Нейронна модель Ходжкіна-Хакслі Hodgkin-Huxley neuron model

Наслідки та застосування

Олександр Бурилко

Відділ диференціальних рівнянь та теорії коливань

Алан Ходжкін, Ендрю Хакслі

1

Figure 2.22: Alan Hodgkin (right) and Andrew Huxley (left) in their Plymouth Marine Lab in 1949 (photo was kindly provided by National Marine Biological Library, Plymouth, UK).

Знаменита стаття

J. Physiol. (1952) 117, 500–544

A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

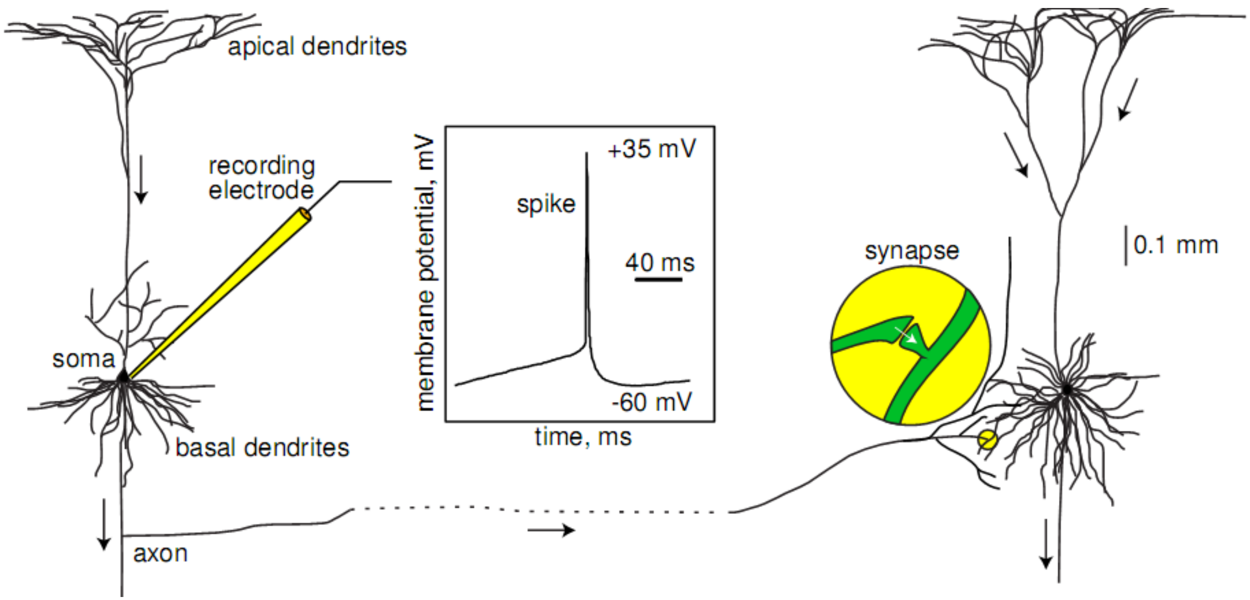
BY A. L. HODGKIN AND A. F. HUXLEY

From the Physiological Laboratory, University of Cambridge

(*Received* 10 *March* 1952)

1 This article concludes a series of papers concerned with the flow of electric current through the surface membrane of a giant nerve fibre (Hodgkin, Huxley & Katz, 1952; Hodgkin & Huxley, 1952 *a–c*). Its general object is to discuss the results of the preceding papers (Part I), to put them into mathematical form (Part II) and to show that they will account for conduction and excitation in quantitative terms (Part III).

Spike



apical dendrites
recording electrode
soma
basal dendrites
axon
membrane potential, mV
+35 mV
spike
40 ms
-60 mV
time, ms
synapse
0.1 mm

Signaling in chemical synapses

1. The process begins with a wave of electrochemical excitation called an action potential traveling along the membrane of the presynaptic cell, until it reaches the synapse.

2. The electrical depolarization of the membrane at the synapse causes channels to open that are permeable to calcium ions.

3. Calcium ions flow through the presynaptic membrane, rapidly increasing the calcium concentration in the interior.

4. The high calcium concentration activates a set of calcium-sensitive proteins attached to vesicles that contain a neurotransmitter chemical.

5. These proteins change shape, causing the membranes of some "docked" vesicles to fuse with the membrane of the presynaptic cell, thereby opening the vesicles and dumping their neurotransmitter contents into the synaptic cleft, the narrow space between the membranes of the pre- and post-synaptic cells.

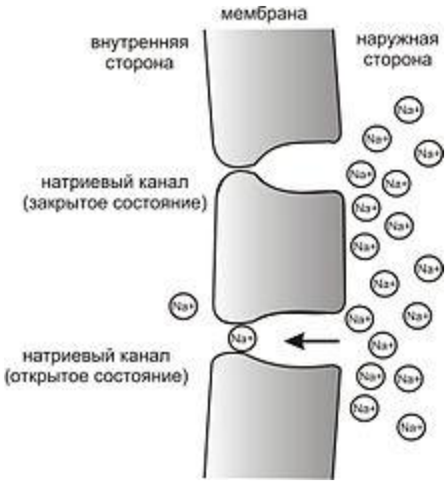
6. The neurotransmitter diffuses within the cleft. Some of it escapes, but some of it binds to chemical receptor molecules located on the membrane of the postsynaptic cell.

7. The binding of neurotransmitter causes the receptor molecule to be *activated* in some way. Several types of activation are possible, as described in more detail below. In any case, this is the key step by which the synaptic process affects the behavior of the postsynaptic cell.

8. Due to thermal shaking, neurotransmitter molecules eventually break loose from the receptors and drift away.

9. The neurotransmitter is either reabsorbed by the presynaptic cell, and then repackaged for future release, or else it is broken down metabolically.

Схема мембрани з двома каналами



Провідність на одиницю площі для Калія і Натрія

$$G_K = G_{Kmax} n^4$$

$$G_{Na} = G_{Na(max)} m^3 h$$

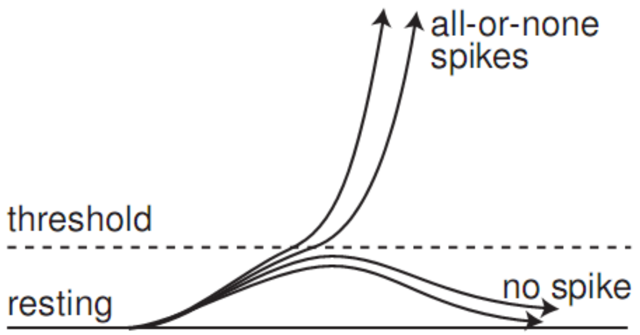
$$dn/dt = \alpha_n (1-n) - \beta_n n$$

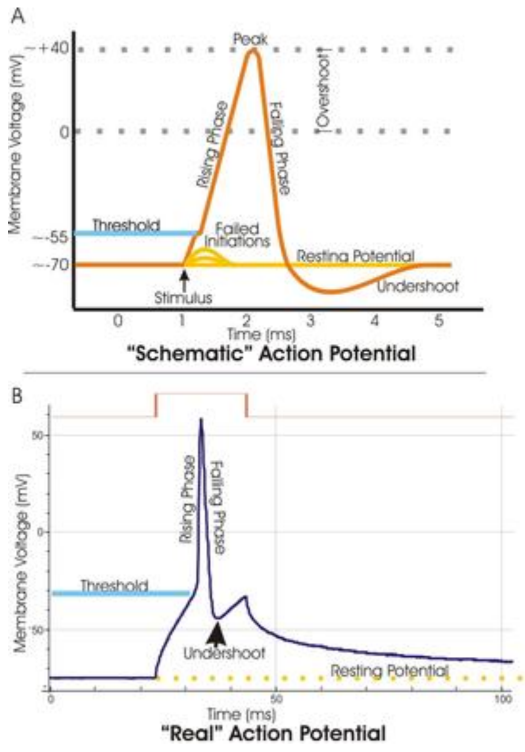
$$dm/dt = \alpha_m (1-m) - \beta_m m$$

$$dh/dt = \alpha_h (1-h) - \beta_h h$$

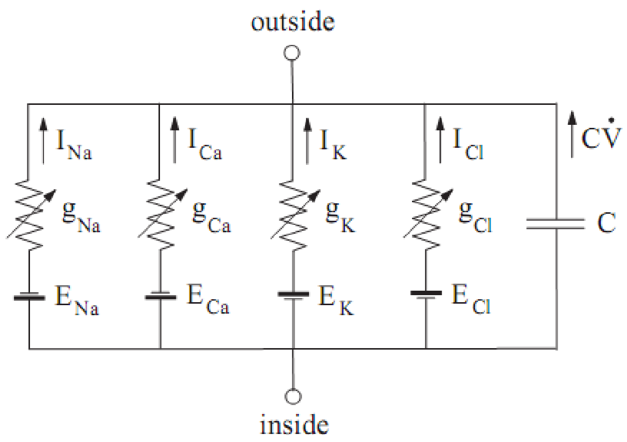
α_m — коефіцієнт трансферу з зякритого стану у відкритий,
β_m — коефіцієнт трансферу з відкритого стану у закритий,
m — фракція каналів у відкритому стані,
$(1-m)$ — фракція каналів у закритому стані

