Matematyczne modelowanie elektrofizjologii neuronów

czyli jak systemy dynamiczne ratują gryzonie (i ludzi)

Dr inż. Jakub Nowacki

whoami

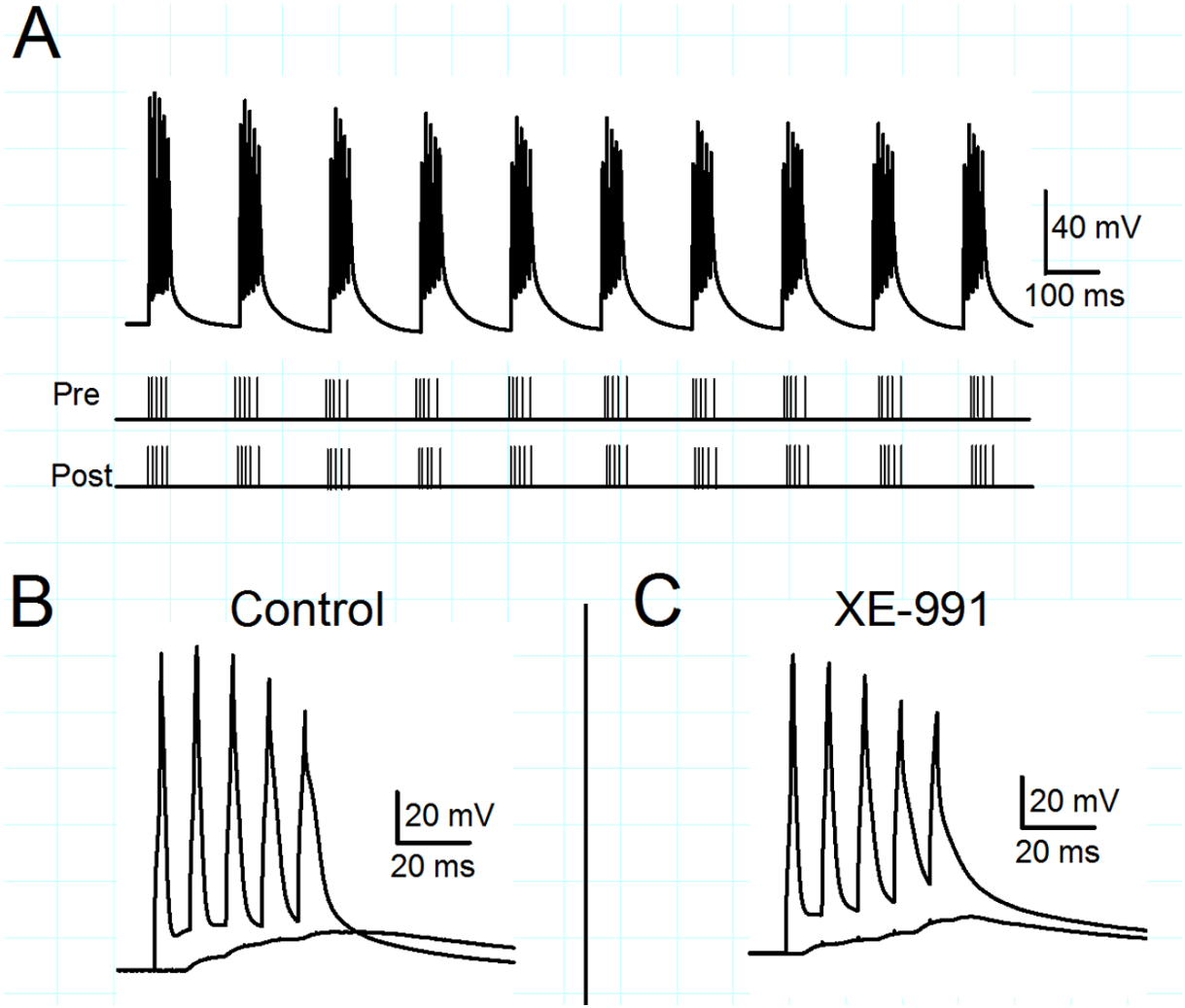
Lead Machine Learning Engineer @ Sotrender (sotrender.com)

Trainer @ Sages (sages.com.pl)

I can code, I do maths

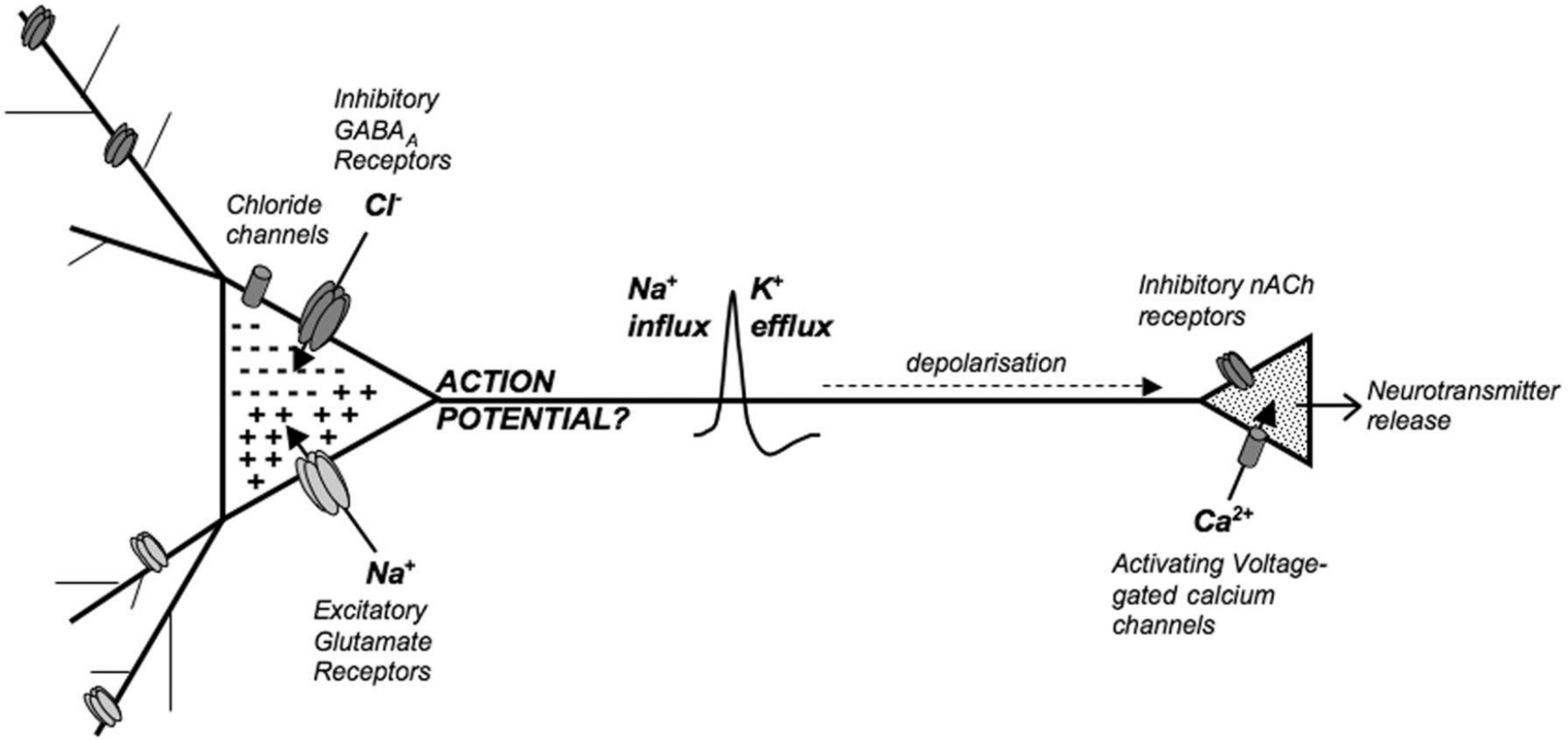
@jsnowacki

Elektrofizjologia



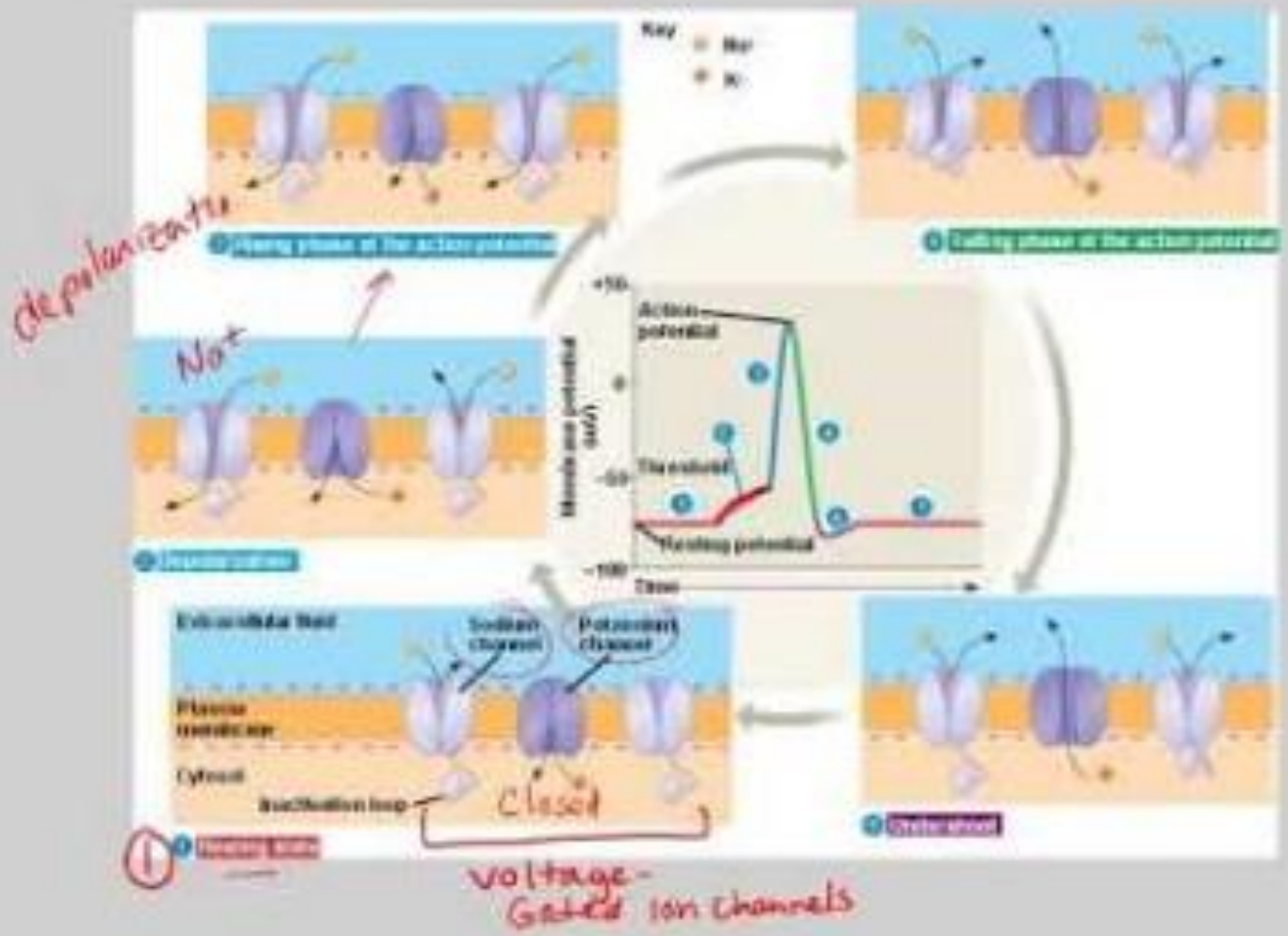
Petrovic MM, Nowacki J, Olivo V, Tsaneva-Atanasova K, Randall AD, Mellor JR (2012) Inhibition of Post-Synaptic Kv7/KCNQ/M Channels Facilitates Long-Term Potentiation in the Hippocampus. PLoS ONE 7(2): e30402.

