

NeuroMat webinars 2021 Sao Paulo Brasil Available at https://www.youtube.com/watch?v=BJ-5O-HJg_Y

Bruno Cessac

▶ **To cite this version:**

Bruno Cessac. NeuroMat webinars 2021 Sao Paulo Brasil Available at https://www.youtube.com/watch?v=BJ-5O-HJg_Y. NeuroMat webinars 2021 Sao Paulo Brasil, Jun 2021, Sao Paulo, Brazil. hal-03331825

HAL Id: hal-03331825
https://inria.hal.science/hal-03331825

Submitted on 2 Sep 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

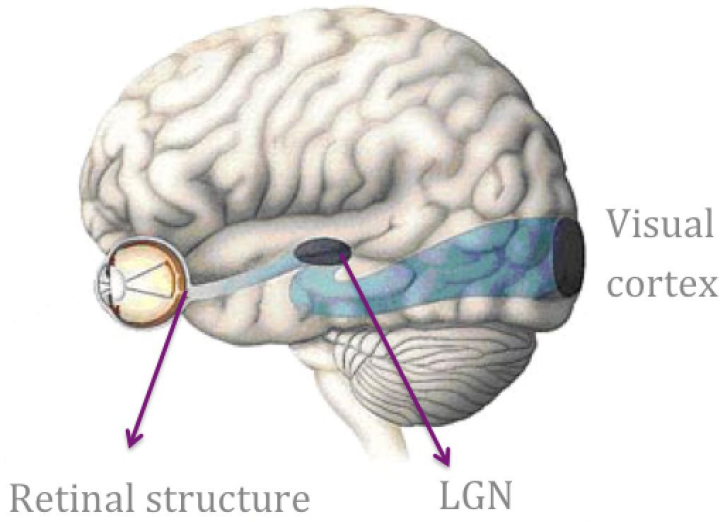
L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

The retina as a dynamical system

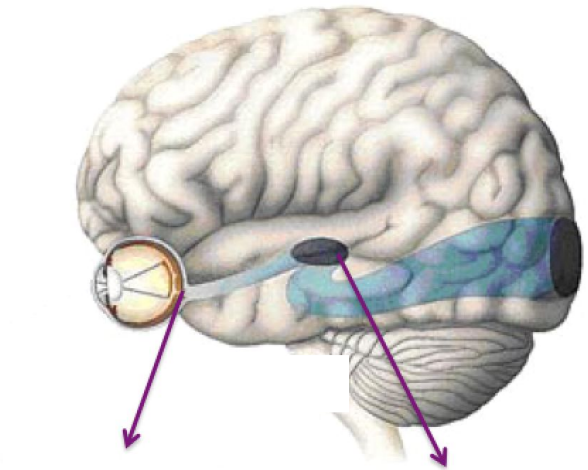
B. Cessac, Université Côte d'Azur, INRIA,
Biovision team and Neuromod Institute
Sophia Antipolis, France