Поріг


all-or-none
spikes
threshold
resting
no spike


A
Peak
Overshoot
Rising Phase
Falling Phase
Threshold
Failed
Initiations
Resting Potential
Undershoot
Stimulus
Membrane Voltage (mV)
~+40
0
~-55
~-70
0
1
2
3
4
5
Time (ms)
"Schematic" Action Potential
B
Rising Phase
Falling Phase
Threshold
Undershoot
Resting Potential
Membrane Voltage (mV)
50
0
-50
0
50
100
Time (ms)
"Real" Action Potential

Модель



$$I_K = g_K (V - E_K) ,$$

$$I_{Na} = g_{Na} (V - E_{Na}) ,$$

$$I_{Ca} = g_{Ca} (V - E_{Ca}) , \qquad I_{Cl} = g_{Cl} (V - E_{Cl})$$

$$E_{ion} = \frac{RT}{zF} \ln \frac{[\mathrm{Ion}]_{out}}{[\mathrm{Ion}]_{in}}$$

where $[\mathrm{Ion}]_{in}$ and $[\mathrm{Ion}]_{out}$ are concentrations of the ions inside and outside the cell, respectively, R is the universal gas constant (8, 315 mJ/(K°·Mol)), T is temperature in degrees Kelvin (K° = 273.16+C°), F is Faraday's constant (96, 480 Coulombs/Mol), z is the valence of the ion ($z = 1$ for Na^+ and K^+, $z = -1$ for Cl^-, and $z = 2$ for Ca^{2+}).

$$I = C\dot{V} + I_{Na} + I_{Ca} + I_K + I_{Cl}$$

$$C\dot{V} = I - g_{Na}(V - E_{Na}) - g_{Ca}(V - E_{Ca}) - g_K(V - E_K) - g_{Cl}(V - E_{Cl})$$

$$C\,\dot{V} = I - \sum_i g_i \cdot (V - E_i)$$

Модель Ходжкіна-Хакслі (1952)

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
\dot{n} &= \alpha_n(V)(1-n) - \beta_n(V) n \\
\dot{m} &= \alpha_m(V)(1-m) - \beta_m(V) m \\
\dot{h} &= \alpha_h(V)(1-h) - \beta_h(V) h \,,
\end{aligned}
$$

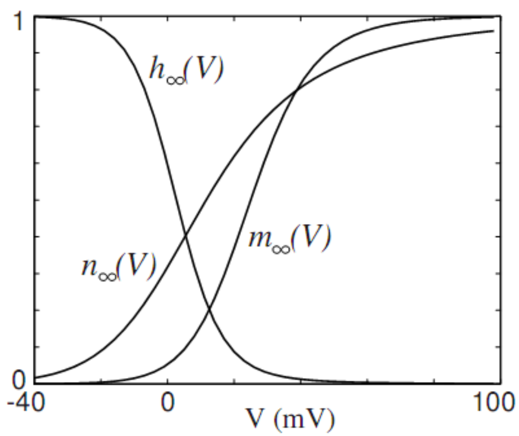
де

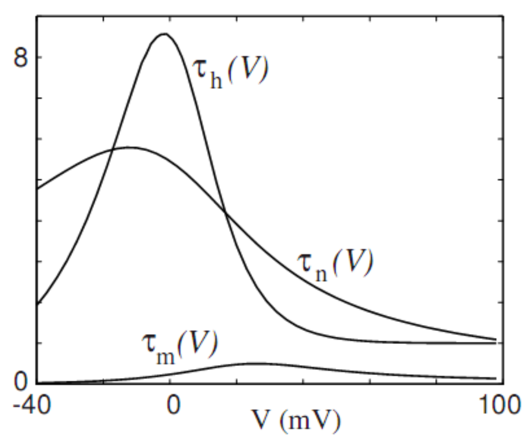
$$
\begin{aligned}
\alpha_m(V) &= \frac{(V+40)/10}{1-\exp(-(V+40)/10)}\,, &\qquad \beta_m(V) &= 4\,\exp(-(V+65)/18) \\
\alpha_h(V) &= 0.07\,\exp(-(V+65)/20)\,, &\qquad \beta_h(V) &= 1/\left(1+\exp(-(V+35)/10)\right) \\
\alpha_n(V) &= \frac{(V+55)/100}{1-\exp(-(V+55)/10)}\,, &\qquad \beta_n(V) &= 0.125\,\exp(-(V+65)/80).
\end{aligned}
$$

Модель Ходжкіна-Хакслі (1952)

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
\dot{n} &= (n_\infty(V) - n)/\tau_n(V)\ , \\
\dot{m} &= (m_\infty(V) - m)/\tau_m(V)\ , \\
\dot{h} &= (h_\infty(V) - h)/\tau_h(V)\ ,
\end{aligned}
$$

$$
\begin{aligned}
n_\infty &= \alpha_n/(\alpha_n + \beta_n)\ , \qquad & \tau_n &= 1/(\alpha_n + \beta_n)\ , \\
m_\infty &= \alpha_m/(\alpha_m + \beta_m)\ , \qquad & \tau_m &= 1/(\alpha_m + \beta_m)\ , \\
h_\infty &= \alpha_h/(\alpha_h + \beta_h)\ , \qquad & \tau_h &= 1/(\alpha_h + \beta_h)
\end{aligned}
$$