Kanały jonowe



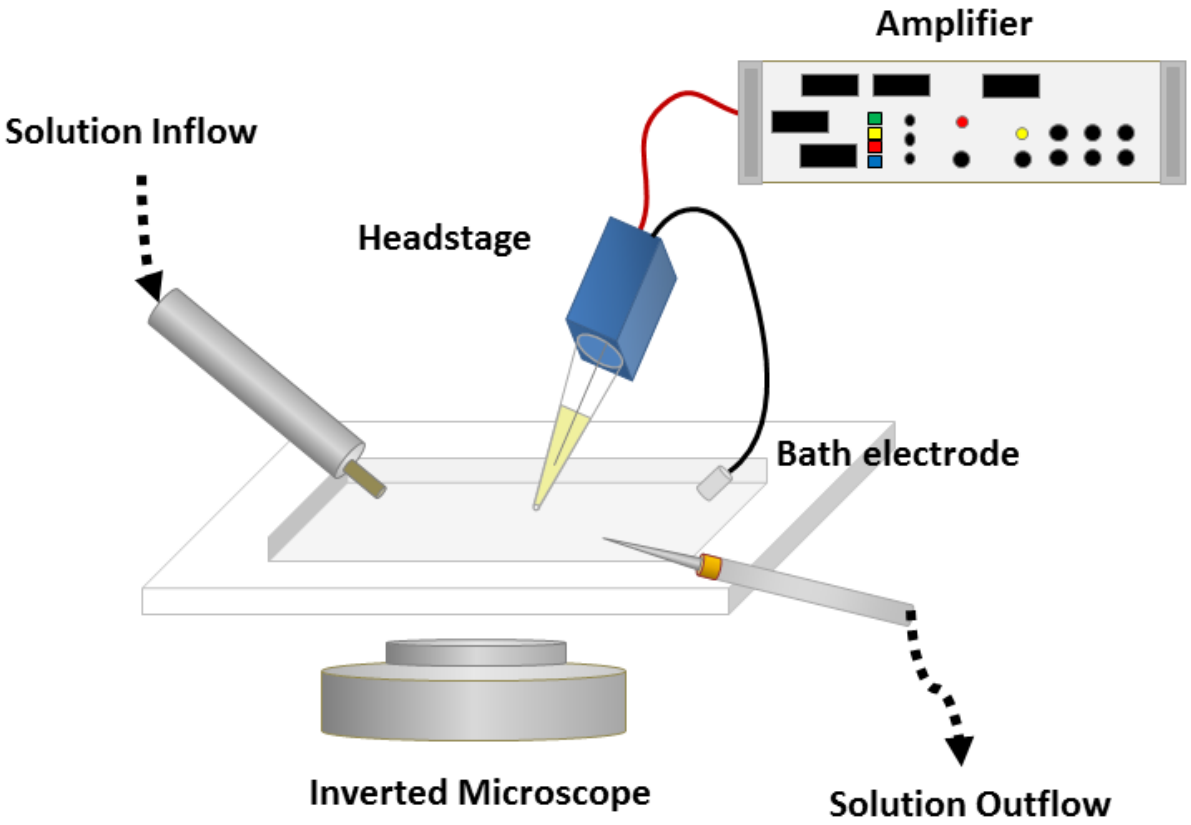
Ion channels in epilepsy, S.M. Mizielinska, Biochemical Society Transactions, Nov 2007, 35 (5) 1077-1079; DOI: 10.1042/BST0351077