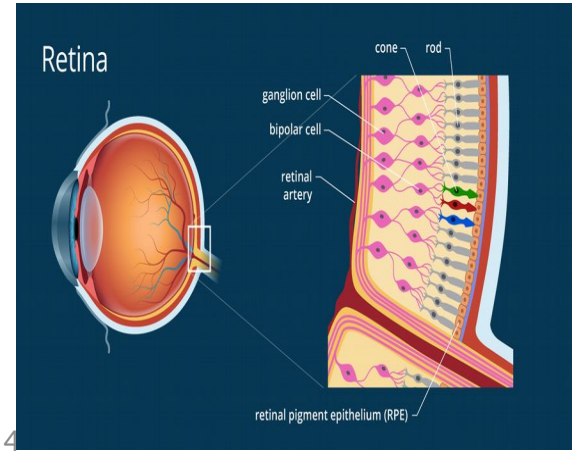
The retina and its dynamics

The visual system



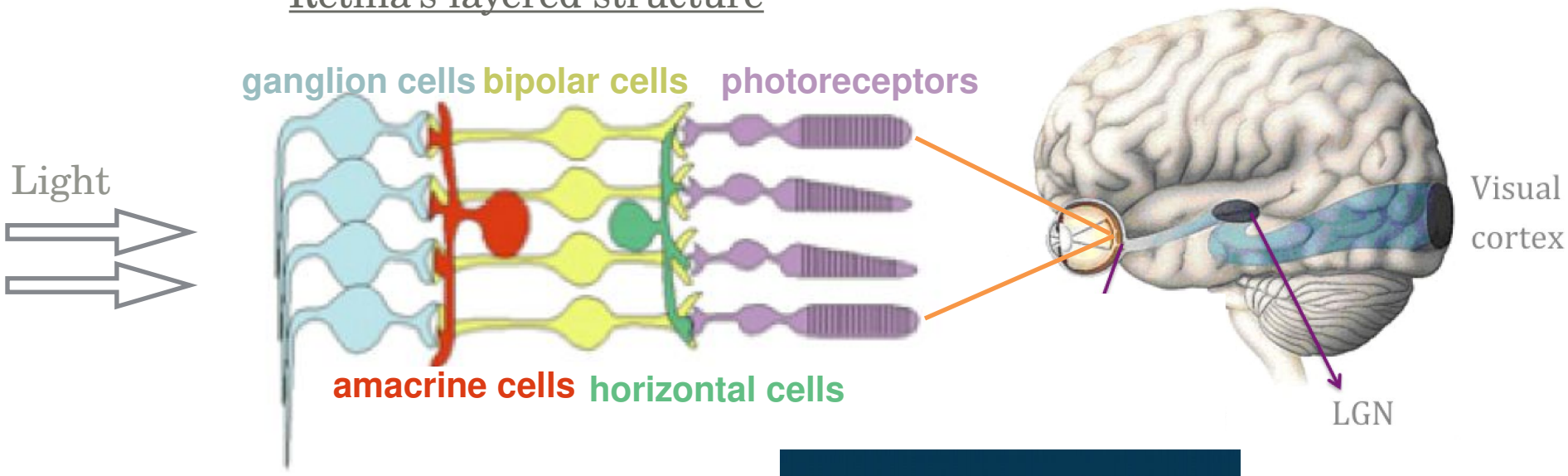
The visual system

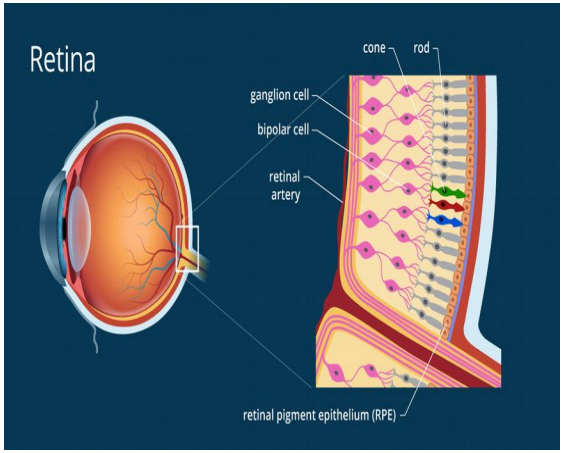




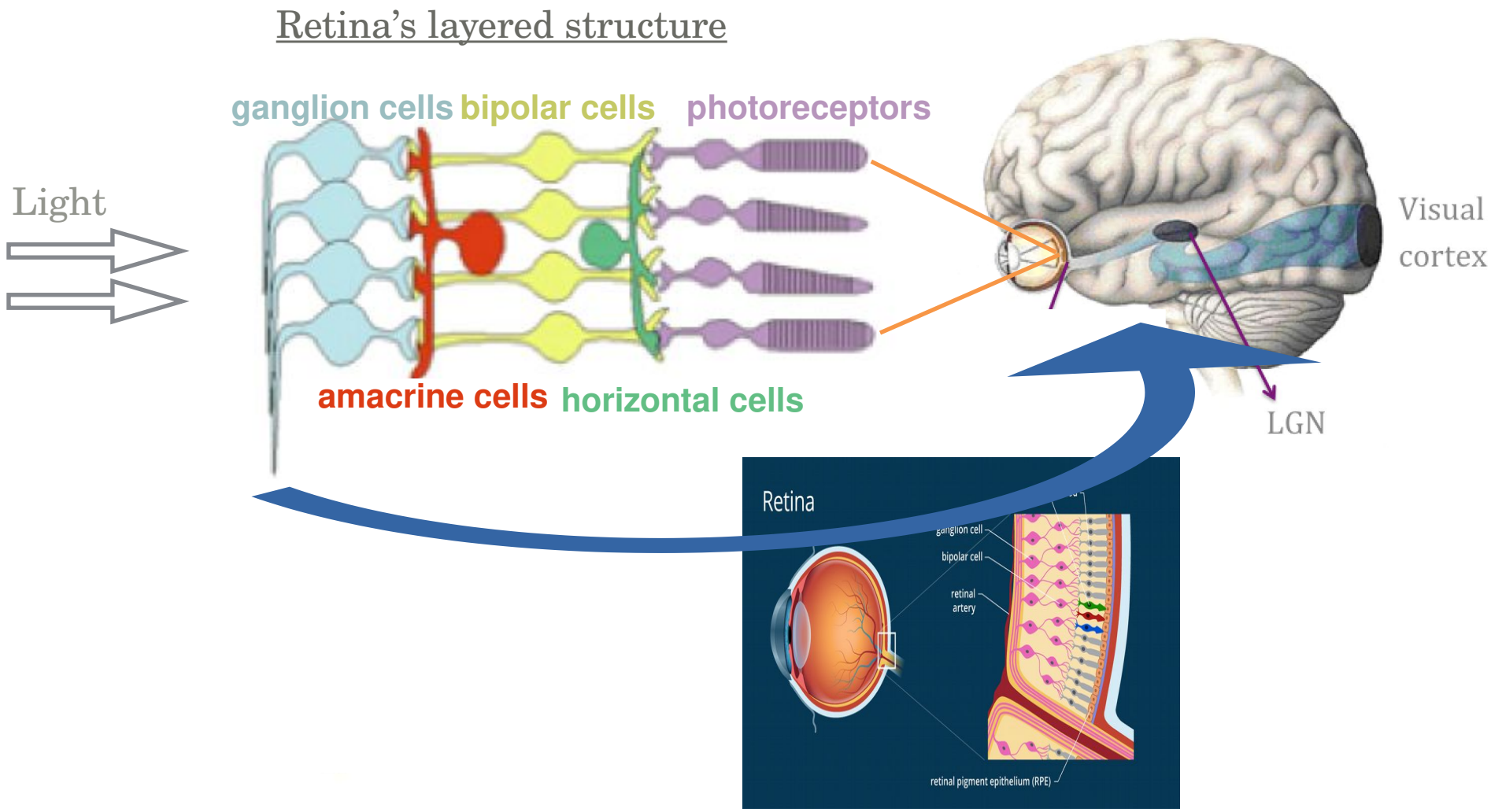
The visual system

Retina's layered structure

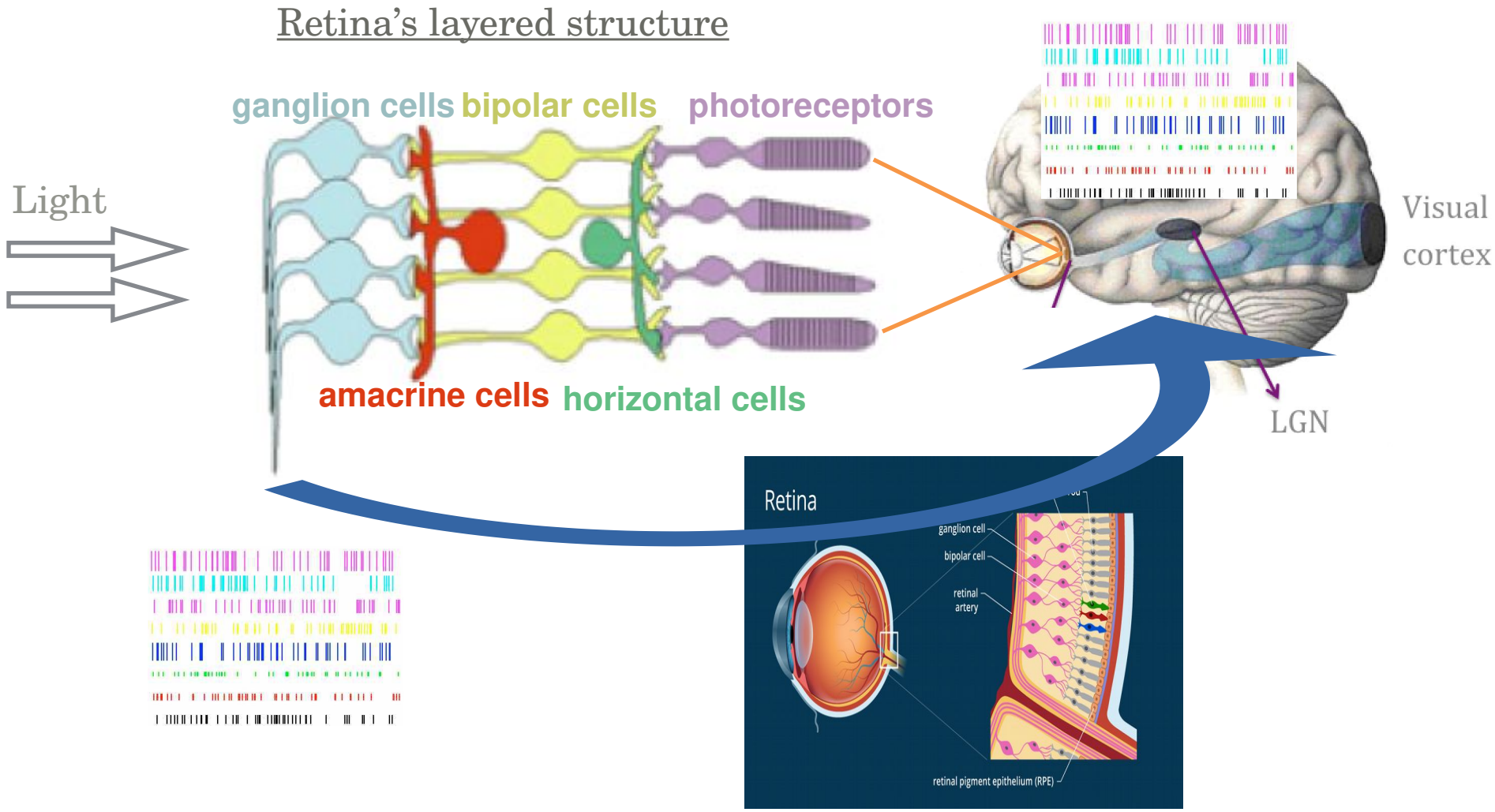




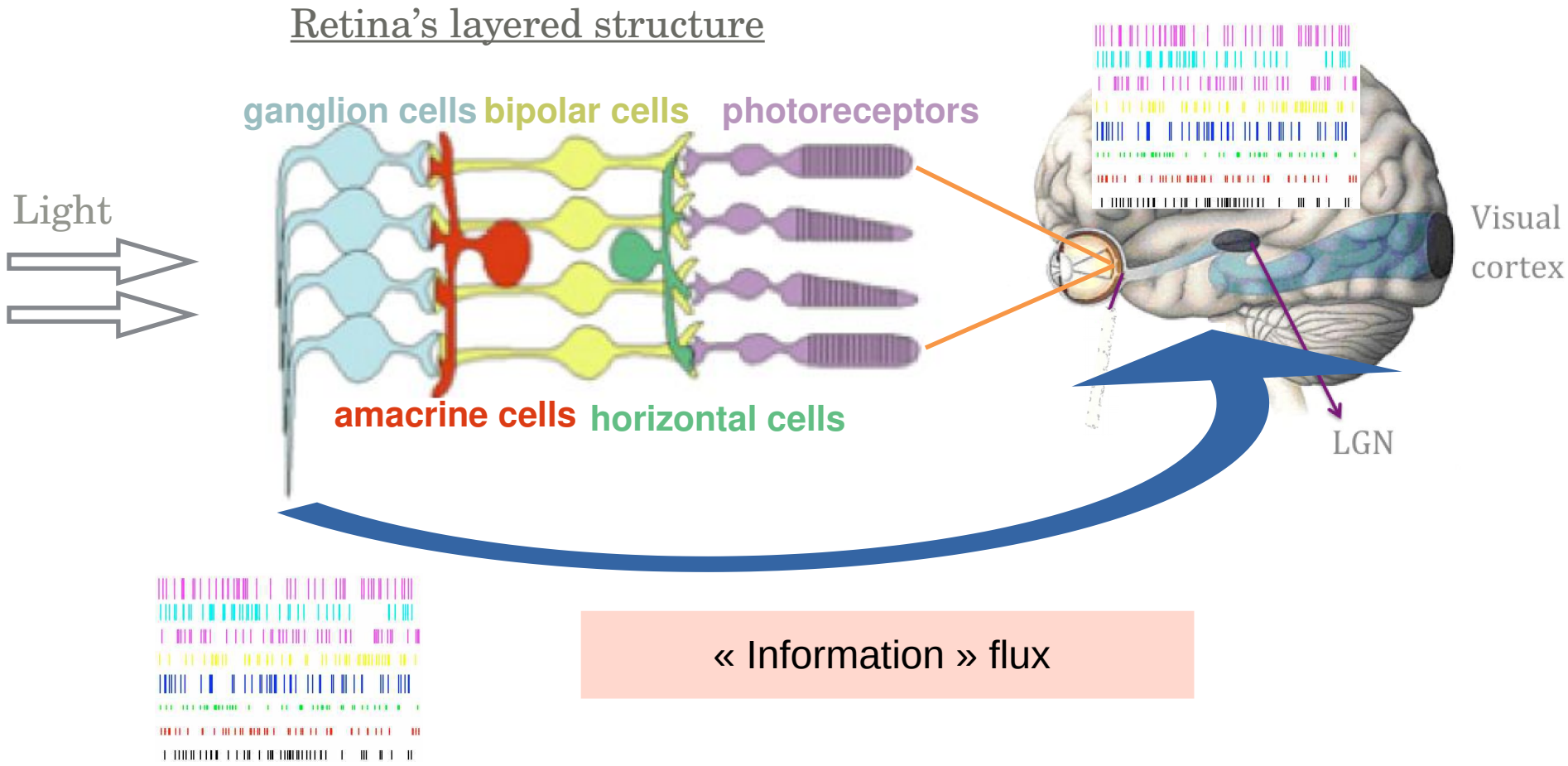
The visual system



The visual system



The visual system

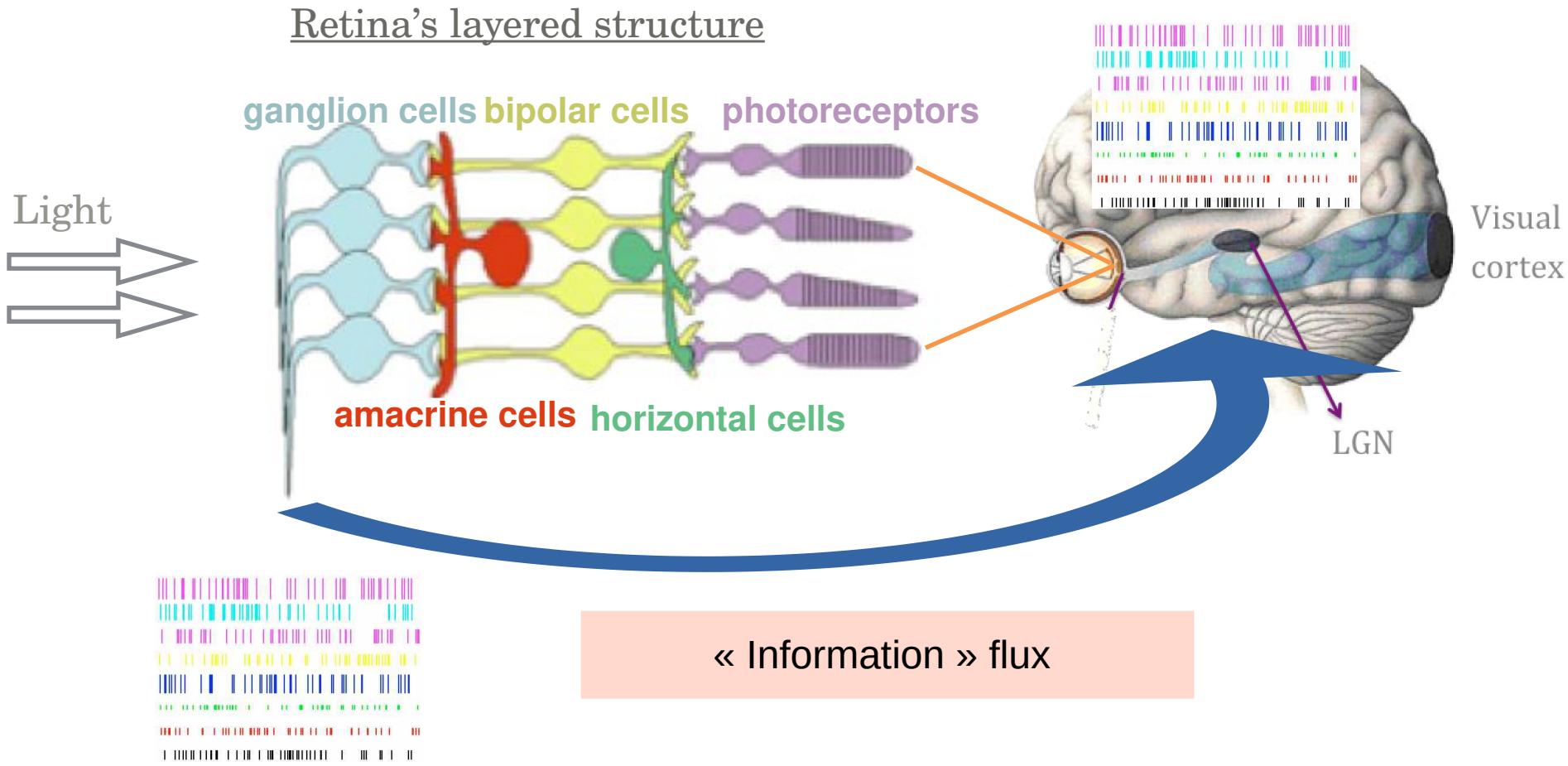


« Information » flux

The visual system

Encoder

Decoder

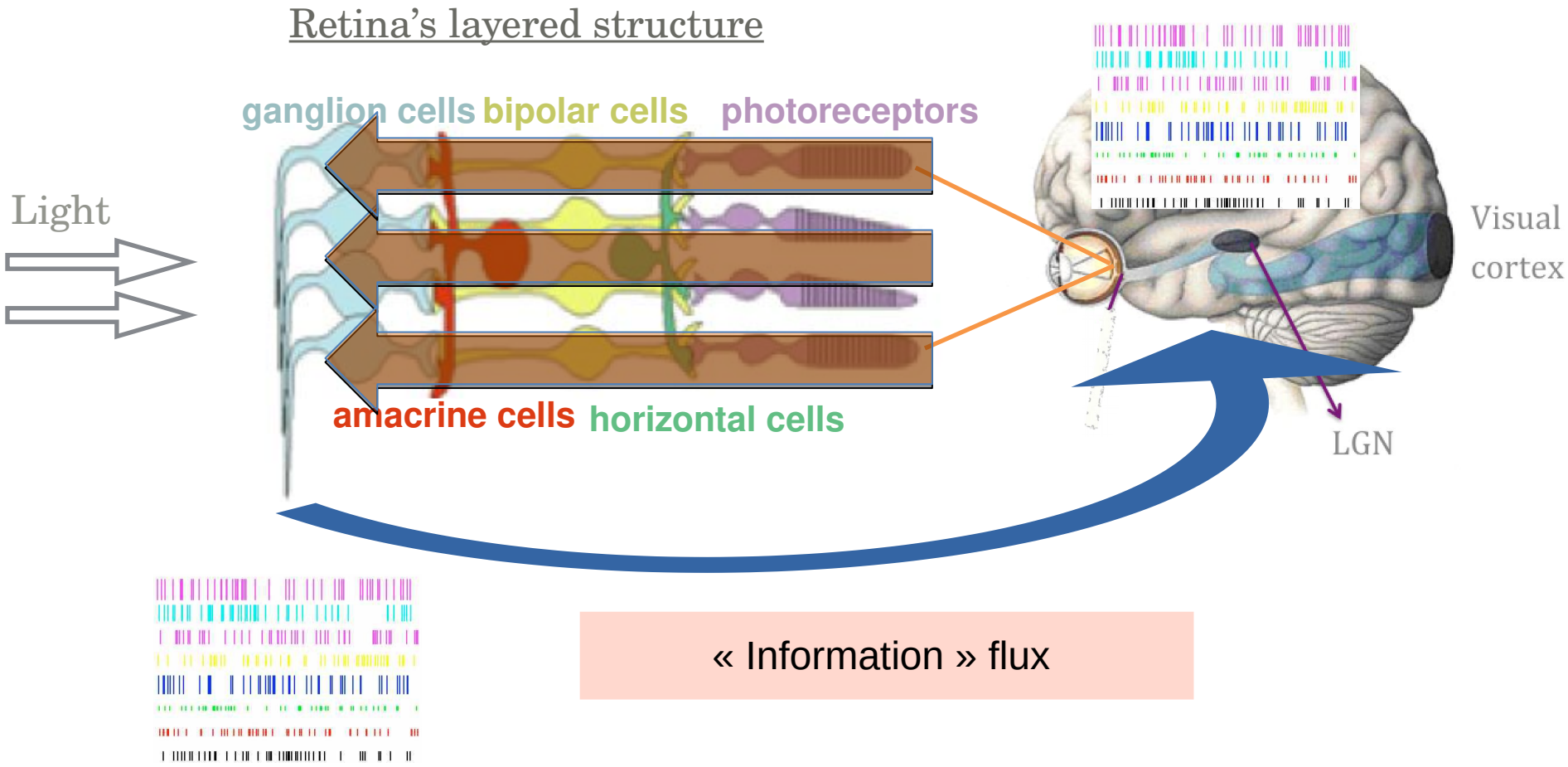


« Information » flux

The visual system

Encoder

Decoder

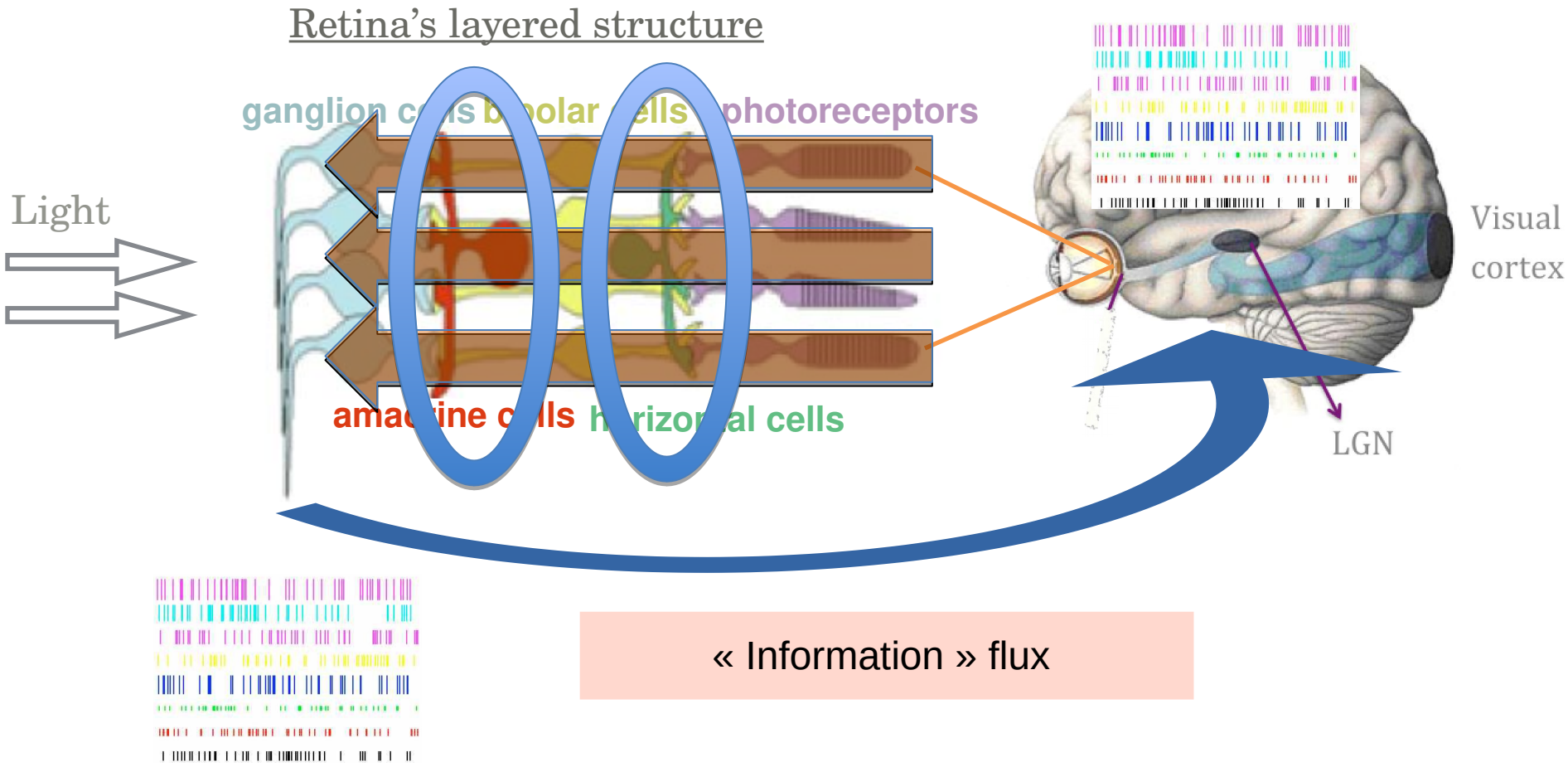


« Information » flux

The visual system

Encoder

Decoder

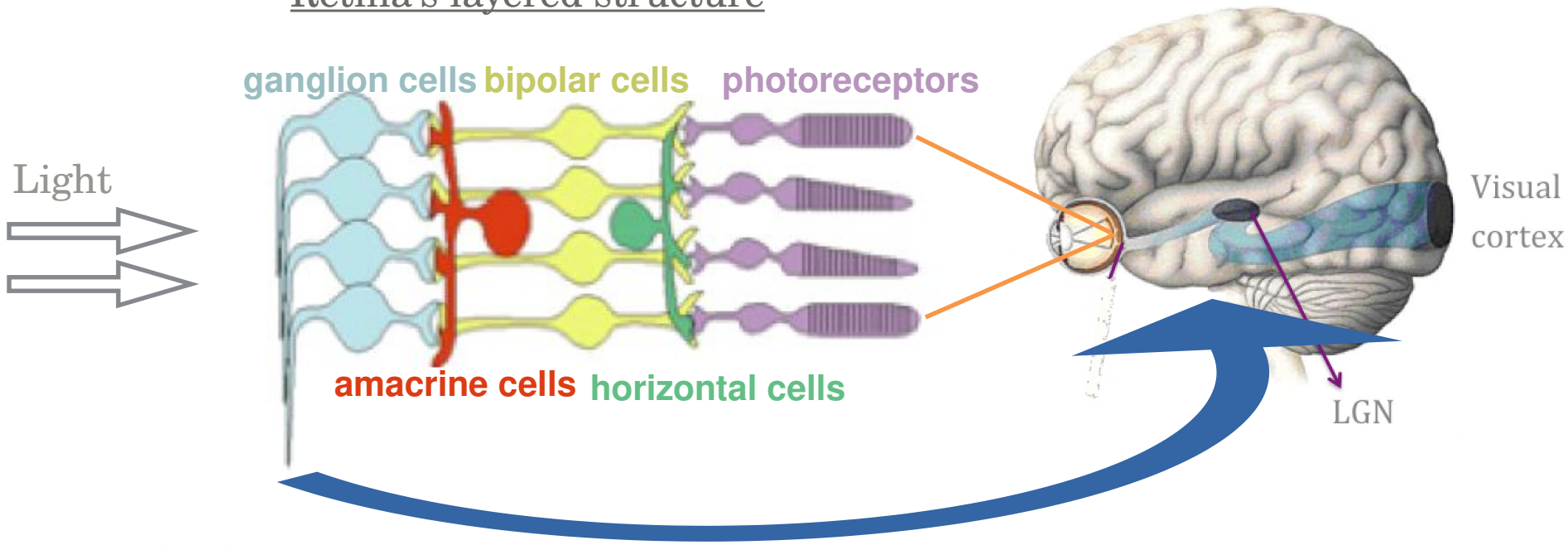


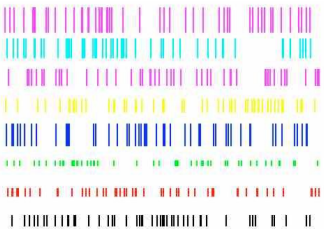
The visual system

Encoder

Decoder

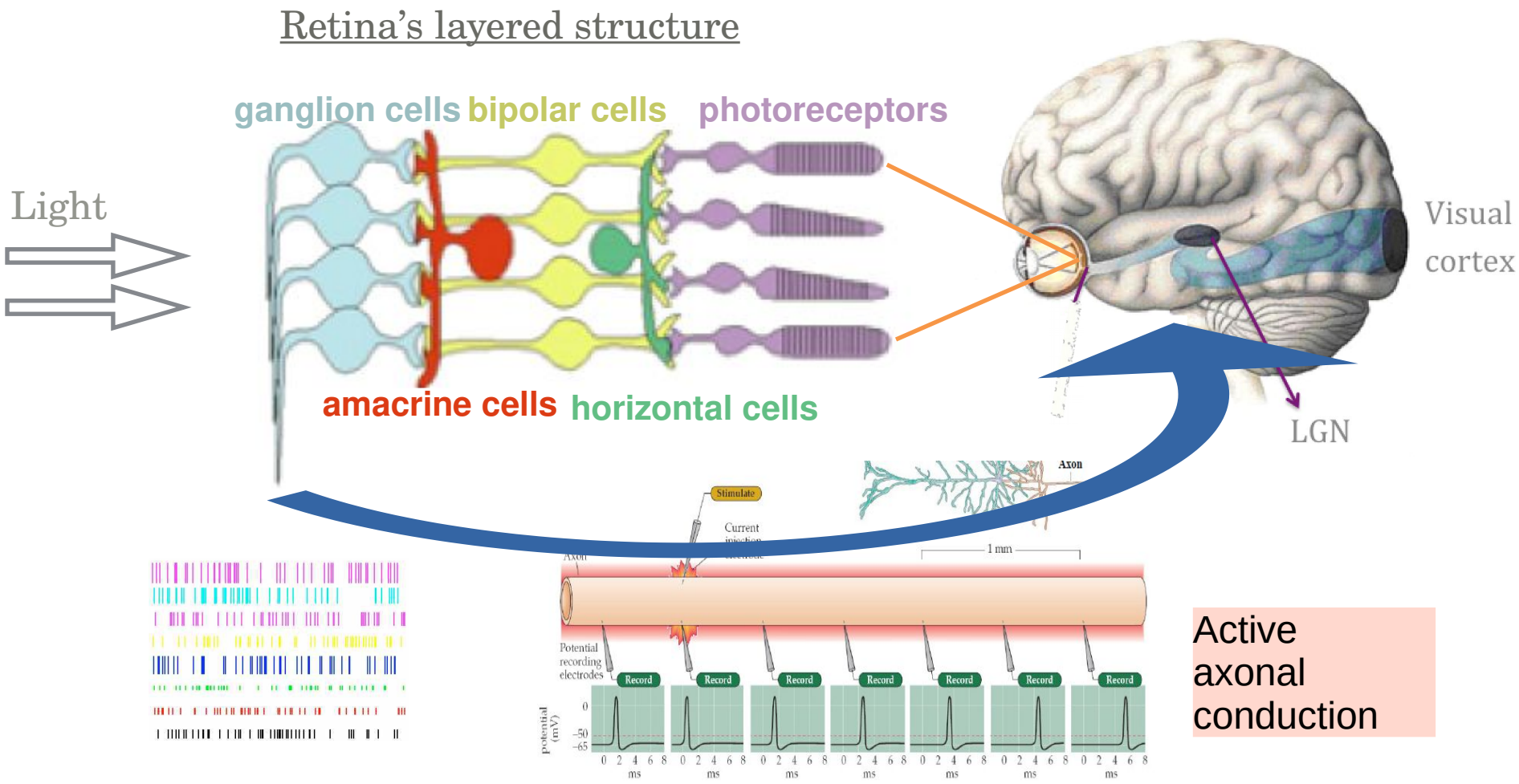
Retina's layered structure





« Information » flux

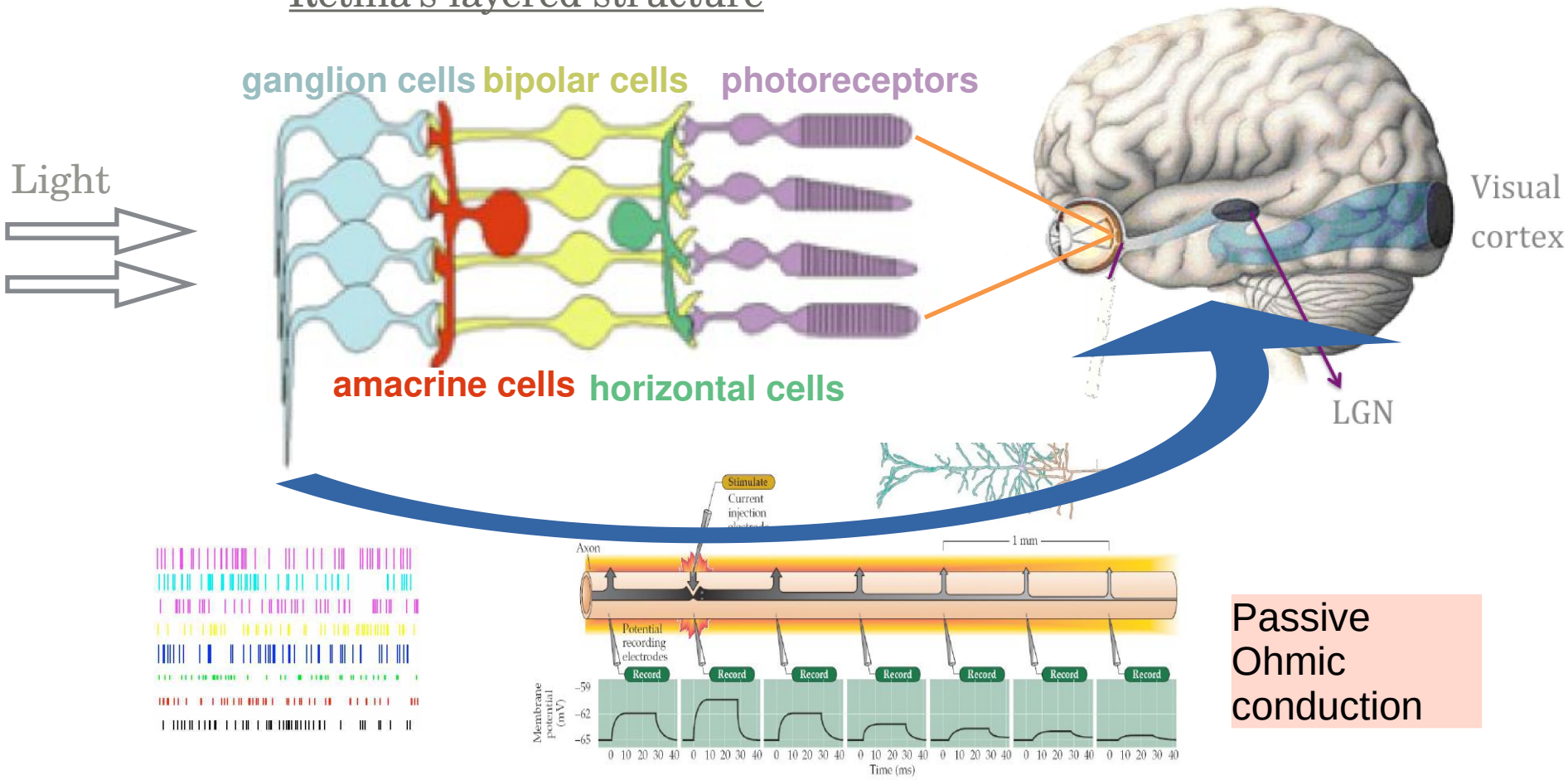
The visual system



Active axonal conduction

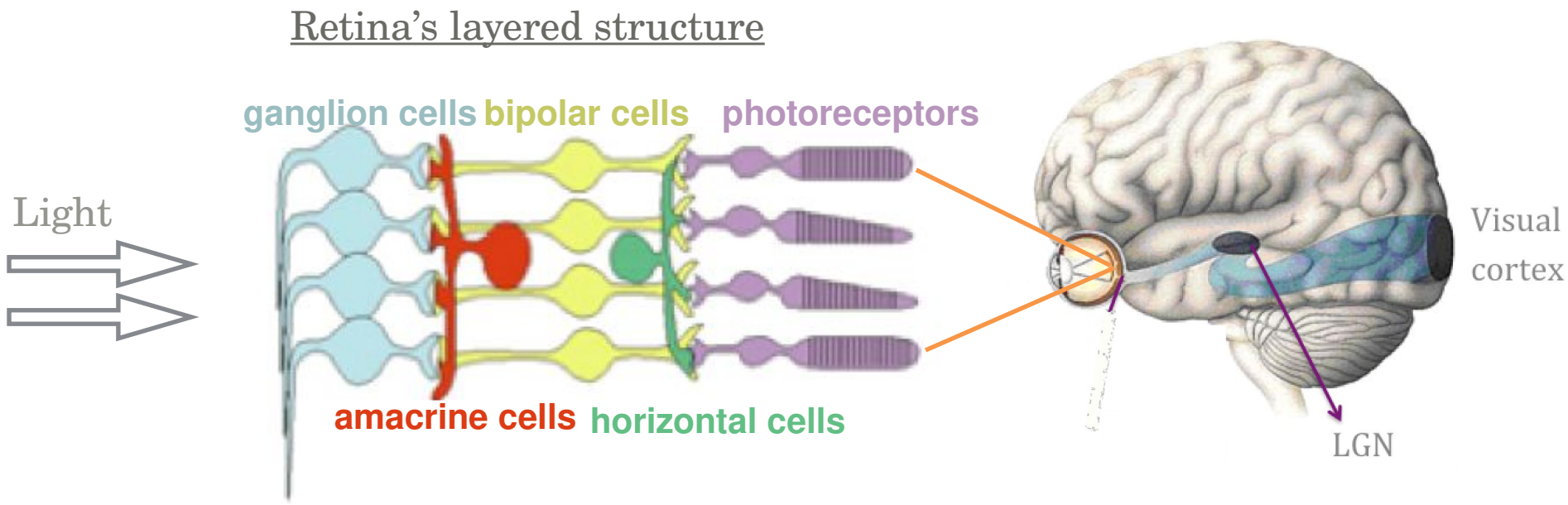
The visual system

Retina's layered structure



Passive Ohmic conduction

The visual system

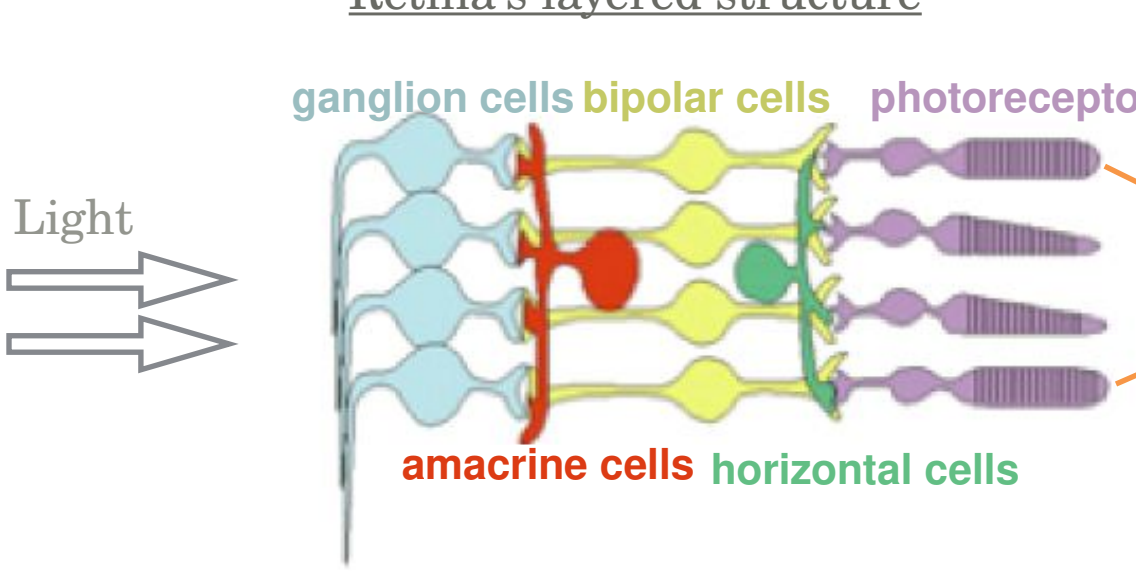


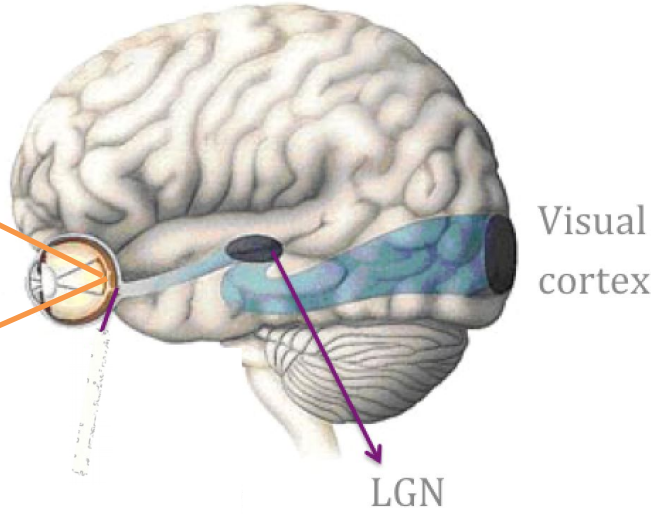
Most neurons in the retina do not spike (except Gcells) =>

« Analogic » computing.

The visual system

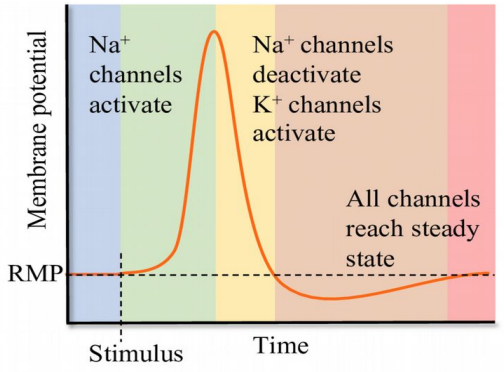
Retina's layered structure



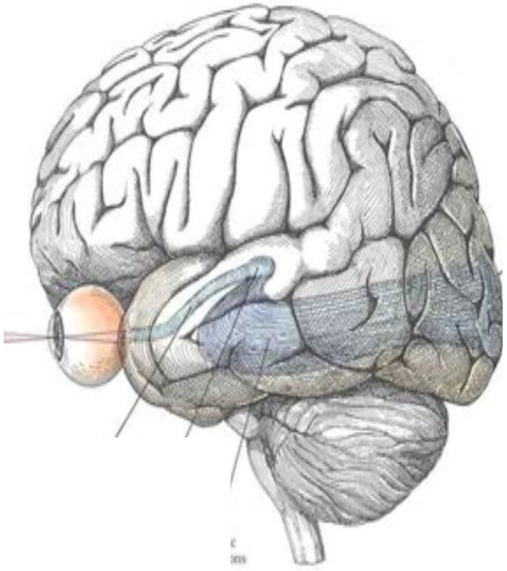


Most neurons in the retina do not spike (except Gcells) =>

« Analogic » computing.

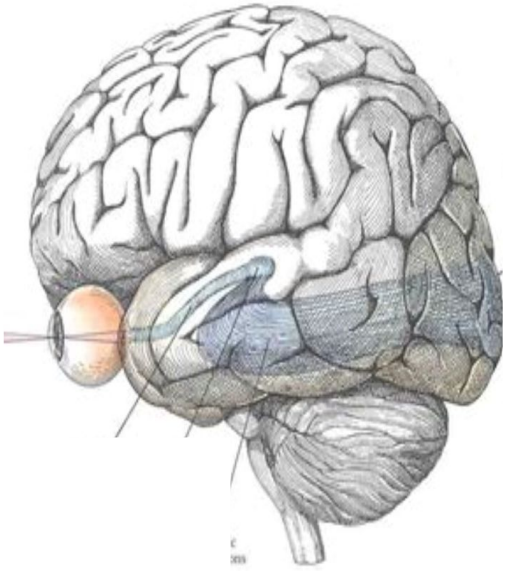


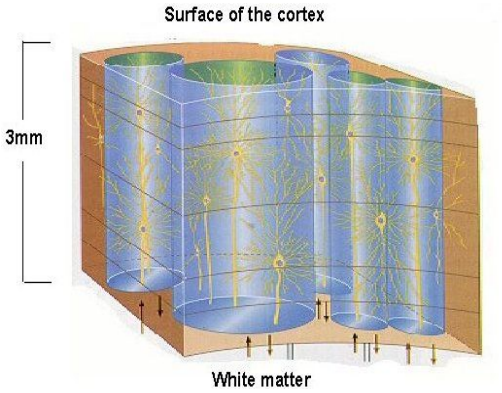
The visual system



The visual system

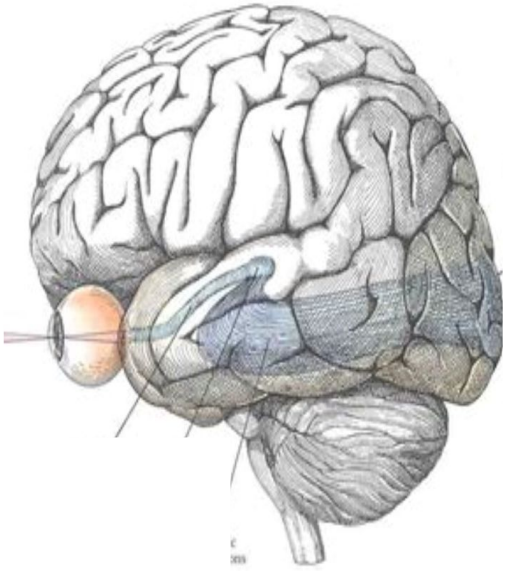
Cortical columns

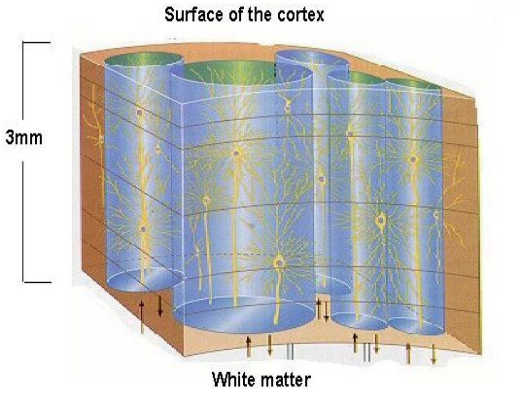


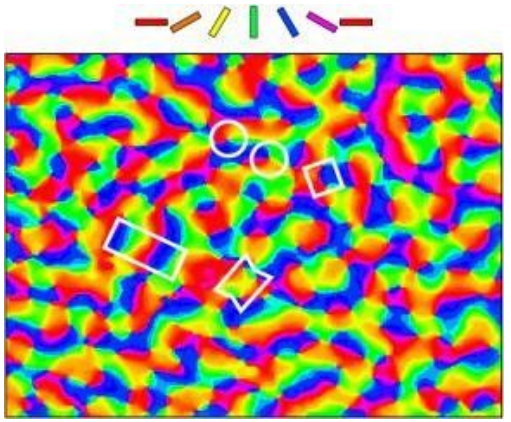


The visual system

Cortical columns



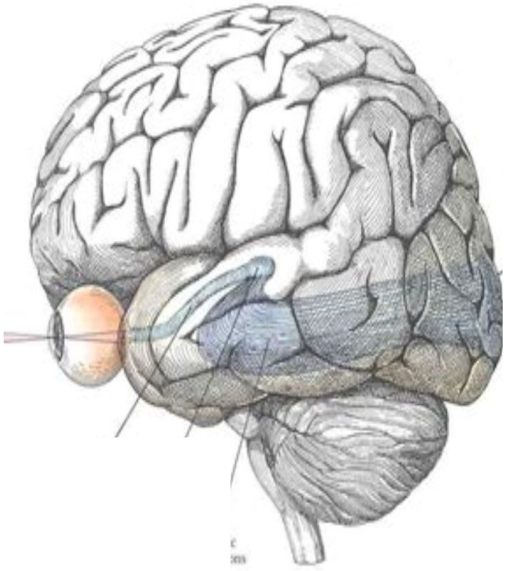


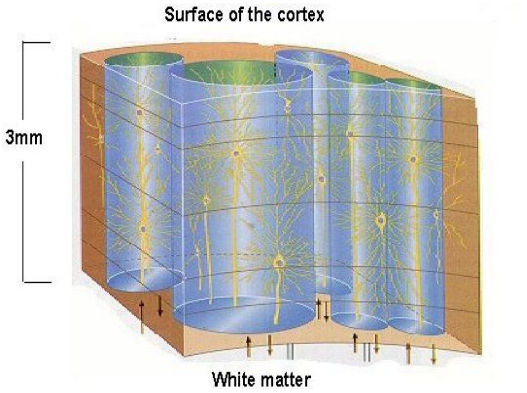


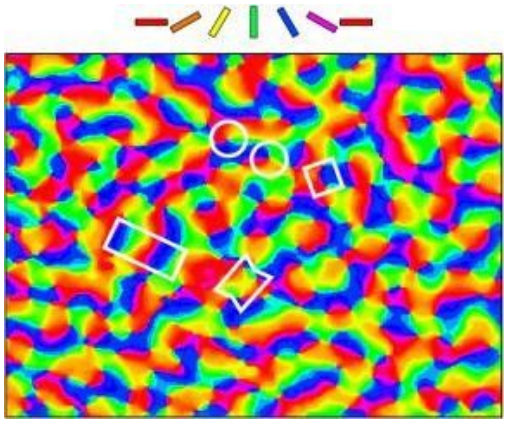
The visual system

Small cylinders, of diameter 0.1~1mm, crossing cortex layers, with about 10^3-10^4 neurons, from different types, strongly connected.

Cortical columns



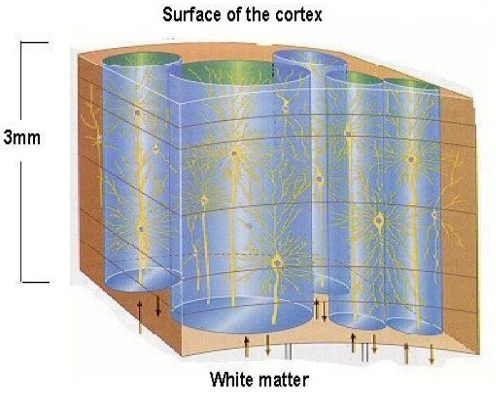




The visual system

Small cylinders, of diameter 0.1~1mm, crossing cortex layers, with about 10^3-10^4 neurons, from different types, strongly connected.

Cortical columns

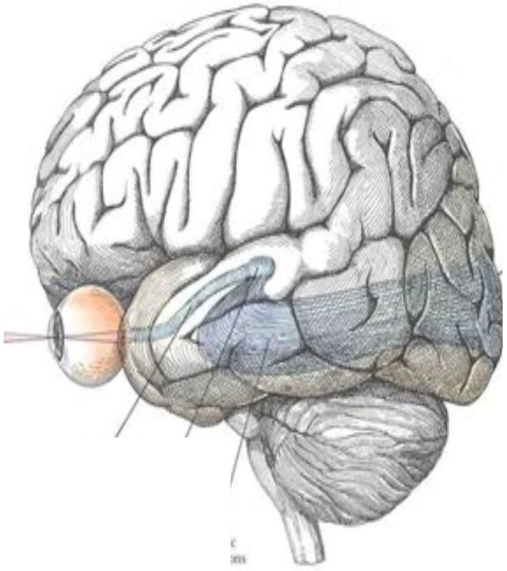


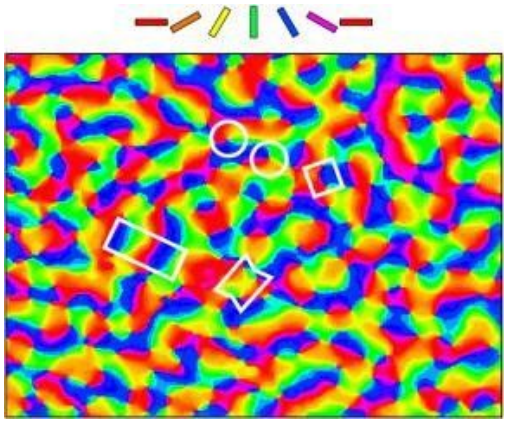
=>

« Field » mesoscopic description (mean-field, neural fields).

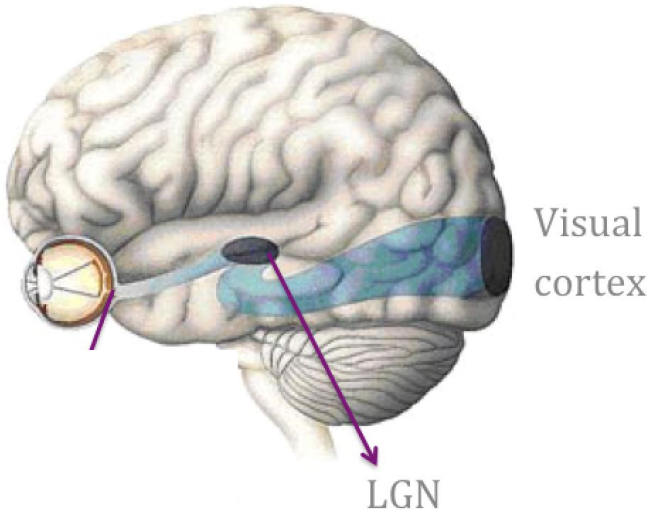
Individual neurons and synapses do not matter.

Population dynamics, PDEs, statistical physics, large deviations ...





The visual system

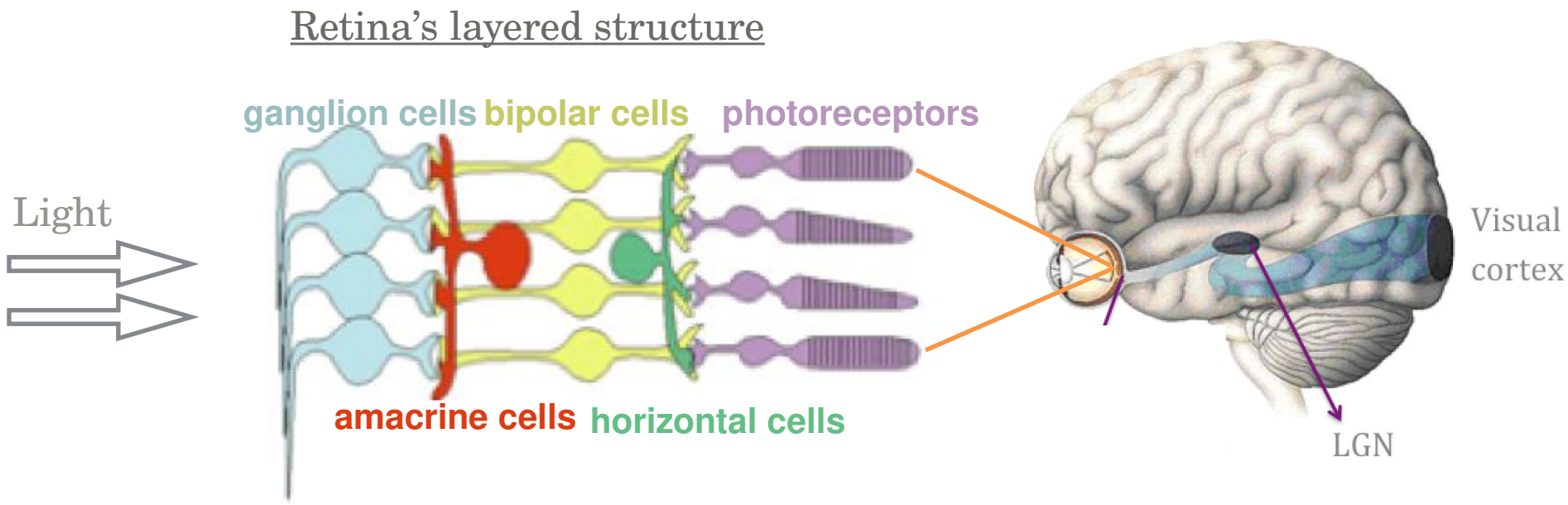


« Information » is processed by spikes.

Individual neurons and synapses do not matter.

Population dynamics, PDEs, statistical physics, large deviations ...

The visual system

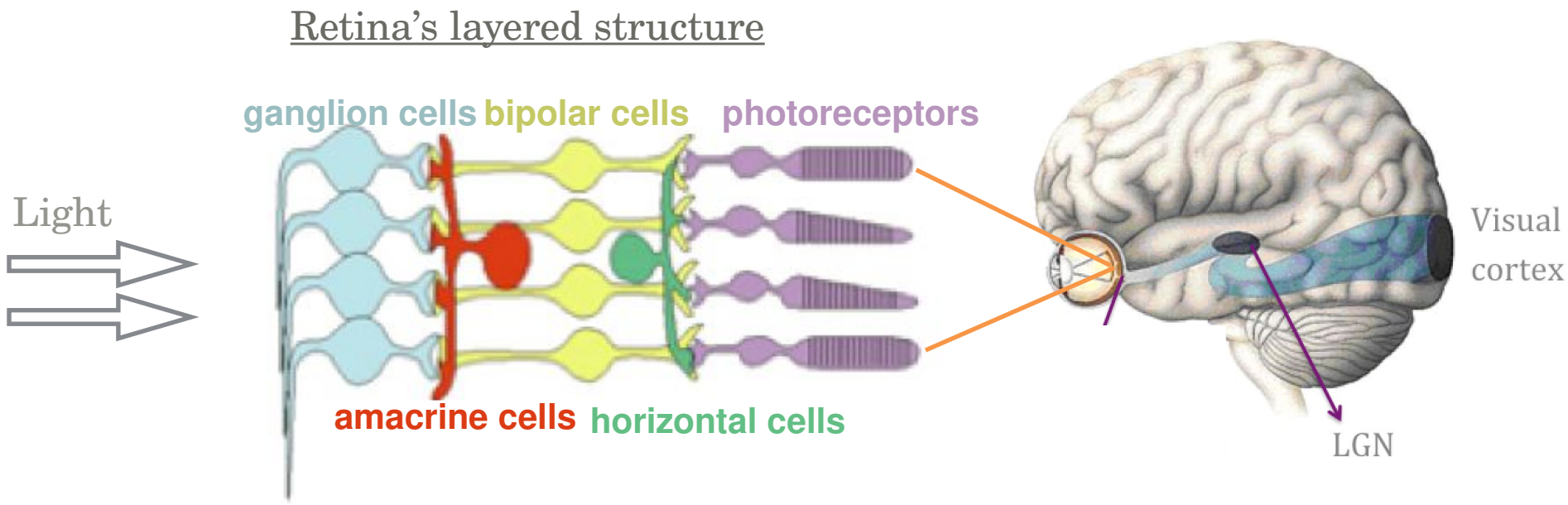


« Information » is processed by spikes.