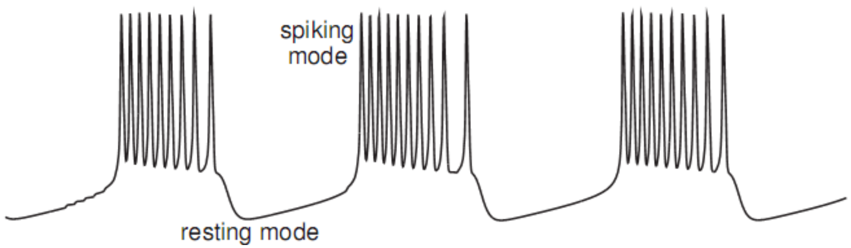


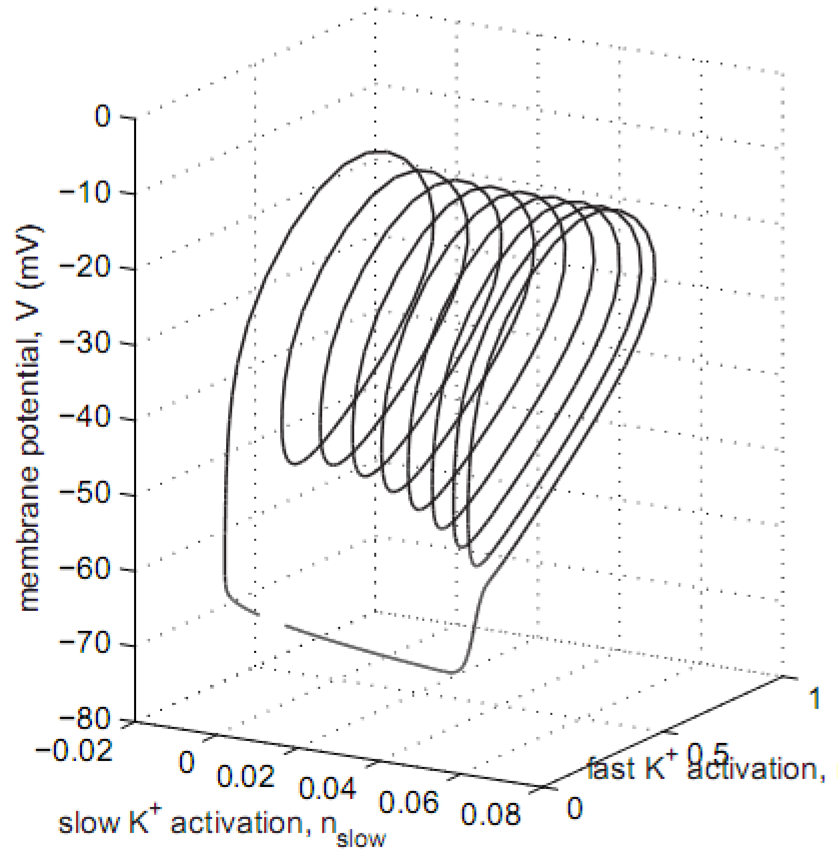


$$
f(A, B, V) = \frac{1}{1 + e^{A(V-B)}}
$$

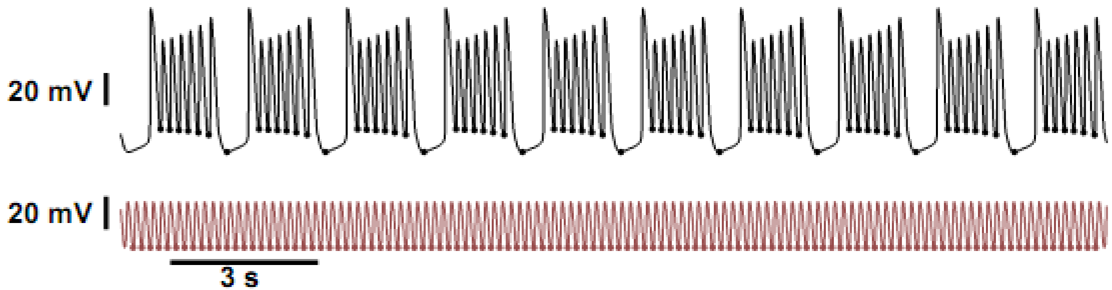
— функція Больцмана (Boltzmann)

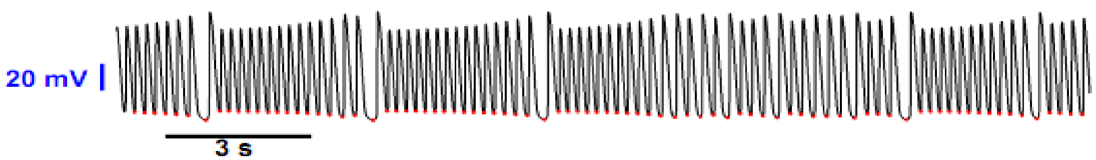
Birst

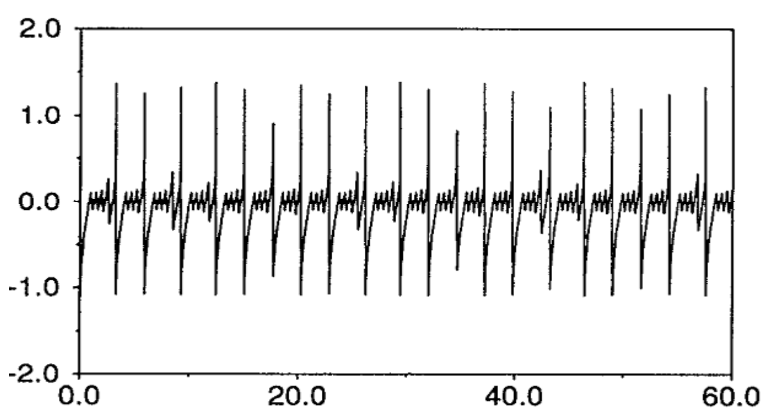

spiking
mode
resting mode


0
−10
−20
−30
−40
−50
−60
−70
−80
membrane potential, V (mV)
−0.02
0
0.02
0.04
0.06
0.08
slow K+ activation, nslow
0
0.5
1
fast K+ activation, n

Birsting, Tonic spiking, Chaos, MMO



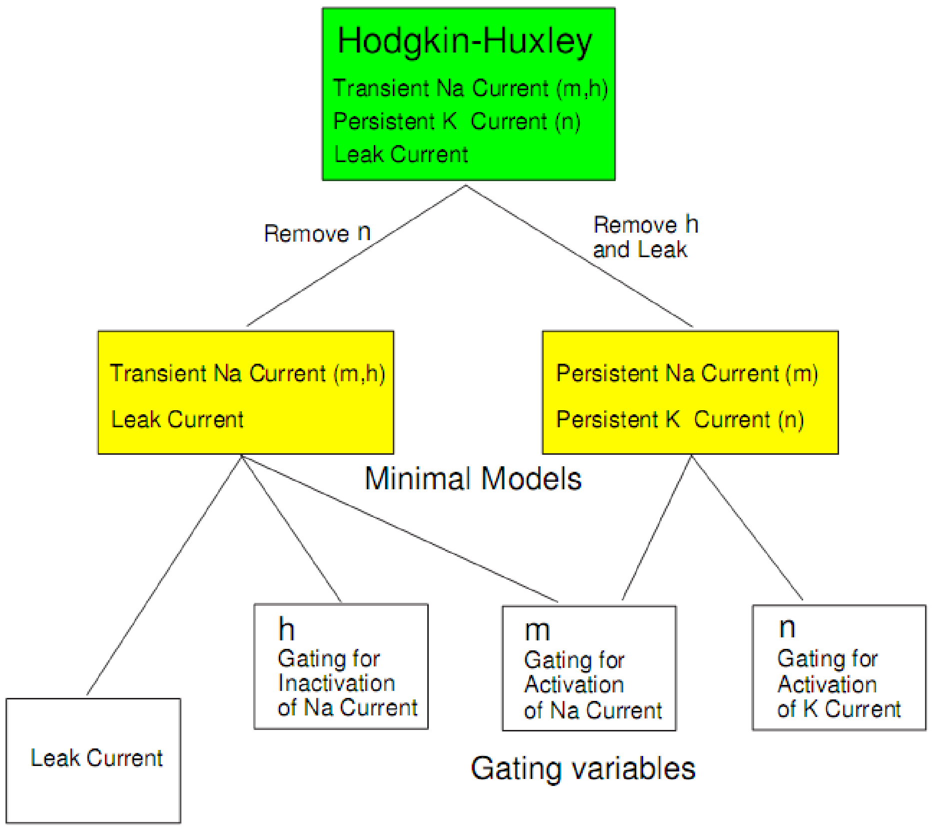




Наслідки.   Дослідження.

1. Узагальнення (розповсюдження) моделі
2. Спрощення моделі
3. Мультистабільність
4. Зовнішній вплив
5. Моделі нейронних сіток
6. Моделі з різними типами зв’язків
7. Синхронізація

Спрощені моделі



Спрощені моделі

Integrate-and-fire (Lapicque, 1907)

$$C\dot{V} = I - \overbrace{g_{\text{leak}}(V - E_{\text{leak}})}^{\text{Ohmic leakage}} ,$$

$$\dot{v} = b - v , \qquad \text{if } v = 1, \text{ then } v \leftarrow 0,$$
$$\dot{v} = b + v^2 , \qquad \text{if } v = v_{\text{peak}}, \text{ then } v \leftarrow v_{\text{reset}},$$

Resonate-and-fire

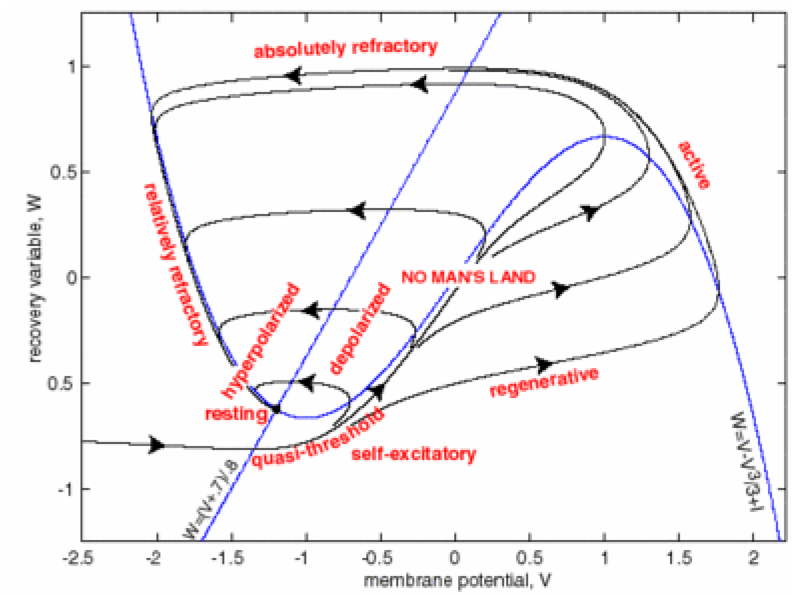
$$\begin{aligned} C\dot{V} &= I - g_{\text{leak}}(V - E_{\text{leak}}) - W , \\ \dot{W} &= (V - V_{1/2})/k - W . \end{aligned}$$

