Excitable behaviors

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Collective dynamics, control and Imaging,
Institute for Theoretical Studies, ETH, June 2017

What is an excitable behavior ?

From google …

Excitability | definition of excitability by Medical dictionary

ex·cit·a·bil·i·ty (ek-sīt'ă-bil'i-tē),
Having the capability of being excitable.

Farlex Partner Medical Dictionary © Farlex 2012

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Definition of *excitable*

1. *1* : capable of being readily roused into action or a state of excitement or irritability

From google …

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ex·cit·a·bil·i·ty (ek-sīt'ă-bil'i-tē),

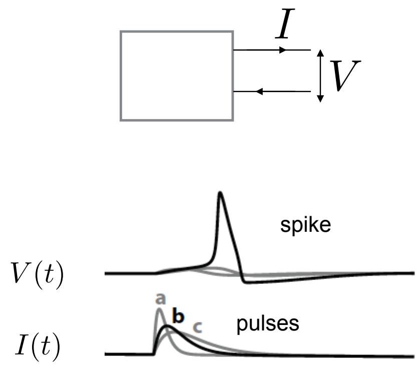
Having the capability of being excitable.

Farlex Partner Medical Dictionary © Farlex 2012

Definition of *excitable*

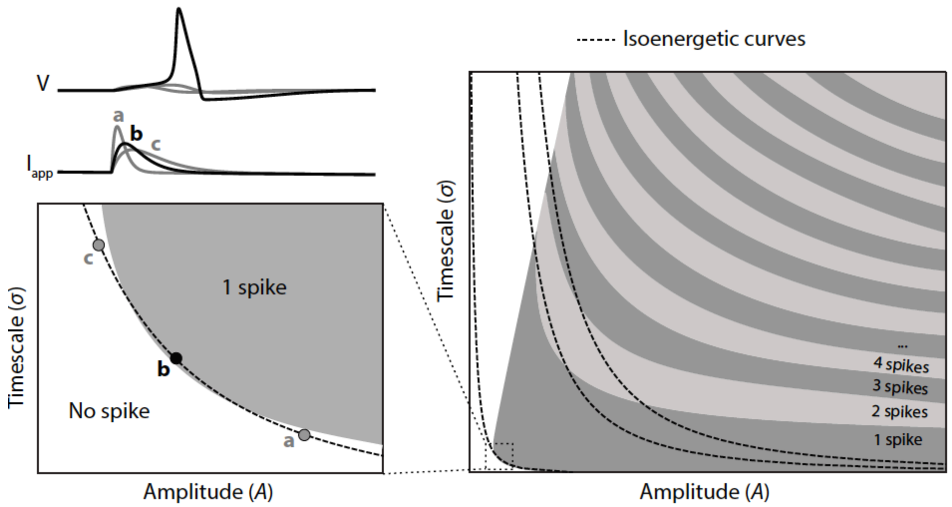
1. *1* : capable of being readily roused into action or a state of excitement or irritability
2. *2* : capable of being activated by and reacting to stimuli <*excitable cells*>

A behavioral property



A family of trajectories characterised by current *pulses* and all-or-none voltage *spikes*

A threshold phenomenon : *localised* sensitivity + *analog-digital* conversion



Excitable behaviors

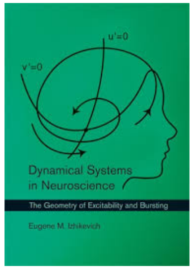
- Neuronal networks are interconnections of neurons and synapses. In neurons, the *current* is the input. In synapses, the *voltage* is the input.
- The all-or-none nature of the spike makes the behavior *nonlinear and hybrid.* Intractable ?
- Excitable behaviors have a characteristic scale, or *resolution*. Tractable ?