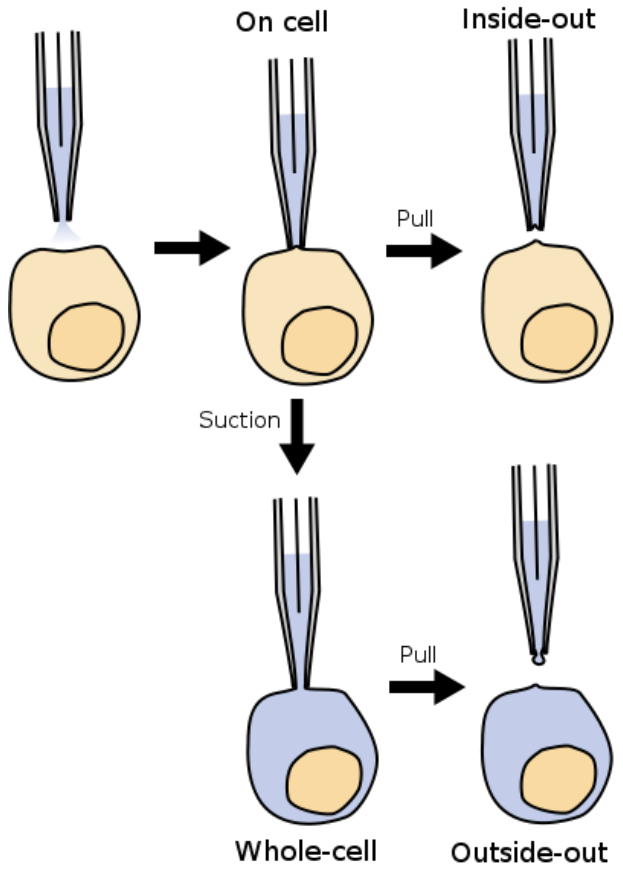
Action potential



https://www.youtube.com/watch?v=MJ8-AzWe0VA

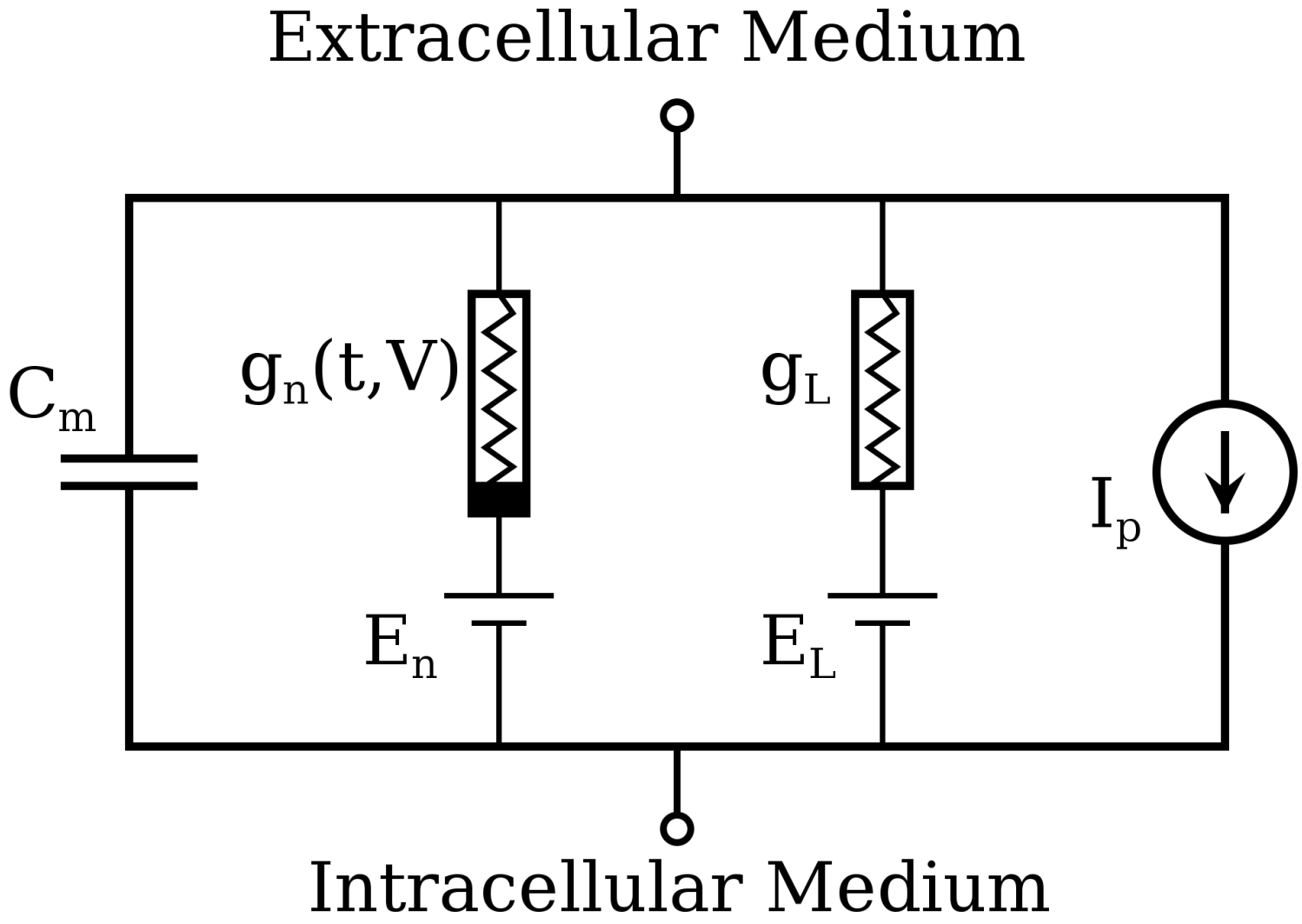
Eksperymenty





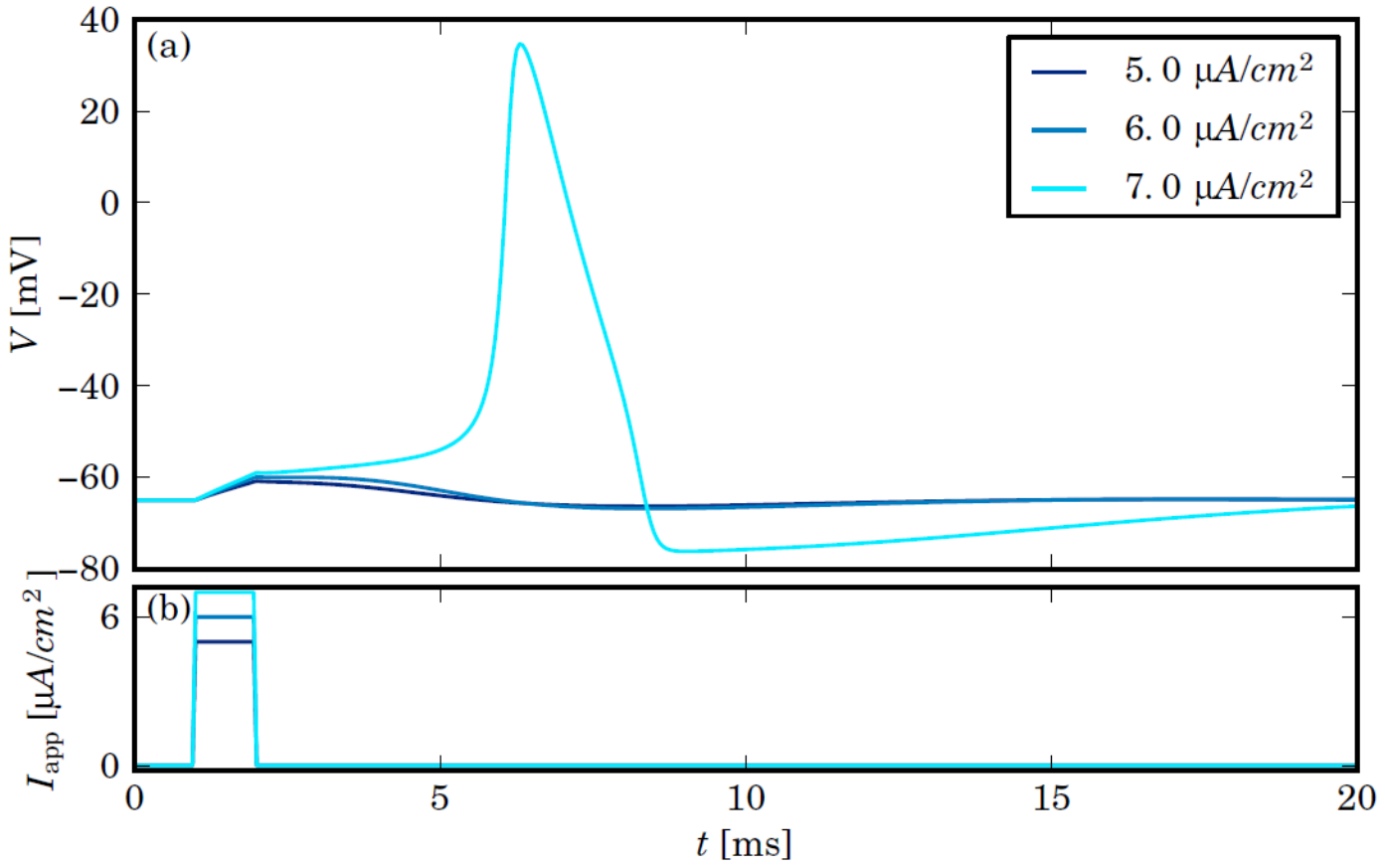
https://en.wikipedia.org/wiki/Patch_clamp

Model Hodgkin–Huxley



Źródło: Wikipedia

Model Hodgkin–Huxley



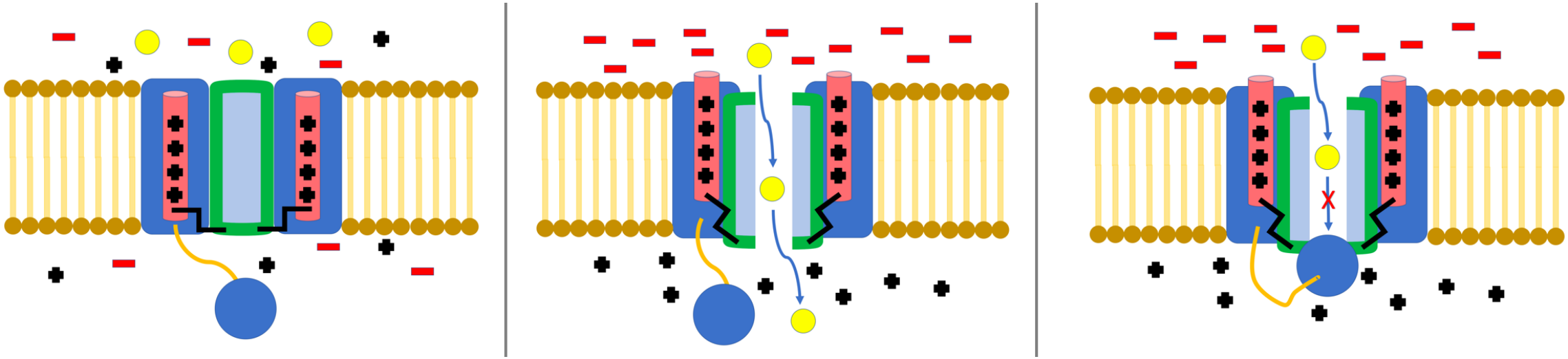
$$C_m \frac{dV}{dt} = -I_{\text{ion}}(V,t) + I_{\text{app}} = -I_{\text{K}}(V,t) - I_{\text{Na}}(V,t) - I_{\text{L}}(V,t) + I_{\text{app}},$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n,$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m,$$

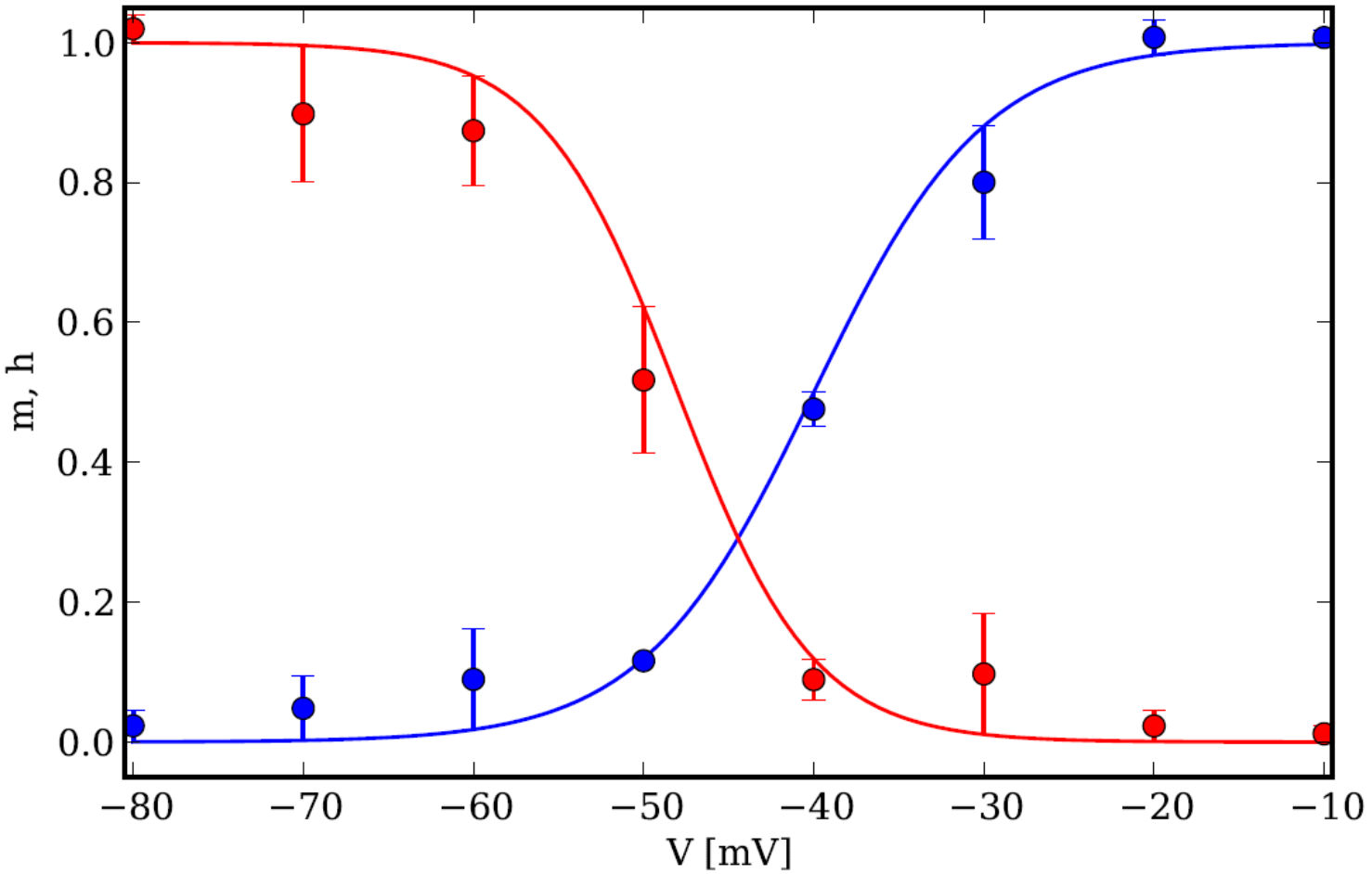
$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h.$$

(In)aktywacja kanałów jonowych



Źródło: https://en.wikipedia.org/wiki/Gating_(electrophysiology)