Theta-model (Koppel-Ermetrout)

$$\dot{\vartheta} = (1 - \cos\vartheta) + (1 + \cos\vartheta)r$$

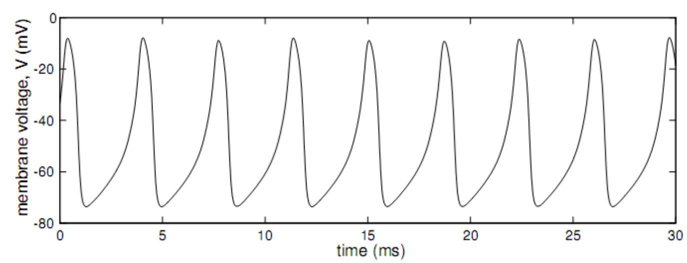
Модель ФіцХью-Нагумо (FizHug-Nagumo) 1961

$$
\begin{aligned}
\dot{V} &= V - V^3/3 - W + I \\
\dot{W} &= 0.08(V + 0.7 - 0.8W)
\end{aligned}
$$



V – мембранний потенціал
W – зворотня змінна
I – зовнішній струм (стимул)

$$
\begin{aligned}
\dot{V} &= f(V) - W + I \\
\dot{W} &= a(bV - cW)
\end{aligned}
$$



Модель Морріс-Лекара (Morris-Lecar) 1981

$$CV' = -g_{\mathrm{Ca}} M_{\mathrm{ss}}(V)(V - V_{\mathrm{Ca}}) - g_{\mathrm{K}} W(V - V_{\mathrm{K}}) - g_{\mathrm{L}}(V - V_{\mathrm{L}}) + I_{\mathrm{app}}$$

$$W' = (W_{\mathrm{ss}}(V) - W)/T_{\mathrm{W}}(V)$$

V – мембранний потенціал
W – зворотня змінна

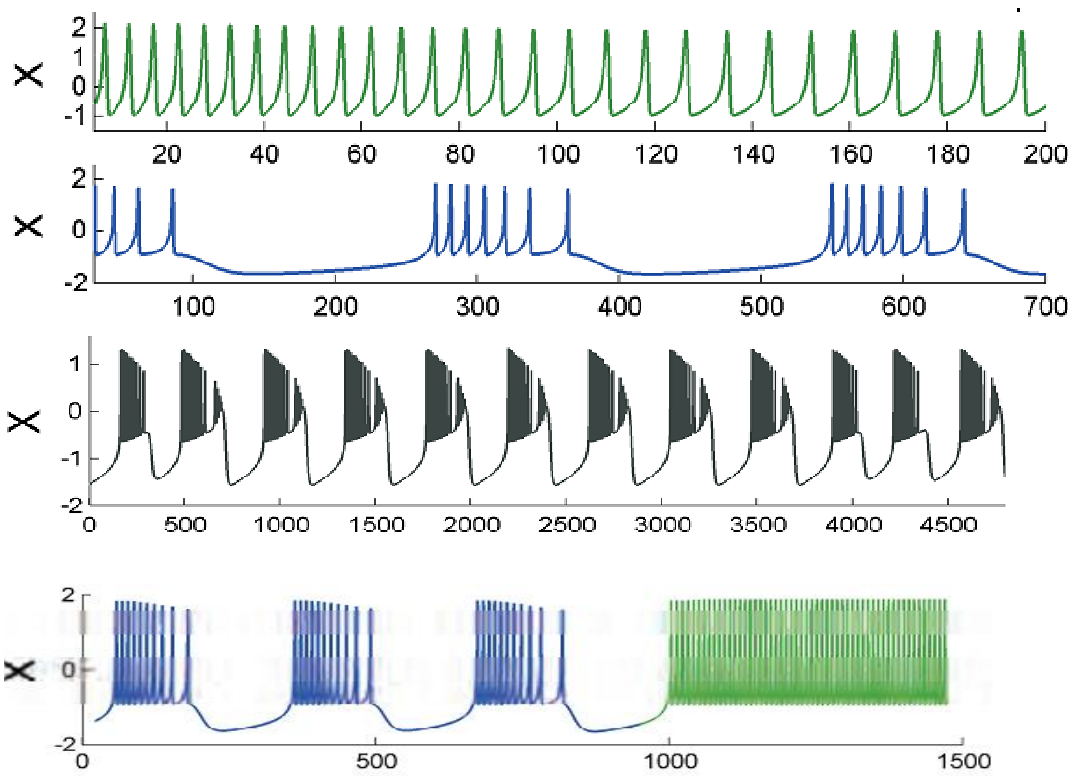
$$W_{\mathrm{ss}}(V) = (1 + \tanh[(V - V_3)/V_4])/2$$

$$M_{\mathrm{ss}}(V) = (1 + \tanh[(V - V_1)/V_2])/2$$

$$T_W(V) = T_0 \mathrm{sech}[(V - V_3)/2V_4]$$

Модель Хіндмарш-Роуз (Hindmarsh-Rose) 1984

$$x' = y - ax^3 + bx^2 + I - z = P(x, y, \alpha) - z,$$
$$y' = c - dx^2 - y = Q(x, y, \alpha),$$
$$z' = \varepsilon(s(x - x_0) - z) = \varepsilon R(x, z, \alpha),$$



Редукція моделі Калабріза-Цимбалюка (Calabrese-Cymbalyuk) 1999

$$
\begin{aligned}
CV' &= -\Big(\overline{g}_{K2}\; m_{K2}^2(V - E_K) + g_I(V - E_I) + I_{Pol} + \\
&\quad \overline{g}_{Na}\; f\left(-150,\; 0.027 + V_{Nam}^{shift}, V\right)^3 h_{Na}(V - E_{Na})\Big), \\
m'_{K2} &= \frac{f\left(-83,\; 0.018 + V_{K2}^{shift}, V\right) - m_{K2}}{\tau_{K2}}, \\
h'_{Na} &= \frac{f\left(500,\; 0.026 + V_{Nah}^{shift}, V\right) - h_{Na}}{\tau_{Na}},
\end{aligned}
$$

$$f(A, B, X) = 1/\left(1 + e^{A(X+B)}\right)$$

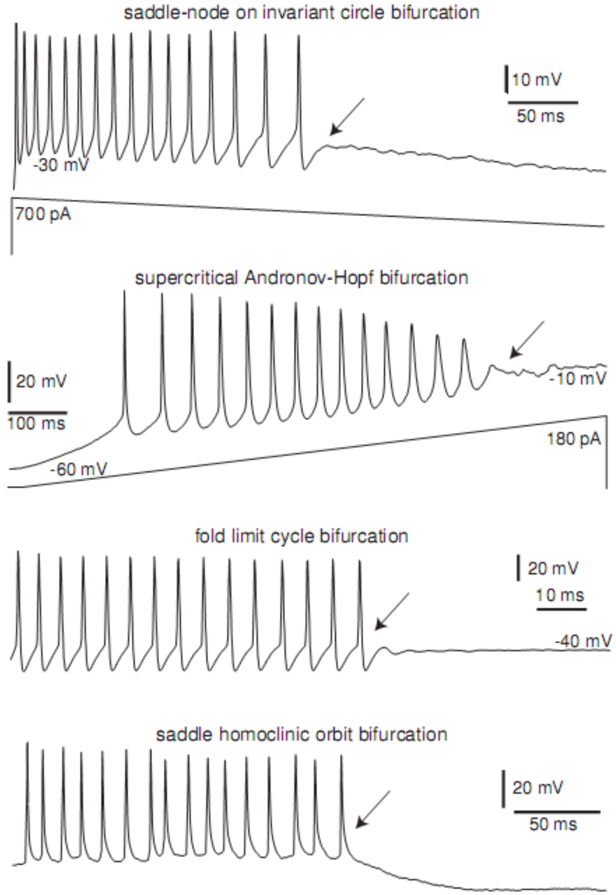
Редукція з 14D до 3D

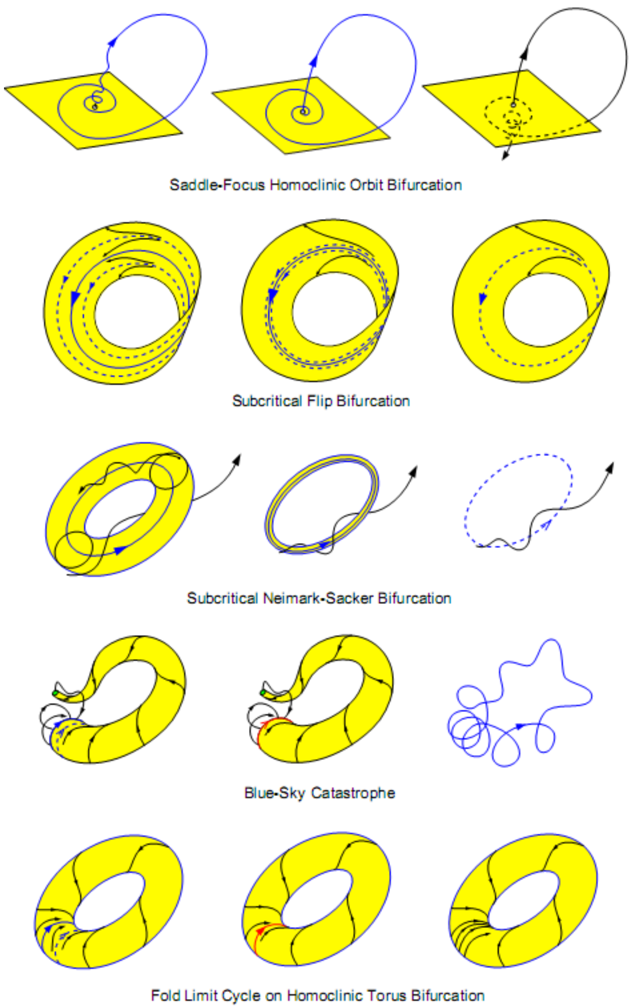
Модель Рубіна-Термана (GPe) (Rubin-Terman) 2002