Individual neurons and synapses do not matter.

Population dynamics, PDEs, statistical physics, large deviations ...

The visual system



Analogic computing.

No spikes except at GCells

Individual neurons and synapses DO matter.

Dedicated circuits made of a few neurons and synapses process the local visual information.

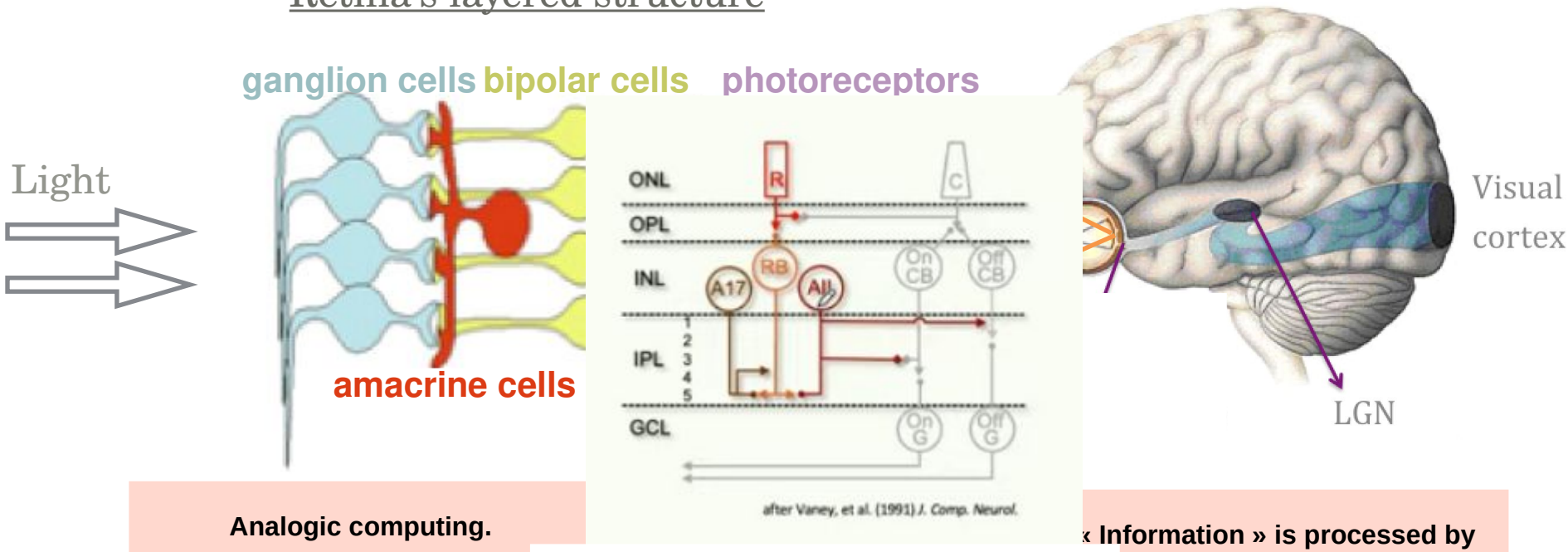
« Information » is processed by spikes.

Individual neurons and synapses do not matter.

Population dynamics, PDEs, statistical physics, large deviations ...

The visual system

Retina's layered structure



Analogic computing.

No spikes except at GCells

Individual neurons and synaps DO matter.

Dedicated circuits made of a f neurons and synapses process the local visual information.

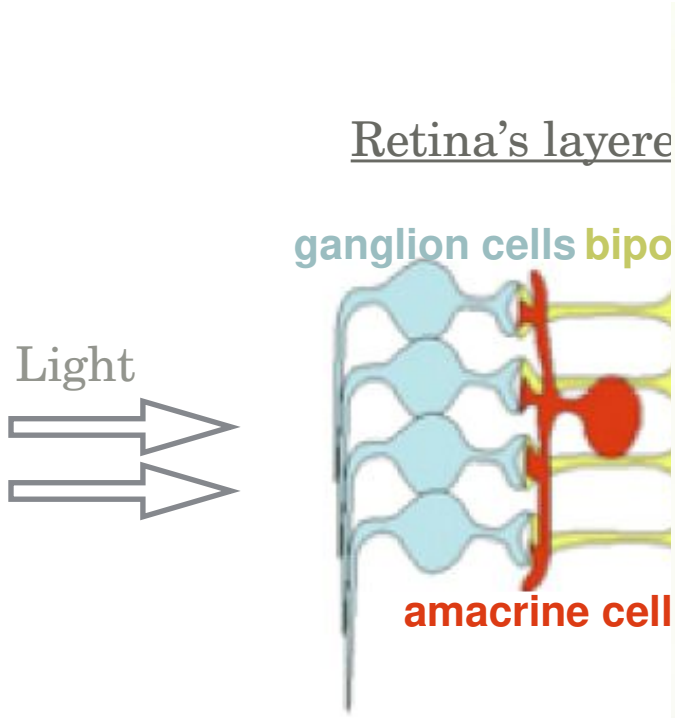
See J. Diamond talk at https://www.youtube.com/watch?v=sB29yq-ewYI&t=1036s

« Information » is processed by spikes.

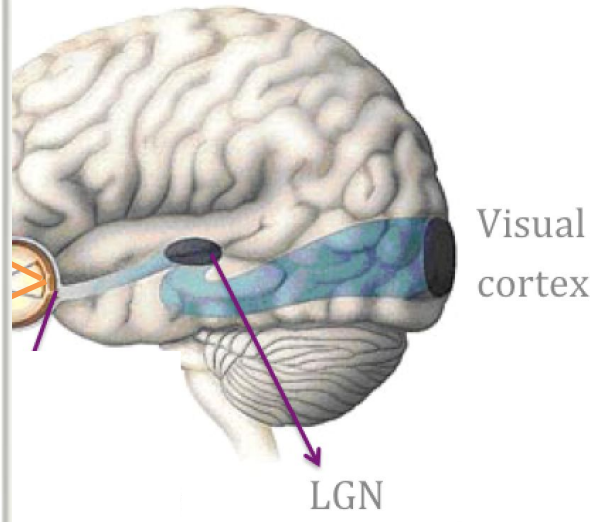
dual neurons and synapses do not matter.

opulation dynamics, PDEs, statistical physics, large deviations ...

The visual system







Analogic computing.

No spikes except at GCells

Individual neurons and synaps DO matter.

Dedicated circuits made of a f neurons and synapses process the local visual information.

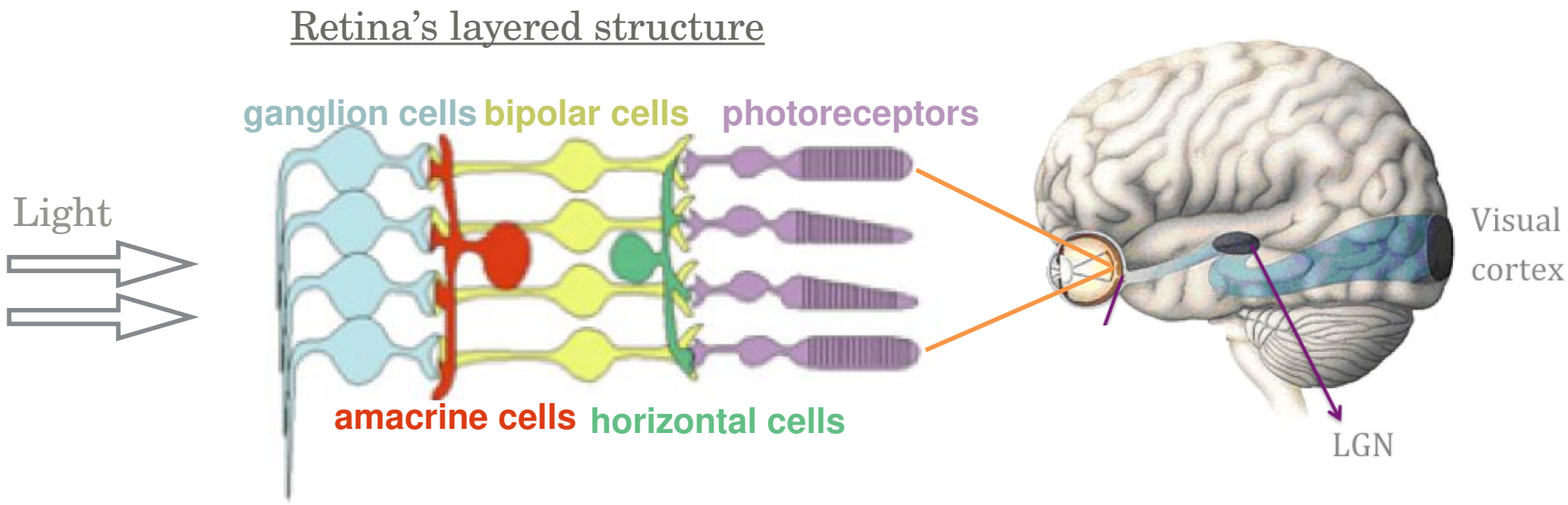
See J. Diamond talk at https://www.youtube.com/watch?v=sB29yq-ewYI&t=1036s

Information » is processed by spikes.

dual neurons and synapses do not matter.

opulation dynamics, PDEs, statistical physics, large deviations ...

The visual system



Analogic computing.

No spikes except at GCells

Individual neurons and synapses DO matter.

Dedicated circuits made of a few neurons and synapses process the local visual information.

« Information » is processed by spikes.

Individual neurons and synapses do not matter.

Population dynamics, PDEs, statistical physics, large deviations ...

A modeller point of view

1. The retina is a ***high dimensional***, ***non autonomous and noisy*** dynamical system, layered and structured, with ***non stationary and spatially inhomogeneous entries*** (visual scenes).

A modeller point of view

1. The retina is a ***high dimensional***, ***non autonomous and noisy*** dynamical system, layered and structured, with ***non stationary and spatially inhomogeneous entries*** (visual scenes).

2. ***Local circuits*** of non linear cells, connected with non linear synapses efficiently process the ***local visual information***. These local circuits are connected together, spanning the whole retina in a ***regular tiling***.

A modeller point of view

1. The retina is a ***high dimensional***, ***non autonomous and noisy*** dynamical system, layered and structured, with ***non stationary and spatially inhomogeneous entries*** (visual scenes).

2. ***Local circuits*** of non linear cells, connected with non linear synapses efficiently process the ***local visual information***. These local circuits are connected together, spanning the whole retina in a ***regular tiling***.

3. The conjunction of non linearities and regular structure can produce a highly ***disordered spatio-temporal*** dynamics.

A modeller point of view

1. The retina is a ***high dimensional***, ***non autonomous and noisy*** dynamical system, layered and structured, with ***non stationary and spatially inhomogeneous entries*** (visual scenes).

2. ***Local circuits*** of non linear cells, connected with non linear synapses efficiently process the ***local visual information***. These local circuits are connected together, spanning the whole retina in a ***regular tiling***.

3. The conjunction of non linearities and regular structure can produce a highly ***disordered spatio-temporal*** dynamics.

4. The retina is sensitive to ***changes in its physiology*** (development, pharmacology, pathologies). These changes can be addressed from the point of view of ***bifurcations theory***.

The Biovision lab

Understanding the normal visual system at neuronal and perceptual levels

- *Better understanding the early visual system*
- *Reading, moving, behaving in 3D virtual environments*
- *Analysis of visual media and user perception*

Understanding the impact of low vision at neuronal and perceptual levels

- *Modeling of retinal prostheses stimulation and cortical responses*
- *Understanding eccentric vision pointing for selection and identification*
- *Understanding low vision impact on attentional and oculo-motor behaviors when reading*
- *Attentional and behavioural studies using virtual reality*

Diagnosis, rehabilitation, and low vision aids

- *Exploring new solutions for diagnosis*
- *Designing rehabilitation methods in virtual reality (VR)*
- *Developing innovative vision-aid digital systems*

Retinal waves

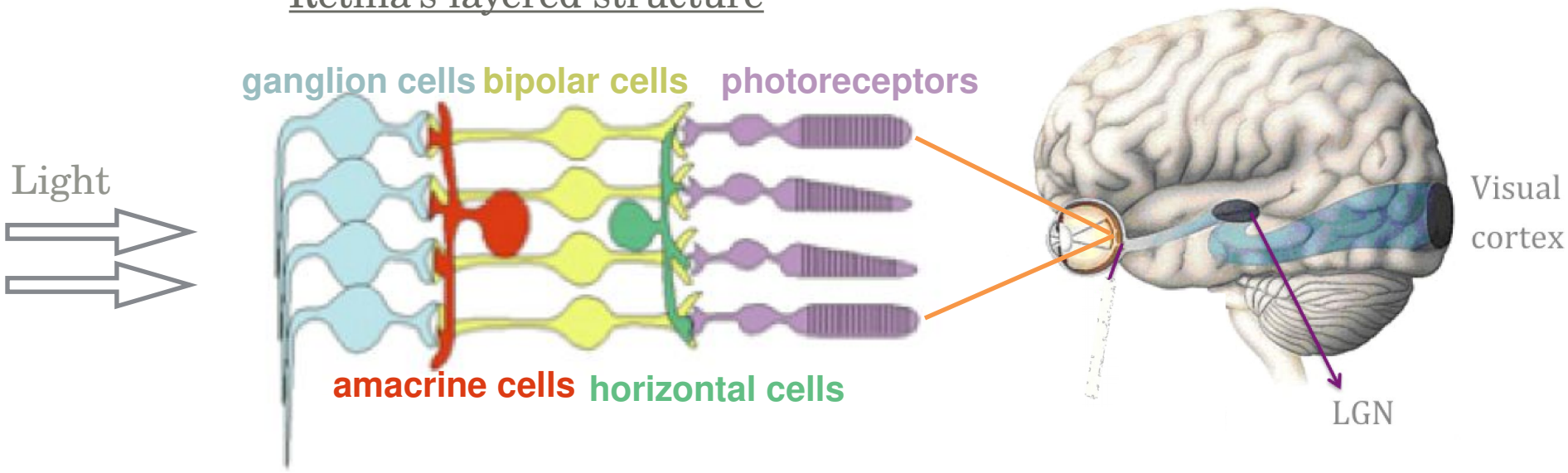
Random dynamical structures in the developing visual system

D. Karvouniari (PhD 2014-2018), Biovision team, INRIA, Sophia Antipolis
L. Gil, InPhyNi, Nice-Sophia-Antipolis
O. Marre, Institut de la Vision, Paris
S. Picaud, Institut de la Vision, Paris
B. Cessac, Biovision team, INRIA, Sophia Antipolis

Acknowledgement: M. Hennig (U. Edinburgh), E. Sernagor (U. Newcastle).

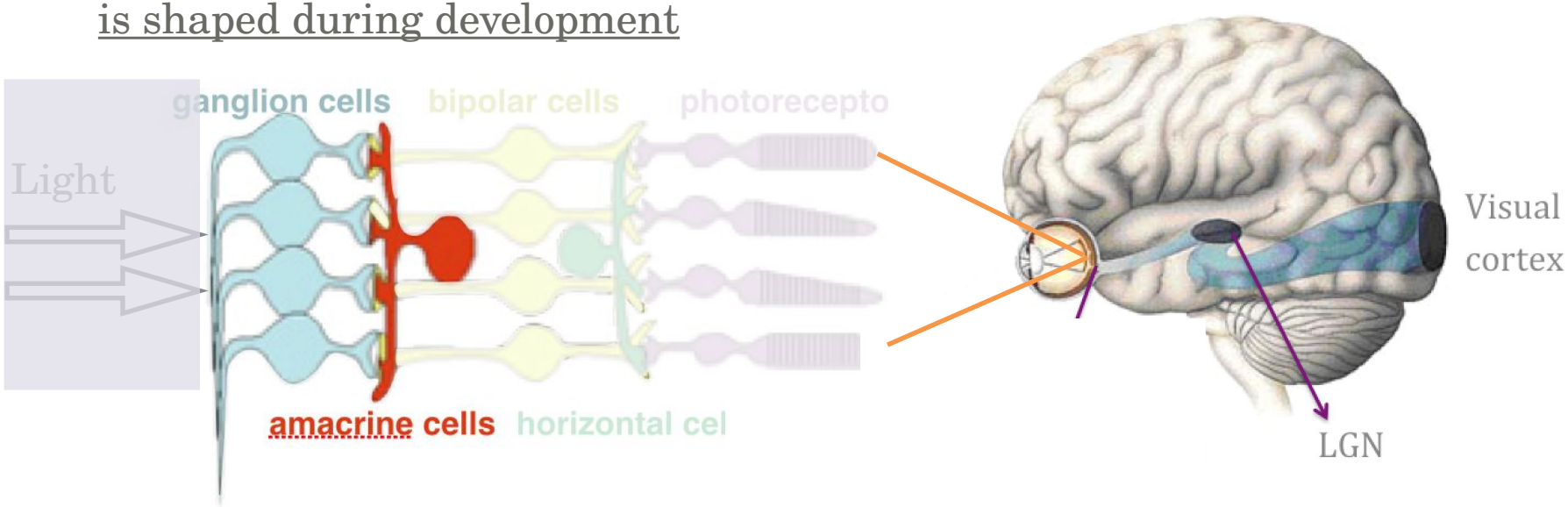
The structure of the adult retina

Retina's layered structure



The structure of the retina during development

Retina's layered structure
is shaped during development

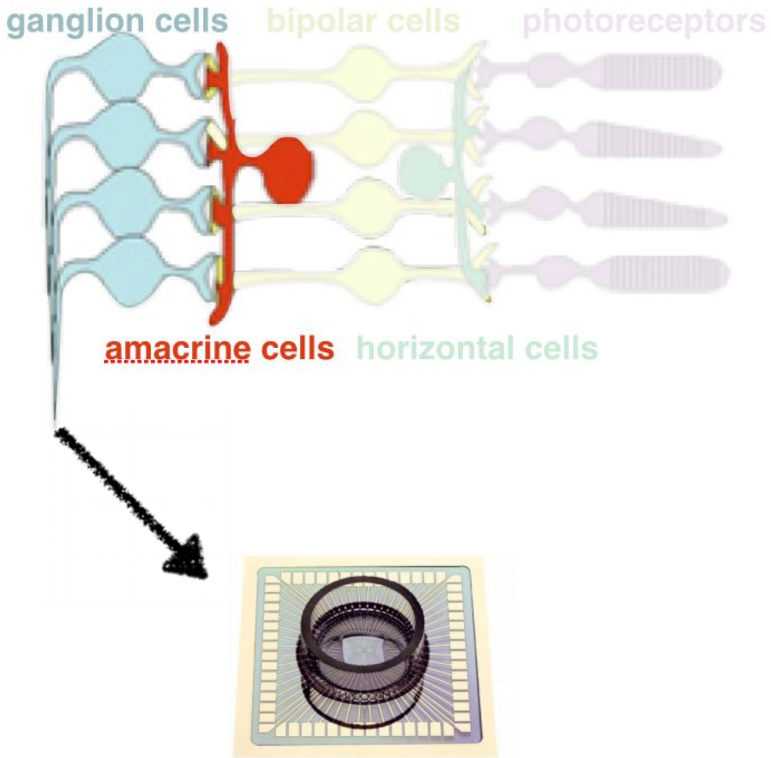


But How? ⇒ **Retinal waves!**

Retinal waves

Spontaneous spatio-temporal waves during development
Disappear short after birth when vision is functional

Recordings from the retina

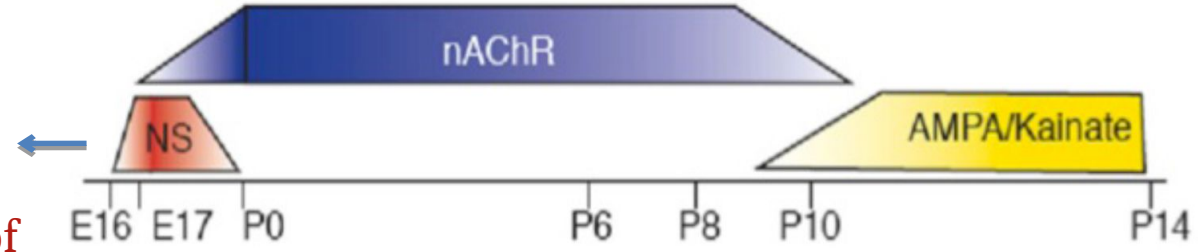


Multi-electrode array (MEA)

MEA recording of the voltage from a mouse retina (courtesy E Sernagor).

Stages of Retinal Waves During Development

Stage I

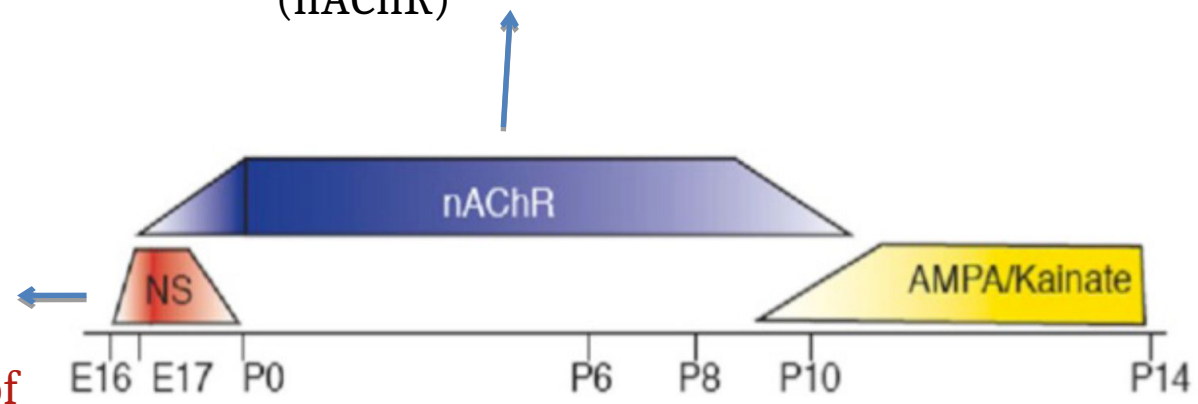


- Formation of retina circuitry
- Chemical synapses not formed yet
- Gap juction-mediated

Stages of Retinal Waves During Development

Stage II

- Retinotopic mapping
- Nicotinic Acetylcholine Receptors (nAChR)



Stage I

- Formation of retina circuitry
- Chemical synapses not formed yet
- Gap juction-mediated

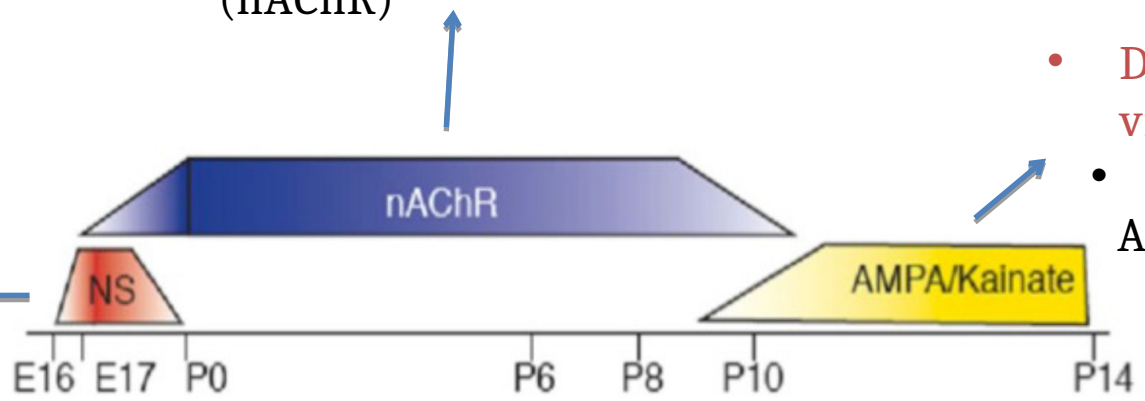
Stages of Retinal Waves During Development

Stage II

- Retinotopic mapping
- Nicotinic Acetylcholine Receptors (nAChR)

Stage III

- Disappear when vision is functional
- Glutamate – AMPA receptors



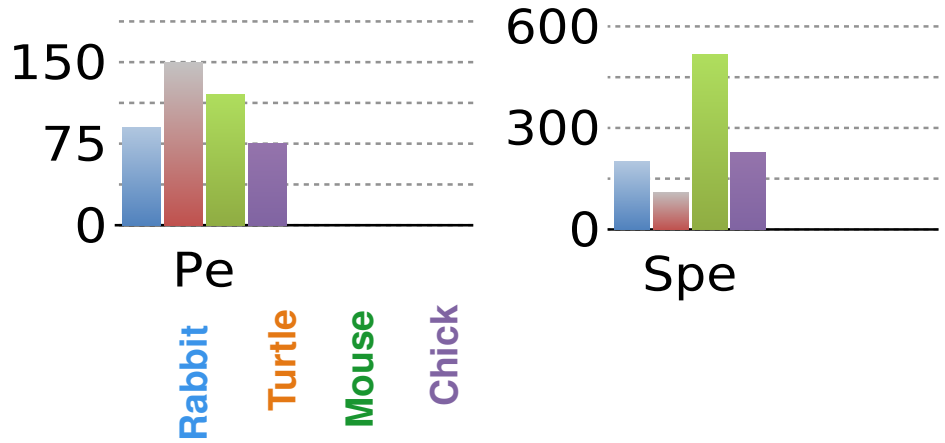
Stage I

- Formation of retina circuitry
- Chemical synapses not formed yet
- Gap juction-mediated

