_m_CaH(X) = t0_m_CaH;

I_CaH(X,m) = g_CaH.*m.*(X-E_Ca)

% ODEs and ICs
m'=((m_inf_CaH(X) - m)./tau_m_CaH(X))

m(0)=m_inf_CaH(-65)+IC_noise.*rand(1,Npop)

% Linkers
@current += -I_CaH(X,m)
@I_CaH += I_CaH(X,m)
```

Slow HCN current

```
%hyperpolarization-activated cyclic nucleotide-modulated cation current HCN for GPe
    neurons (Fujita 2012)

% Parameters
g_HCN4 = 0.3;
E_Cat = -40; % Reversal potential for Cat, mV
IC_noise=0;

q_m_HCN = -76.4; k_m_HCN =-3.3;
%t0_m_HCN = 2000; t1_m_HCN = 3000
t0_m_HCN = 5000; t1_m_HCN = 7000;
fm_HCN = -76.4;
s0_m_HCN = 6.56; s1_m_HCN = -7.48;

% Functions
m_inf_HCN(X)=1./(1 + exp((q_m_HCN - X)./k_m_HCN));

tau_m(X) =t0_m_HCN + (t1_m_HCN - t0_m_HCN)./(exp((fm_HCN-X)./s0_m_HCN) + exp((fm_HCN
    -X)./s1_m_HCN));

tau_m_HCN(X) = 0.01*(tau_m(X)< 0.01) + (tau_m(X))*(tau_m(X) >= 0.01)

I_HCN(X,m) = g_HCN4.*m.*(X-E_Cat)

% ODEs and ICs
m'=((m_inf_HCN(X) - m)./tau_m_HCN(X))

m(0)=m_inf_HCN(-45)+IC_noise.*rand(1,Npop)

% Linkers
@current += -I_HCN(X,m)
```

Fast HCN current

```
%hyperpolarization-activated cyclic nucleotide-modulated cation current HCN for GPe
    neurons (Fujita 2012)

% Parameters
g_HCN1 = 0.1;
E_Cat = -40; % Reversal potential for Cat, mV
IC_noise=0;

q_m_HCN = -76.4; k_m_HCN =-2.3;
%t0_m_HCN = 2000; t1_m_HCN = 3000
t0_m_HCN = 500; t1_m_HCN = 800;
fm_HCN = -76.4;
s0_m_HCN = 6.56; s1_m_HCN = -7.48;

% Functions
m_inf_HCN(X)=1./(1 + exp((q_m_HCN - X)./k_m_HCN));

tau_m(X) =t0_m_HCN + (t1_m_HCN - t0_m_HCN)./(exp((fm_HCN-X)./s0_m_HCN) + exp((fm_HCN
    -X)./s1_m_HCN));

tau_m_HCN(X) = 0.01*(tau_m(X)< 0.01) + (tau_m(X))*(tau_m(X) >= 0.01)

I_HCN(X,m) = g_HCN1.*m.*(X-E_Cat)

% ODEs and ICs
m'=((m_inf_HCN(X) - m)./tau_m_HCN(X))

m(0)=m_inf_HCN(-45)+IC_noise.*rand(1,Npop)

% Linkers
@current += -I_HCN(X,m)
```

Noise

```

db = 20
ruido(t) = wgn(1,1,db);
@rr += ruido(t);
```

Referências

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