$$
\begin{aligned}
v' &= -0.1\,(v+55) - 30n^4\,(v+80) - 120\,(m_\infty(v))^3\,h\,(v-55) - 0.5\,(a_\infty(v))^3\,r\,(v-120) - \\
&\quad -0.15\,(s_\infty(v))^2\,(v-120) - 30\,(v+80)\,\frac{[\mathrm{Ca}]}{[\mathrm{Ca}]+30} + I_{\mathrm{app}}, \\
n' &= 0.05\left(\frac{1}{1+\exp[-(v+50)/14]} - n\right) \Big/ \left(0.05 + \frac{0.27}{1+\exp[(v+40)/12]}\right), \\
h' &= 0.05\left(\frac{1}{1+\exp[(v+58)/12]} - h\right) \Big/ \left(0.05 + \frac{0.27}{1+\exp[(v+58)/12]}\right), \\
r' &= \left(\frac{1}{1+\exp[(v+70)/2]} - r\right)/30, \\
[\mathrm{Ca}]' &= 10^{-4}\left(-0.15\,(s_\infty(v))^2\,(v-120) - 0.5\,(a_\infty(v))^3\,r\,(v-120) - 20\,[\mathrm{Ca}]\right).
\end{aligned}
$$

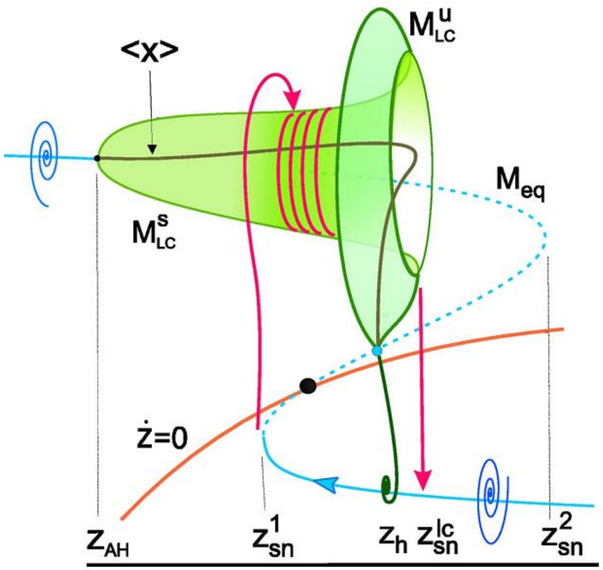
STN, GPe, GPi, TC

Біфуркації

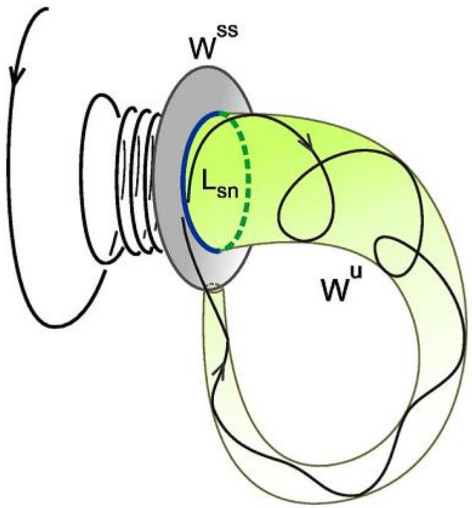

saddle-node on invariant circle bifurcation
10 mV
50 ms
-30 mV
700 pA
supercritical Andronov-Hopf bifurcation
20 mV
100 ms
-10 mV
180 pA
-60 mV
fold limit cycle bifurcation
20 mV
10 ms
-40 mV
saddle homoclinic orbit bifurcation
20 mV
50 ms


Saddle-Focus Homoclinic Orbit Bifurcation
Subcritical Flip Bifurcation
Subcritical Neimark-Sacker Bifurcation
Blue-Sky Catastrophe
Fold Limit Cycle on Homoclinic Torus Bifurcation

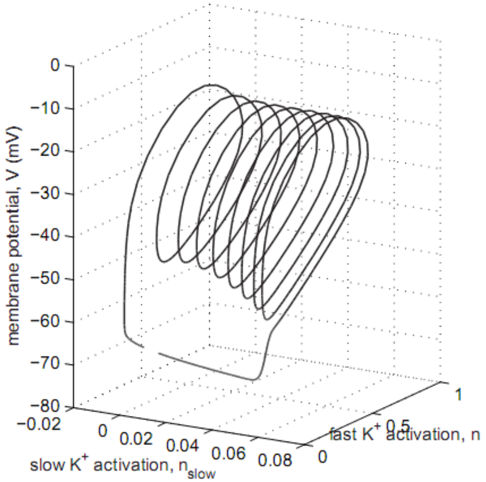
Біфуркації



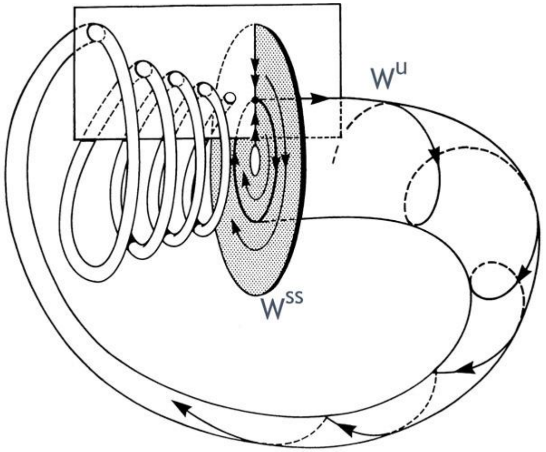
M^u_{LC}
<x>
M_{eq}
M^s_{LC}
$\dot{z}=0$
z_{AH}
z^1_{sn}
z_h z^{lc}_{sn}
z^2_{sn}



W^{ss}
L_{sn}
W^u



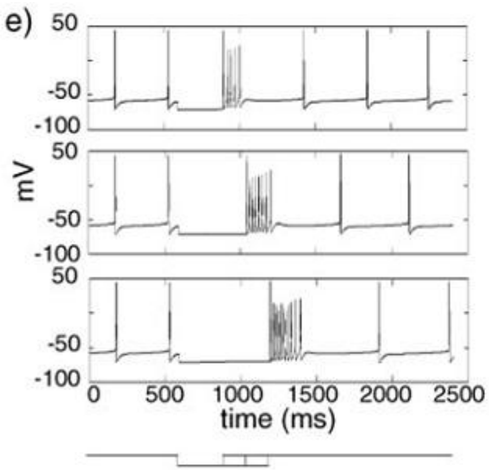
membrane potential, V (mV)
0
−10
−20
−30
−40
−50
−60
−70
−80
−0.02
0
0.02
0.04
0.06
0.08
slow K+ activation, n_{slow}
0
0.5
1
fast K+ activation, n