Variability within retinal waves

i) Across species

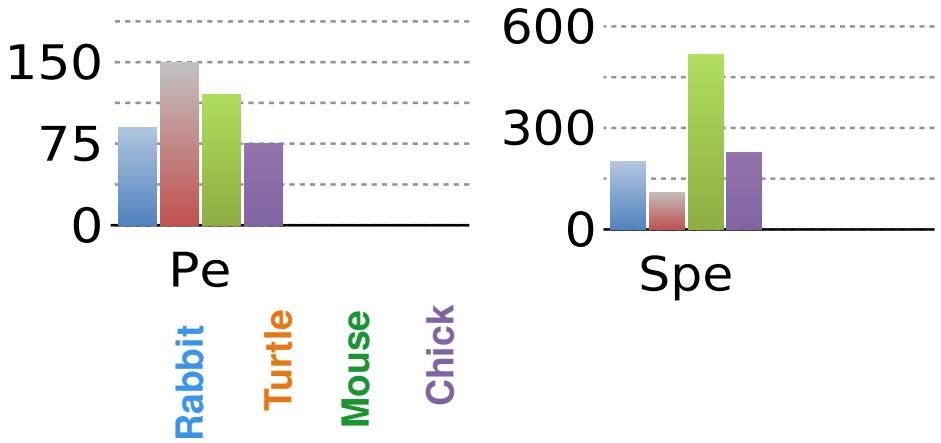
Godfrey et al. 2007



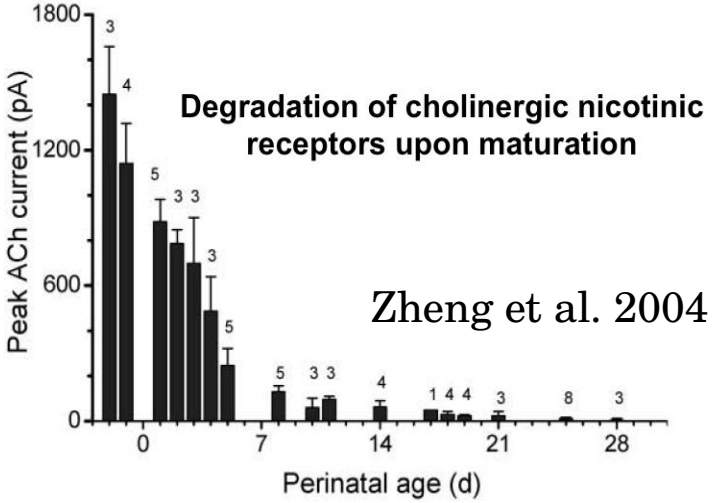
Variability within retinal waves

i) Across species

Godfrey et al. 2007



ii) Development

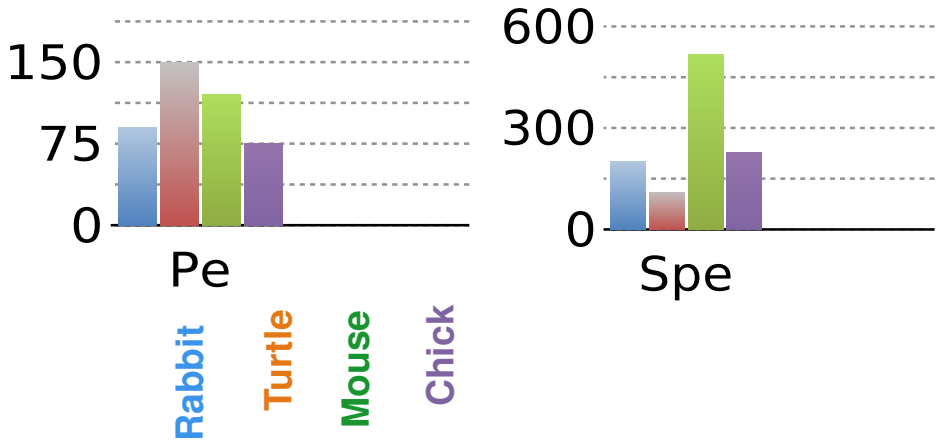


Zheng et al. 2004

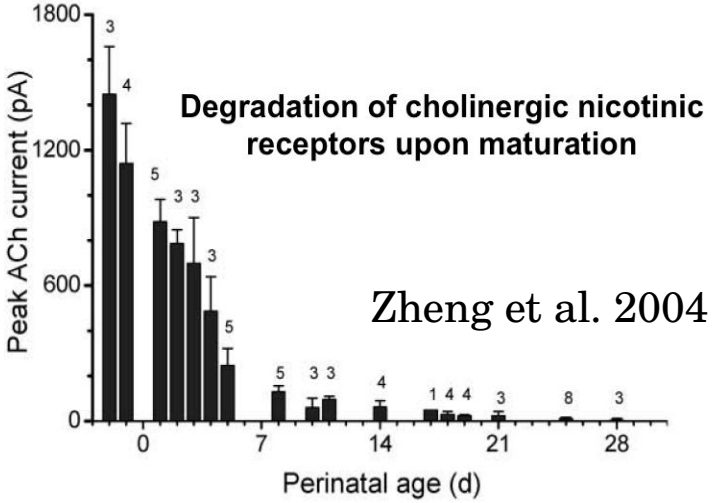
Variability within retinal waves

i) Across species

Godfrey et al. 2007

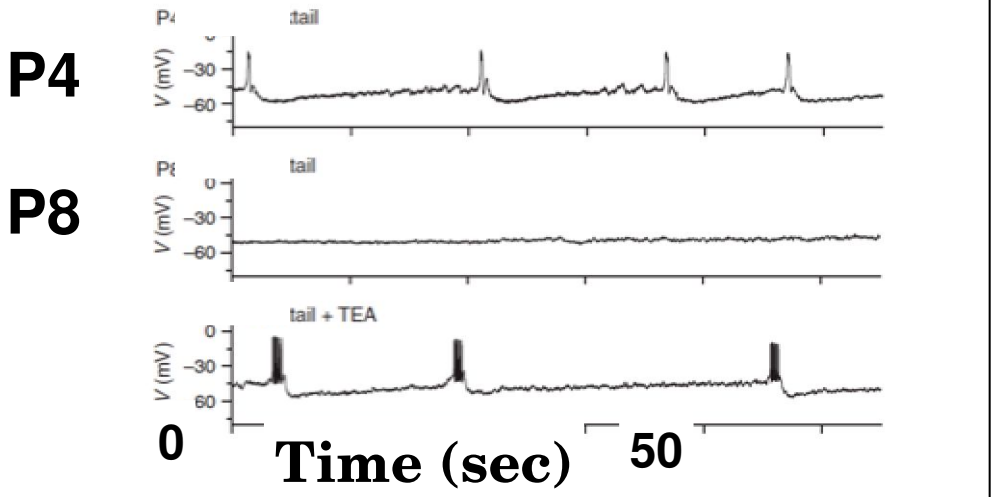


ii) Development



Zheng et al. 2004

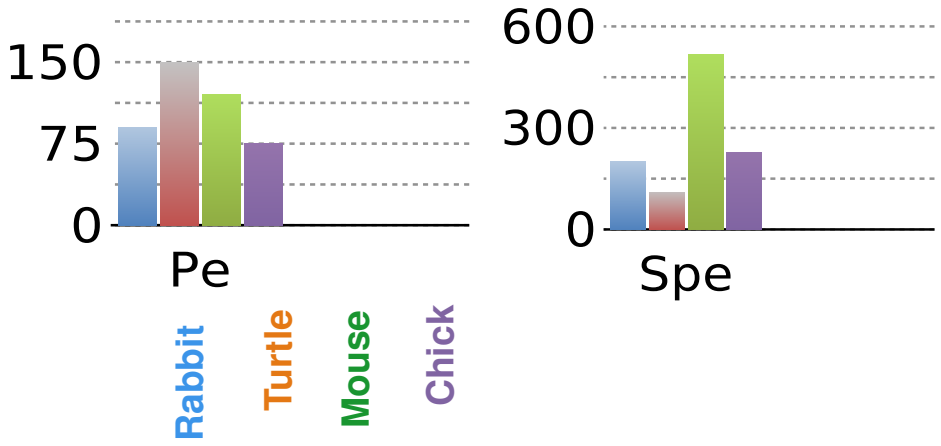
iii) Pharmacology



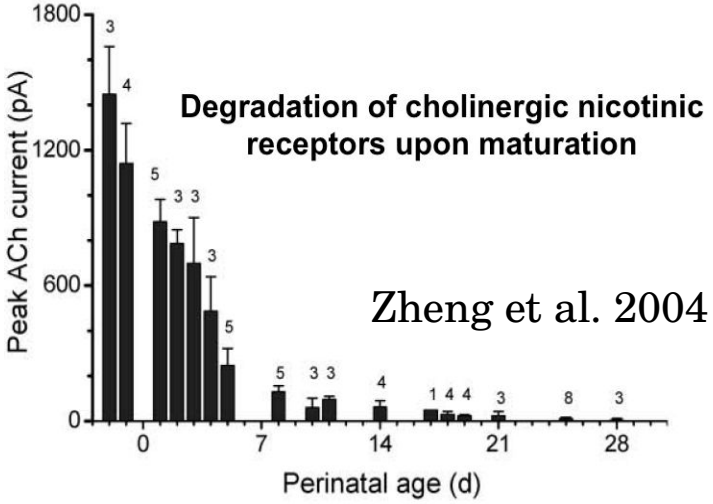
Variability within retinal waves

i) Across species

Godfrey et al. 2007

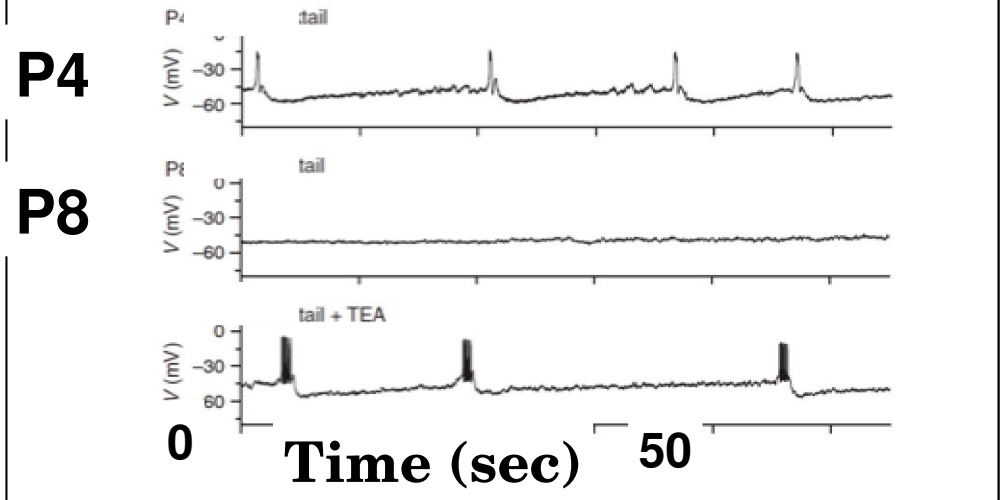


ii) Development



Zheng et al. 2004

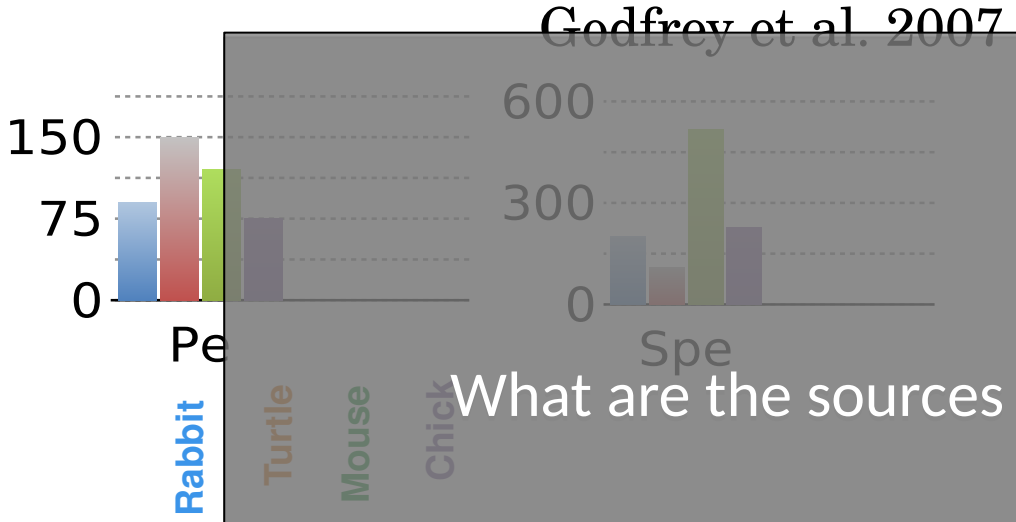
iii) Pharmacology



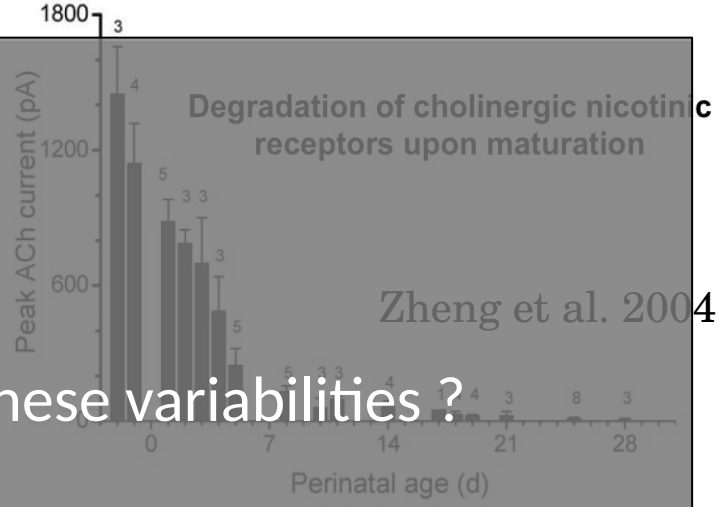
iv) Spatial Variability

Variability within retinal waves

i) Across species



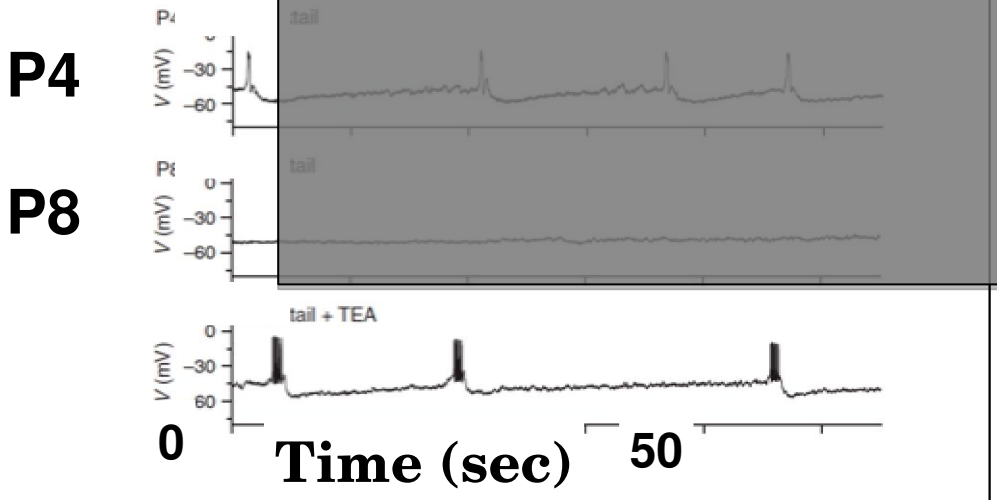
ii) Development



What are the sources of these variabilities ?

Is there a unique, global, mechanism explaining them ?

iii) Pharmacology

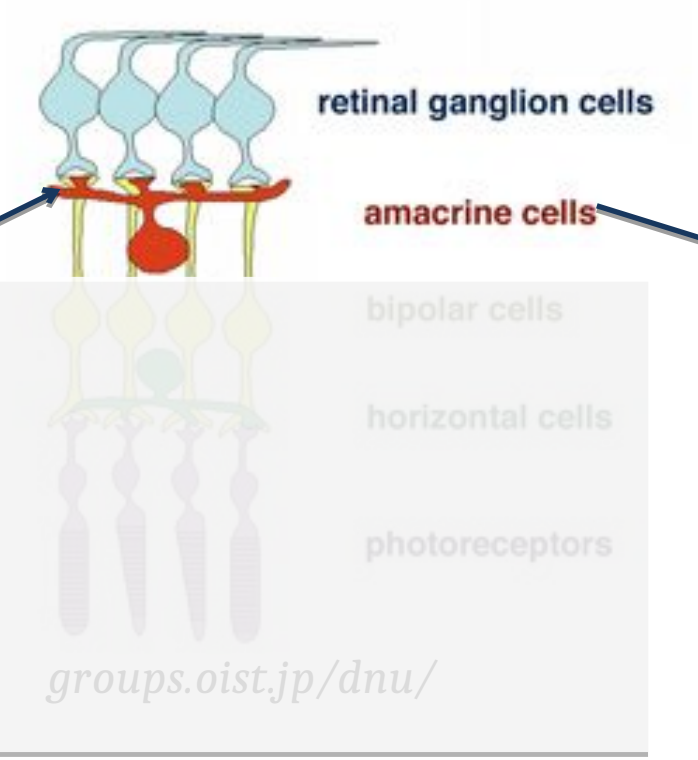


iv) Spatial Variability

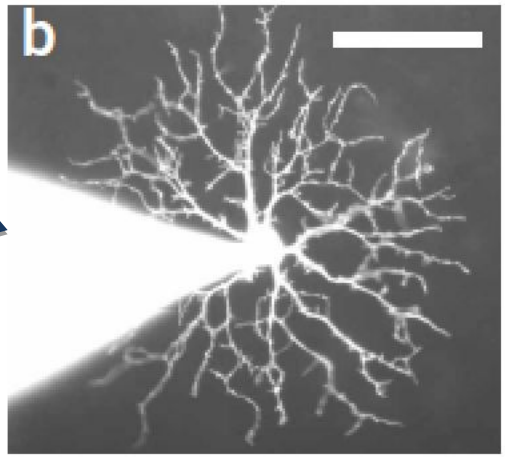
Focus on stage II retinal waves

Stage II retinal waves are well studied experimentally and there is already existing work on their modeling

Stage II (cholinergic retinal waves)



Starburst Amacrine Cell (SAC)

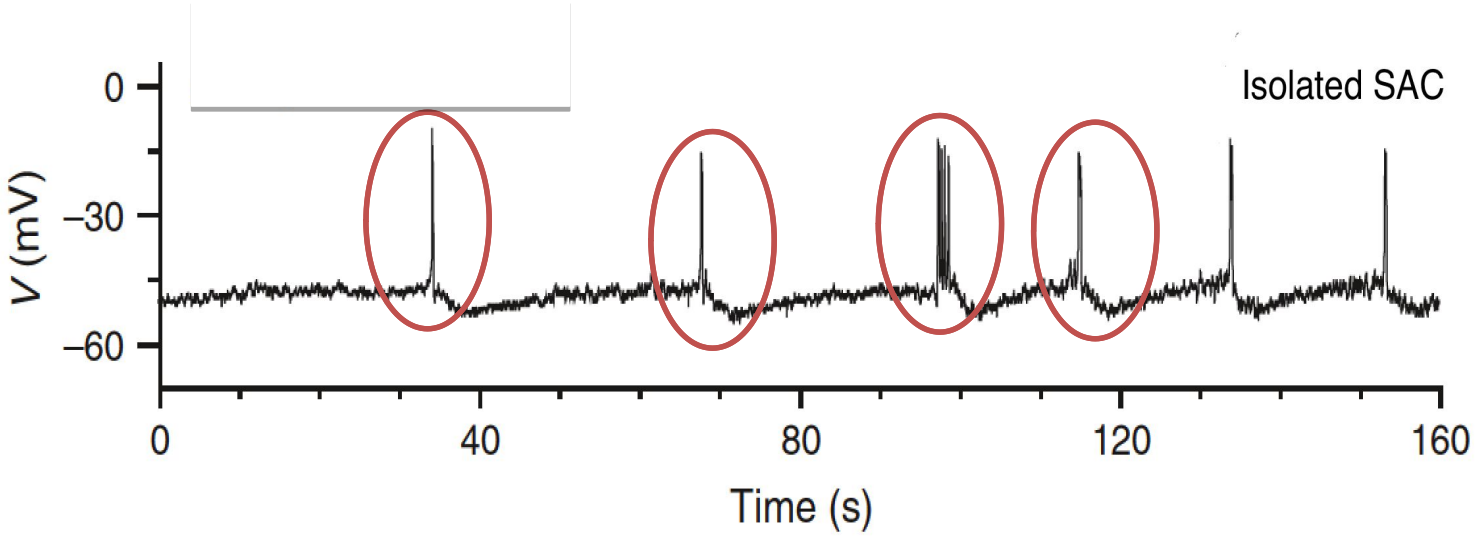


Zheng et al. 2006

Experiments for the emergence of retinal waves

Retinal waves require three components:

i) Spontaneous bursting activity



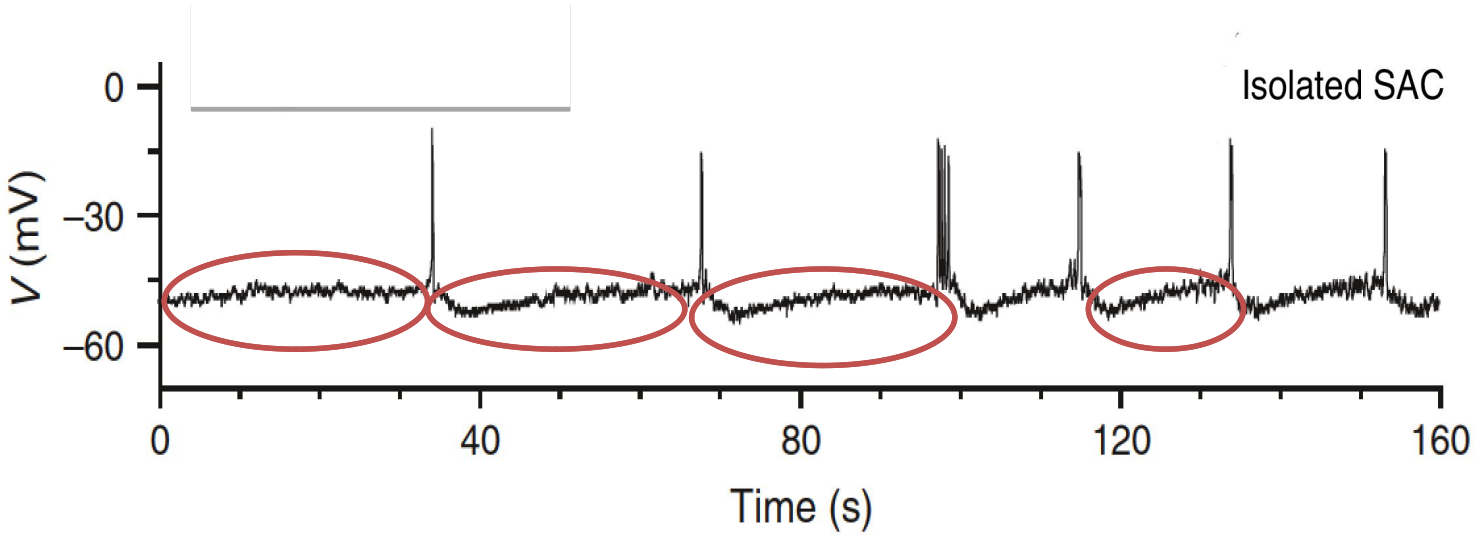
Experiment for isolated neurons,
Zheng et al., 2006, Nature

Experiments for the emergence of retinal waves

Retinal waves require three components:

i) Spontaneous bursting activity

ii) Refractory mechanism (slow After HyperPolarisation- sAHP)



Experiment for isolated neurons,
Zheng et al., 2006, Nature

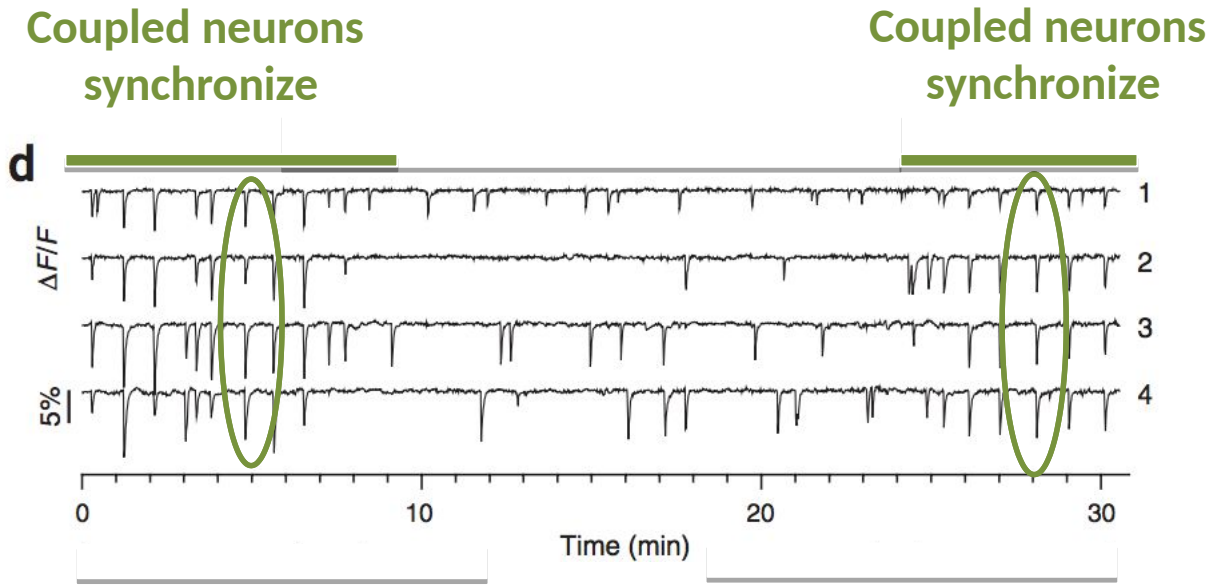
Experiments for the emergence of retinal waves

Retinal waves require three components:

i) Spontaneous bursting activity

ii) Refractory mechanism (slow After HyperPolarisation- sAHP)

iii) Coupling (through Acetylcholine neurotransmitter)



Experiment for coupled and isolated neurons, Zheng et al., 2006, Nature

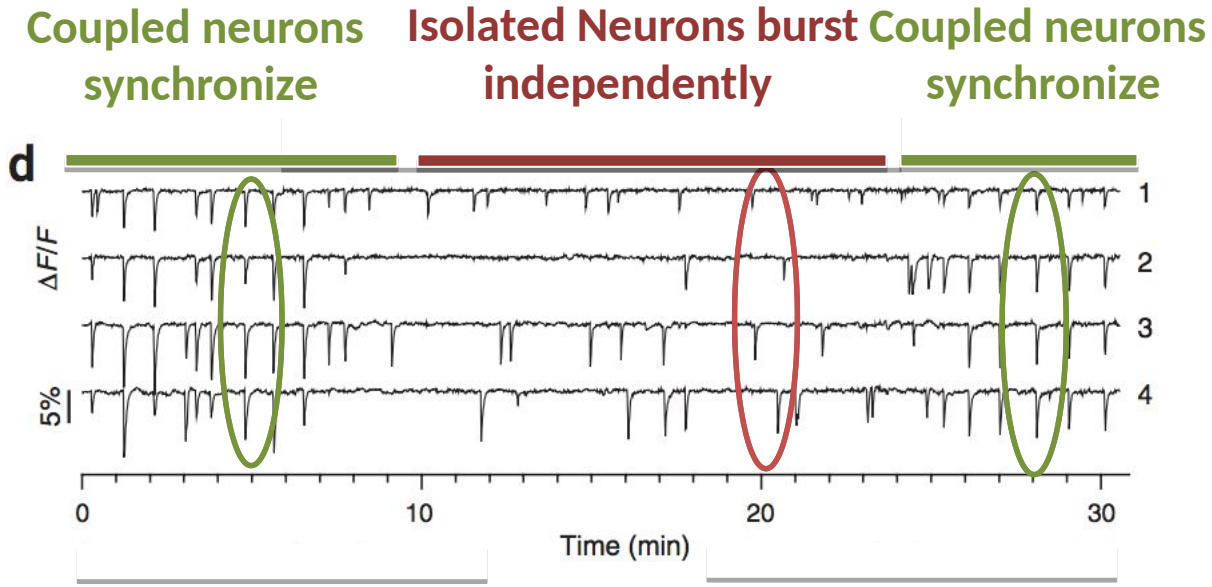
Experiments for the emergence of retinal waves

Retinal waves require three components:

i) Spontaneous bursting activity

ii) Refractory mechanism (slow After HyperPolarisation- sAHP)

iii) Coupling (through Acetylcholine neurotransmitter)



Experiment for coupled and isolated neurons, Zheng et al., 2006, Nature

Experiments for the emergence of retinal waves

Several models of stage II retinal waves have been proposed already:

- **Feller et all Neuron, 1997.**
- **Eglen et al, J. Neuroscience 2000.**
- **Godfrey & Swindale. PLoS Comput Biol, 2007.**
- **Hennig et al, J. Neuroscience, 2009**
- **Lansdell et al, PLoS Computational Biology, 2014.**

But none of them as studied simultaneously these 3 aspects:

(i) realistic model of spontaneous bursting
(ii) sAHP biophysical modelling
(iii) realistic Ach interaction.

Experiment for coupled and isolated neurons, Zheng et al., 2006, Nature

A network model for stage II retinal waves

A biophysical model explains the spontaneous bursting behavior in the developing retina
Dora Matzakos-Karvouniari, Lionel Gil, Elaine Orendorff, Olivier Marre, Serge Picaud, Bruno Cessac
Scientific Reports, Nature Publishing Group, 2019, 9 (1), pp.1-23. ⟨10.1038/s41598-018-38299-4⟩

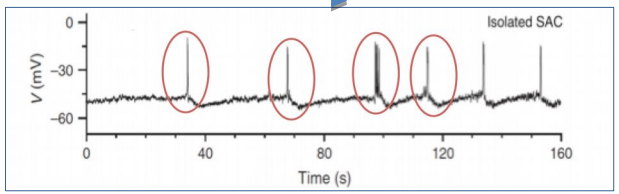
A network model for stage II retinal waves

Membrane potential dynamics

$$C_m \frac{\partial V}{\partial t} = -g_L^M (V - V_L) - g_{Ca}(V)(V - V_{Ca}) - g_K N (V - V_K)$$

$$\tau_N \frac{\partial N}{\partial t} = \Lambda(V)(N_\infty(V) - N)$$

Morris-Lecar & Fast K+ channels



A network model for stage II retinal waves

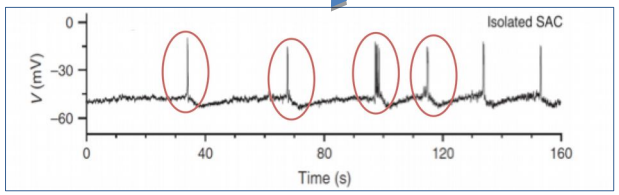
Membrane potential dynamics

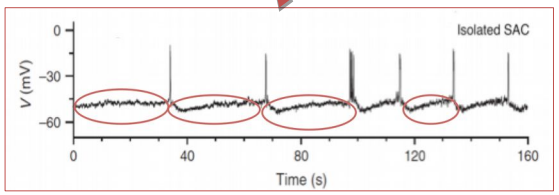
$$C_m \frac{\partial V_i}{\partial t} = -g_L^M (V_i - V_L) - g_{Ca}(V_i)(V_i - V_{Ca}) - g_K N_i (V_i - V_K) - g_{sAHP} R_i^4 (V_i - V_K) - \sum_j g_{j,Ach}(A_j)(V_i - V_{Ach})$$

$$\tau_N \frac{\partial N}{\partial t} = \Lambda(V)(N_\infty(V) - N)$$

Morris-Lecar & Fast K+ channels

sAHP current Refractory mechanism

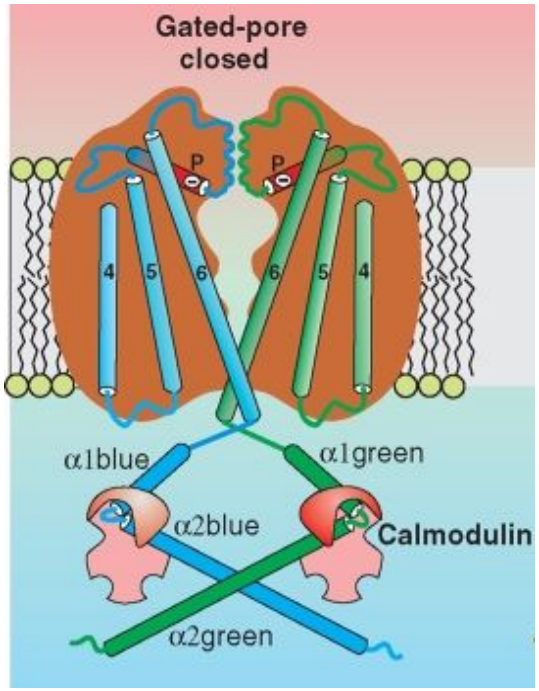




sAHP current

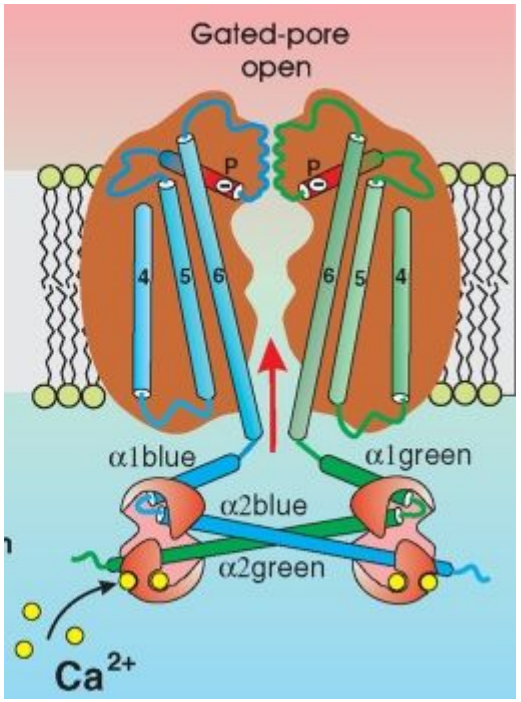
- ***Definition***
  - Slow After Hyperpolarisation Current
  - Calcium-dependent slow potassium channels

- **Mechanism**
  - Model SK-like channels (Abel et al. 2004)
  - Gating Mechanism: Four ions Ca^{2+} bind to Calmodulin (CaM)



Closed

Ca^{2+}



Open

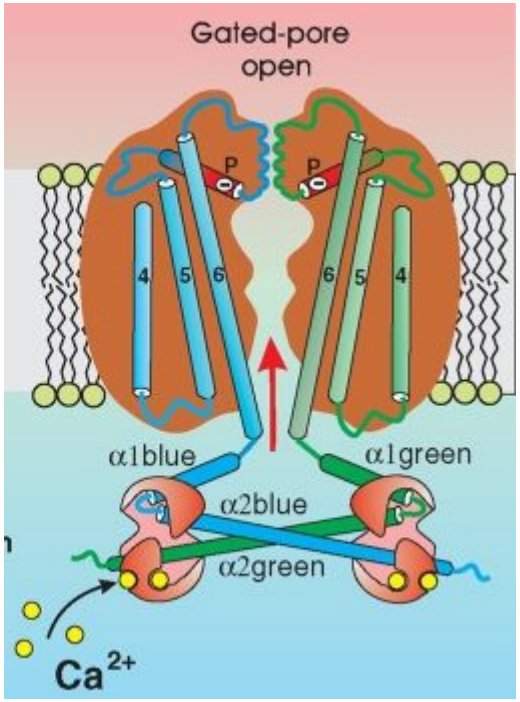
Calcium gated potassium channel

superhimik.livejournal.com/

sAHP current

- Four Ca^{2+} ions bound to calmodulin open the channel
- I_{sAHP} current depends on gating variable R as follows:

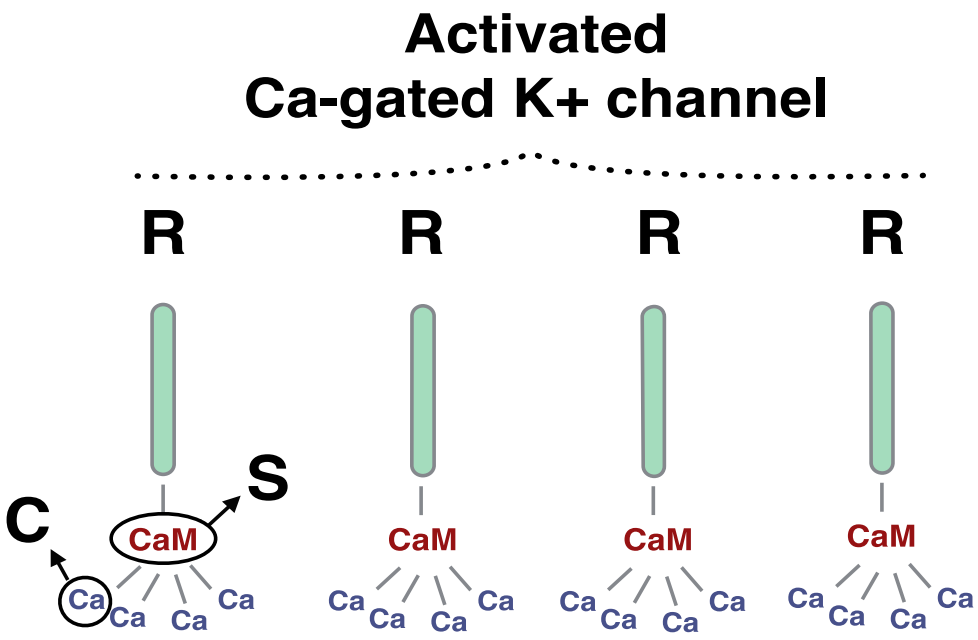
$$I_{sAHP} = g_{sAHP}^{m} R^{4} (V - V_K)$$ (Hennig et al. 2009)