(In)aktywacja kanałów jonowych

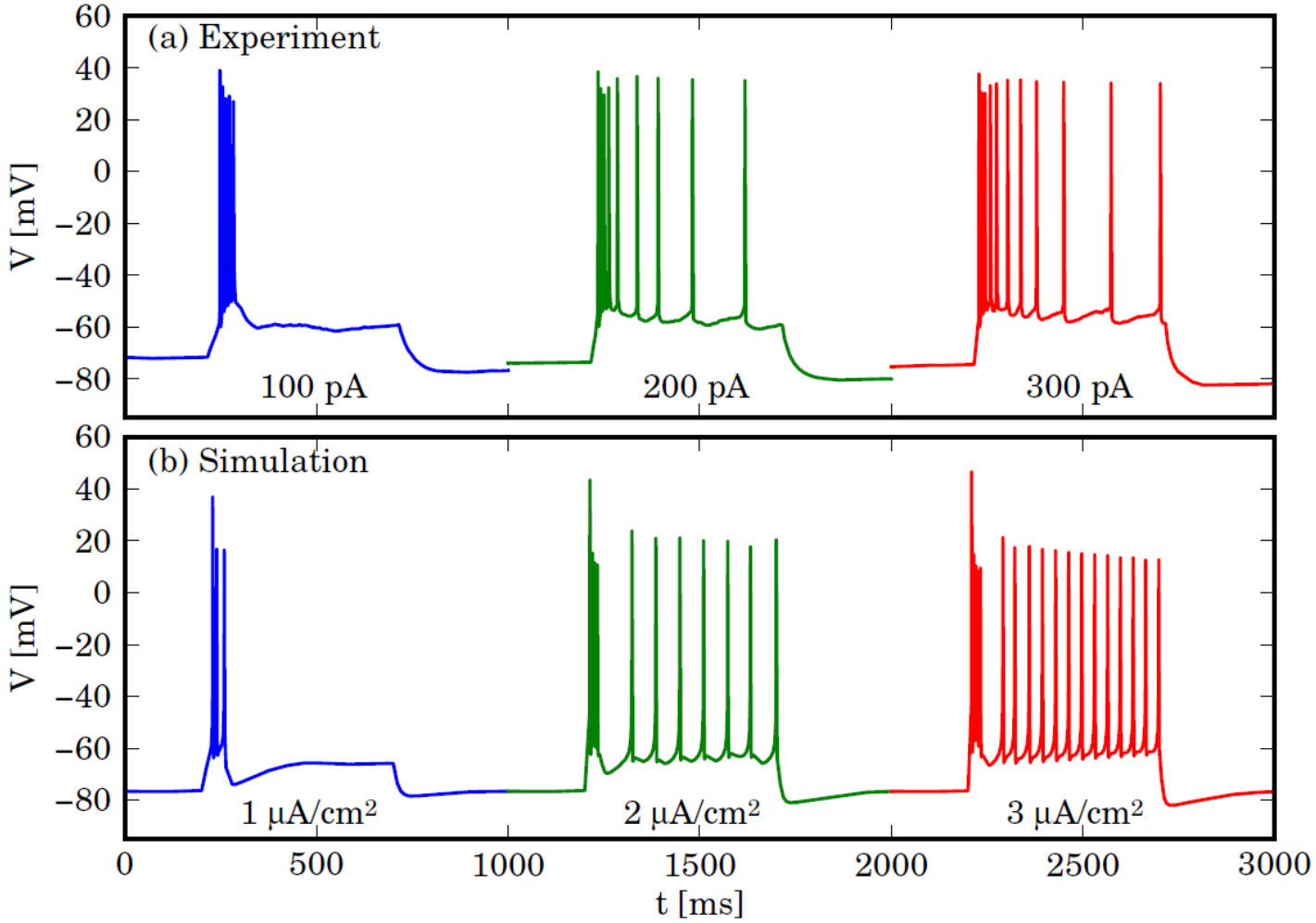


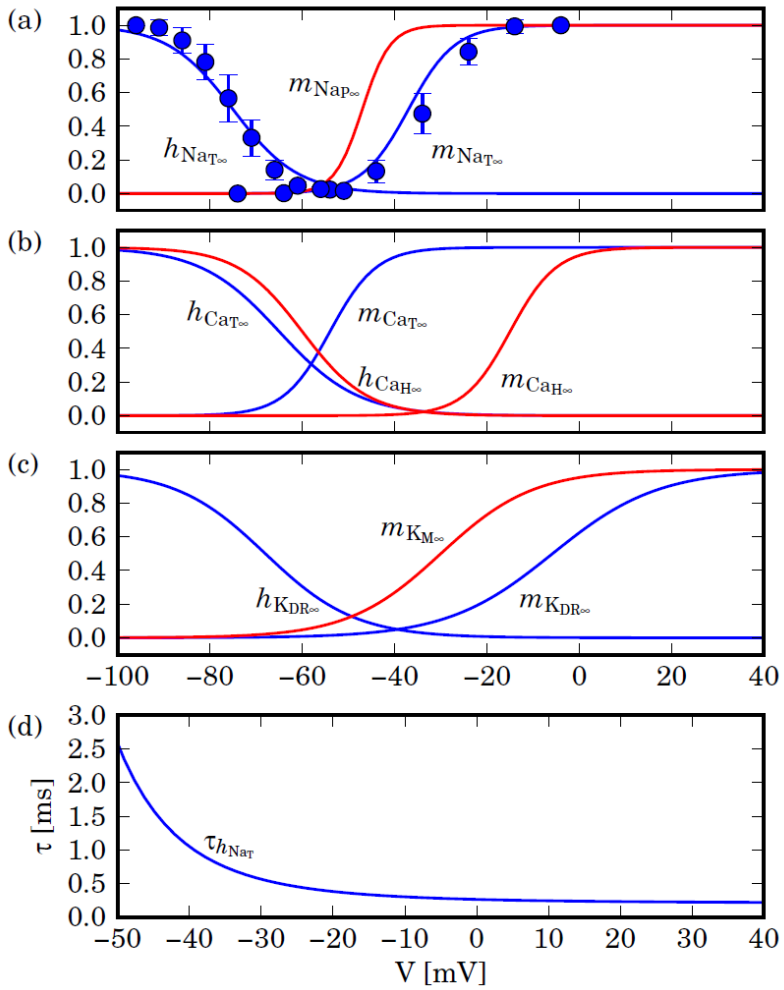
$$y_{x_\infty}(V) = \frac{1}{1 + \exp\left(-\frac{V - V_{\mathrm{yx}}}{k_{\mathrm{yx}}}\right)},$$

$$y_{x_\infty}(V) = \frac{\alpha_{\mathrm{x}}}{\alpha_{\mathrm{x}} + \beta_{\mathrm{x}}}$$