The switchlet project: a system theory of excitability

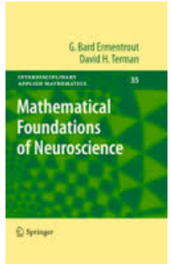
- What is an excitable behavior ? How is it regulated ?
- How can we study interconnections of excitable systems ?
- What makes those nonlinear systems tractable ?
- What makes those systems worth studying beyond their relevance in neurophysiology ?

European Research Council
Advanced Grant
erc

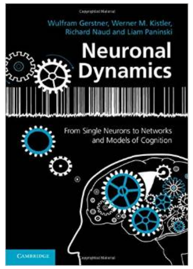
A state-space paradigm ?



2007



2010



2014

Great for computations but limited for system theoretic questions

Tractability of high-dimensional NL models ?
spatiotemporal modeling ? stochastic modeling ?
Interconnections ? Robustness ? Modulation ?

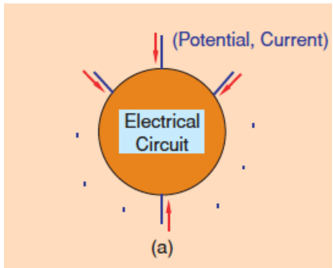
A historical hint

The typical regulator system can frequently be described, in essentials, by differential equations of no more than perhaps the second, third or fourth order. …In contrast, the order of the set of differential equations describing the typical negative feedback amplifier used in telephony is likely to be very much greater. As a matter of idle curiosity, I once counted to find out what the order of the set of equations in an amplifier I had just designed would have been, if I had worked with the differential equations directly. It turned out to be 55.

Henrik Bode, Feedback: the history of an idea, 1960

Bode developed loop-shaping analysis to overcome the intractability of sensitivity analysis of electrical circuits aimed at signal transmission

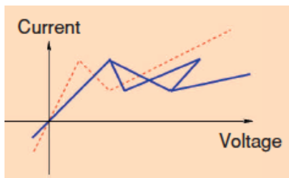
The behavioral approach to system theory



The Behavioral Approach

The behavioral approach is based on the following premises.

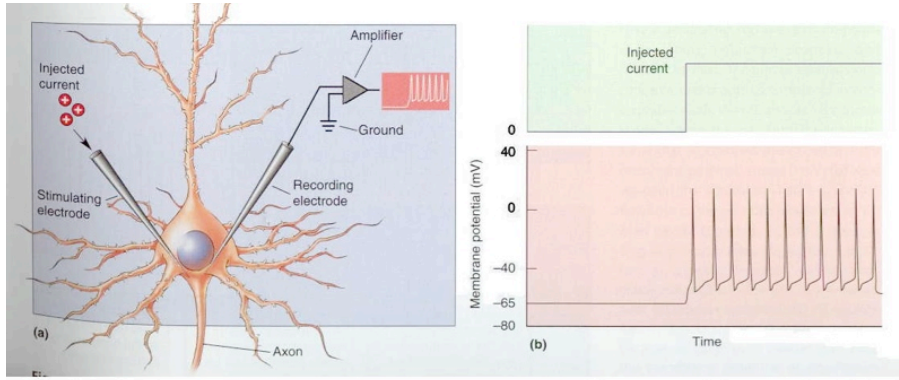
1) A mathematical model is a subset of a set of a priori possibilities. This subset is the behavior of the model. For a dynamical system, the behavior consists of the time trajectories that the model declares possible.
2) The behavior is often given as a set of solutions of equations. Differential and difference equations are an effective, but highly nonunique, way of specifying the behavior of a dynamical system.
3) The behavior is the central concept in modeling. Equivalence of models, properties of models, model representations, and system identification must refer to the behavior.



See J. Willems, CSM 2007 for more …

Modelling excitability

The textbook picture

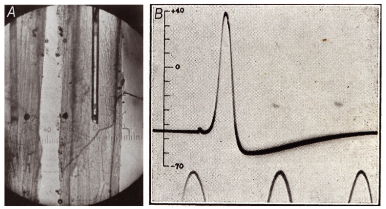


A one-port circuit.
Neurons are electrical circuits classified according to their step response.