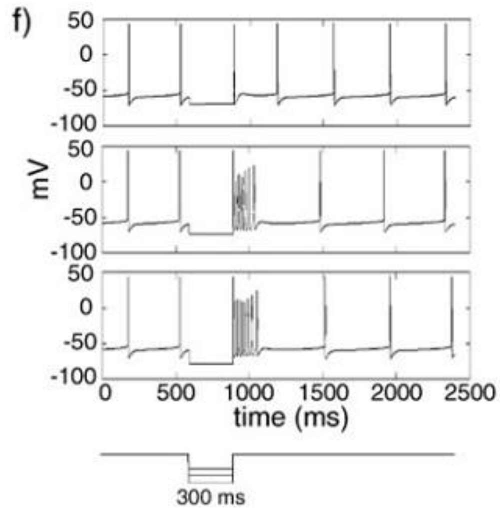


W^u
W^{ss}

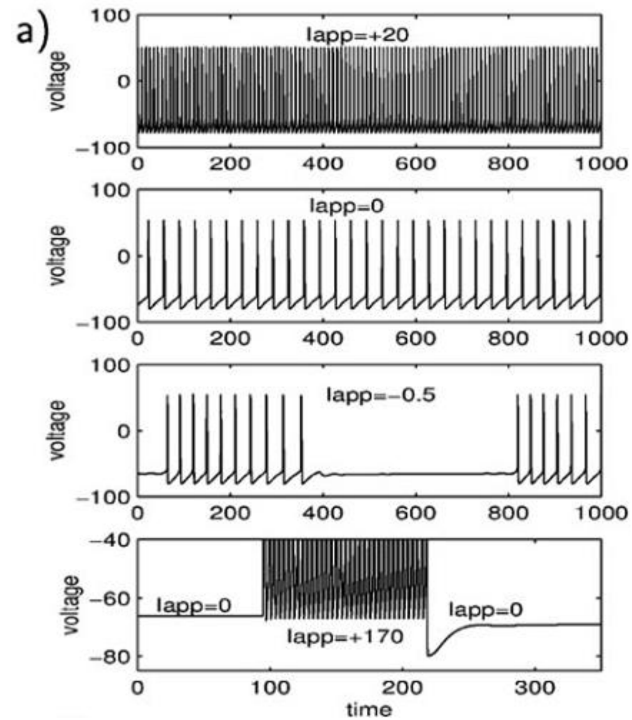
Зовнішній вплив
Rubin-Terman model

STN



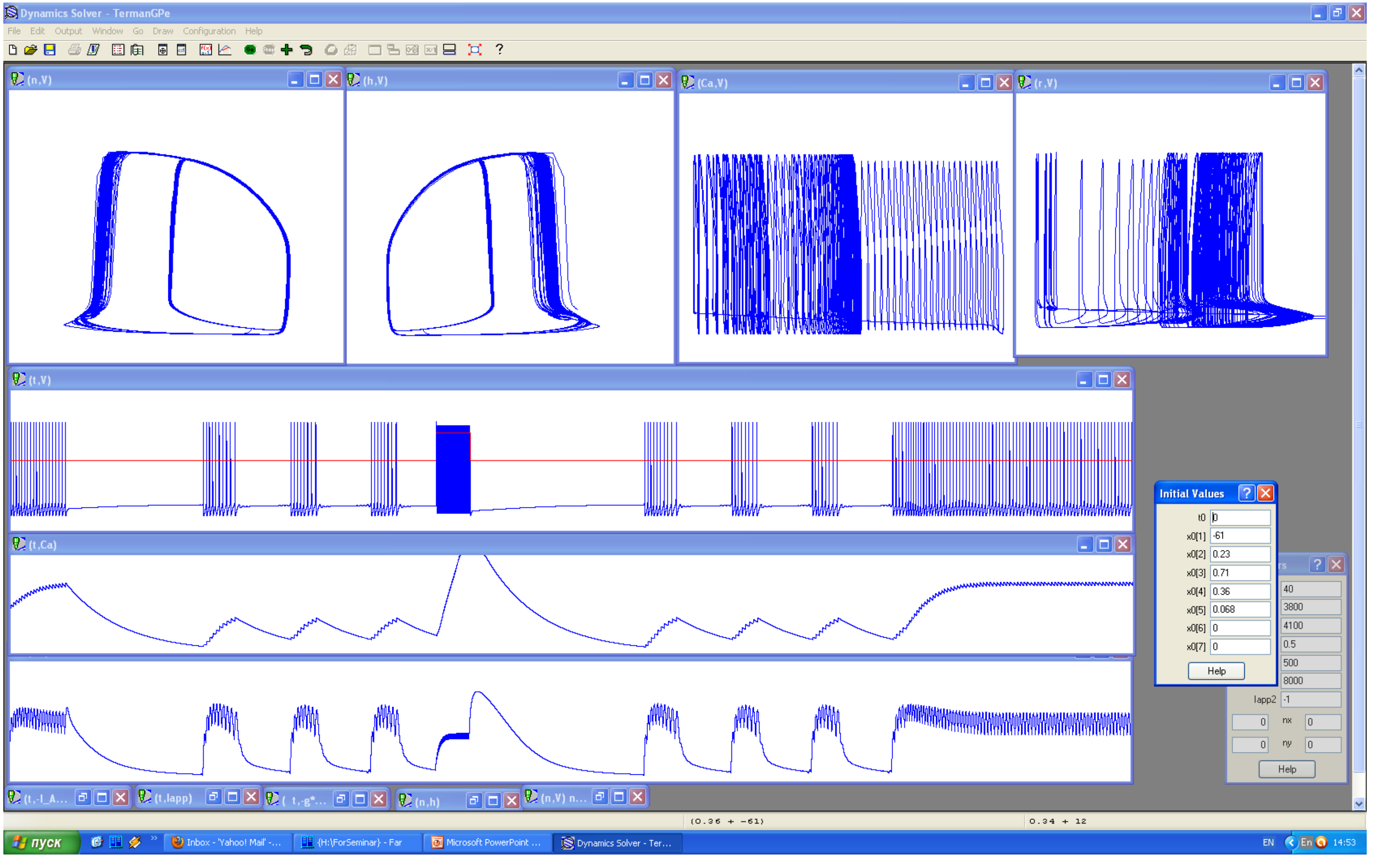


GPe

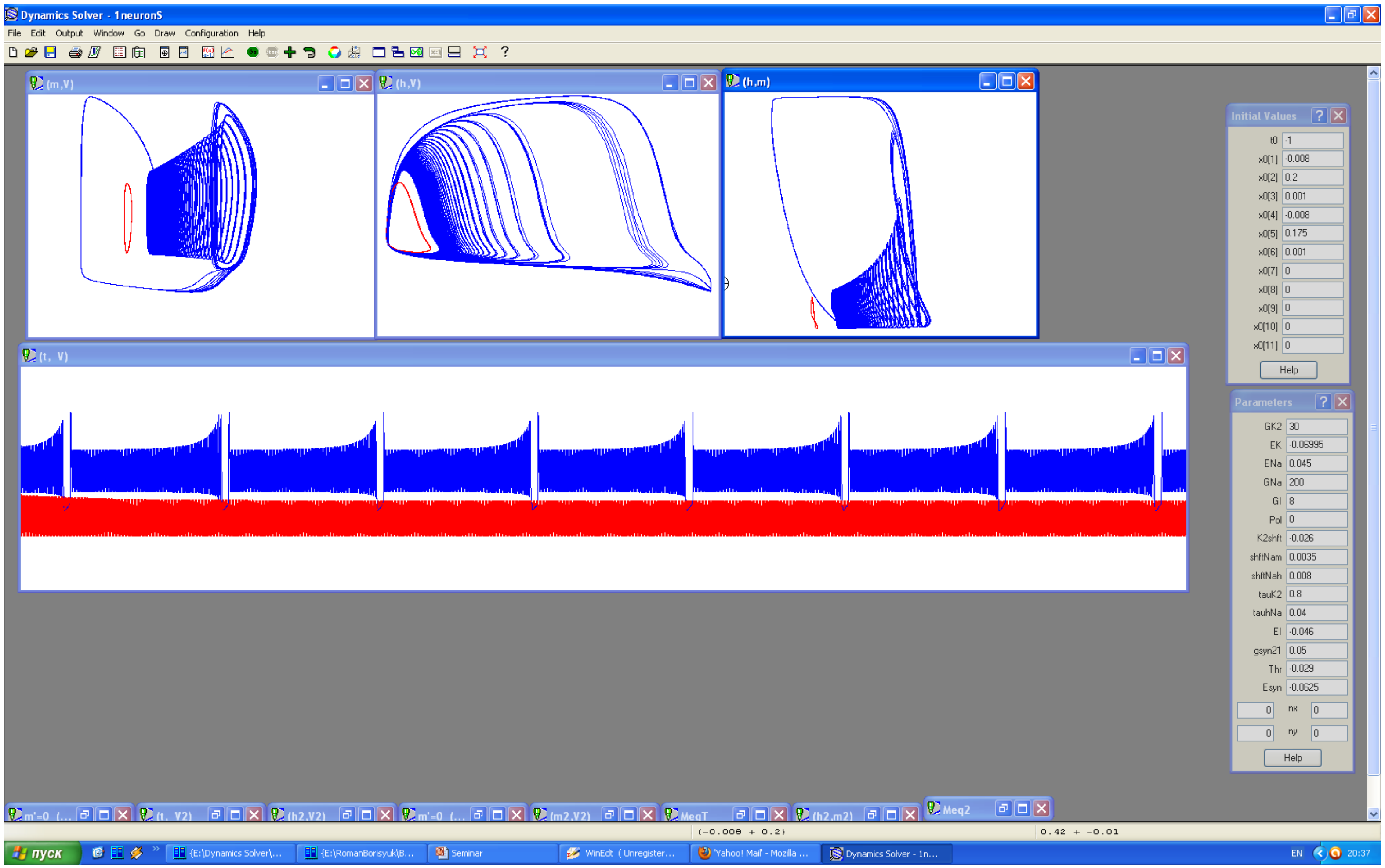


Зовнішній вплив

Rubin-Terman model (GPe)