$$\tau_{\mathrm{x}}(V) = \frac{1}{\alpha_{\mathrm{x}} + \beta_{\mathrm{x}}}$$

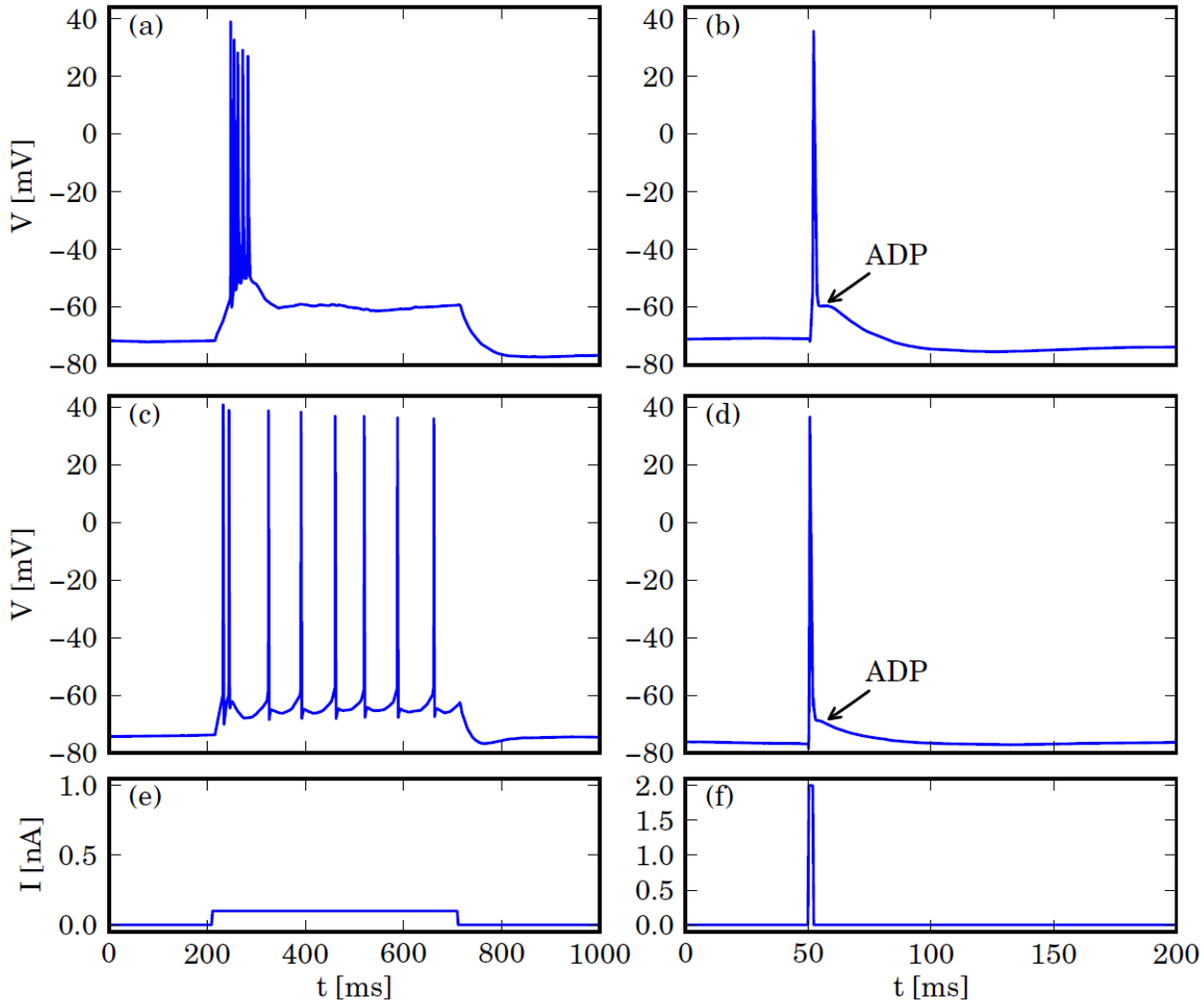
Model neuronów piramidalnych CA1/3



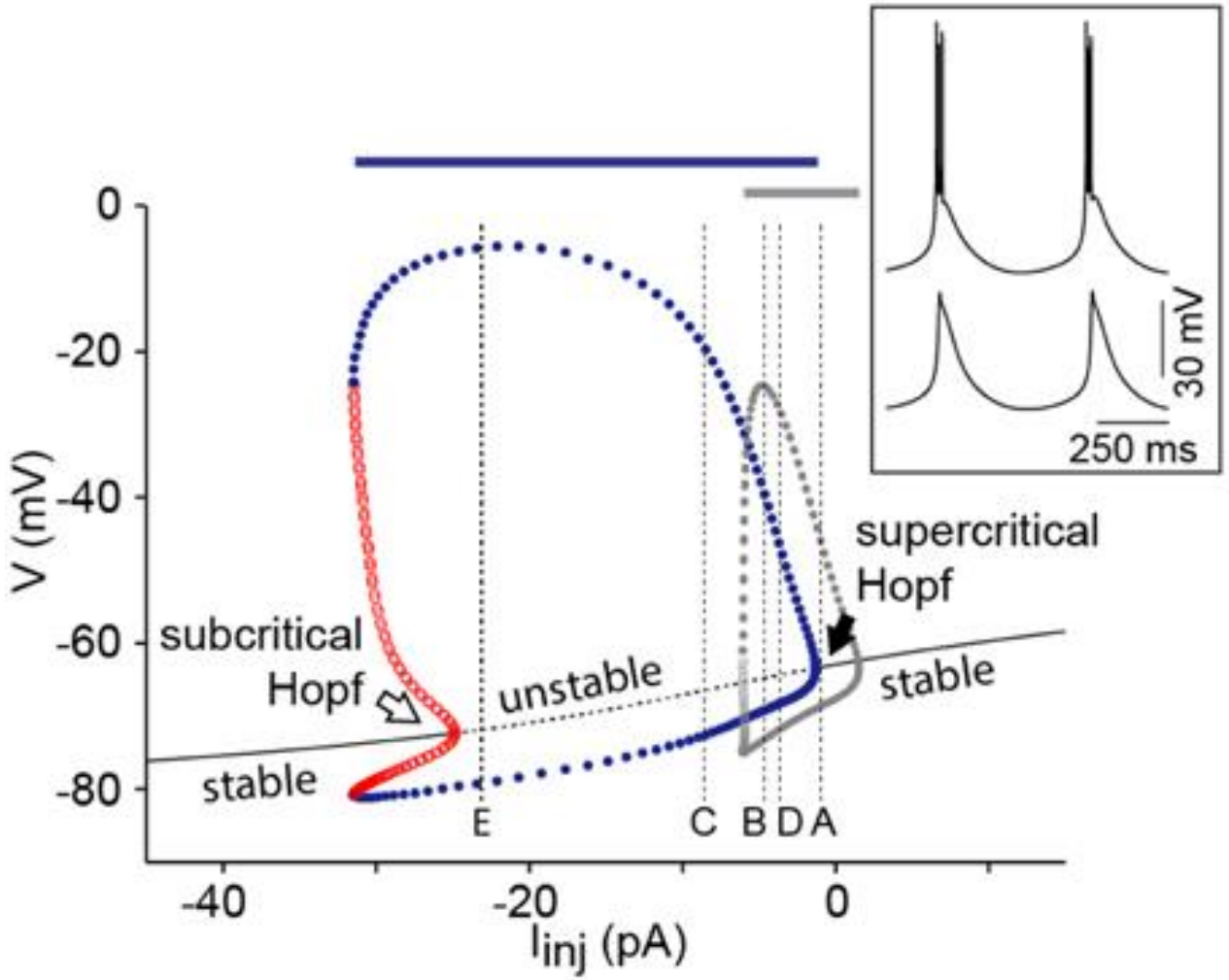


A unified model of CA1/3 pyramidal cells: an investigation into excitability, J Nowacki, HM Osinga, JT Brown, AD Randall, K Tsaneva-Atanasova, Progress in biophysics and molecular biology 105 (1-2), 34-48

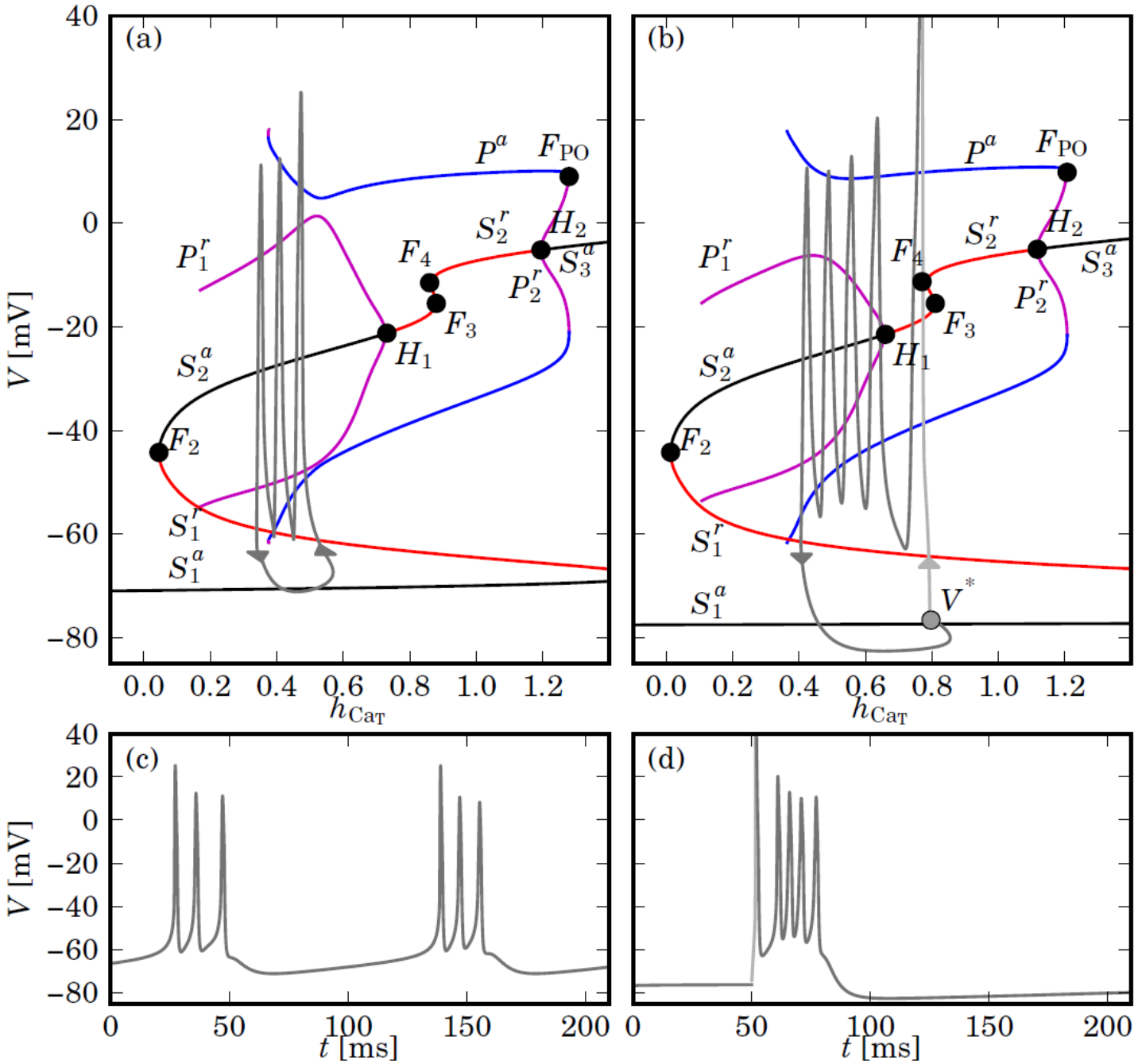
Model neuronów piramidalnych CA1/3



Analiza bifurkacyjna



Amarillo, Yimy & Mato, German & Nadal, Marcela. (2015). Analysis of the role of the low threshold currents I T and I h in intrinsic delta oscillations of thalamocortical neurons. Frontiers in Computational Neuroscience. 1. 52. 10.3389/fncom.2015.00052.