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



The action potential

A circuit model

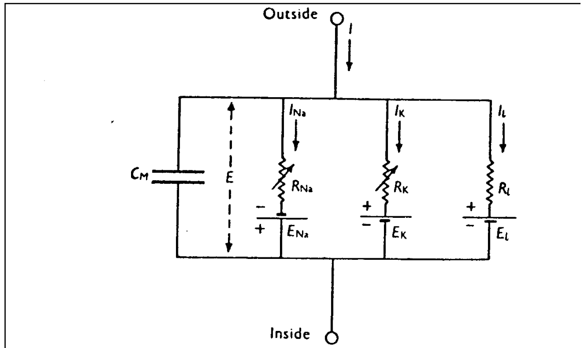
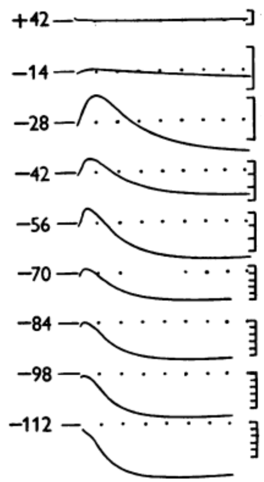


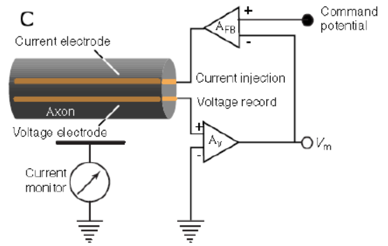
Fig. 1. Electrical circuit representing membrane. $R_{Na}=1/g_{Na}$; $R_K=1/g_K$; $R_l=1/\bar{g}_l$. R_{Na} and R_K vary with time and membrane potential; the other components are constant.

What Hodgkin and Huxley did (1)

The voltage clamp experiment :

identifying a system through its inverse





$$\frac{\Delta I}{\Delta V} = g(V,t)$$

“Input conductance”
=
“step response of the inverse”
=
“local gain “

A voltage-dependent transfer function

$$\frac{\Delta I}{\Delta V} = G(s;V)$$

e.g. $$\frac{K(V)}{\tau(V)s+1}$$

Admittance identified from the step response at an operating point of the circuit.

! NOT from the state-space model

$$\tau(V)\frac{dg}{dt} = -g + \int^{V} K(x)dx$$

What Hodgkin and Huxley did (2)

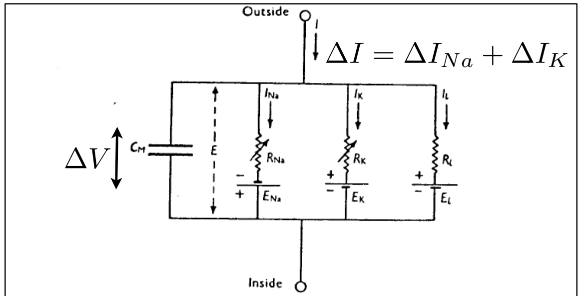
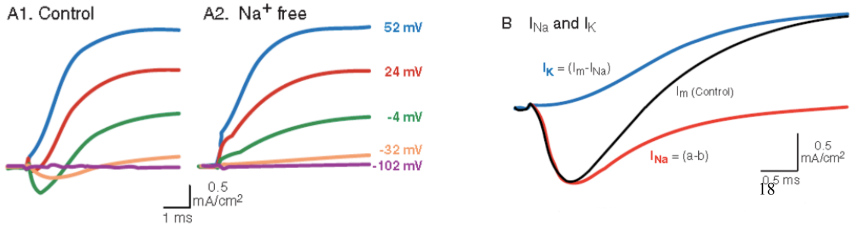


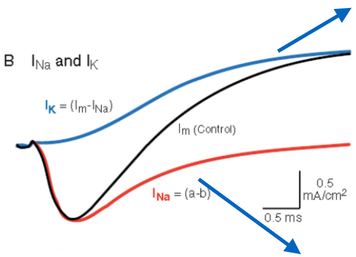
Fig. 1. Electrical circuit representing membrane. $R_{Na}=1/g_{Na}$; $R_K=1/g_K$; $R_l=1/\bar{g}_l$. R_{Na} and R_K vary with time and membrane potential; the other components are constant.