The conductance is proportional to the fourth power of R because four terminals are needed to open the channel.

superhimik.livejournal.com/

Set of equations for sAHP current



Gating mechanism

All 4 subunits R of the channel are bound to activate the channel

⇧

Saturated Calmodulin molecule (CaM) bind to each channel subunit

⇧

4 Calcium ions bound to each saturated Calmodulin complex S

Set of equations for sAHP current

Activated
Ca-gated K+ channel

$$\tau_R \frac{dR}{dt} = a_R S(1 - R) - R$$

R : Probability that one terminal of the channel is open

$$\tau_S \frac{dS}{dt} = -S + a_s C^4 (1 - S)$$

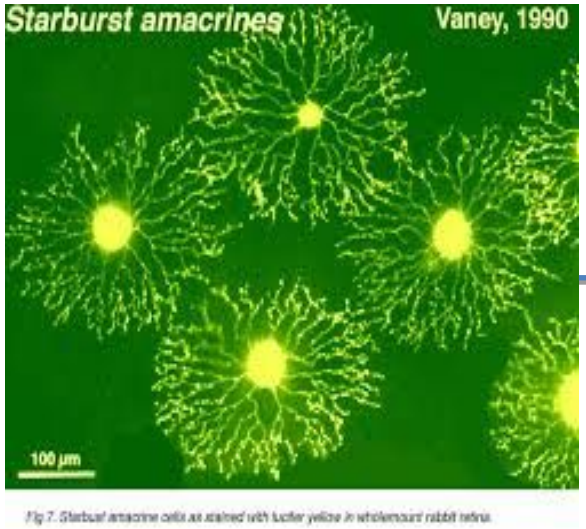
S : Fraction of saturated calmodulin concentration (CaM)

$$\tau_{Ca} \frac{dC}{dt} = -a_R \frac{C}{H_x} + C_o + \delta_{Ca} I_{Ca}(V)$$

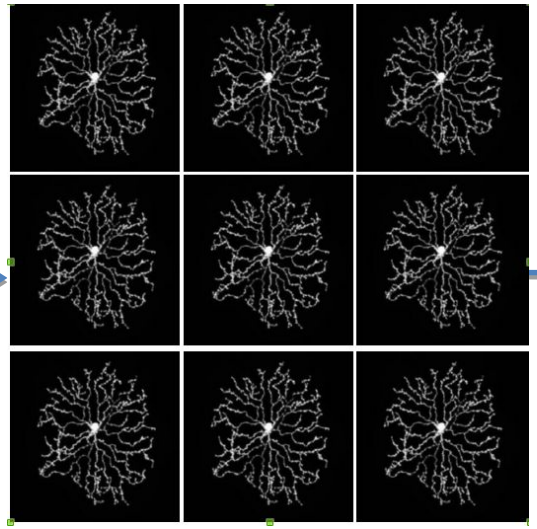
C : Intracellular Calcium concentration

SACs Network

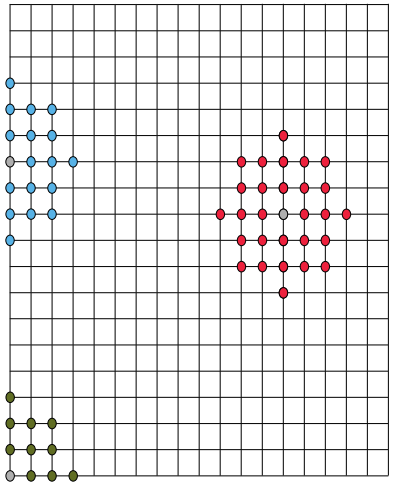
Model synaptic interactions



SACs realistic connections



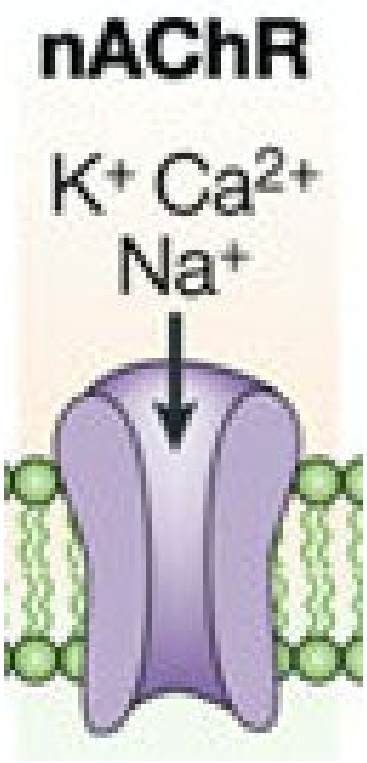
SACs on a lattice



SACs become points on a lattice

Acetylcholine current

- Molecular nicotinic receptors (nAchR)
- Two molecules of acetylcholine bind to open a nicotinic channel
- The nicotinic conductance depends on the second power of the acetylcholine neurotransmitter concentration A



$$g_{Ach} = g_{Ach}^{m} \frac{A^2}{K_d^2 + A^2}$$

A network model for stage II retinal waves

Membrane potential dynamics

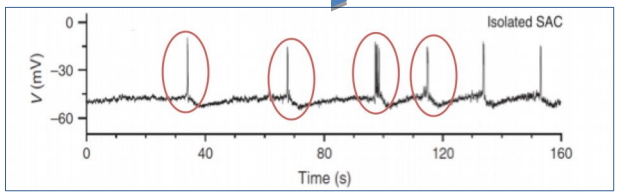
$$C_m \frac{\partial V_i}{\partial t} = -g_L^M(V_i - V_L) - g_{Ca}(V_i)(V_i - V_{Ca}) - g_K N_i(V_i - V_K) - g_{sAHP} R_i^4(V_i - V_K) - \sum_j g_{j,Ach}(A_j)(V_i - V_{Ach})$$

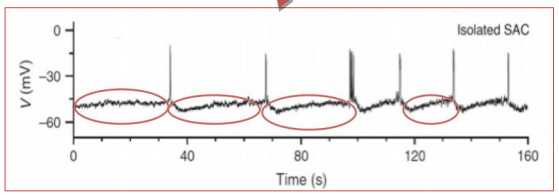
$$\tau_N \frac{\partial N}{\partial t} = \Lambda(V)(N_\infty(V) - N)$$

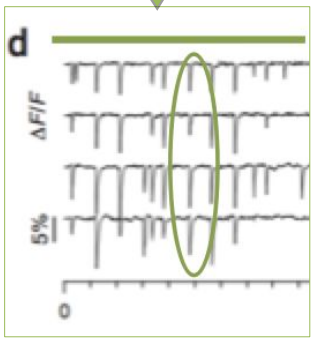
Morris-Lecar & Fast K+ channels

sAHP current
Refractory mechanism

Ach current
Network effect







A network model for stage II retinal waves

A biophysical model explains the spontaneous bursting behavior in the developing retina
Dora Matzakos-Karvouniari, Lionel Gil, Elaine Orendorff, Olivier Marre, Serge Picaud, Bruno Cessac
Scientific Reports, Nature Publishing Group, 2019, 9 (1), pp.1-23. ⟨10.1038/s41598-018-38299-4⟩

$$
\begin{cases}
C_m \frac{dV_i}{dt} &= -g_L(V_i - V_L) - g_C M_\infty(V_i)(V_i - V_C) - g_K N_i (V_i - V_K) \\
&\quad - G_{sAHP}(R_i)(V_i - V_K) - G_A(\{A_k\}_{k\in\mathcal{B}_i})(V_i - V_A) \\
\tau_N \frac{dN_i}{dt} &= \Lambda(V_i)(N_\infty(V_i) - N_i) \\
\tau_C \frac{dC_i}{dt} &= -\frac{\alpha_C}{H_X} C_i + C_0 - \delta_C g_C M_\infty(V_i)(V_i - V_C) \\
\tau_S \frac{dS_i}{dt} &= \alpha_S(1 - S_i) C_i^4 - S_i \\
\tau_R \frac{dR_i}{dt} &= \alpha_R S_i (1 - R_i) - R_i \\
\frac{dA_i}{dt} &= -\mu A_i + \beta_A T_A(V_i),
\end{cases}
$$

A network model for stage II retinal waves

N neurons, 6 N equations

~ 20 parameters per neuron

(But neurons are assumed identical)

$$
\begin{cases}
C_m \frac{dV_i}{dt} &= -g_L(V_i - V_L) - g_C M_\infty(V_i)(V_i - V_C) - g_K N_i (V_i - V_K) \\
&\quad - G_{sAHP}(R_i)(V_i - V_K) - G_A(\{A_k\}_{k \in n})(V_i - V_A) \\
\tau_N \frac{dN_i}{dt} &= \lambda(V_i)(N_\infty(V_i) - N_i) \\
\tau_C \frac{dC_i}{dt} &= -\frac{\alpha_C}{H_X} C_i + C_0 - \delta_C g_C M_\infty(V_i)(V_i - V_C) \\
\tau_S \frac{dS_i}{dt} &= \alpha_S (1 - S_i) C_i^4 - S_i \\
\tau_R \frac{dR_i}{dt} &= \alpha_R S_i (1 - R_i) - R_i \\
\frac{dA_i}{dt} &= -\mu A_i + \beta_A T_A(V_i),
\end{cases}
$$

A network model for stage II retinal waves

N neurons, 6 N equations

~ 20 parameters per neuron

(But neurons are assumed identical)

Time scale separation

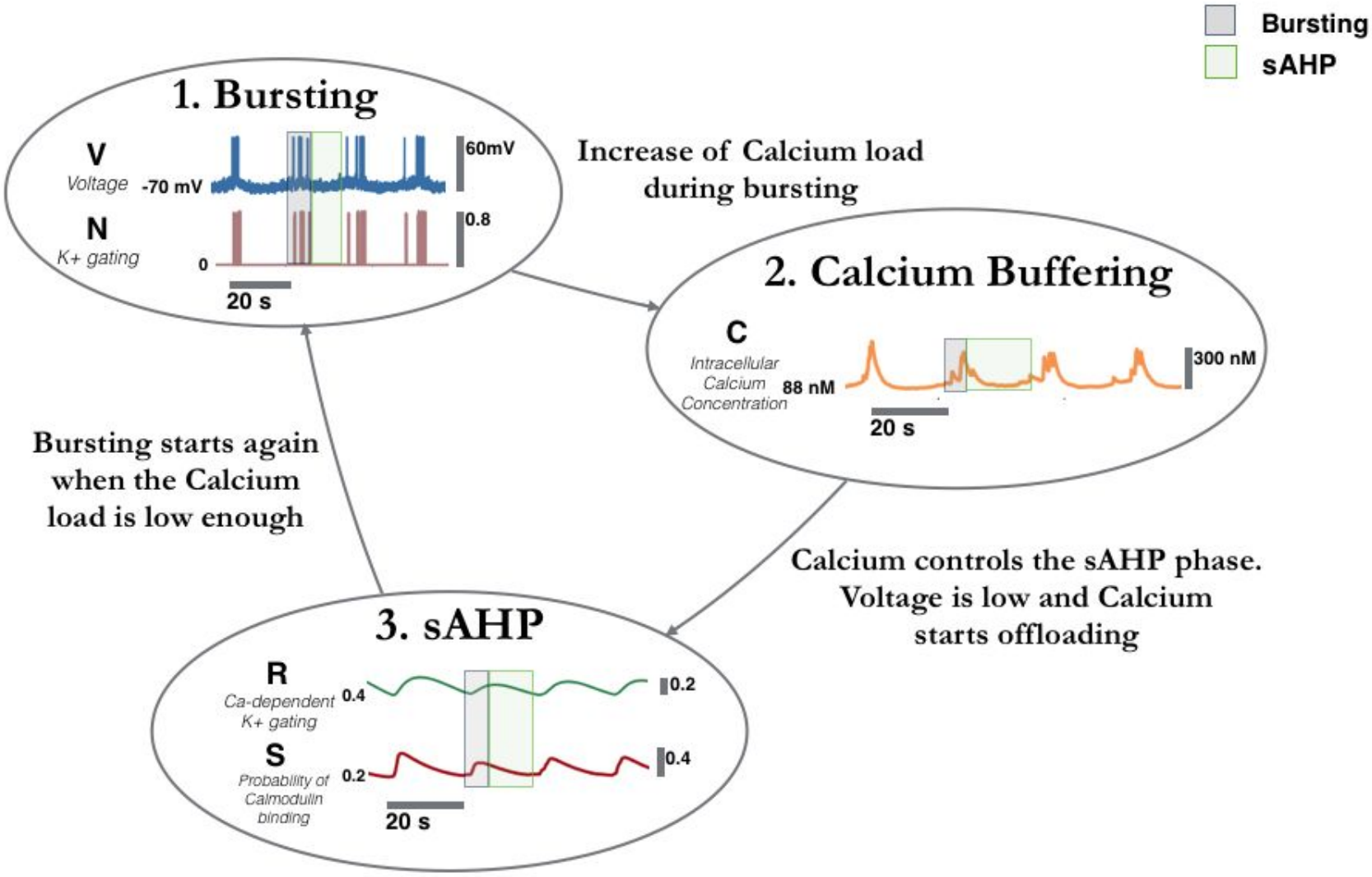
$$\begin{cases} C_m \frac{dV_i}{dt} = -g_L(V_i - V_L) - g_C M_\infty(V_i)(V_i - V_C) - g_K N_i(V_i - V_K) \\ \qquad -G_{sAHP}(R_i)(V_i - V_K) - G_A(\{A_k\}_{k\in n})(V_i - V_A) \\ \tau_N \frac{dN_i}{dt} = \lambda(V_i)(N_\infty(V_i) - N_i) \\ \tau_C \frac{dC_i}{dt} = -\frac{\alpha_C}{H_X} C_i + C_0 - \delta_C g_C M_\infty(V_i)(V_i - V_C) \\ \tau_S \frac{dS_i}{dt} = \alpha_S(1 - S_i)C_i^4 - S_i \\ \tau_R \frac{dR_i}{dt} = \\ \frac{dA_i}{dt} = \end{cases}$$

Fast V, N. $\tau_L = 11$ ms, $\tau_N = 5$ ms.

Medium C, A. $\tau_C = 2$ s, $\tau_A = 1.86$ s.

Slow S, R. $\tau_R = \tau_S = 44$ s.

Spontaneous Bursting Mechanism of SACs



Fast time scale

Fast time scale

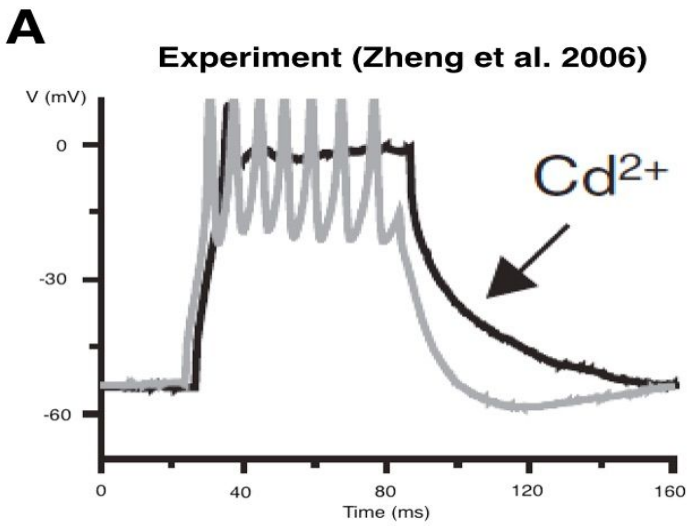
Morris-Lecar model with fast dynamics, in the presence of a slow external current

$$\begin{cases} \frac{dV}{dt_f} &= -\tilde{g}_L(V - V_L) - \tilde{g}_C M_\infty(V)(V - V_C) - \tilde{g}_K N(V - V_K) + I_{ext} \\ \frac{dN}{dt_f} &= \frac{\tau_L}{\tau_N}\Lambda(V)(N_\infty(V) - N) \end{cases}$$

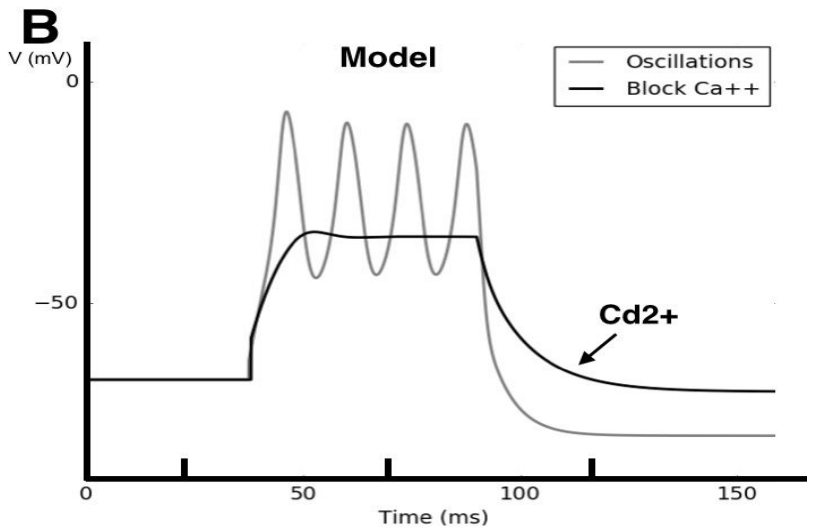
Fast time scale

Morris-Lecar model with fast dynamics, in the presence of a slow external current

$$\begin{cases} \dfrac{dV}{dt_f} = -\tilde{g}_L(V - V_L) - \tilde{g}_C M_\infty(V)(V - V_C) - \tilde{g}_K N(V - V_K) + I_{ext} \\ \dfrac{dN}{dt_f} = \dfrac{\tau_L}{\tau_N}\Lambda(V)(N_\infty(V) - N) \end{cases}$$

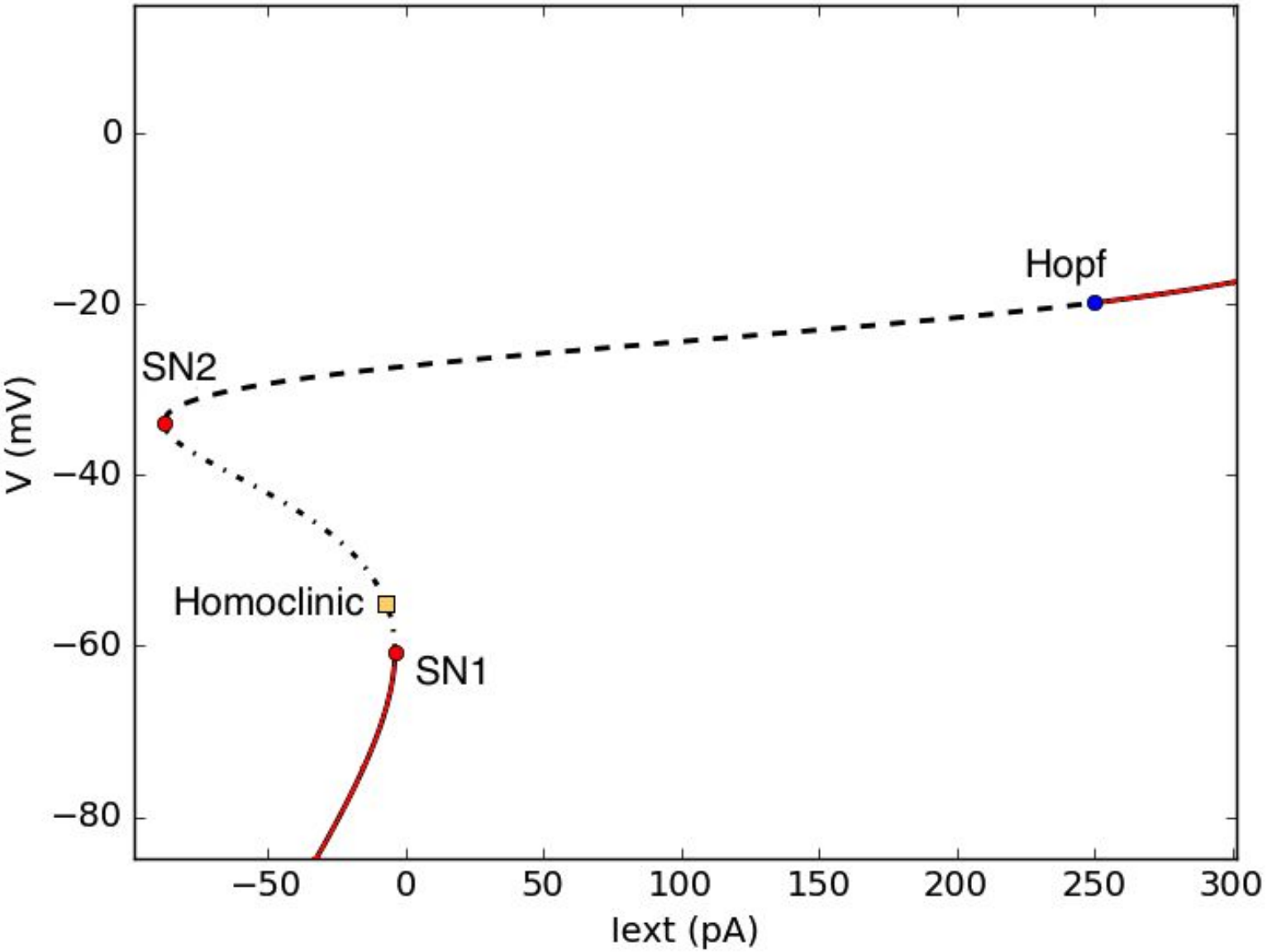


Experiment by Zheng et al. 2006, Nature

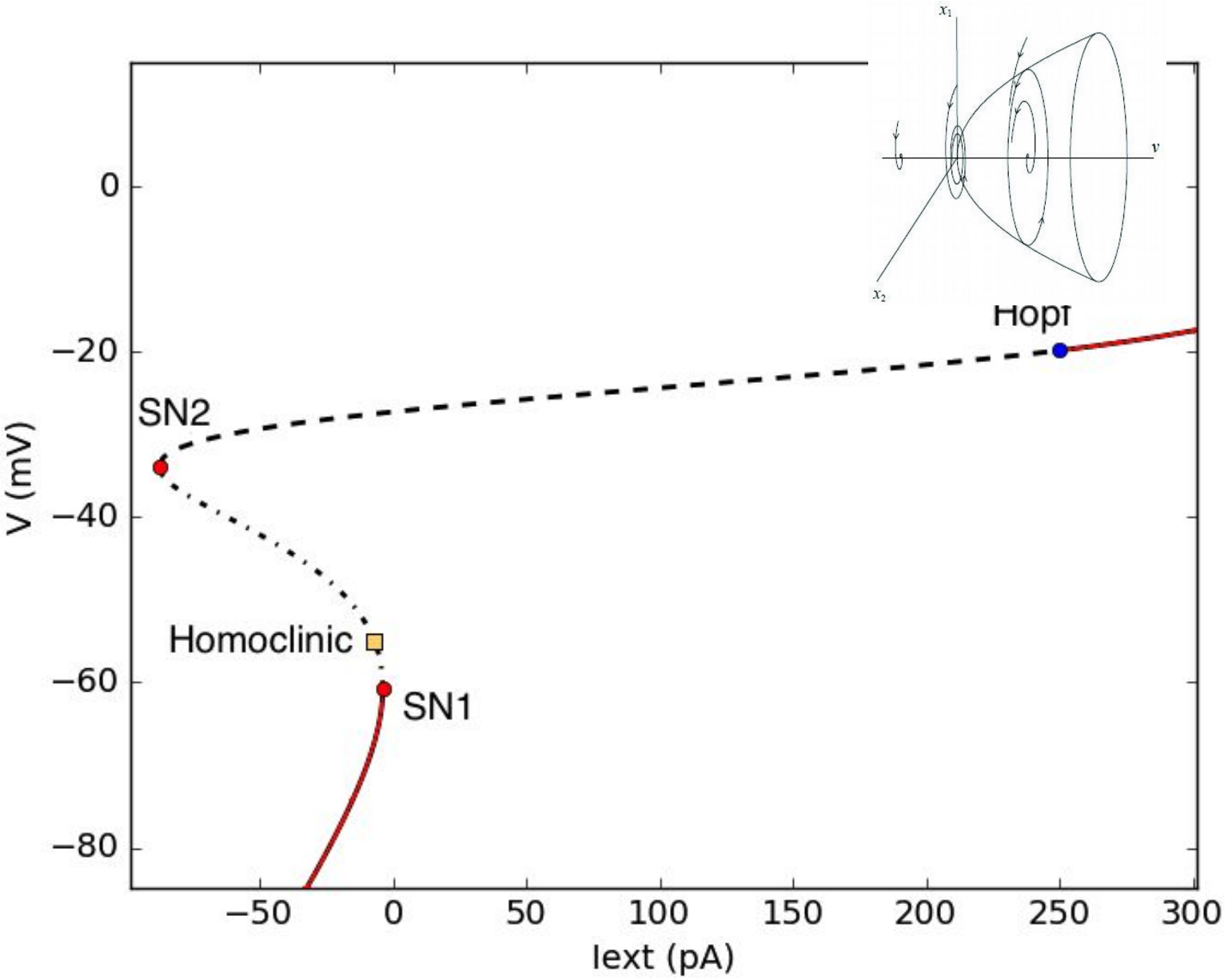


Model. Tuning parameters V1, V2, V3 ,V4 from ML adjusted to reproduce the experiment