Wiele skal czasu

$$\begin{aligned} x' &= f(x,y), \\ y' &= \varepsilon g(x,y), \end{aligned}$$

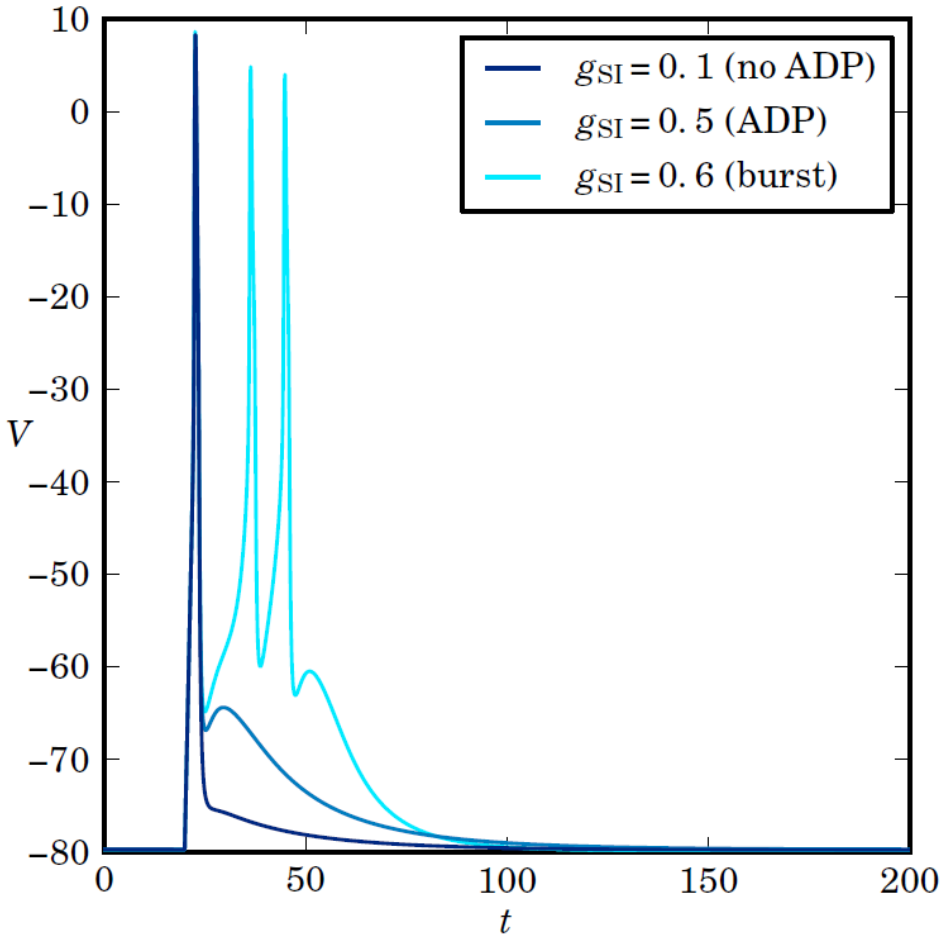
Szybki podsystem

$$\begin{aligned} x' &= f(x,y), \\ y' &= 0. \end{aligned}$$

Wolny podsystem

$$\begin{aligned} 0 &= f(x,y), \\ \dot{y} &= g(x,y). \end{aligned}$$

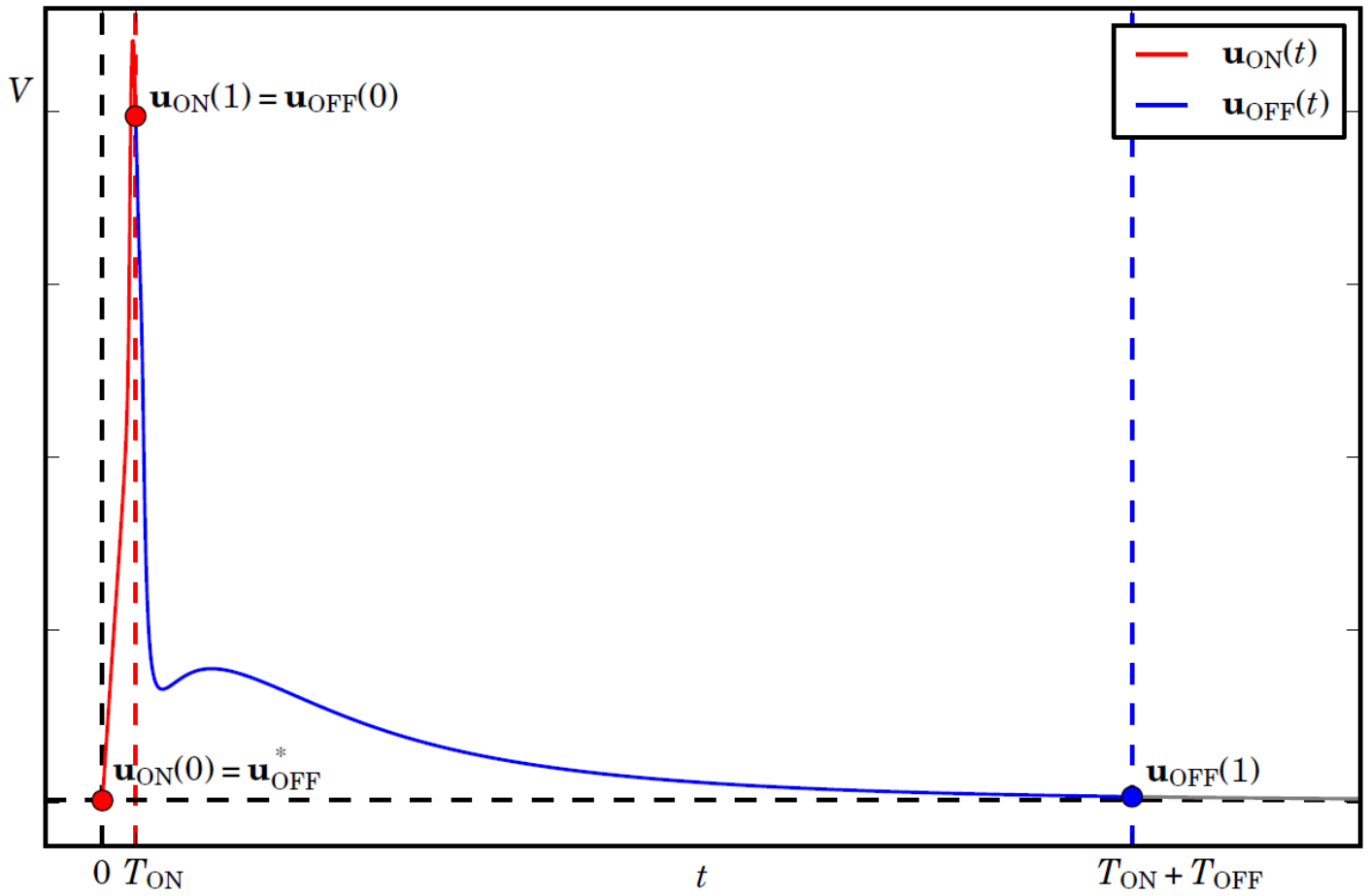
Transient burst

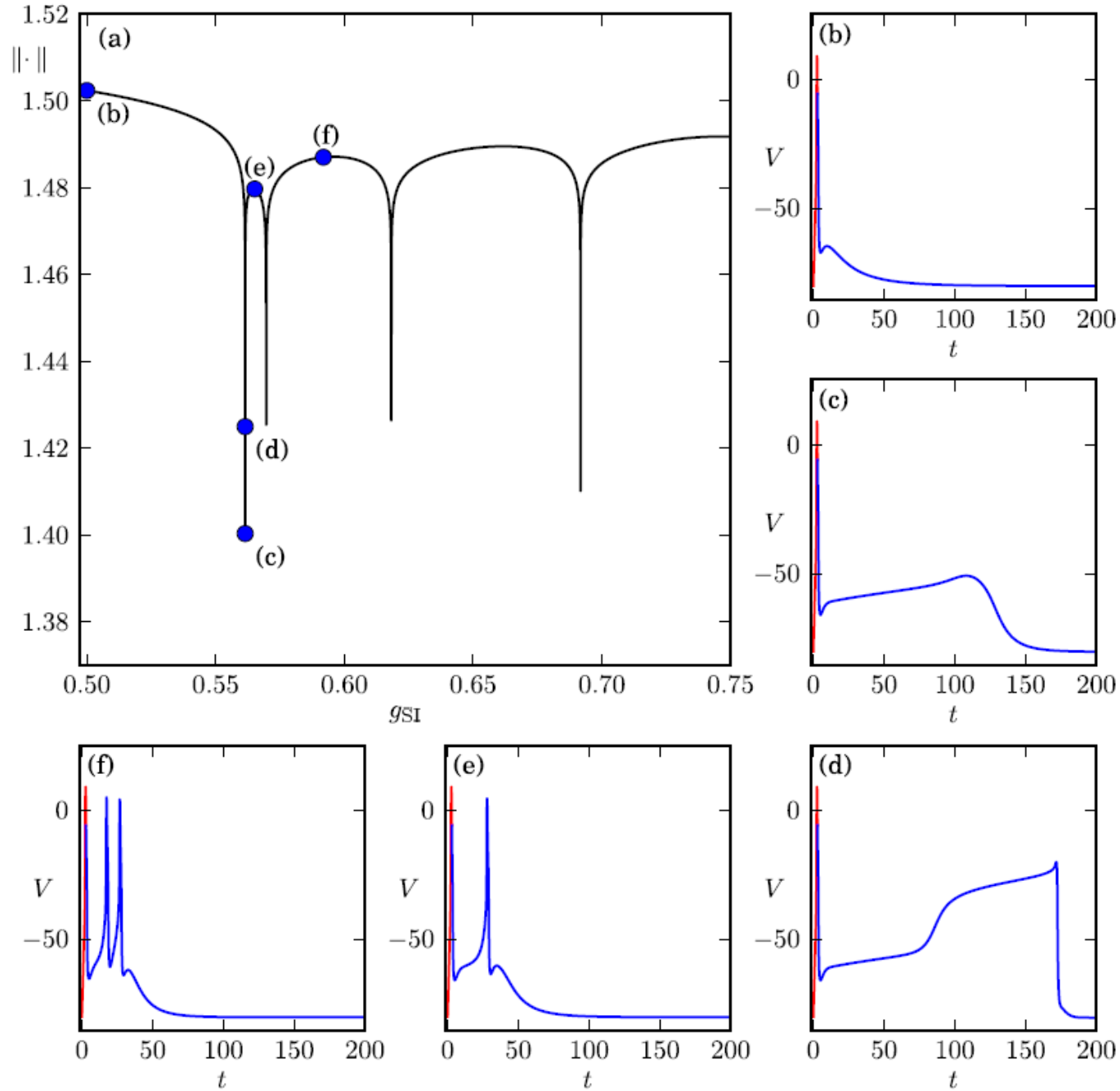


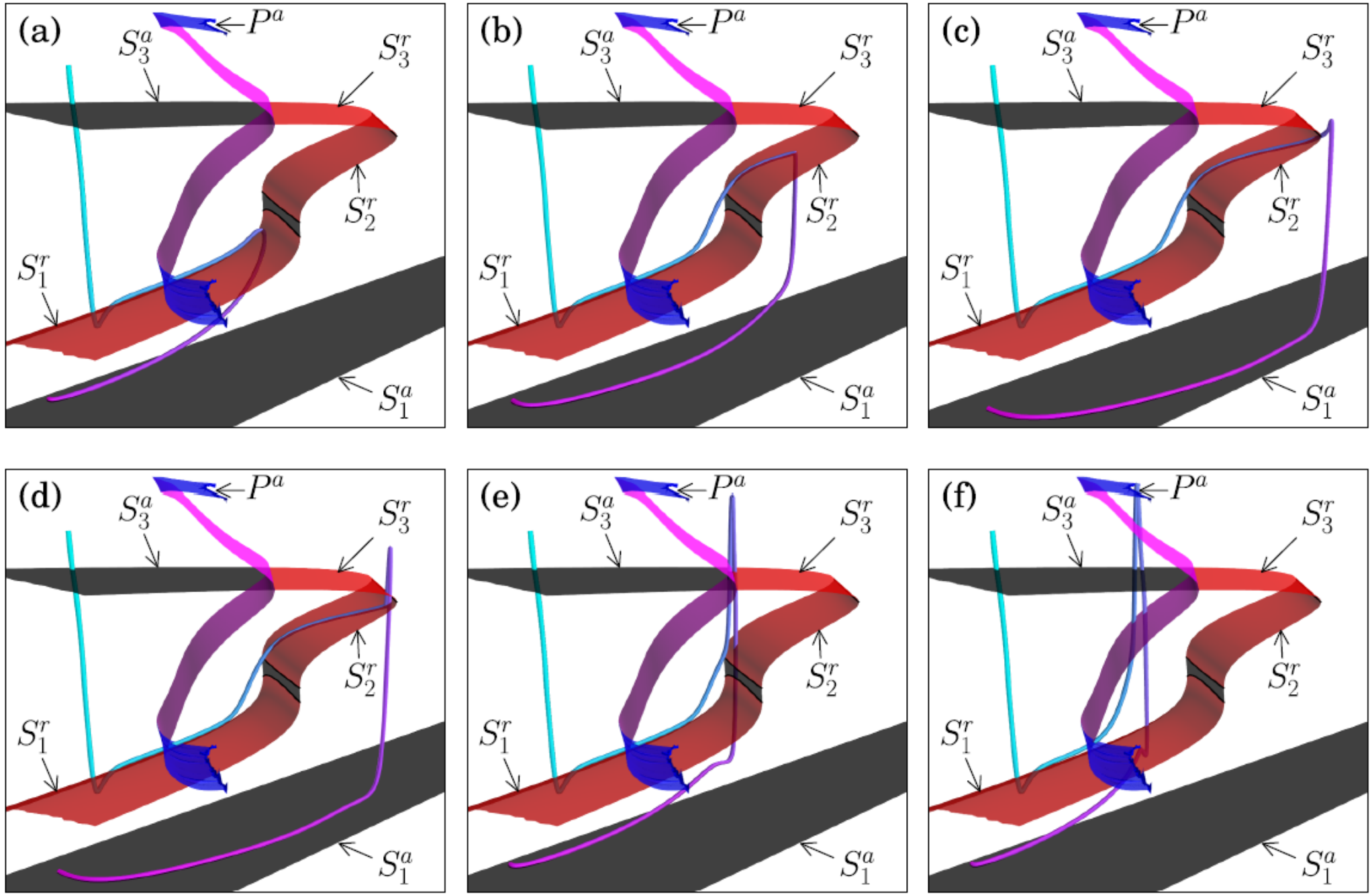
			C_m	=	1.0	μF/cm^2		
Inward currents:								
g_{FI}	=	2.0 mS/cm^2	E_I	=	80.0	mV		
$V_{m_{FI}}$	=	−25.0 mV	g_{SI}	=	0.5	mS/cm^2		
$k_{m_{FI}}$	=	5.0 mV	$V_{m_{SI}}$	=	−54.0	mV	$V_{h_{SI}}$ = −56.0	mV
			$k_{m_{SI}}$	=	5.0	mV	$k_{h_{SI}}$ = 8.5	mV
			$\tau_{m_{SI}}$	=	3.0	ms	$\tau_{h_{SI}}$ = 20.0	ms
Outward currents:								
g_{FO}	=	9.5 mS/cm^2	E_O	=	−80.0	mV		
$V_{m_{FO}}$	=	−6.0 mV	g_{SO}	=	1.2	mS/cm^2		
$k_{m_{FO}}$	=	11.5 mV	$V_{m_{SO}}$	=	−20.0	mV		
$\tau_{m_{FO}}$	=	1.0 ms	$k_{m_{SO}}$	=	10.0	mV		
			$\tau_{m_{SO}}$	=	75.0	ms		