Мультистабільніть
Calabrese-Cymbalyuk model



Зв’язок між нейронами

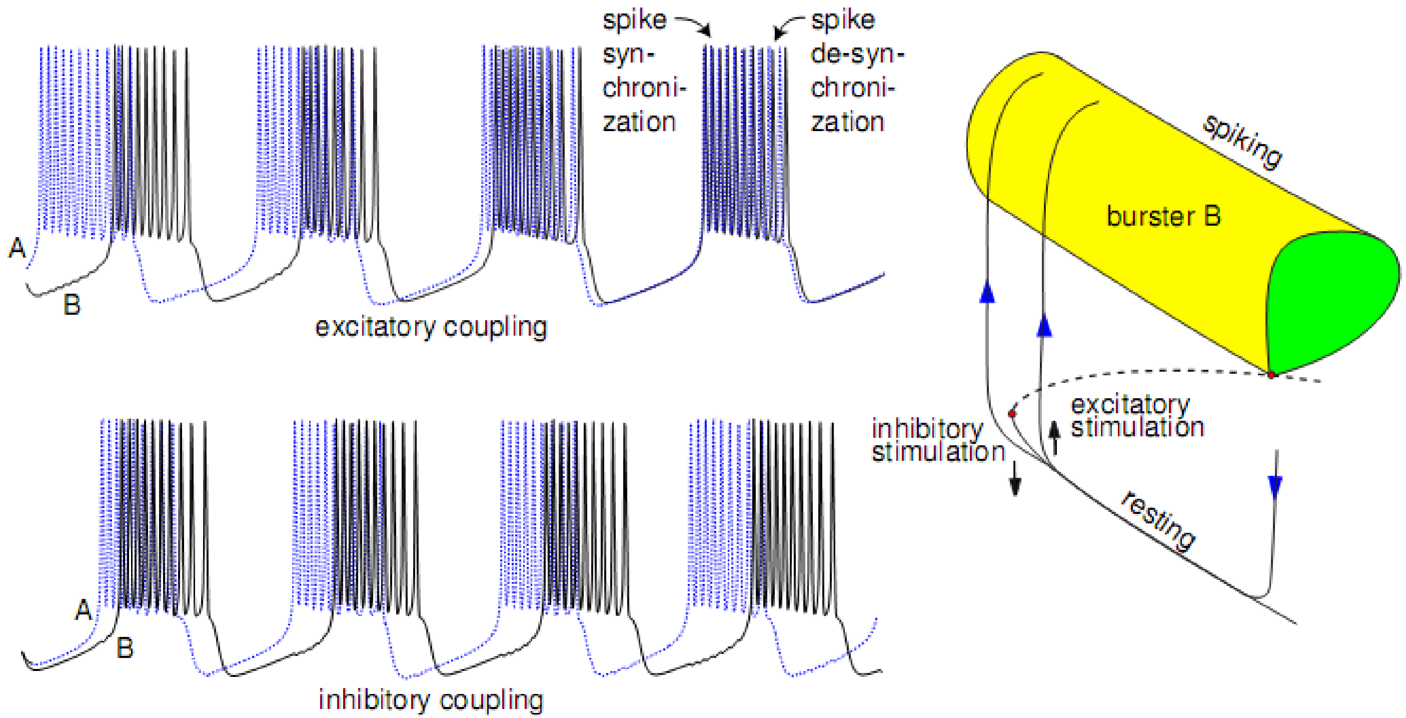
1. Без додаткового рівняння зв’язку

$$
\begin{aligned}
C\dot{V}_i &= -\sum I - (V_i - E_s)\sum_{j=1}^{n} g_{ij}, \Gamma(V_j - \Theta_{syn}), \\
\Gamma(x) &= 1/(1 + e^{-Ax})
\end{aligned}
$$

2. З додатковим рівнянням зв’язку

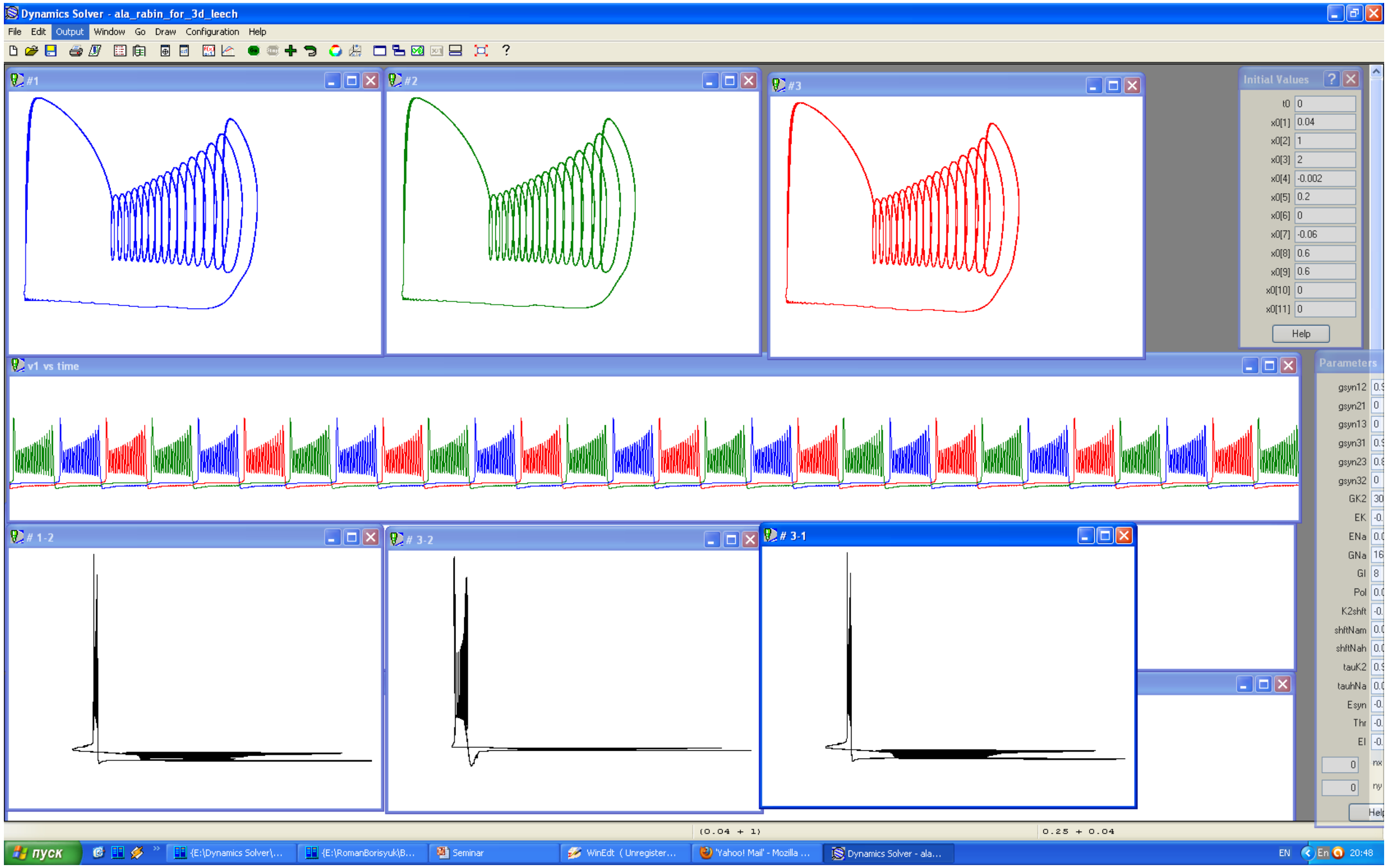
$$
\begin{aligned}
C\dot{V}_i &= -\sum I - (V_i - E_s)\sum_{j=1}^{n} g_{ij} s_j, \Gamma(V_j - \Theta_{syn}), \\
\dot{s}_j &= \alpha_j \Gamma(V_j - \Theta_{syn}) - \beta s_j
\end{aligned}
$$