Tearing apart two

distinct ionic currents …



Modelling conductances



Delayed SLOW first-order response (POSITIVE conductance)

Delayed FAST first-order response (NEGATIVE conductance) + SLOW first-order response (POSITIVE conductance)

Fitting a state space model

$$\frac{a}{2R_2}\frac{\partial^2 V}{\partial x^2} = C_M\frac{\partial V}{\partial t} + \bar{g}_K n^4 (V-V_K) + \bar{g}_{Na} m^3 h (V-V_{Na}) + \bar{g}_l (V-V_l),$$

$$dn/dt = \alpha_n(1-n) - \beta_n n,$$
$$dm/dt = \alpha_m(1-m) - \beta_m m,$$
$$dh/dt = \alpha_h(1-h) - \beta_h h,$$

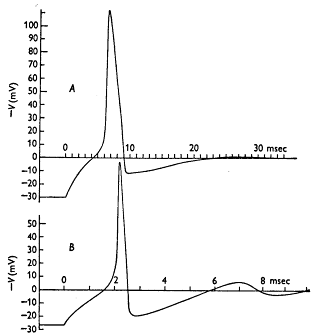
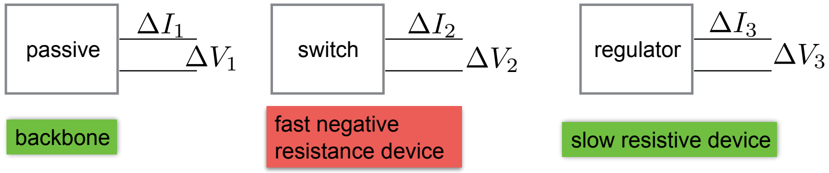


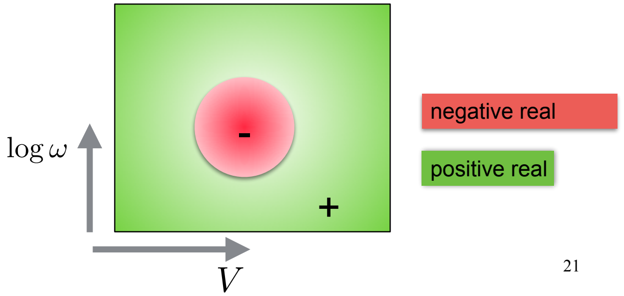
Fig. 22. Theoretical basis of anode break excitation. A, numerical solution of eqn. (26) for boundary condition $-V = -30$ mV for $t<0$; temperature 6° C. B, anode break excitation following sudden cessation of external current which had raised the membrane potential by 26·5 mV; giant axon with long electrode at 18·5° C. Time scales differ by a factor appropriate to the temperature difference.

A differential model of excitability



Kirchoff law:

$$\Delta I = \Delta I_1 + \Delta I_2 + \Delta I_3$$
$$\Delta V = \Delta V_1 = \Delta V_2 = \Delta V_3$$



Differential behavioral theory

How much of a behavior can be inferred from a local description around specific trajectories ?

in particular: from linearised models around equilibrium trajectories ?

$$R(s; w)\delta w = 0$$
$$F(w) = 0$$

Many antecedents:

Kalman vs Aizerman conjecture
Contraction analysis vs Lyapunov analysis
Differential positivity vs monotonicity
Differential dissipativity vs dissipativity
Singularity theory

Analysing excitability

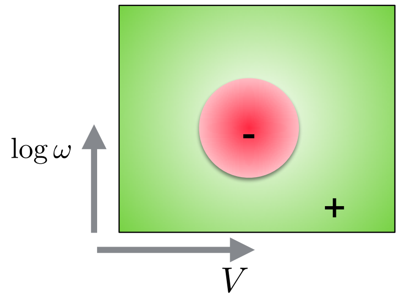
The general ansatz

A differential behavior can be analysed at different resolutions, e.g.