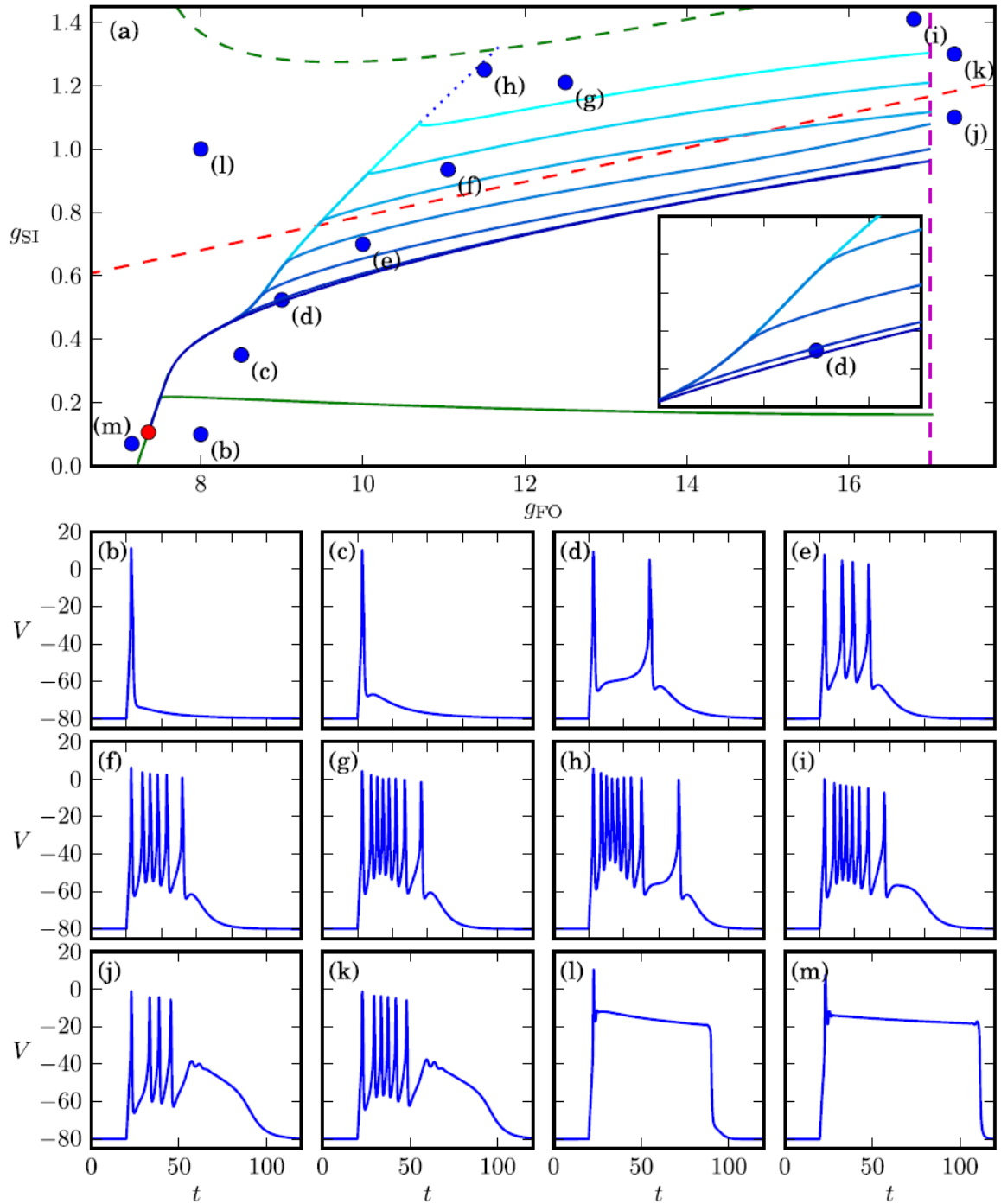
Dynamical systems analysis of spike-adding mechanisms in transient bursts
J Nowacki, HM Osinga, K Tsaneva-Atanasova
The Journal of Mathematical Neuroscience 2 (1), 7

Potencjał akcyjny jako zagadnienie brzegowe



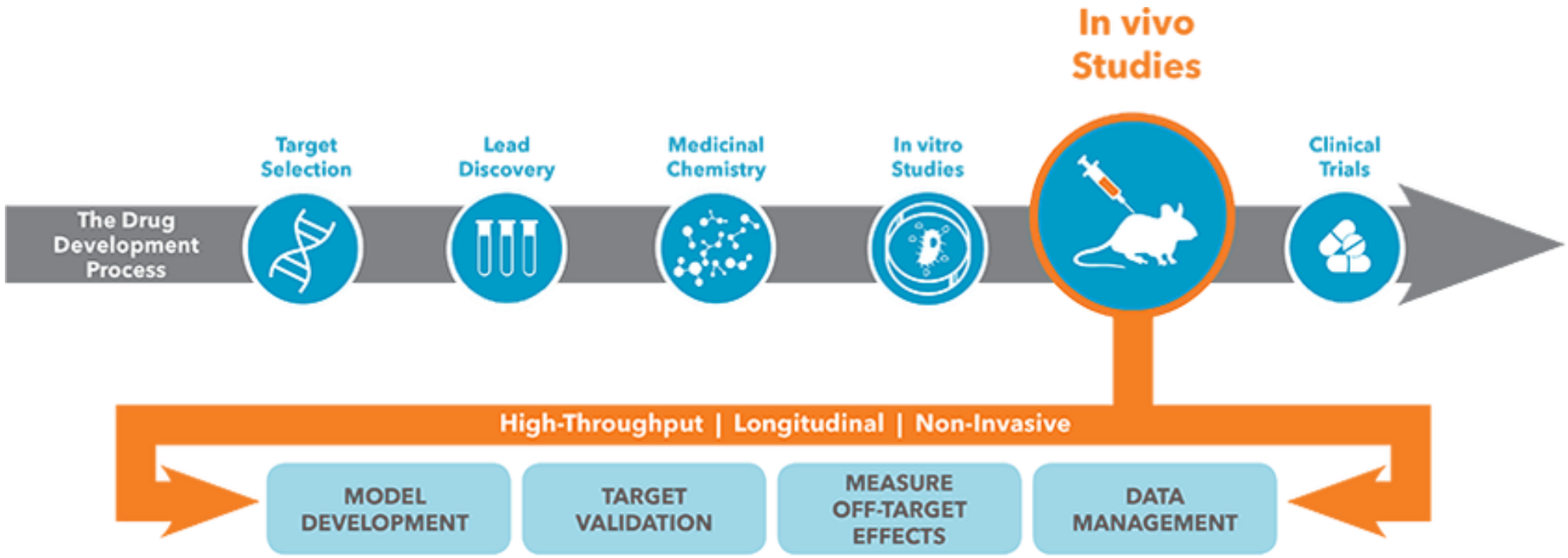

(a)
(b)
(c)
(d)
(e)
(f)
$\|\cdot\|$
1.52
1.50
1.48
1.46
1.44
1.42
1.40
1.38
0.50
0.55
0.60
0.65
0.70
0.75
g_{SI}
V
t
0
−50
50
100
150
200


(a)
P^a
S_3^a
S_3^r
S_2^r
S_1^r
S_1^a
(b)
P^a
S_3^a
S_3^r
S_2^r
S_1^r
S_1^a
(c)
P^a
S_3^a
S_3^r
S_2^r
S_1^r
S_1^a
(d)
P^a
S_3^a
S_3^r
S_2^r
S_1^r
S_1^a
(e)
P^a
S_3^a
S_3^r
S_2^r
S_1^r
S_1^a
(f)
P^a
S_3^a
S_3^r
S_2^r
S_1^r
S_1^a