Синхронізація



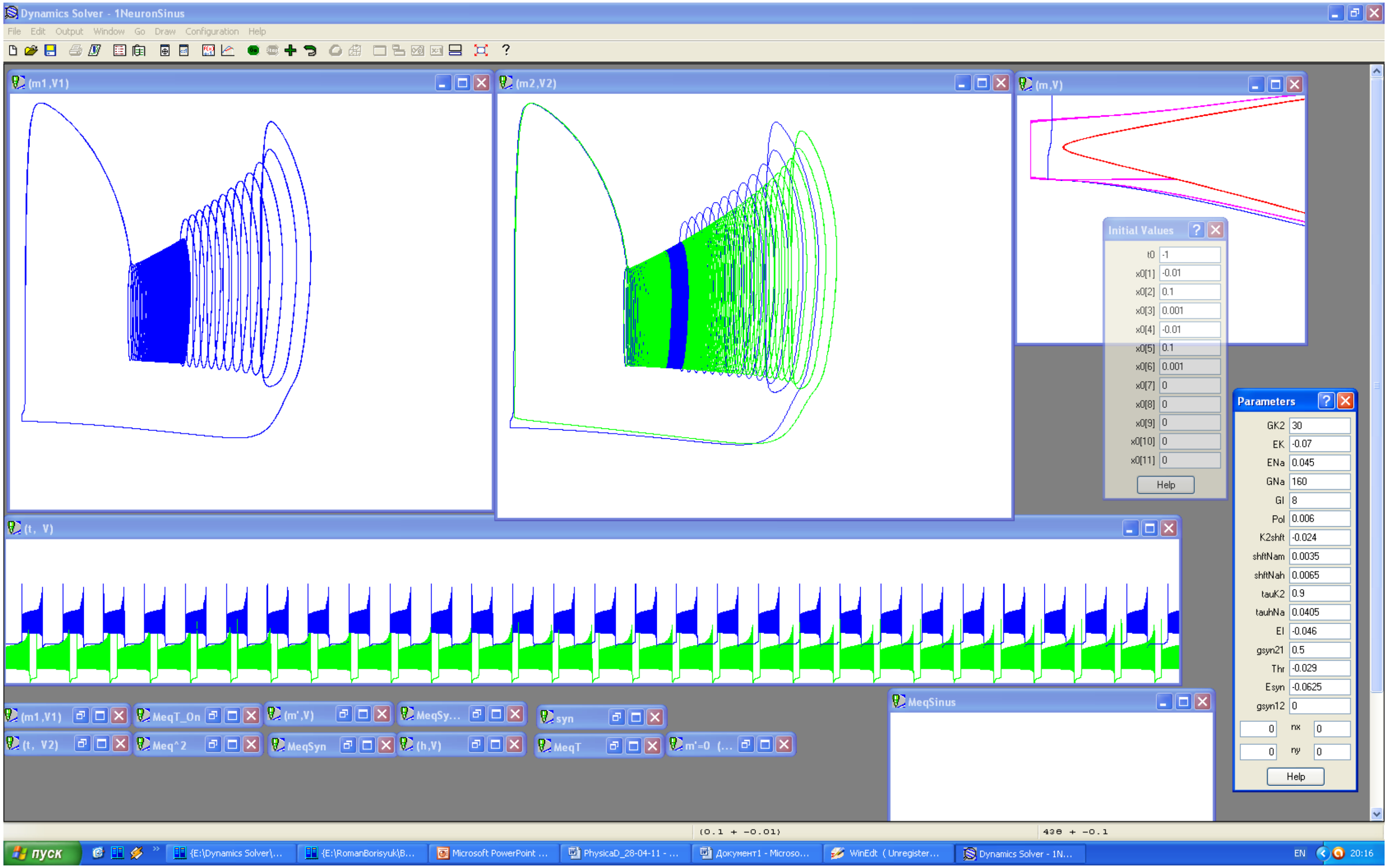
Звя’зані нейрони

Calabrese-Cymbalyuk model



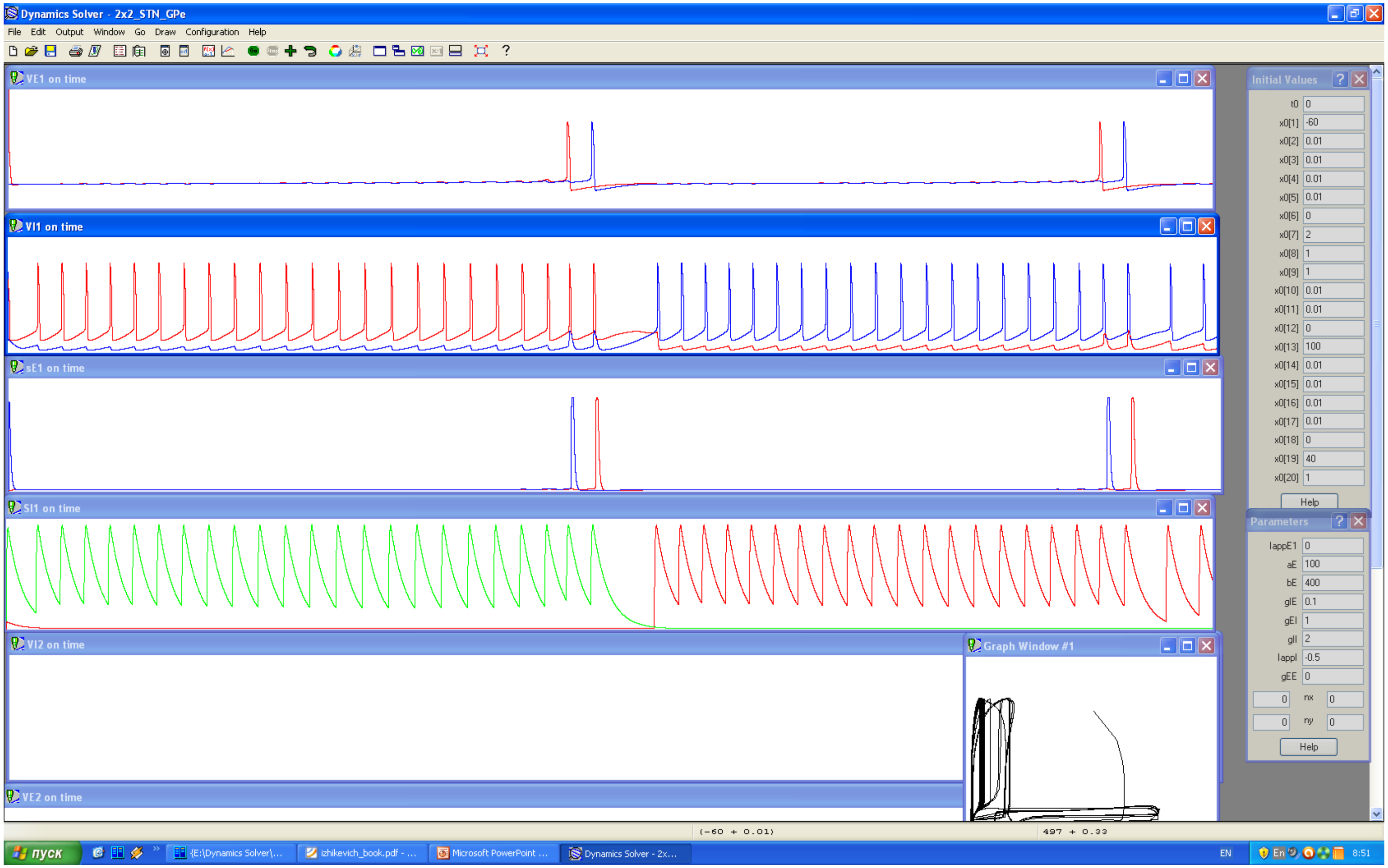
Звя’зані нейрони

Calabrese-Cymbalyuk model



Звя’зані нейрони

Rubin-Terman model (2STN+2GPe)



Література

1. A.L. Hodgkin and A.F. Huxley
   A qualitative description of membrane current and application to conduction and excitation in nerve. Journal Physiol., 117: 500-544 (1951)

2. **Eugene M. Izhikevich**
   Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting (2005)

3. **G. Bard Ermentrout and David H. Terman**
   Mathematical Foundations of Neuroscience (2010)

Програми

1. **NEURON** `http://www.neuron.yale.edu`

NEURON: a Tool for Neuroscientists

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Abstract

NEURON is a simulation environment for models of individual neurons and networks of neurons that are closely linked to experimental data. NEURON provides tools for conveniently constructing, exercising, and managing models, so that special expertise in numerical methods or programming is not required for its productive use. This paper describes two tools that address the problem of how to achieve computational efficiency and accuracy.

2. **GENESIS** `http://www.genesis-sim.org`

3. **XPP**

4. **MATLAB**