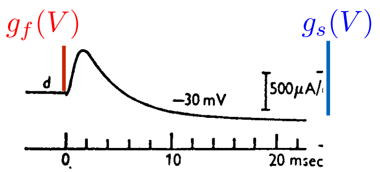
$$R(s'; w') = \int_{\mathbb{C}} \int_{W} R(s; w) h(s - s'; w - w') dw ds$$

h : resolution kernel

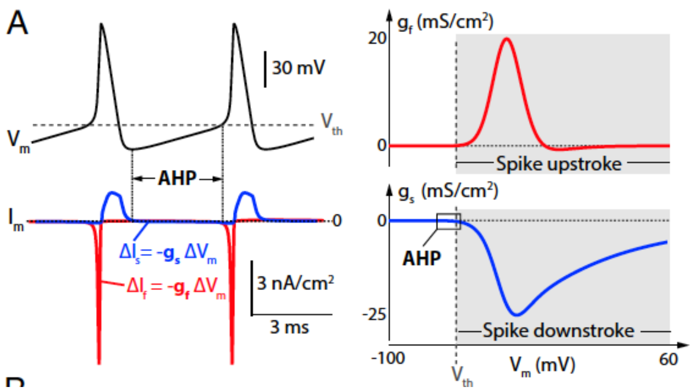
The data dictate the relevant resolutions



The two resolutions of an excitable behavior

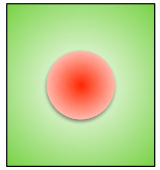


$$g(V,t) \approx g_f(V)e^{-\frac{t}{\tau_f}} + g_s(V)e^{-\frac{t}{\tau_s}}$$



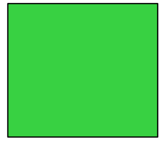
The two resolutions of an excitable behavior

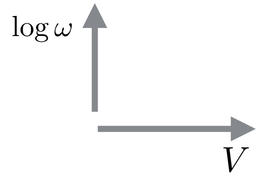
$$G(s;V)$$



$$\approx$$

$$g_l$$





$$+\ g_f(V).\frac{1}{\tau_f s + 1}$$


.


$$+\ g_s(V).\frac{1}{\tau_s s + 1}$$


.


A quasi-static model

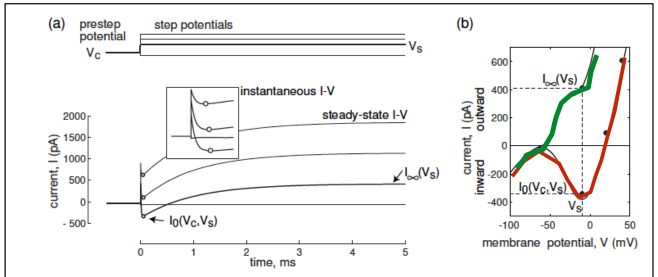


Figure 2.6: Voltage-clamp experiment to measure instantaneous and steady-state I-V relation. Shown are simulations of the I_{Na}+I_K-model (see Fig.4.1b); the continuous curves are theoretically found I-V relations.