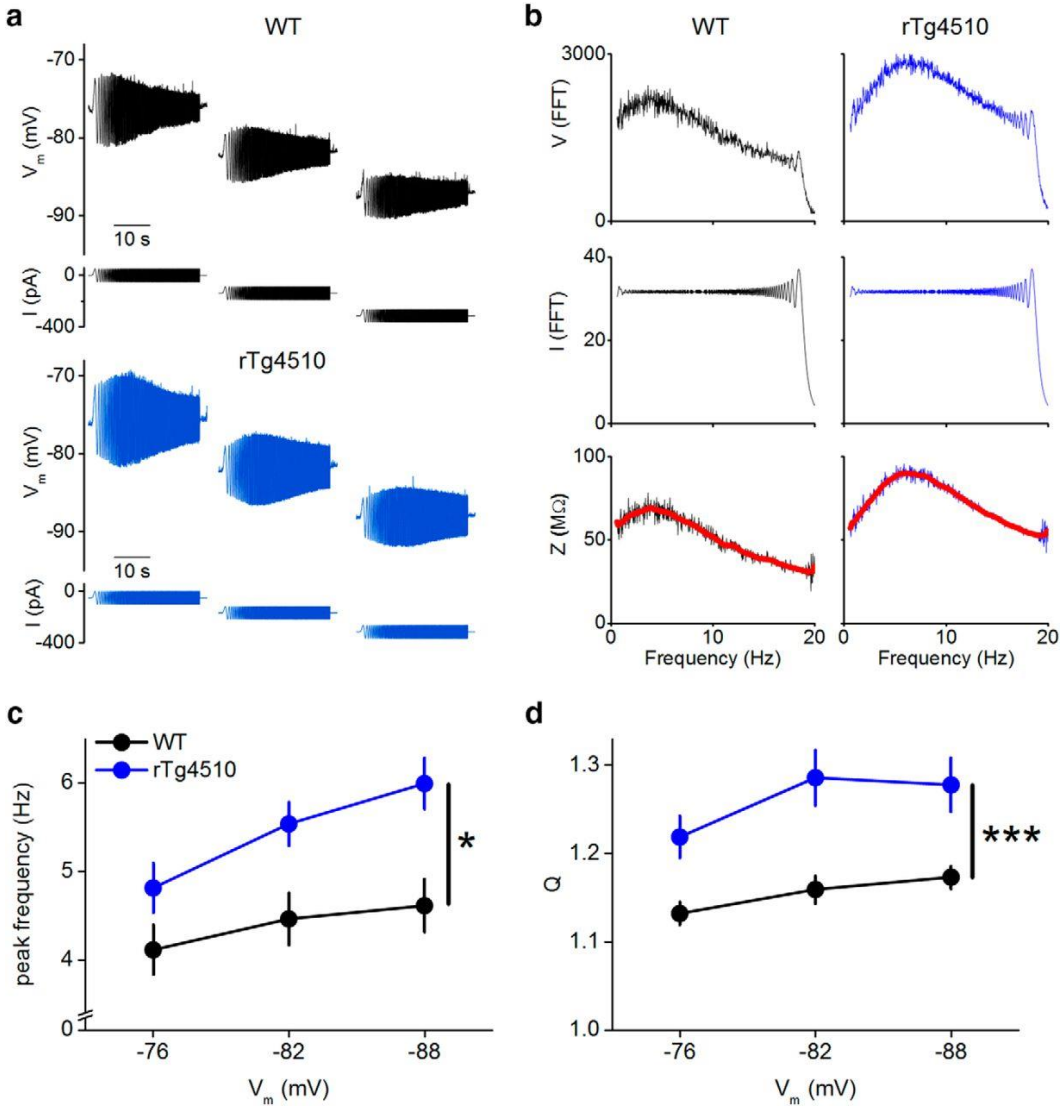

(a)
(b)
(c)
(d)
(e)
(f)
(g)
(h)
(i)
(j)
(k)
(l)
(m)
g_{SI}
g_{FO}
V
t

Po co to wszystko?

Tworzenie leków

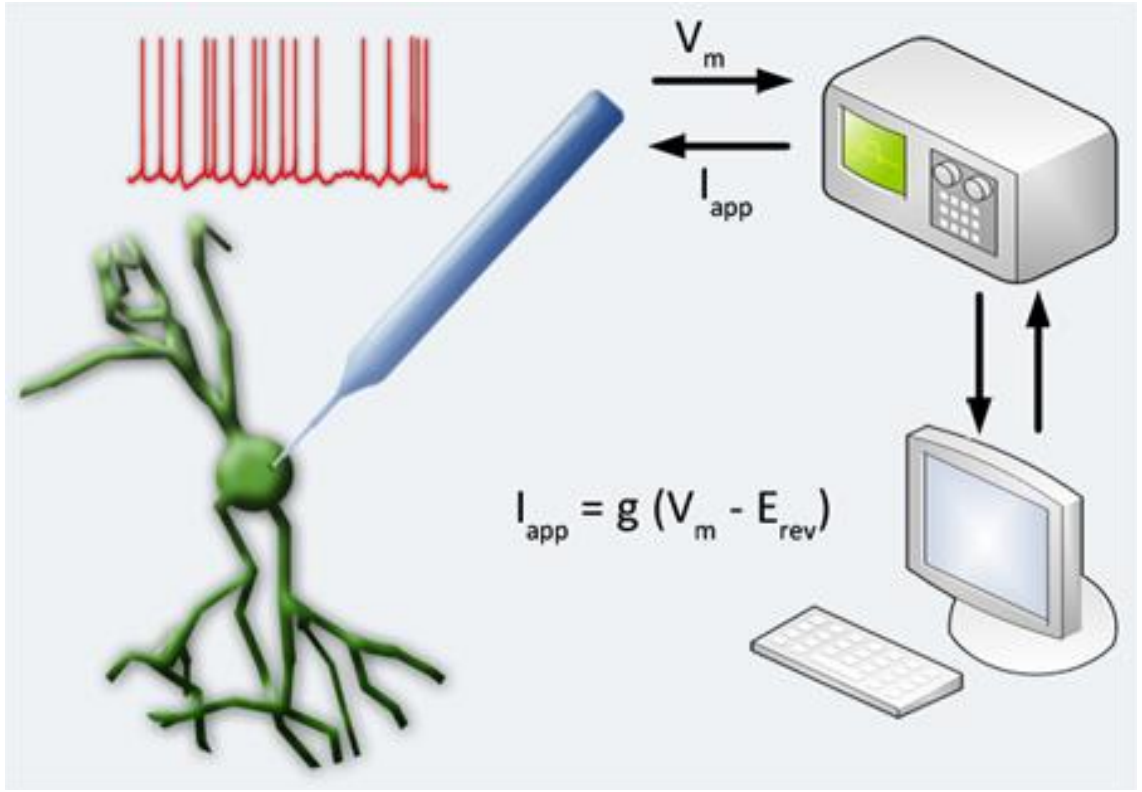


Lepsze zrozumienie eksperymentów



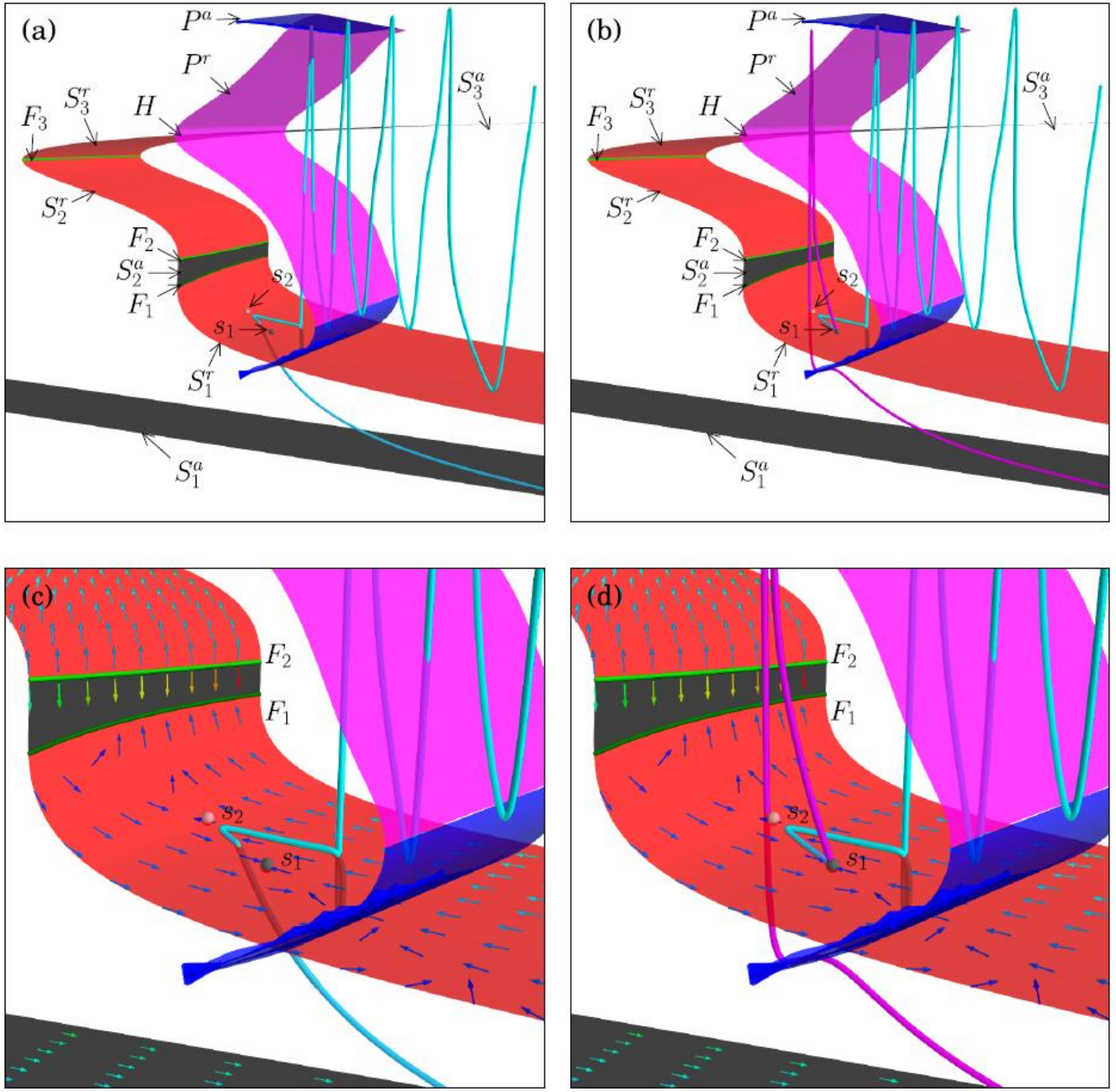
Altered intrinsic pyramidal neuron properties and pathway-specific synaptic dysfunction underlie aberrant hippocampal network function in a mouse model of tauopathy
CA Booth, J Witton, J Nowacki, K Tsaneva-Atanasova, MW Jones, ...
Journal of Neuroscience 36 (2), 350-363

Nowe możliwości eksperymentalne



http://rtxi.org/

Zrozumienie nowych problemów matematycznych



Dziękuję!

Pytania?

https://en.wikipedia.org/wiki/Monument_to_the_laboratory_mouse