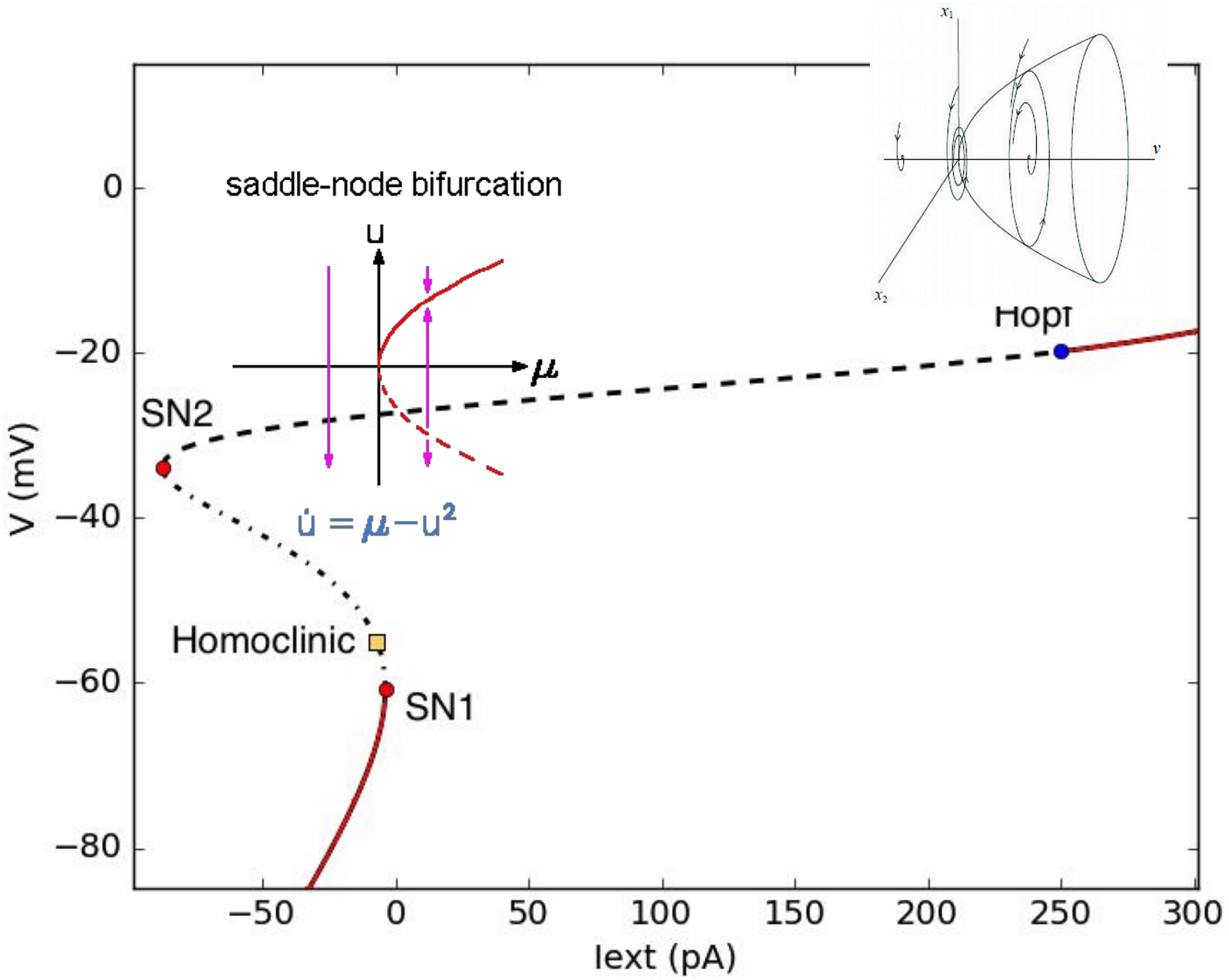
Bifurcation diagram of M-L model



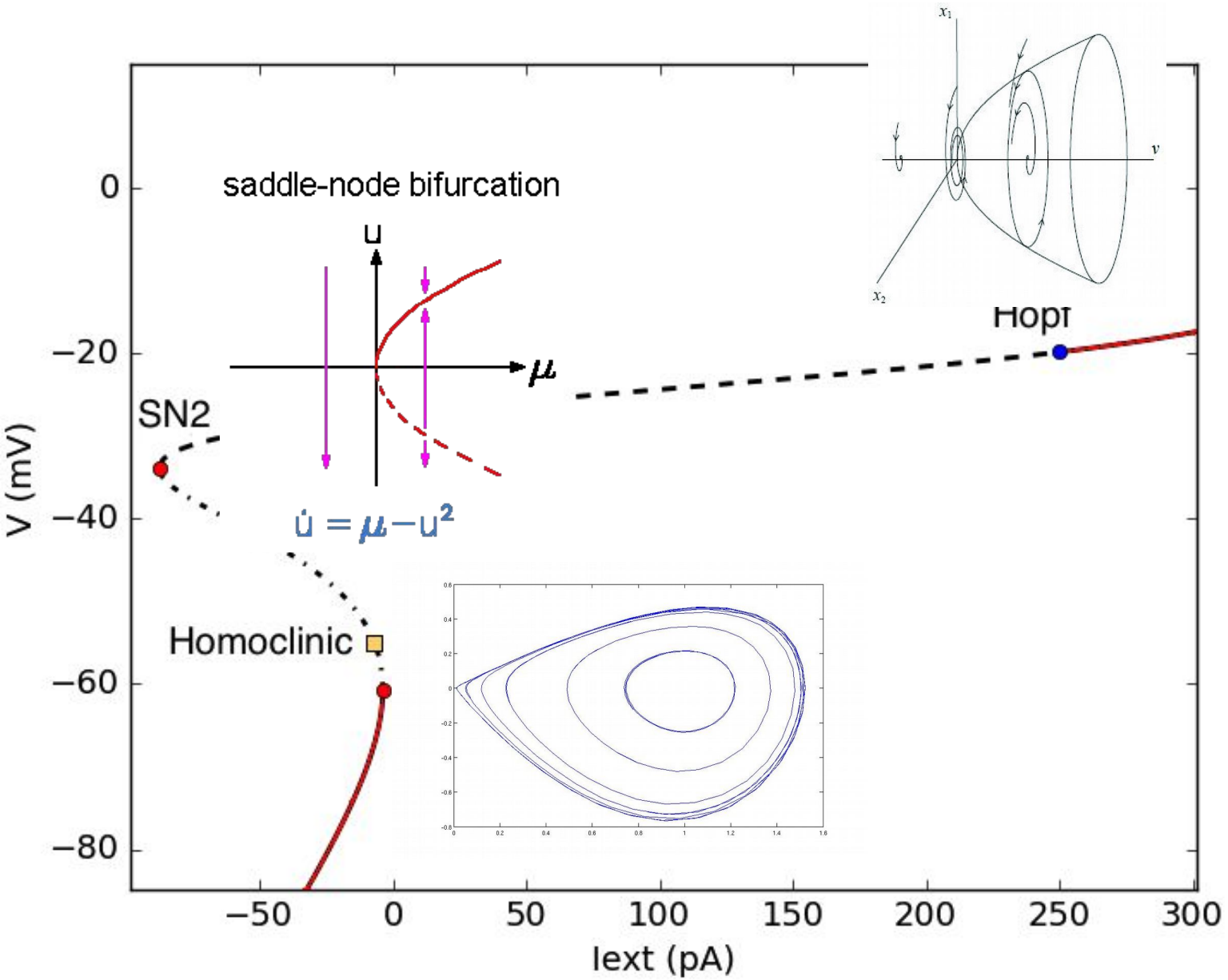
Bifurcation diagram of M-L model



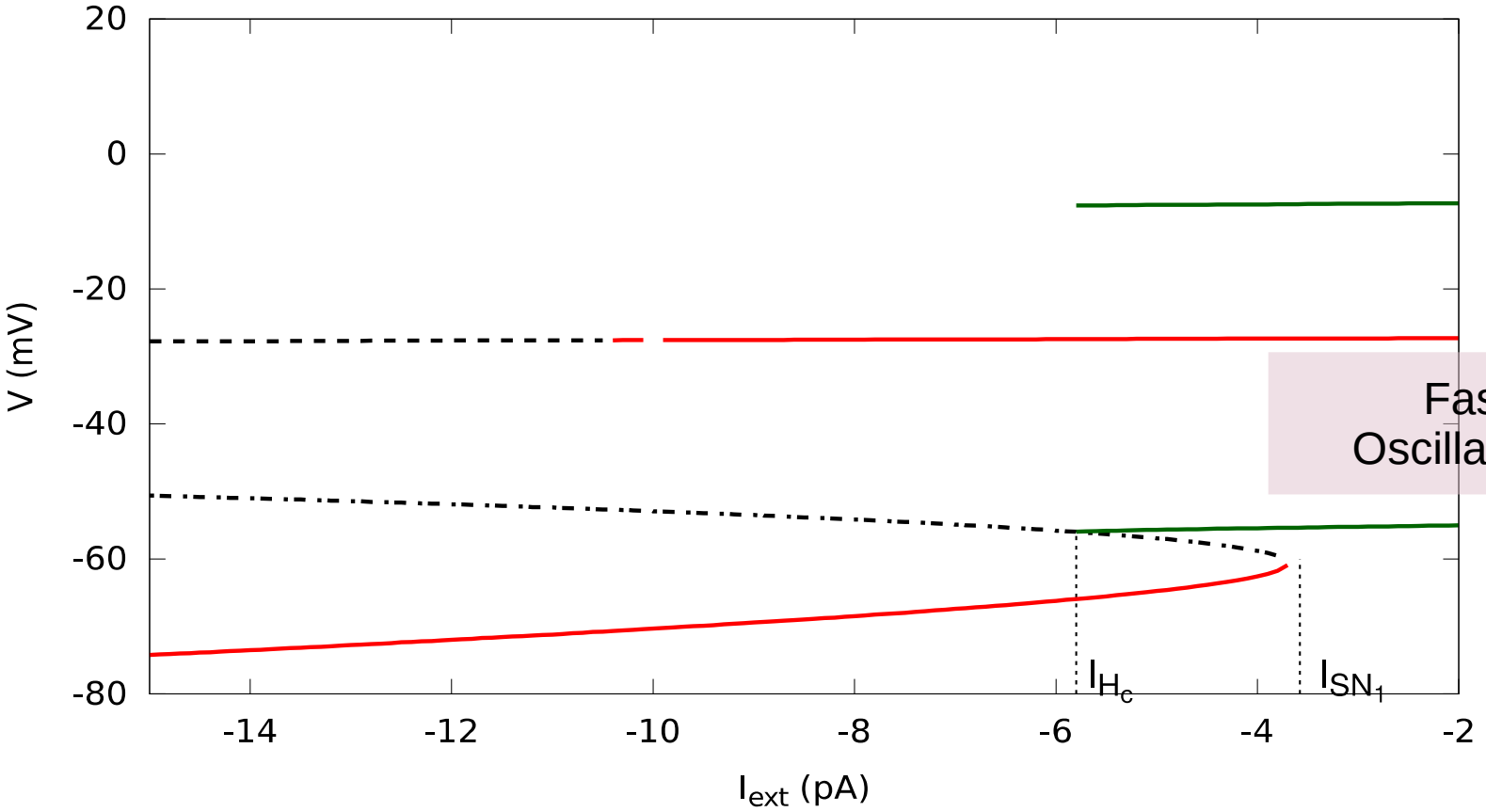
Bifurcation diagram of M-L model



Bifurcation diagram of M-L model



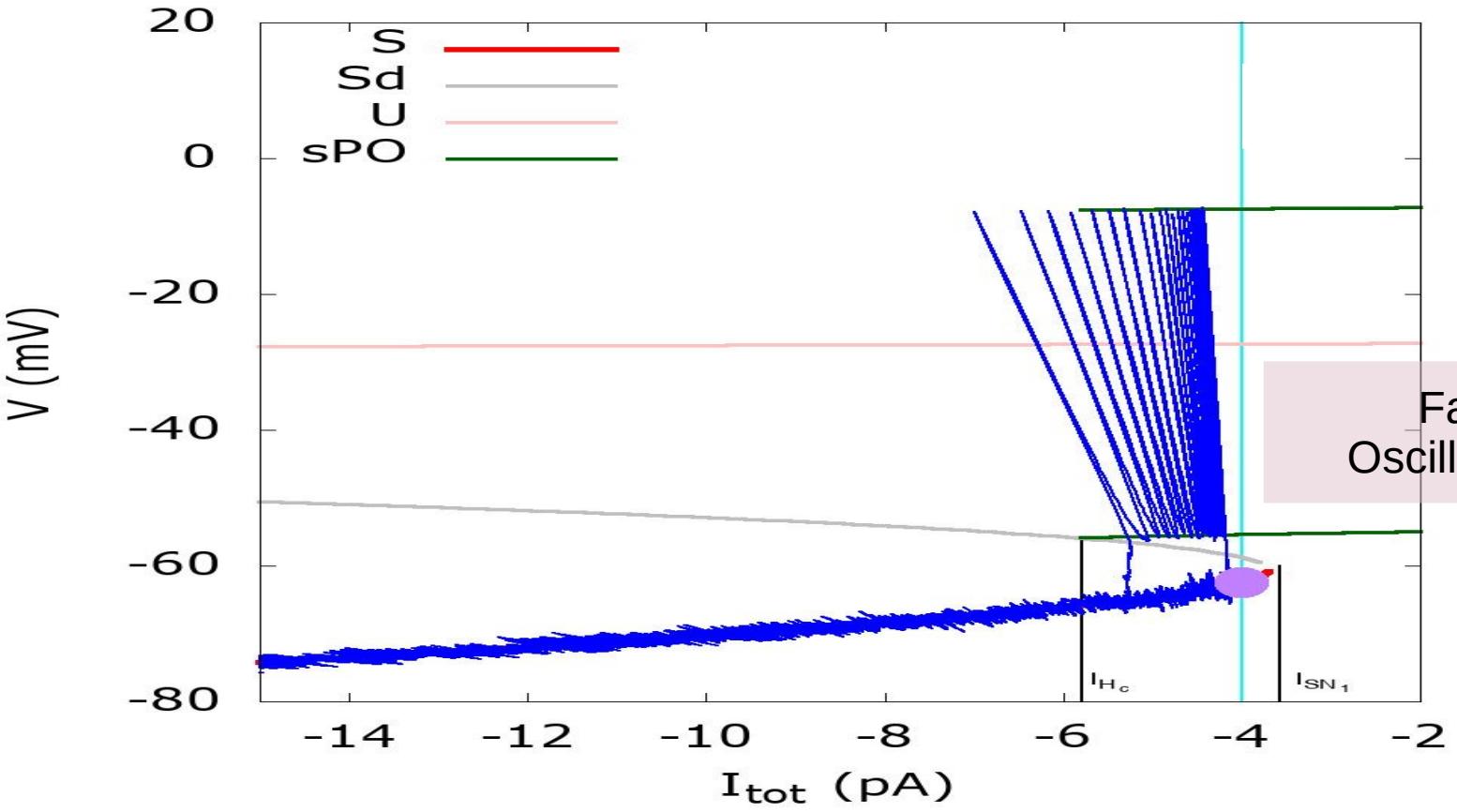
The mechanism of bursting



Fast Oscillations

Stable Fixed point

The mechanism of bursting (noise induced)



Fast Oscillations

Stable Fixed point

Spontaneous Bursting Mechanism of SACs

Bursting
sAHP

1. Bursting

V
Voltage -70 mV
60mV
N
K+ gating
0
0.8
20 s

Increase of Calcium load during bursting

2. Calcium Buffering

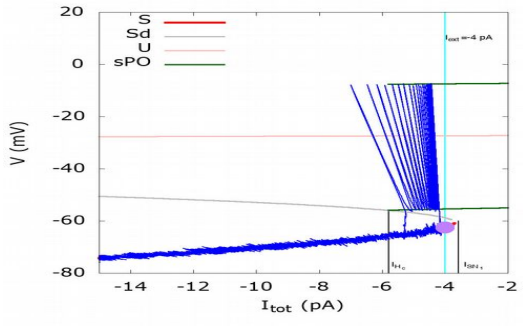
C
Intracellular Calcium Concentration 88 nM
300 nM
20 s

Calcium controls the sAHP phase. Voltage is low and Calcium starts offloading

3. sAHP

R
Ca-dependent K+ gating
0.4
0.2
S
Probability of Calmodulin binding
0.2
0.4
20 s

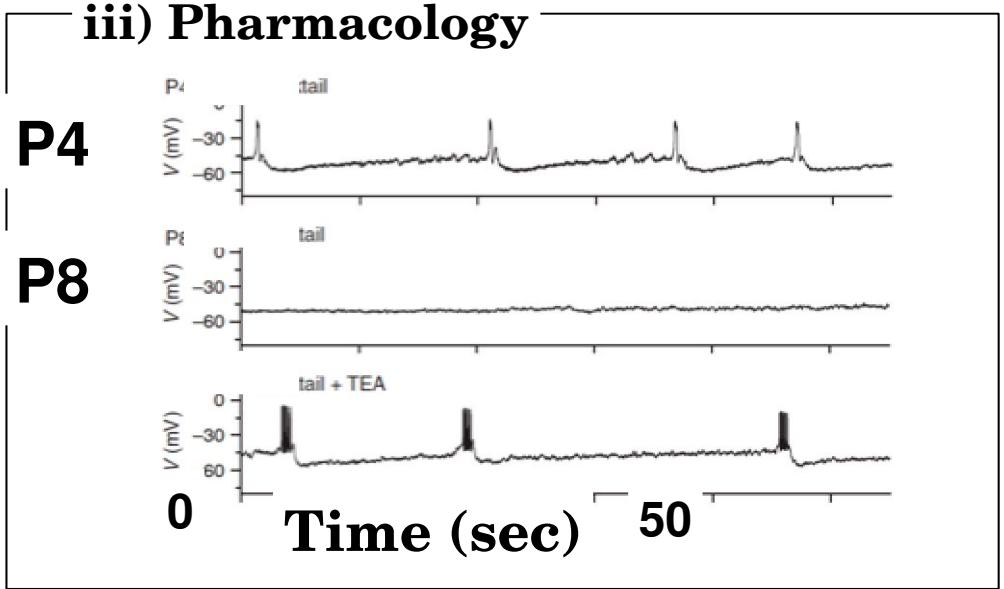
Bursting starts again when the Calcium load is low enough



Variability within retinal waves

Pharmacological effects can be explained and predicted from bifurcations analysis (variations of physiological parameters).

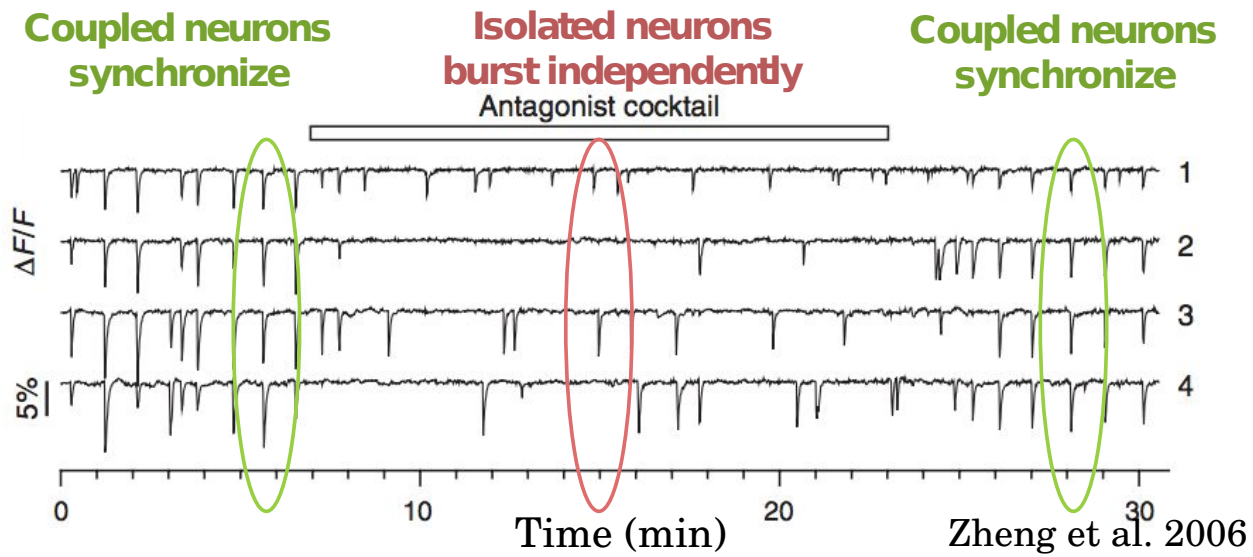
A biophysical model explains the spontaneous bursting behavior in the developing retina
Dora Matzakos-Karvouniari, Lionel Gil, Elaine Orendorff, Olivier Marre, Serge Picaud, Bruno Cessac
Scientific Reports, Nature Publishing Group, 2019, 9 (1), pp.1-23. ⟨10.1038/s41598-018-38299-4⟩



Cellular mechanisms of stage II retinal waves

Cellular mechanisms of stage II retinal waves

C. Synchrony through Acetylcholine



Zheng et al. 2006

Mutual excitatory connections between SACs through Acetylcholine

A network model for stage II retinal waves

Morris-Lecar

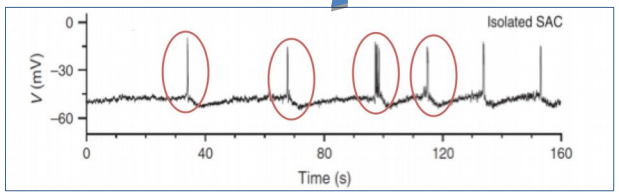
$$C_m \frac{\partial V_i}{\partial t} = -g_L^M(V_i - V_L) - g_{Ca}(V_i)(V_i - V_{Ca}) - g_K N_i(V_i - V_K) - g_{sAHP} R_i^4(V_i - V_K) - \sum_j g_{j,Ach}(A_j)(V_i - V_{Ach})$$

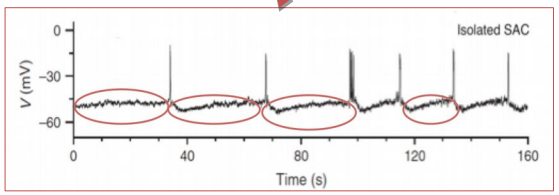
$$\tau_N \frac{\partial N}{\partial t} = \Lambda(V)(N_\infty(V) - N)$$

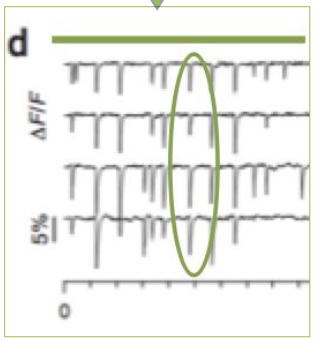
Morris-Lecar & Fast K+ channels (kV3)

sAHP current
Refractory mechanism

Ach current
Network effect

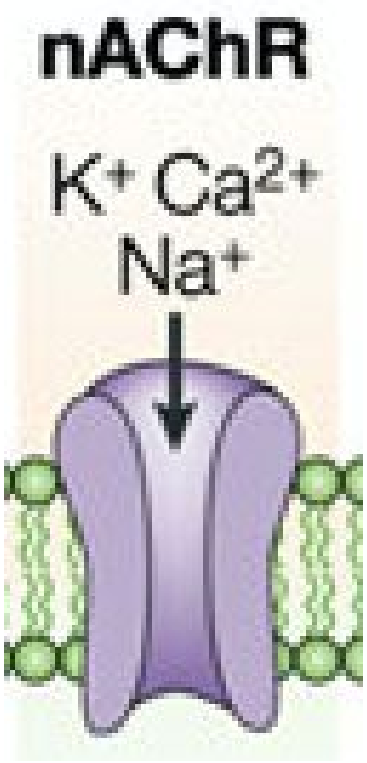






Acetylcholine current

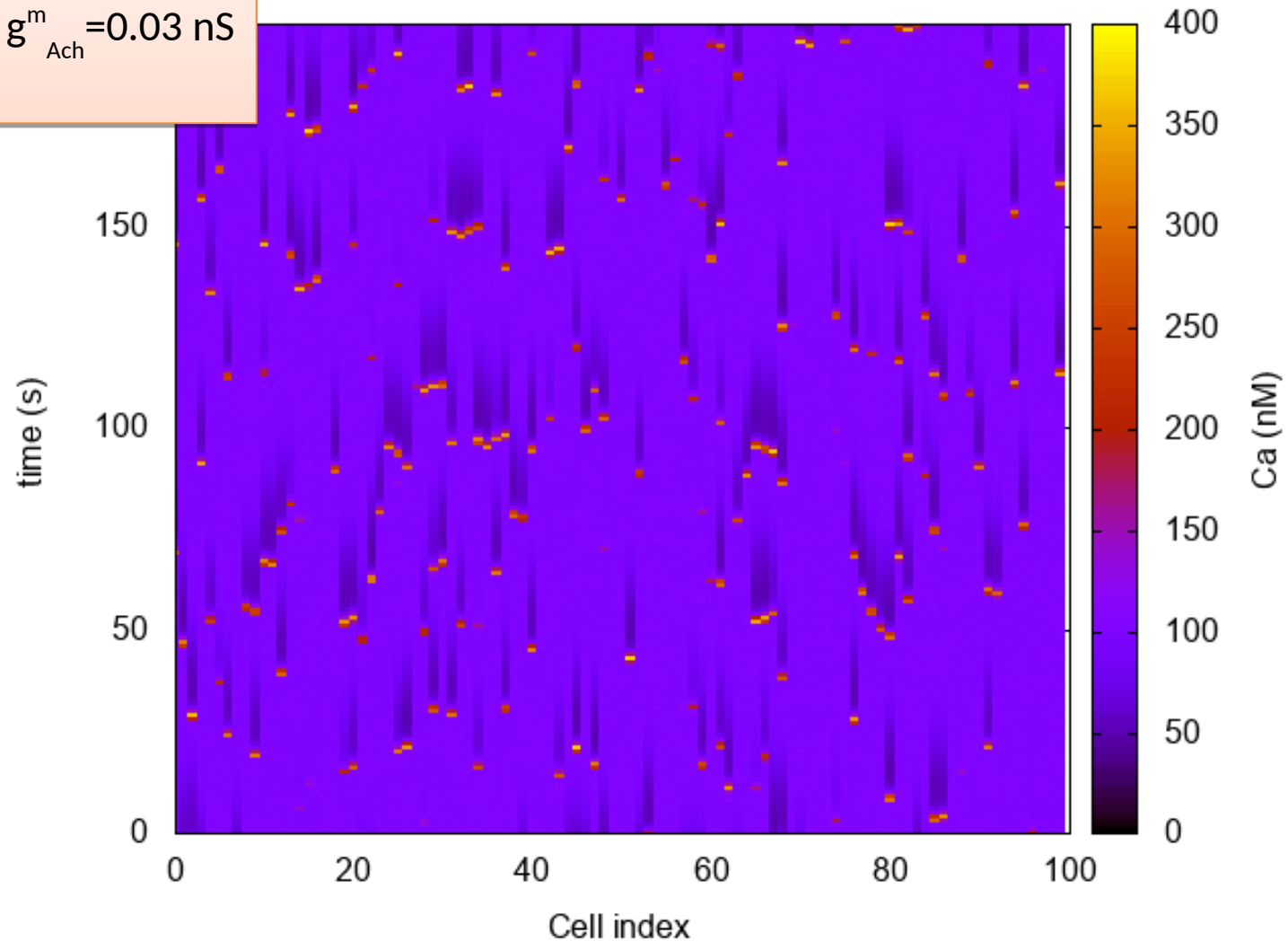
- Molecular nicotinic receptors (nAchR)
- Two molecules of acetylcholine bind to open a nicotinic channel
- The nicotinic conductance depends on the second power of the acetylcholine neurotransmitter concentration A