$$I(V) = \int^V g_l + g_f(x)dx$$

A hysteretic switch
in the fast time scale

$$I(V) = \int^V g_l + g_f(x) + g_s(x)dx$$

A monotone resistor
in the slow time scale

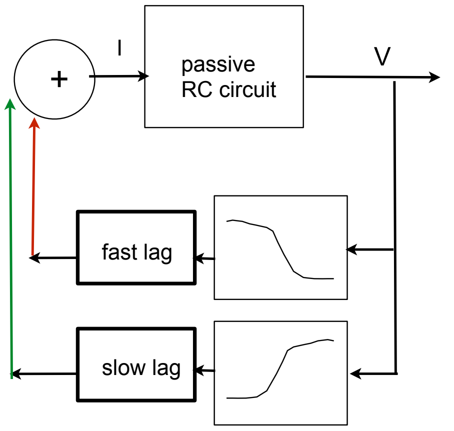
A state-space representation

$$C\dot{V} = I_l(V) + I_f(V_f) + I_s(V_s) + I$$
$$\tau_f \dot{V}_f = -V_f + V$$
$$\tau_s \dot{V}_s = -V_s + V$$

Fitzhugh Nagumo model :

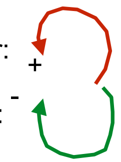
$$C = 0;\ I_l(V) = -\frac{V^3}{3};\ I_f(V) = k_f V;\ I_s(V) = -k_s V$$

A mixed feedback representation



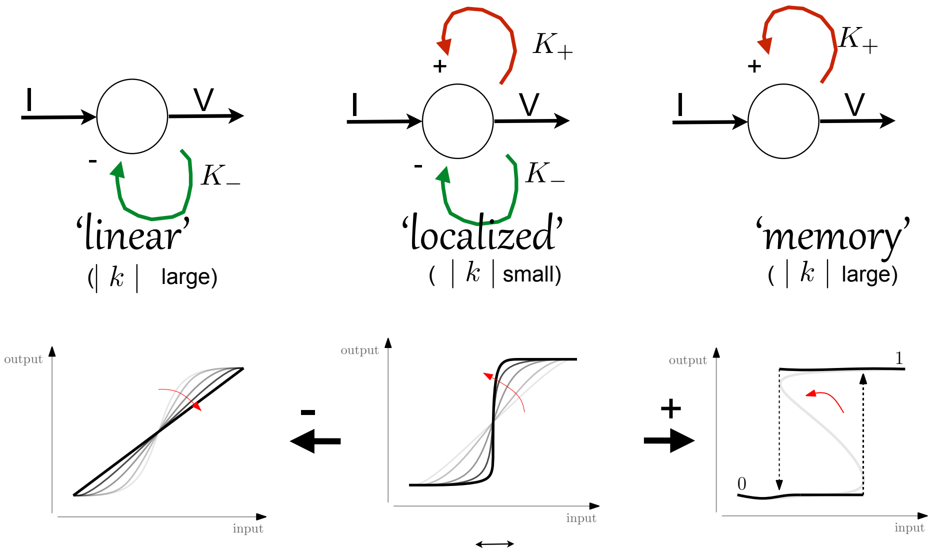
High frequency behavior:

Low frequency behavior:



Necessary localization in some frequency range !

Balanced feedback 'localizes'



$\overleftrightarrow{O}(k)$

$k \approx K_+ - K_-$

Benefits of a differential approach

Modelling / Analysis / Synthesis is *faithful* to the data

A realm of tractable methodologies tools, e.g. from LTI system theory and singularity theory

Extensions are '*straightforward*' : e.g. spatiotemporal excitability replaces LTI by LTSI …

Ongoing research

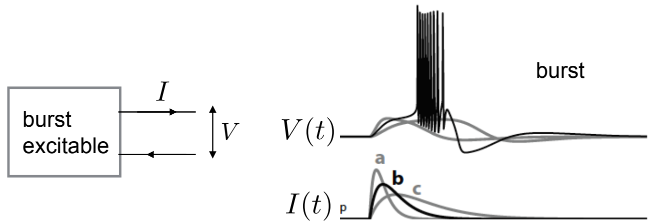
Transfer functions at a resolution

Sensitivity analysis, regulation, and synthesis of excitable circuits

Spatiotemporal excitability, network excitability, …

Interconnecting excitable behaviors

Bursting as interconnection of excitable systems



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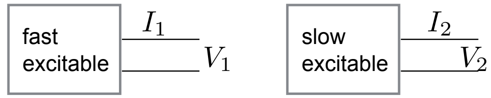
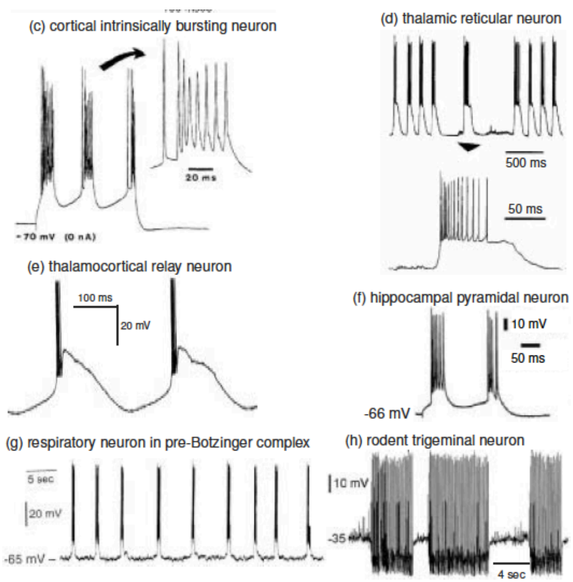


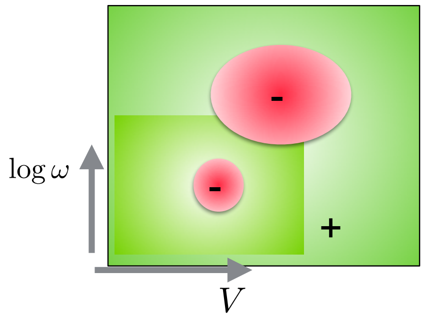
$$I = I_1 + I_2$$

$$V = V_1 = V_2$$

Bursting, an essential component of neuronal signalling



A novel theory of bursting



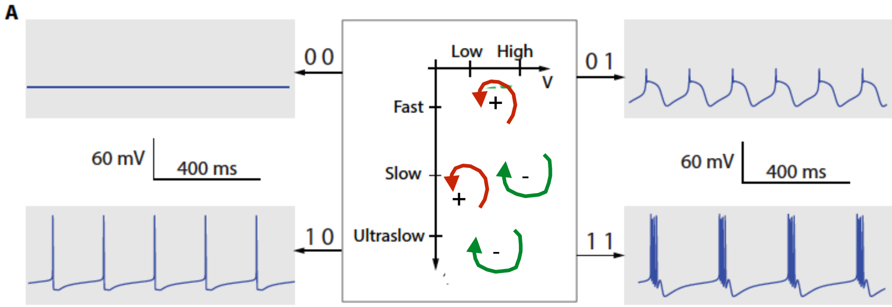
A. Franci, G. Drion, R. Sepulchre. An organizing center in a planar model of neuronal excitability SIAM Journal on Applied Dynamical Systems, 11(4), pp. 1698-1722, 2012

G. Drion, A. Franci, V. Seutin, R. Sepulchre. A Balance Equation Determines a Switch in Neurona Excitability, PLoS Computational Biology 9(5) : e1003040, 2013.