$$g_{Ach} = g_{Ach}^{m} \frac{A^2}{K_d^2 + A^2}$$

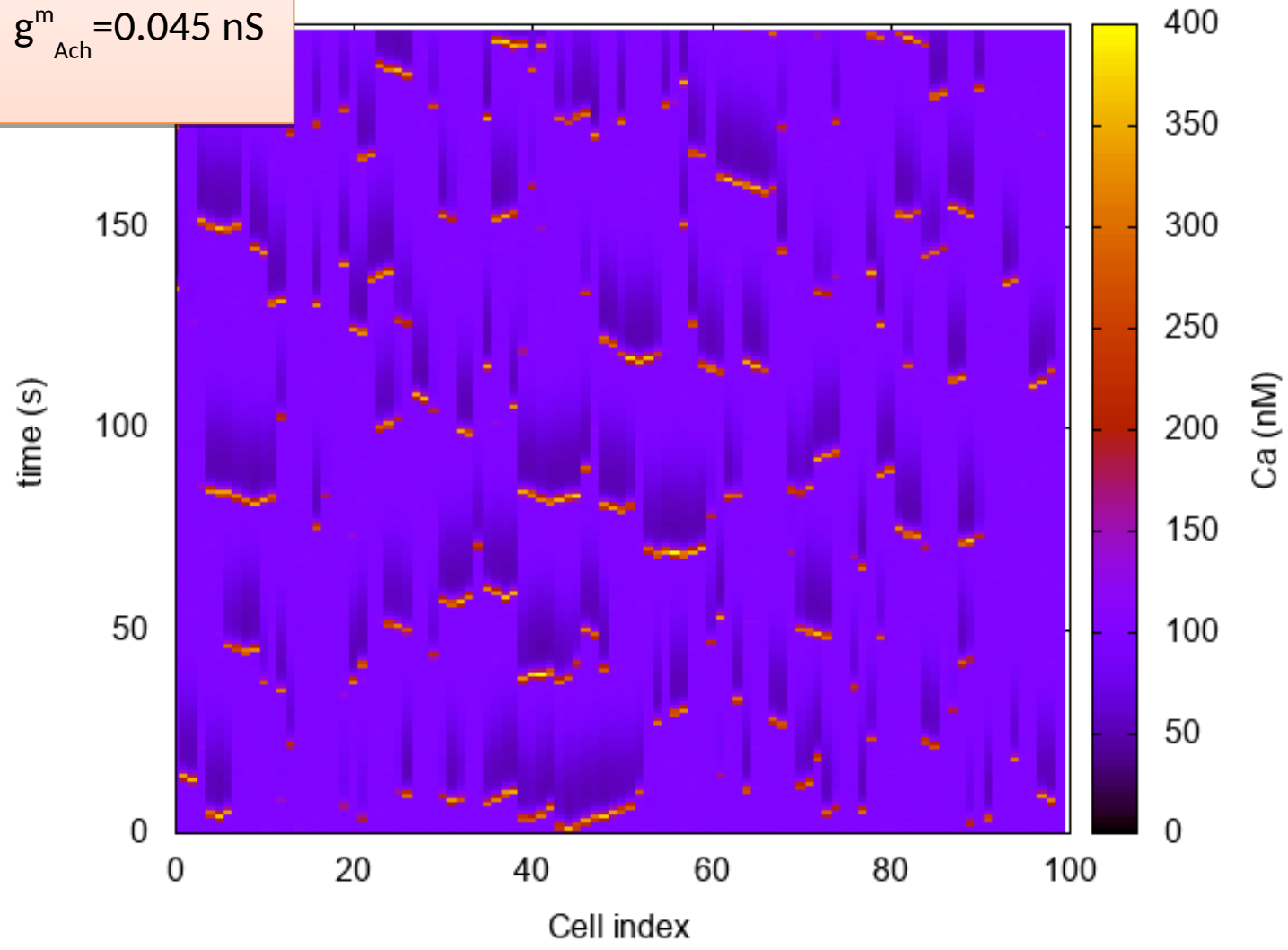
Waves propagation

g^{m}_{Ach}=0.03 nS



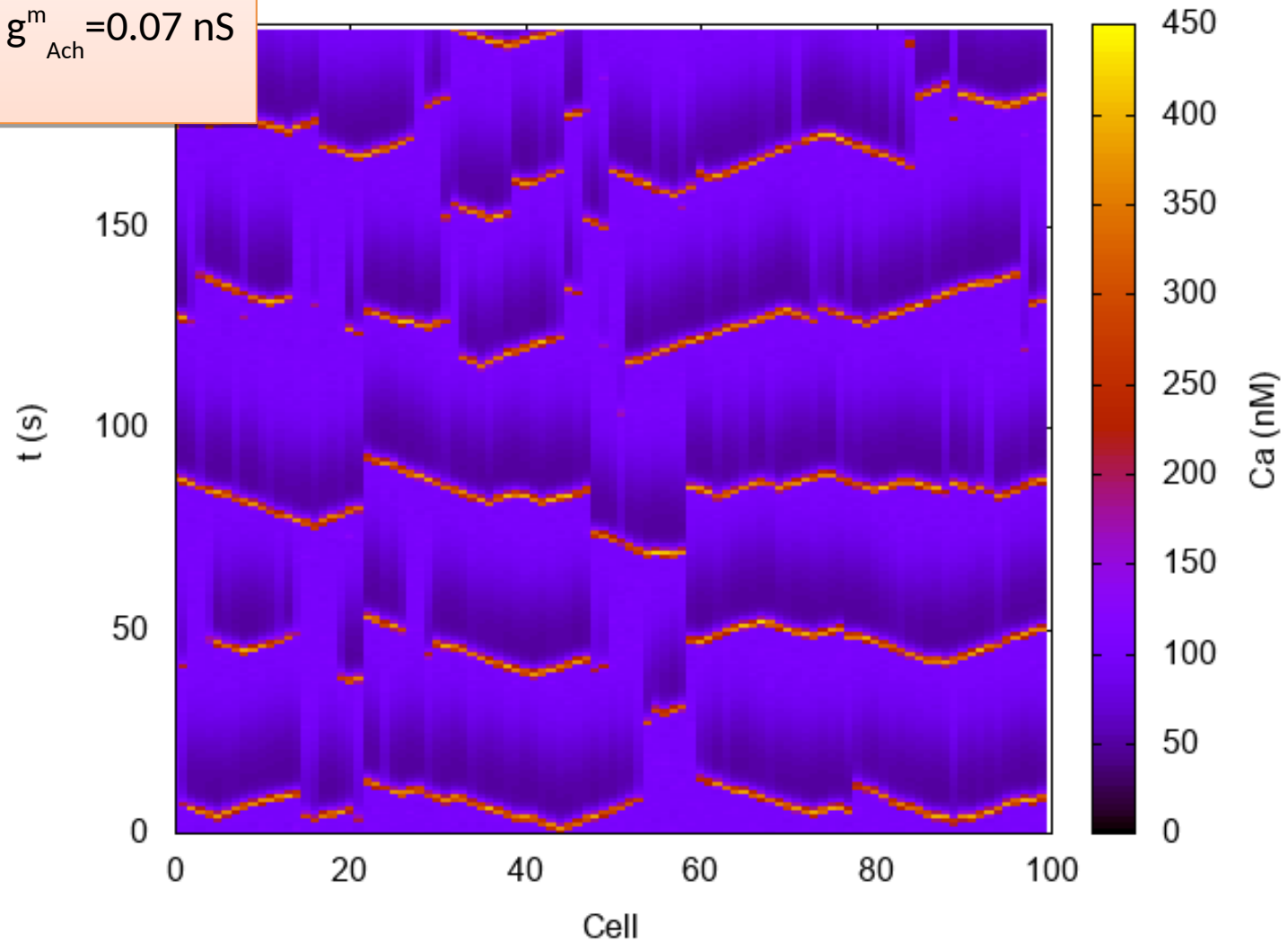
Waves propagation

g^{m}_{Ach}=0.045 nS



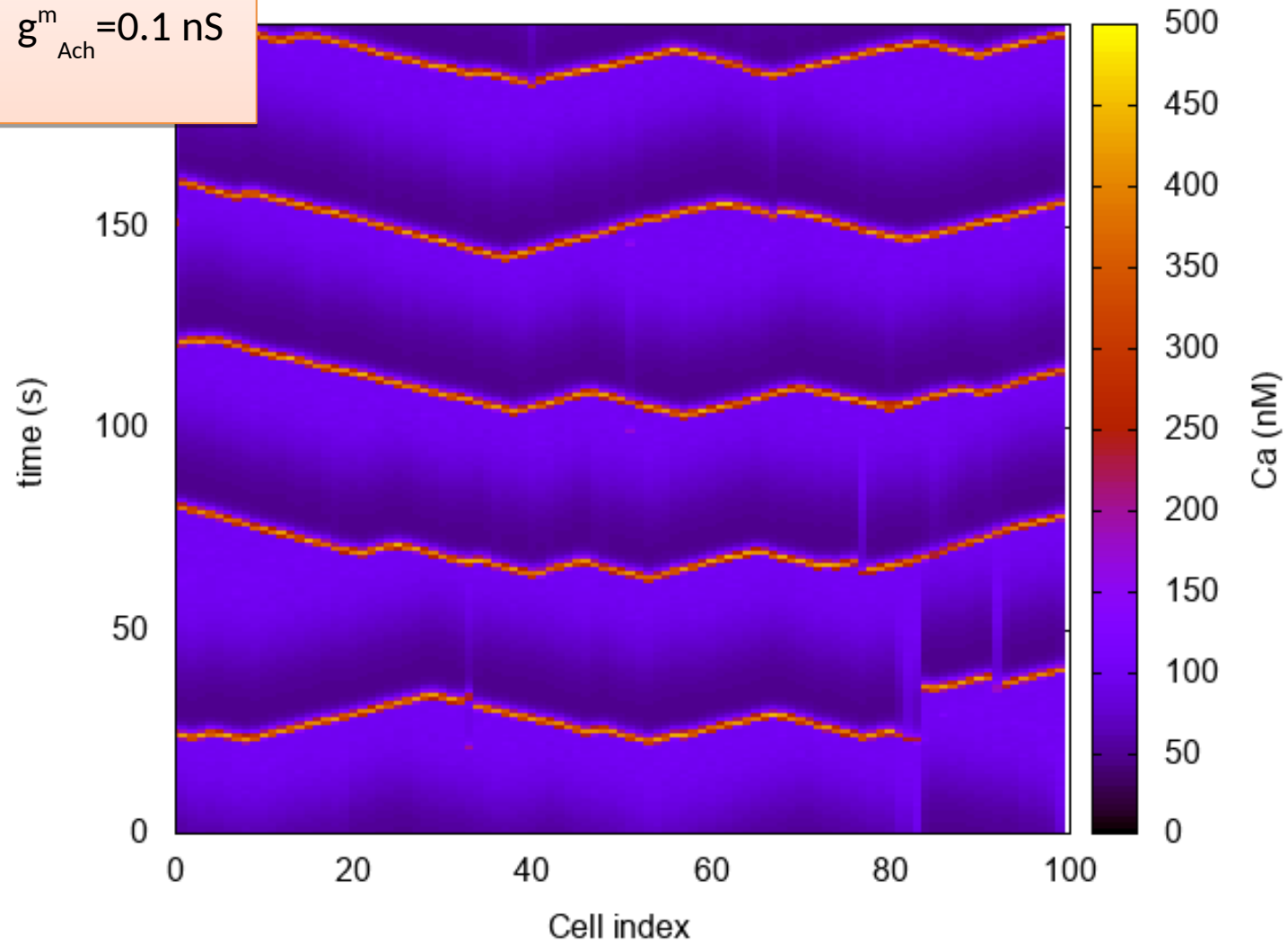
Waves propagation

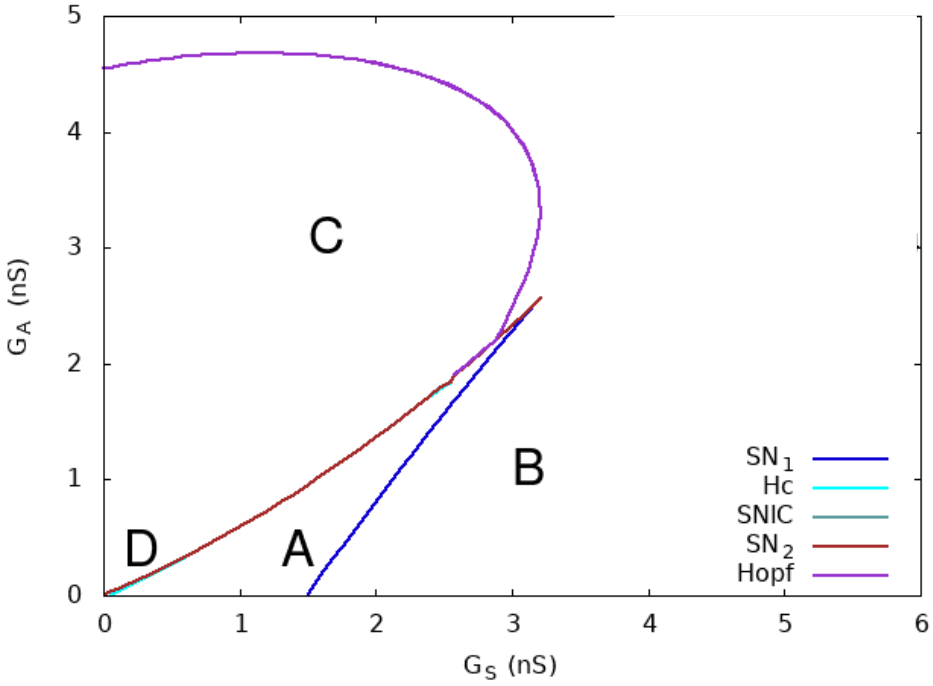
g^{m}_{Ach}=0.07 nS

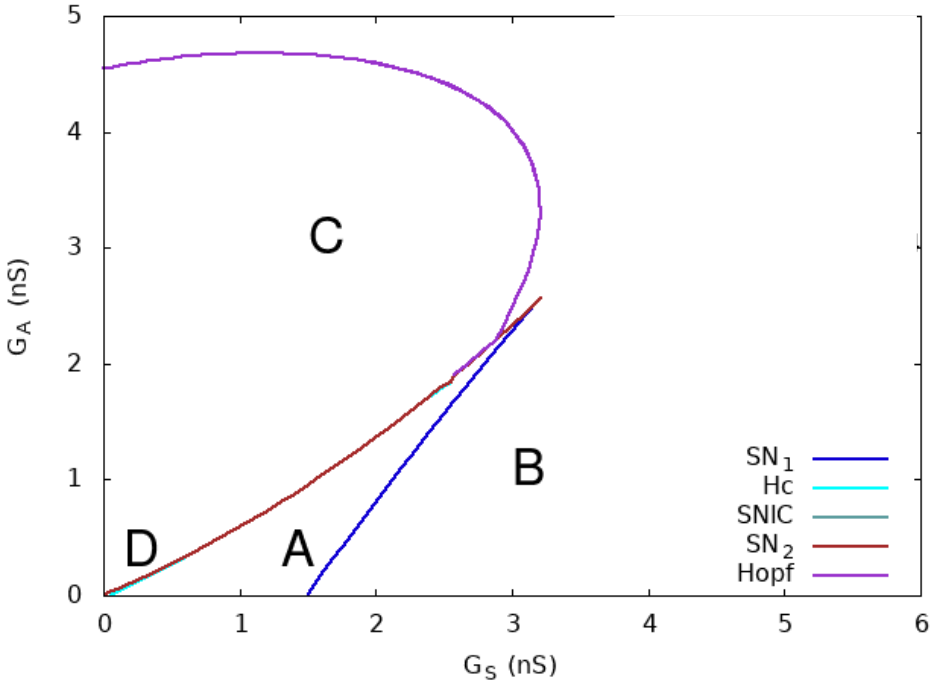


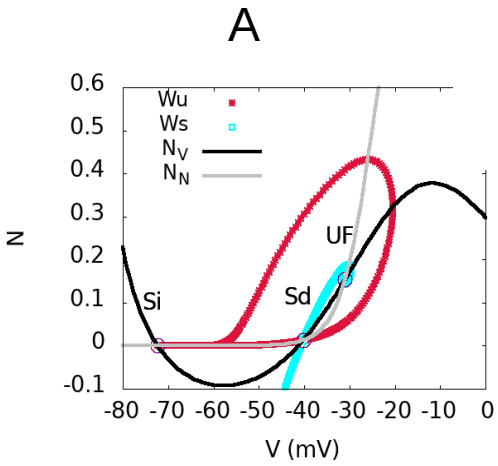
Waves propagation

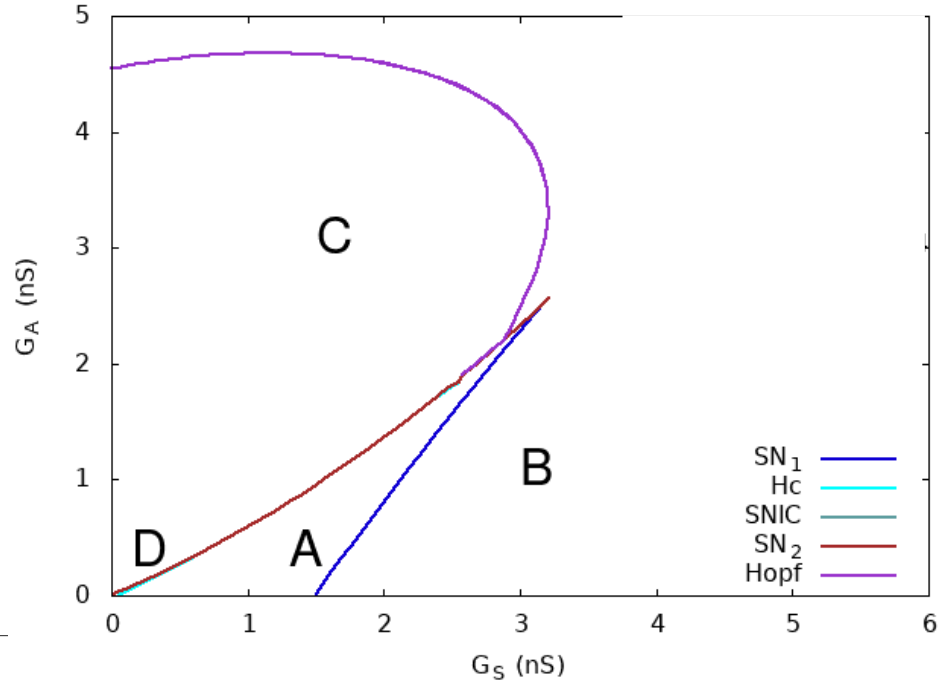
g^{m}_{Ach}=0.1 nS



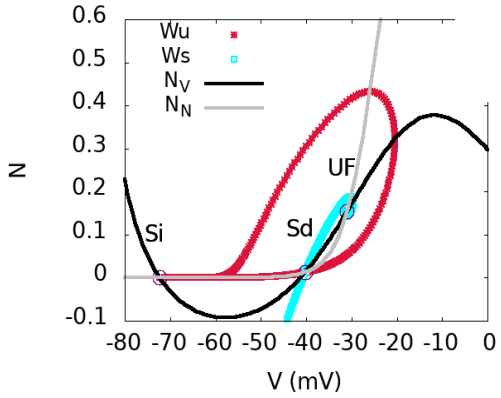

5
4
3
2
1
0
0
1
2
3
4
5
6
G_A (nS)
G_S (nS)
C
B
A
D
SN_1
Hc
SNIC
SN_2
Hopf


5
4
3
2
1
0
0
1
2
3
4
5
6
G_A (nS)
G_S (nS)
C
B
A
D
SN_1
Hc
SNIC
SN_2
Hopf

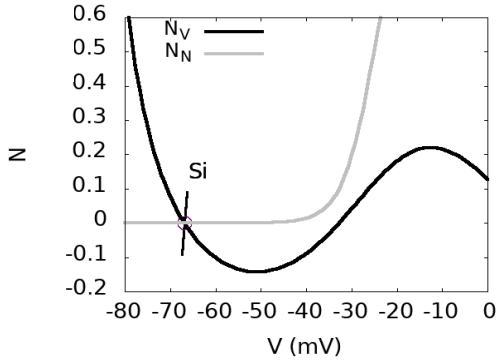

A
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
N
Wu
Ws
N_V
N_N
UF
Si
Sd
-80 -70 -60 -50 -40 -30 -20 -10 0
V (mV)

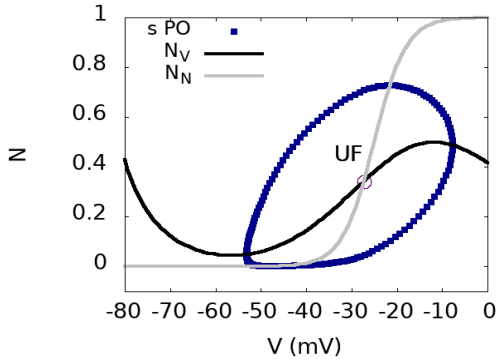

C
B
D
A
SN 1
Hc
SNIC
SN 2
Hopf
G A (nS)
G S (nS)

A

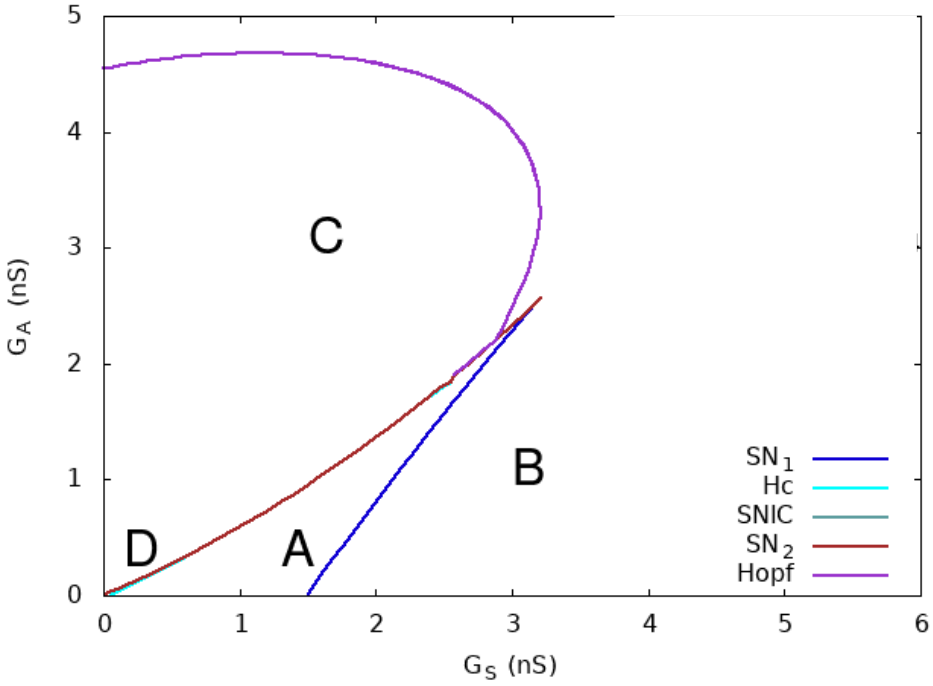

Wu
Ws
N V
N N
UF
Si
Sd
N
V (mV)

B

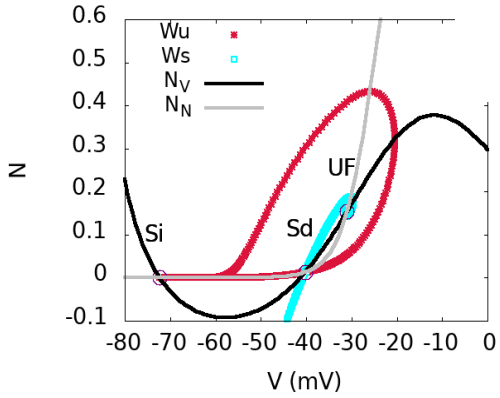

N V
N N
Si
N
V (mV)


s PO
N_V
N_N
UF
N
V (mV)

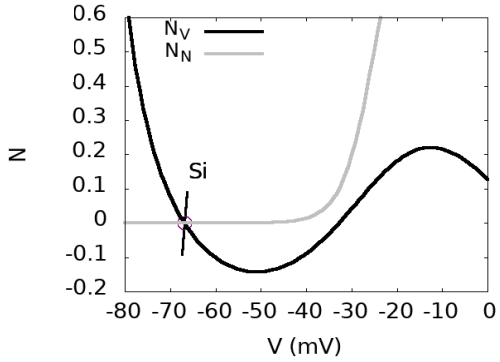
C

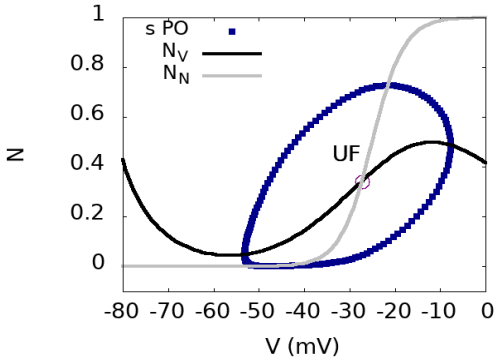

C
B
D
A
SN_1
Hc
SNIC
SN_2
Hopf
G_A (nS)
G_S (nS)

A

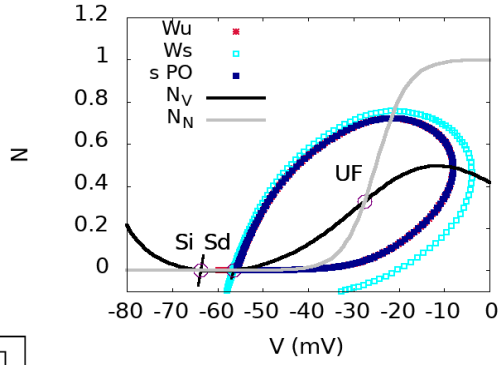

Wu
Ws
N_V
N_N
UF
Si
Sd
N
V (mV)

B

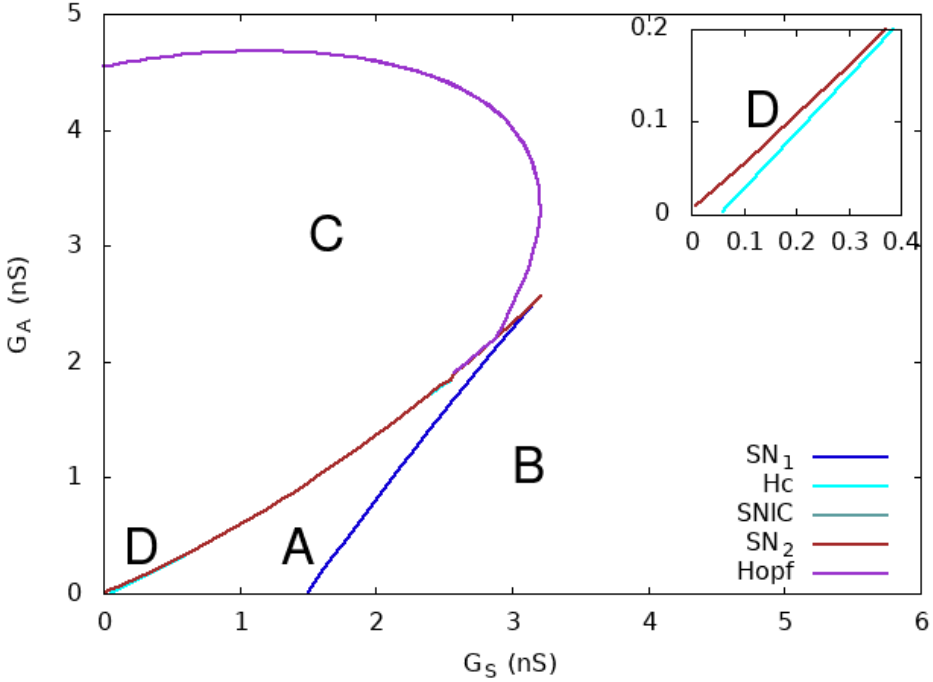

N_V
N_N
Si
N
V (mV)


s PO
N_V
N_N
UF
N
V (mV)

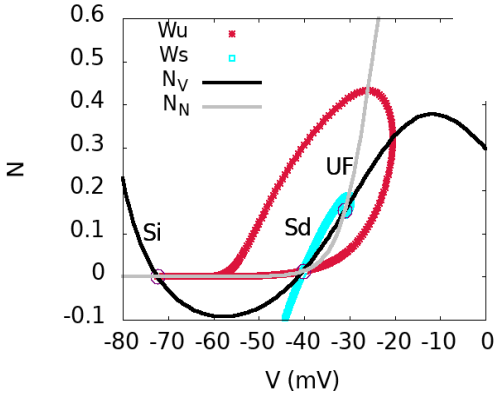
C


Wu
Ws
s PO
N_V
N_N
UF
Si
Sd
N
V (mV)

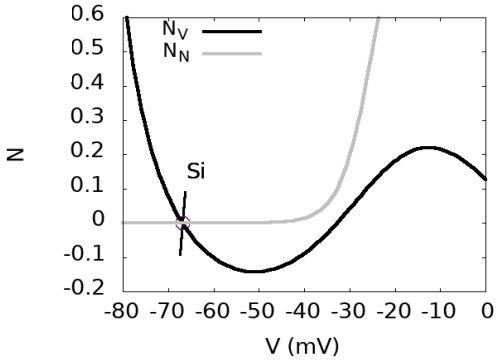
D

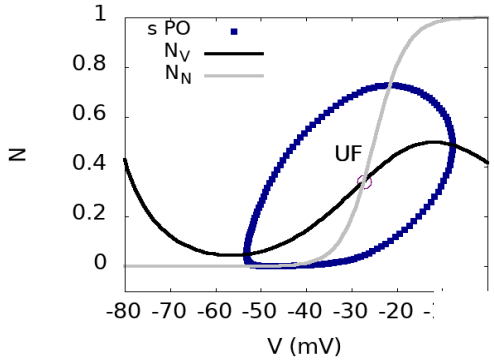

C
D
A
B
G_A (nS)
G_S (nS)
SN_1
Hc
SNIC
SN_2
Hopf

A

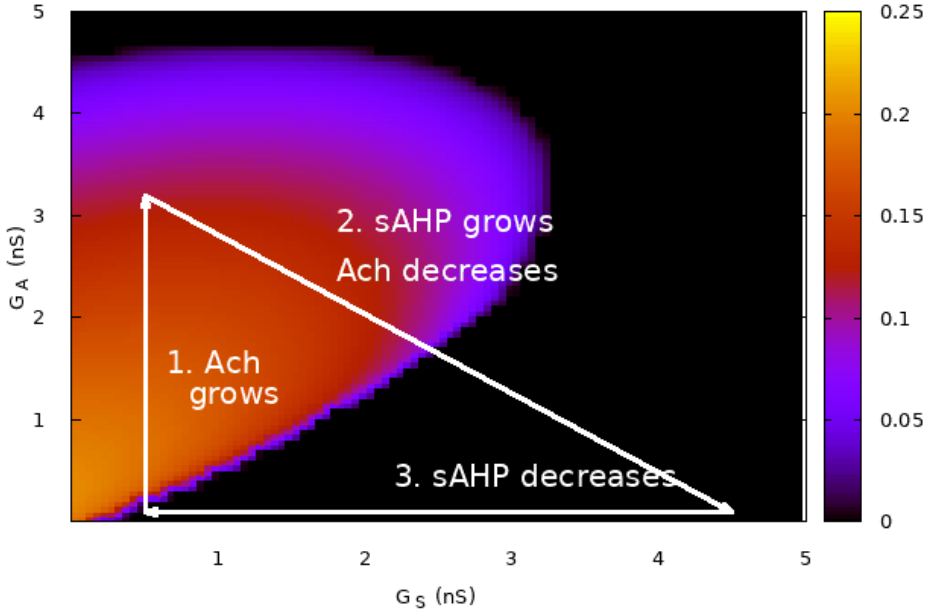

Wu
Ws
N_V
N_N
UF
Si
Sd
N
V (mV)

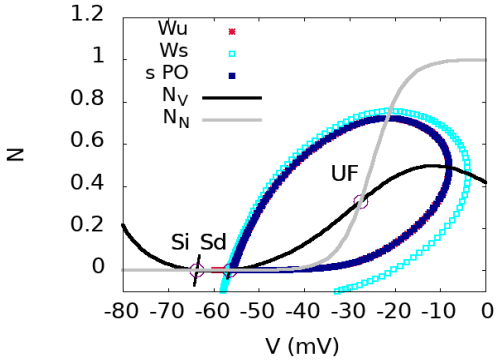
B


N_V
N_N
Si
N
V (mV)


s PO
N_V
N_N
UF
N
V (mV)

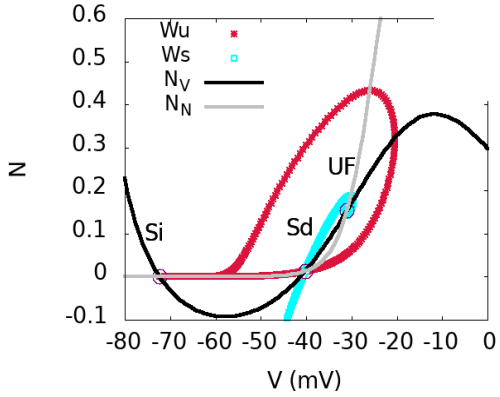
C


2. sAHP grows
Ach decreases
1. Ach grows
3. sAHP decreases
G_A (nS)
G_S (nS)

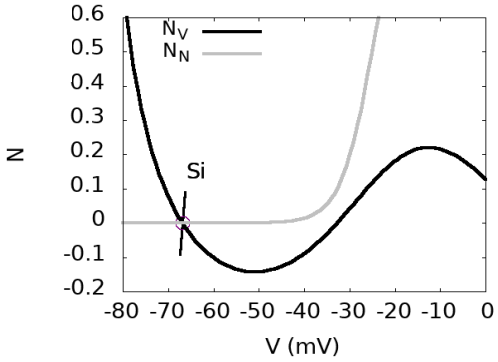

Wu
Ws
s PO
N_V
N_N
UF
Si
Sd
N
V (mV)

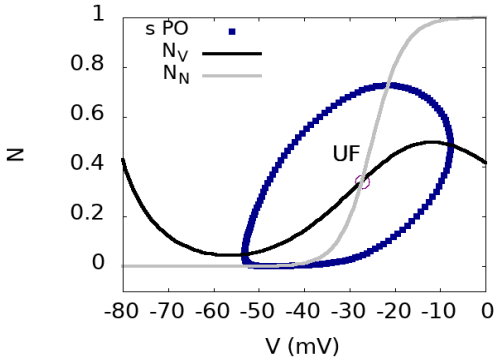
D

A

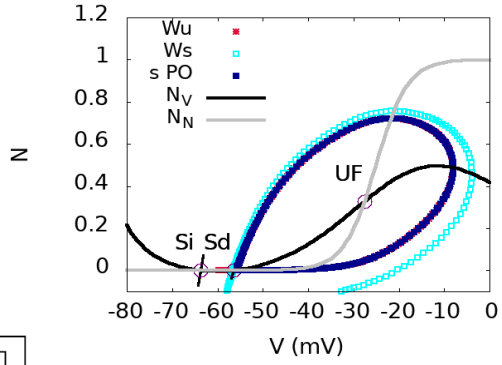

Wu
Ws
N_V
N_N
UF
Si
Sd
N
V (mV)

B

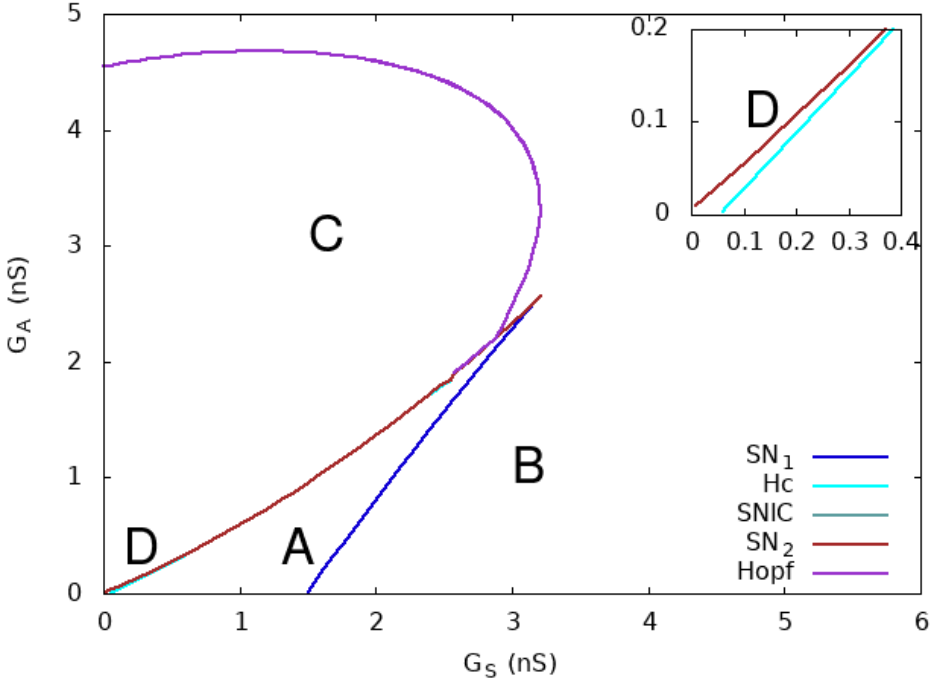

N_V
N_N
Si
N
V (mV)


s PO
N_V
N_N
UF
N
V (mV)

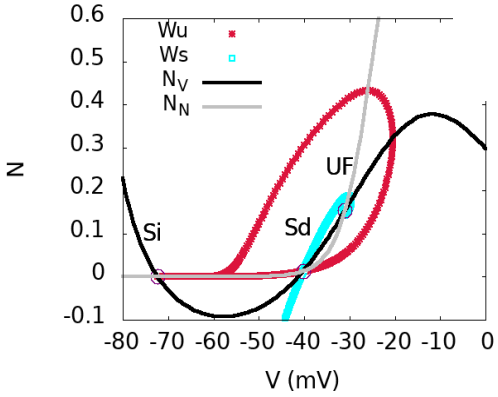
C


Wu
Ws
s PO
N_V
N_N
UF
Si
Sd
N
V (mV)

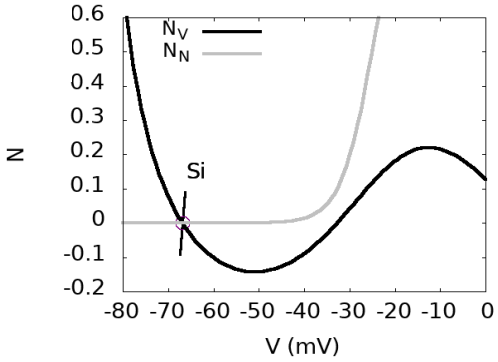
D

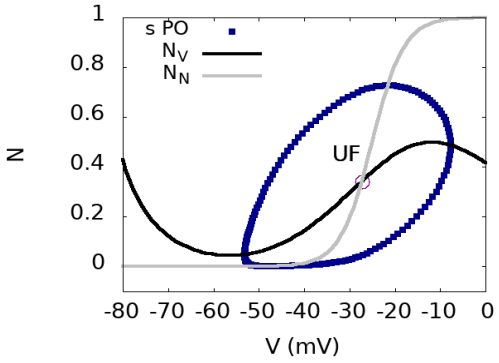

C
D
A
B
G_A (nS)
G_S (nS)
SN_1
Hc
SNIC
SN_2
Hopf

A

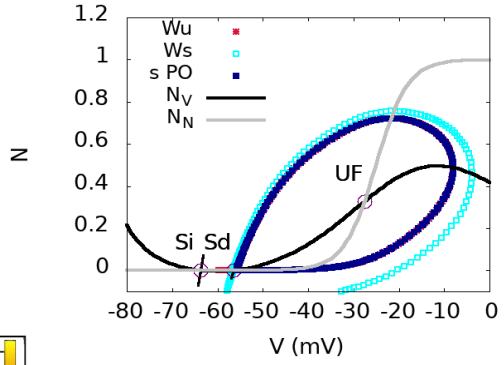

Wu
Ws
N_V
N_N
UF
Si
Sd
N
V (mV)

B

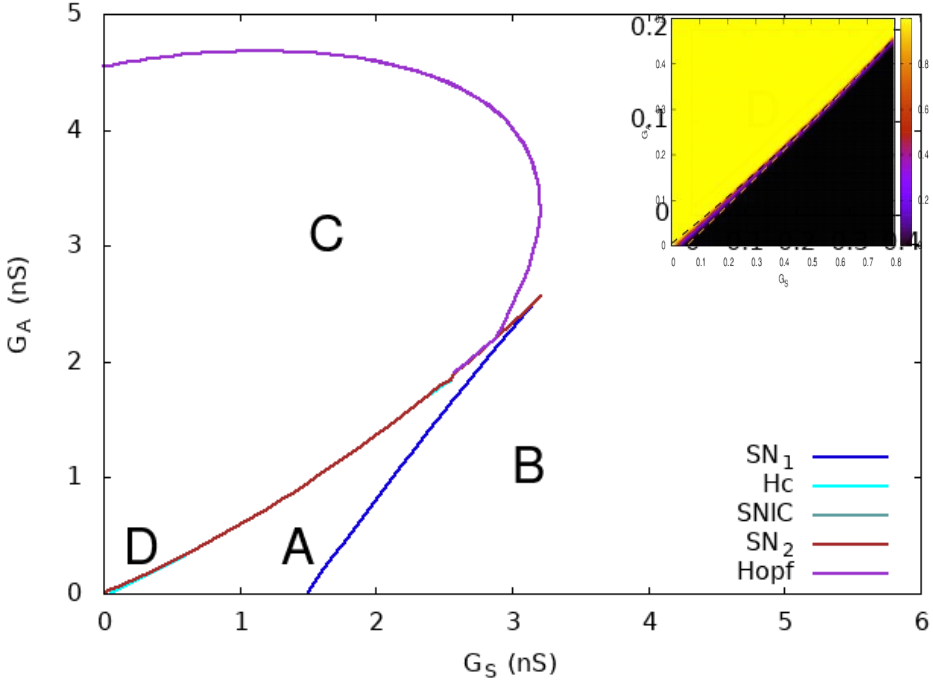

N_V
N_N
Si
N
V (mV)


s PO
N_V
N_N
UF
N
V (mV)