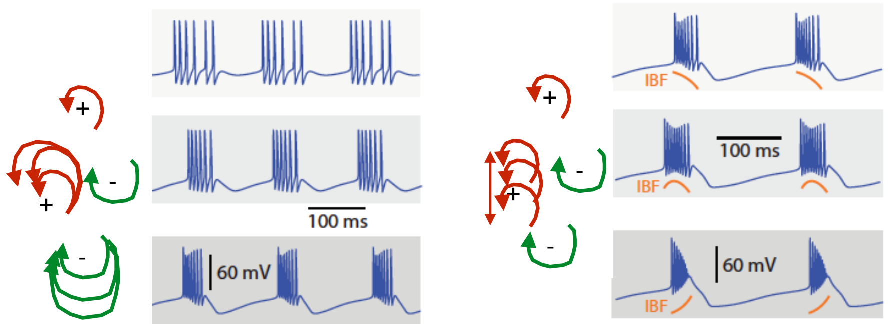
A. Franci, G. Drion, R. Sepulchre. Modeling the modulation of neuronal bursting: a singularity theory approach. SIAM J. Appl. Dyn. Syst. 13-2 (2014), pp. 798-829

G. Drion, A. Franci, J. Dethier, R. Sepulchre. Dynamic input conductances shape neuronal spiking. eNeuro, DOI: 10.1523/ENEURO.0031-14. 2015.

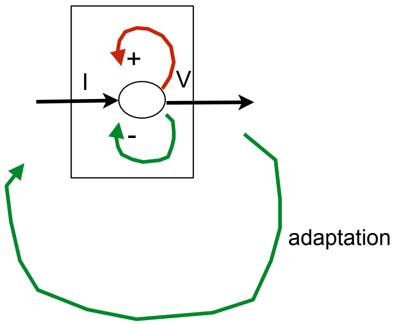
A two-state automaton
(two switches)



continuously regulated
(two regulators)



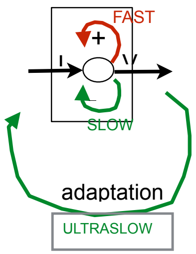
The dominant bursting model of neurodynamics



Endogenous bursting : Slow negative feedback (adaptation) provides the driving oscillating input to the excitable model

Izhikevich, Chapter 9
Terman and Ermentrout, Chapter 5
Keener and Sneyd, Chapter 9

Should we care ?

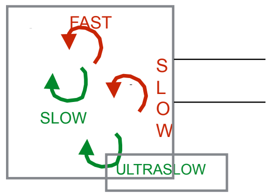


No modulation (no route to burst)

No robustness (fragile to noise and time scale separation)

No interconnections

Classification based on bifurcations



the slow negative conductance controls the modulation between spike and burst

The motif is as robust as the spiking motif

Interconnection based approach

No classification ; loop shaping regulation

Benefits of a differential approach

Modelling / Analysis / Synthesis is *faithful* to the data

A realm of tractable methodologies tools, e.g.
from LTI system theory and singularity theory

Extensions are '*straightforward*' : e.g. spatiotemporal
excitability replaces LTI by LTSI …

Ongoing research

Synthesis of excitable and bursting circuits

Integrate and fire models of excitability and bursting

Spatio-temporal excitable networks

Conclusions

What is an excitable behavior ?

A relationship between current pulses and voltage spikes characterised
by a window of *ultrasensitivity* at a given *scale.*
A *continuous* behavior with a *discrete* readout.

How to model excitability ?

Differential modelling:
The data only provide a local model around specific (e.g. equilibrium)
trajectories of the parts.

How to analyse and design excitable behaviors ?

Integrate the differential models at different resolutions
Switchlets are to systems what wavelets are to signals

Interconnecting excitable behaviors

Interconnecting two excitable systems provides a
system theory of bursting

Conclusions

What is an excitable behavior ?

MODELING BY

A relationship between current pulses and voltage spikes characterised
by a window of *ultrasensitivity* at a given *scale.*
A *continuous* behavior with a *discrete* readout.

How to model excitability ?

TEARING,

Differential modelling:
The data only provide a local model around equilibrium trajectories
of the parts.

How to analyse and design excitable behaviors ?

ZOOMING,

Analyse the differential models at different resolutions
Switchlets are to systems what wavelets are to signals

Interconnecting excitable behaviors

AND LINKING

Interconnecting two excitable systems provides a
system theory of bursting

(J. Willems, CSM, 2007)

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