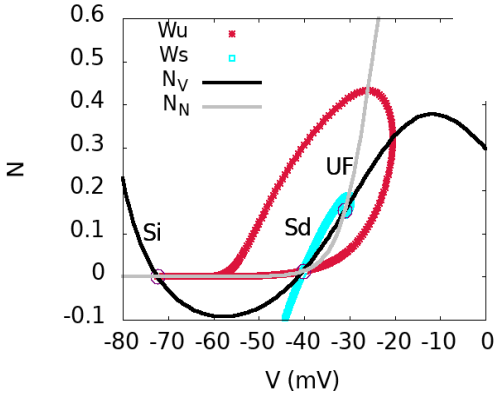
C


Wu
Ws
s PO
N_V
N_N
UF
Si
Sd
N
V (mV)

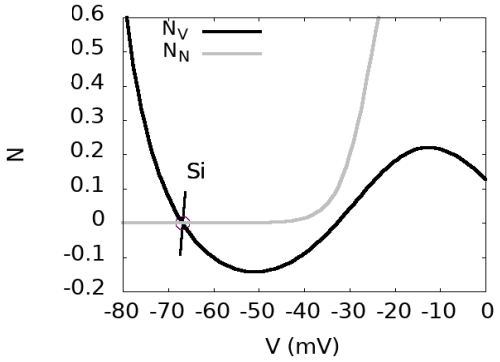
D

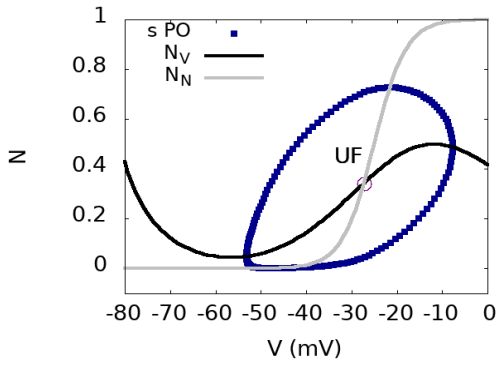

C
B
D
A
SN_1
Hc
SNIC
SN_2
Hopf
G_A (nS)
G_S (nS)

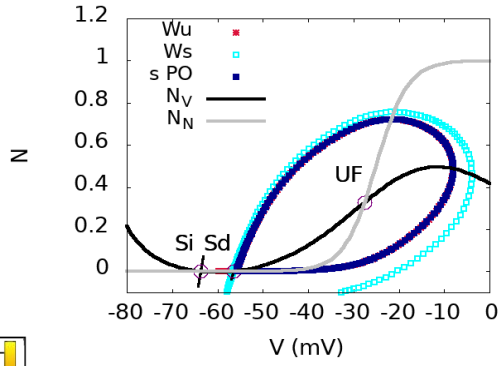
A


Wu
Ws
N_V
N_N
UF
Si
Sd
N
V (mV)

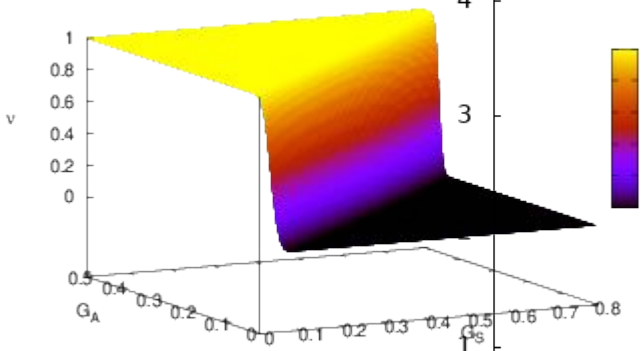
B

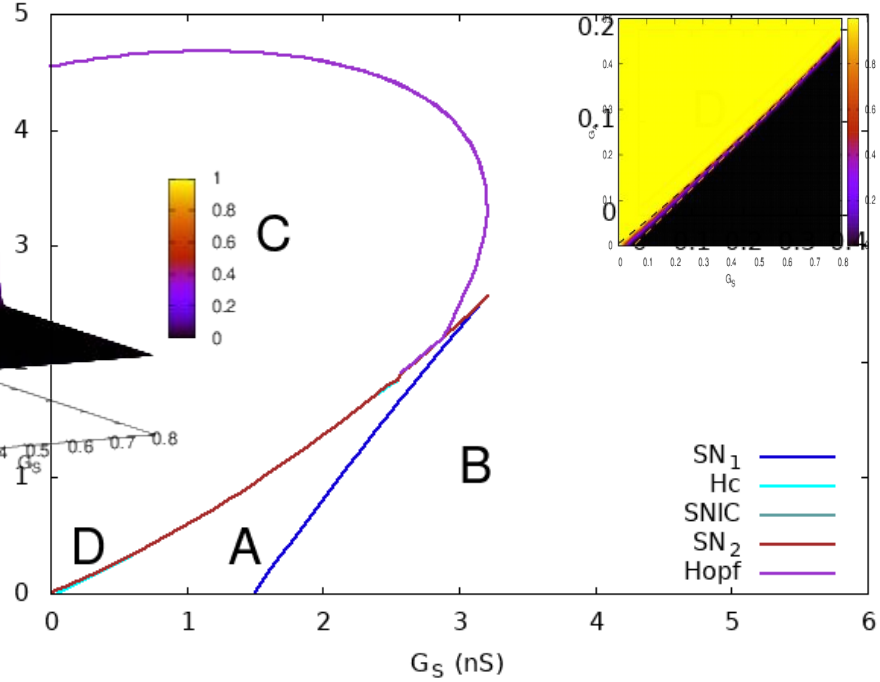

N_V
N_N
Si
N
V (mV)


s PO
N_V
N_N
UF
N
V (mV)


Wu
Ws
s PO
N_V
N_N
UF
Si
Sd
N
V (mV)

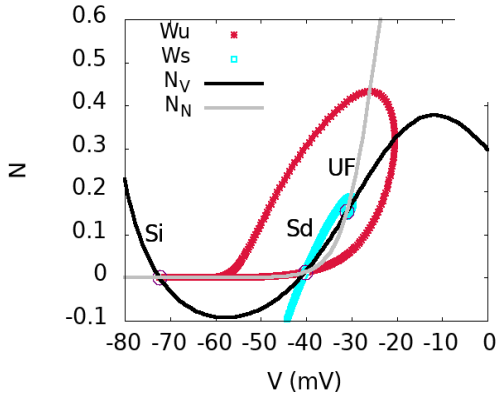
C


v
G_A
G_S

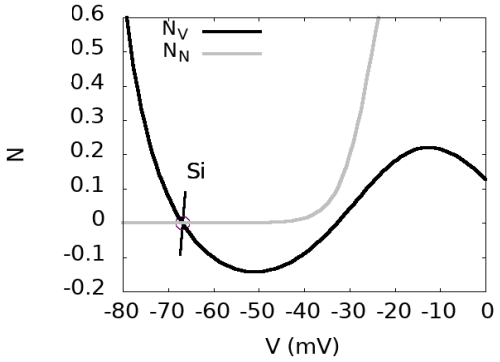

C
B
D
A
SN_1
Hc
SNIC
SN_2
Hopf
G_S (nS)

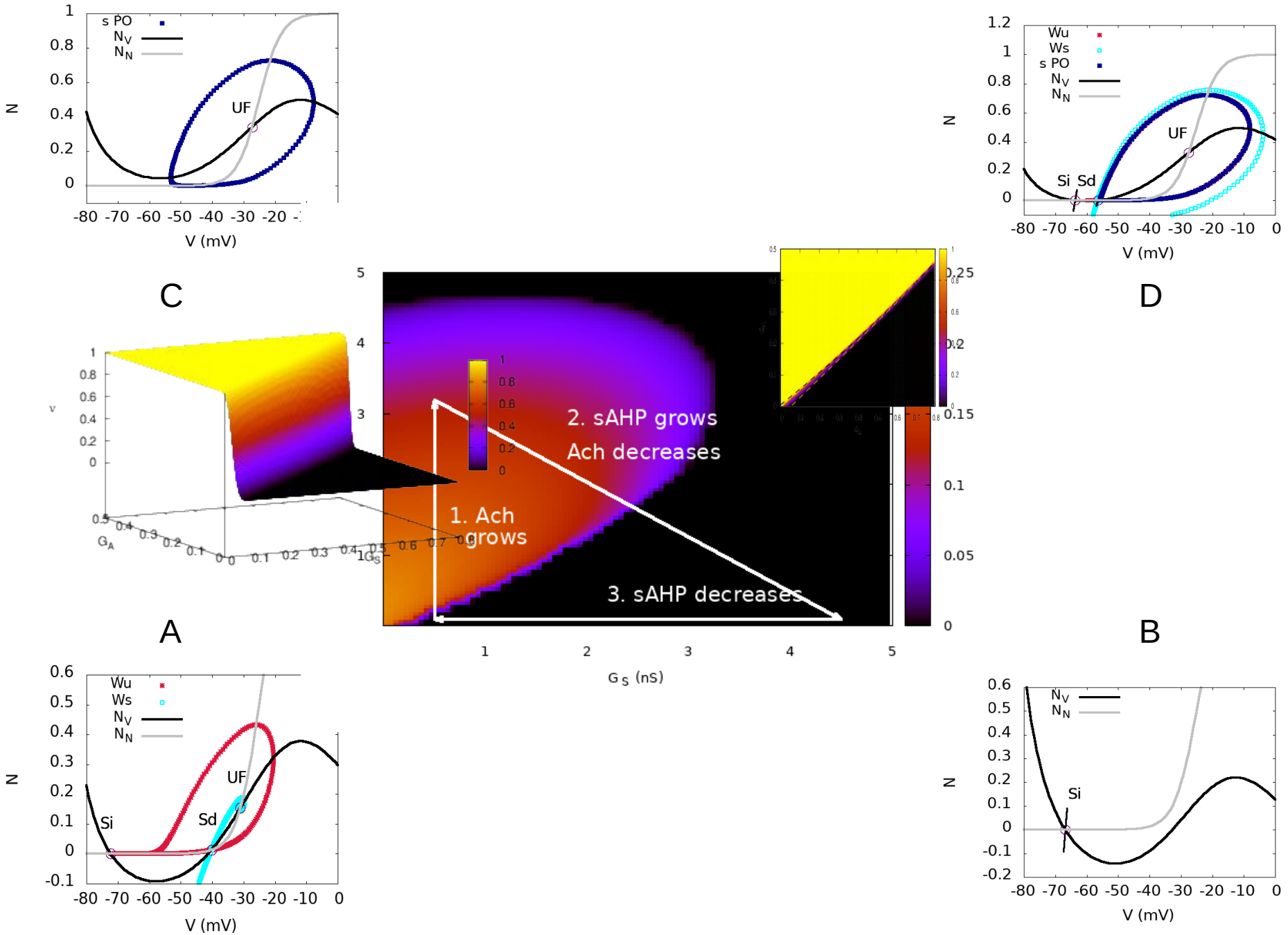
D

A


Wu
Ws
N_V
N_N
UF
Si
Sd
N
V (mV)

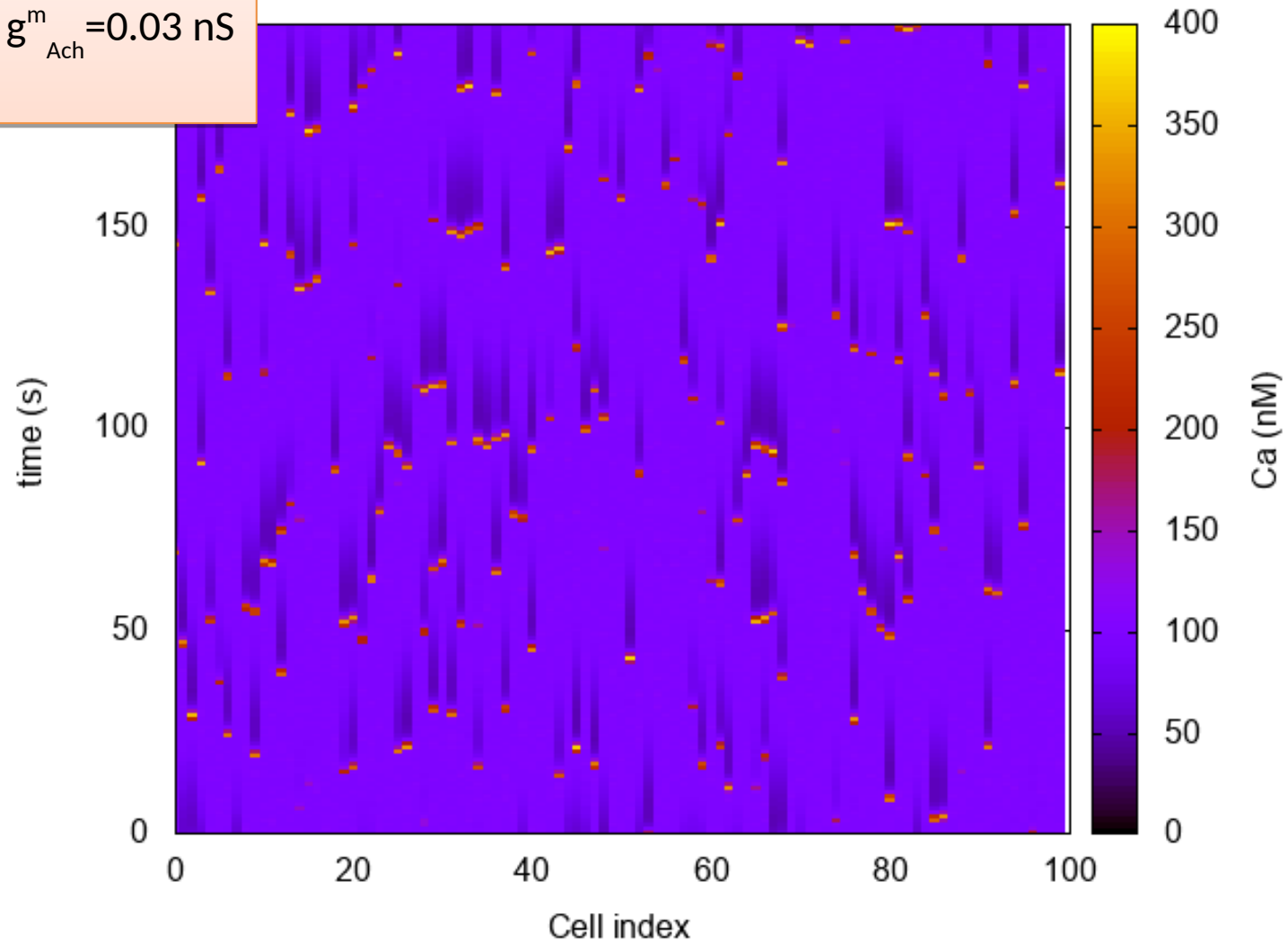
B


N_V
N_N
Si
N
V (mV)


A
B
C
D
s PO
N_V
N_N
Wu
Ws
UF
Si
Sd
N
V (mV)
1. Ach grows
2. sAHP grows
Ach decreases
3. sAHP decreases
G_S (nS)
G_A
V

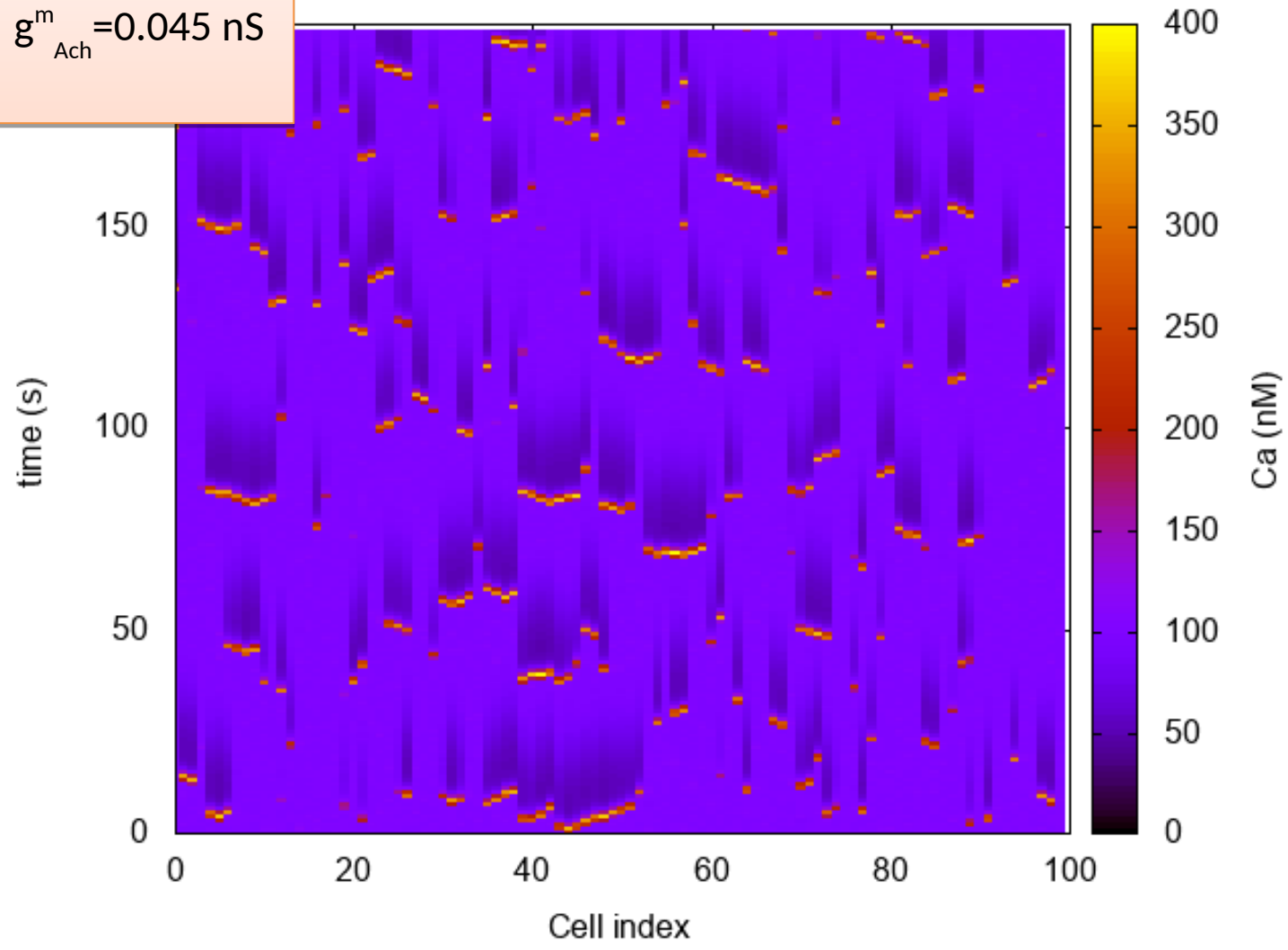
Waves propagation

g^{m}_{Ach}=0.03 nS



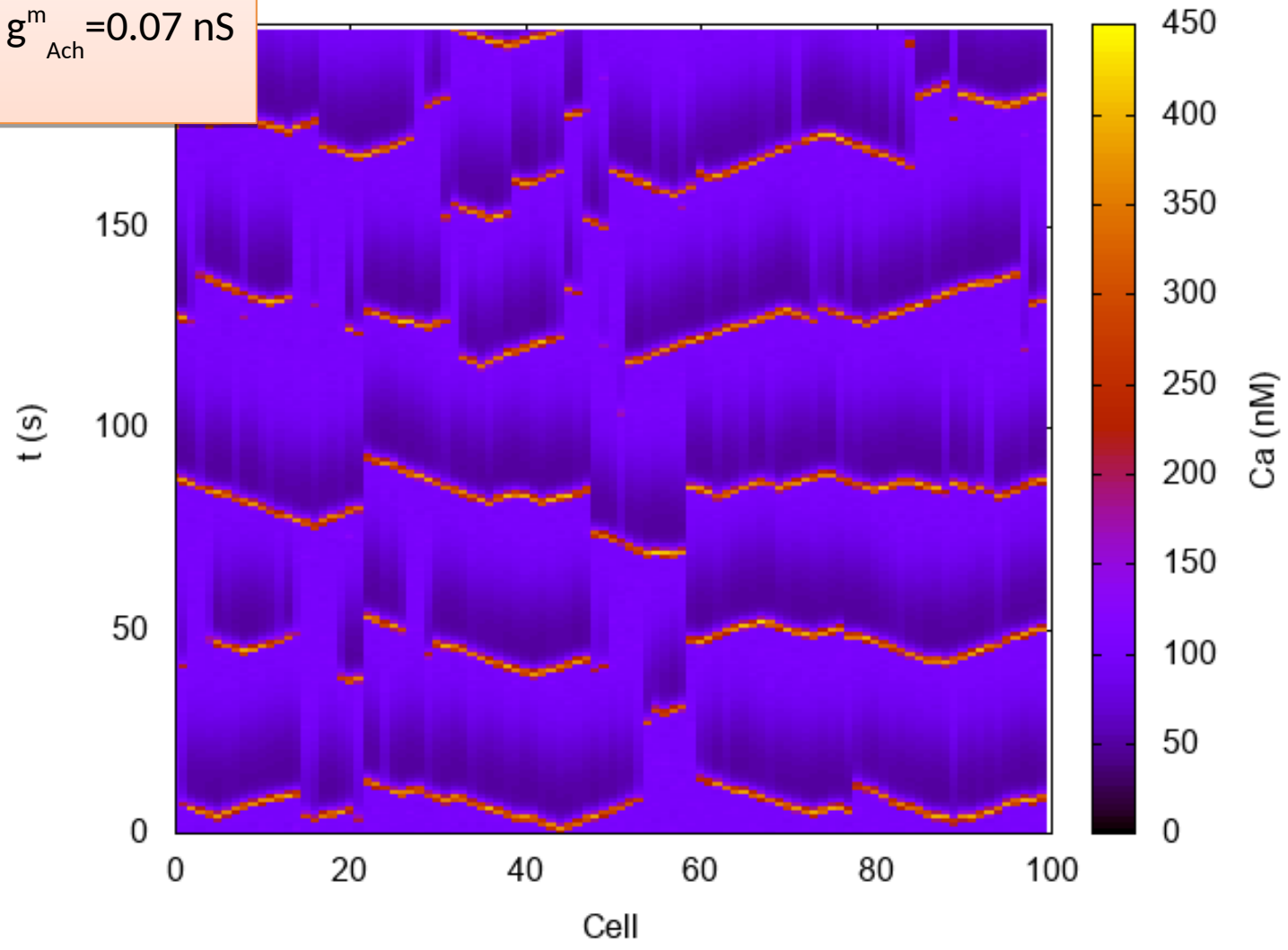
Waves propagation

g^{m}_{Ach}=0.045 nS



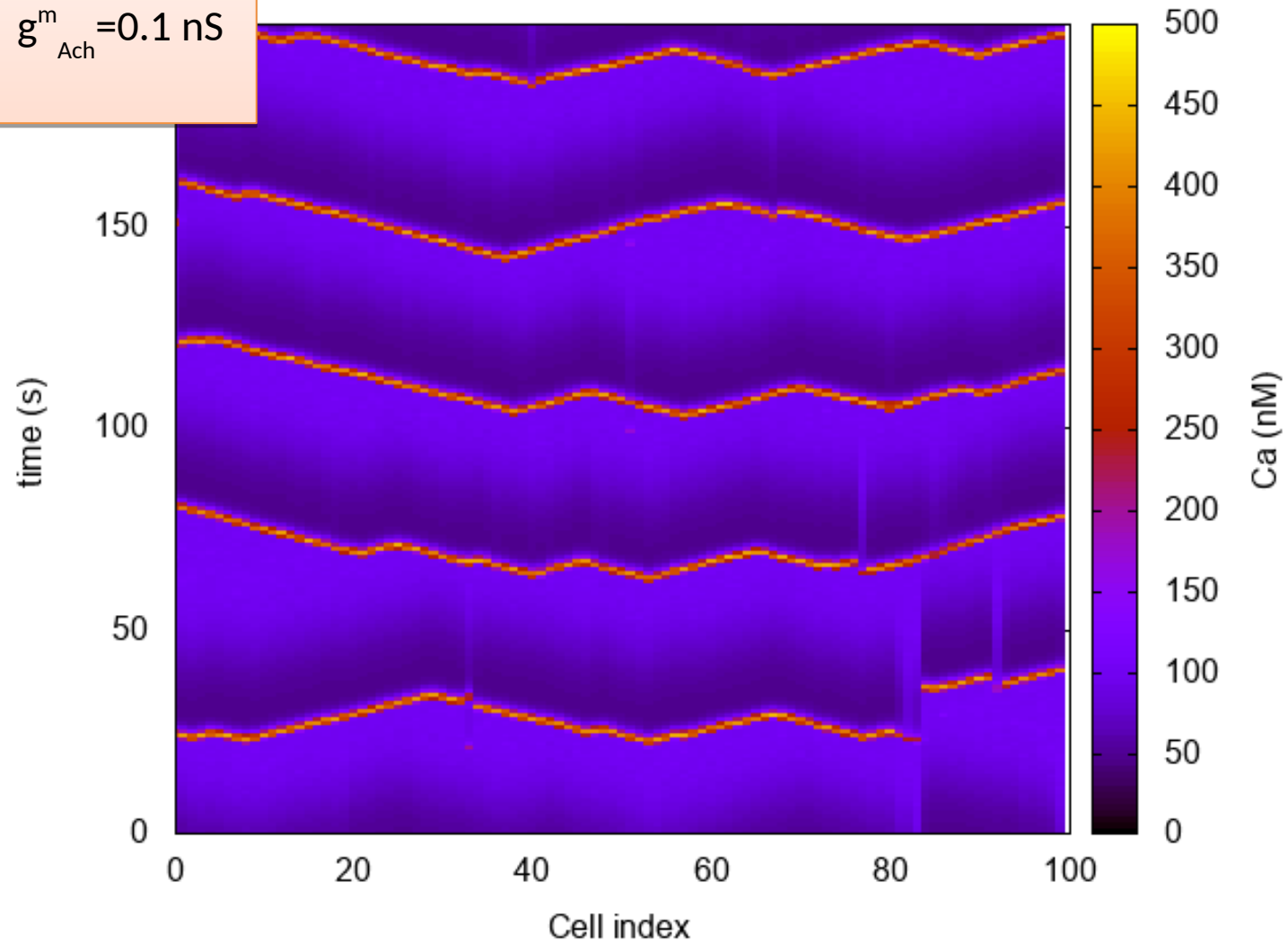
Waves propagation

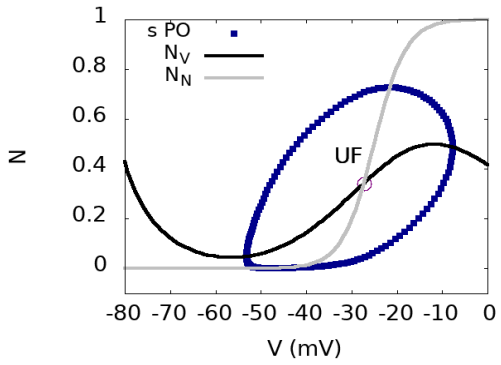
g^{m}_{Ach}=0.07 nS



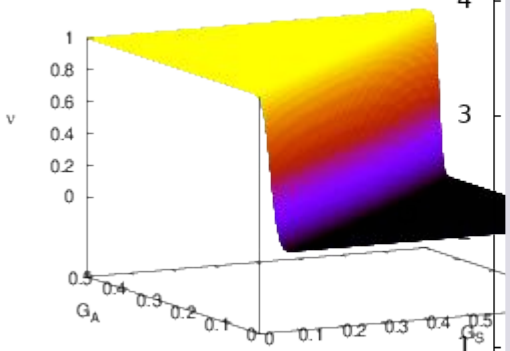
Waves propagation

g^{m}_{Ach}=0.1 nS

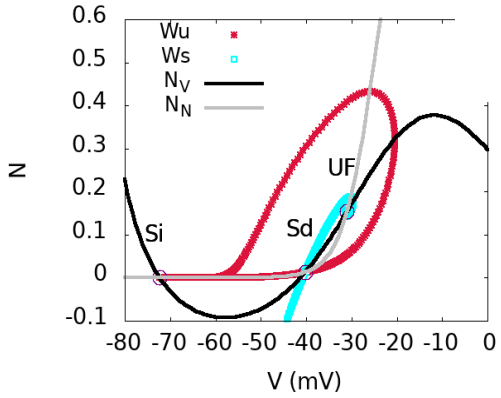


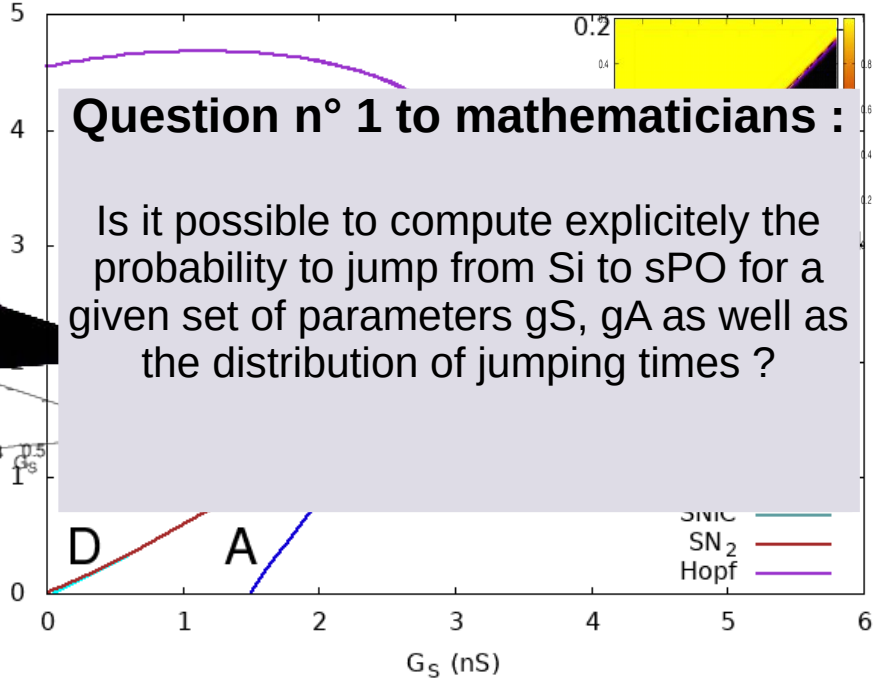


C



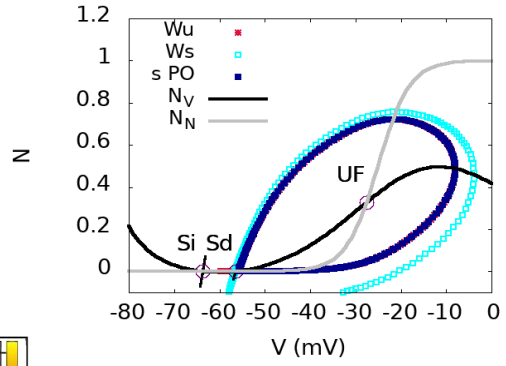
A





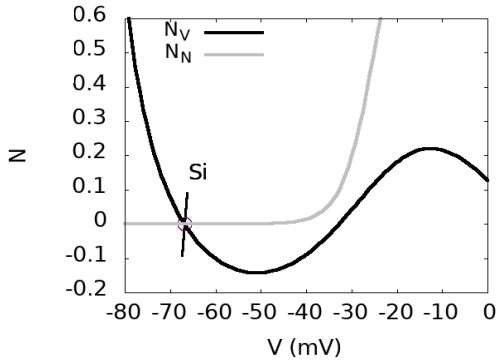
Question n° 1 to mathematicians :

Is it possible to compute explicitely the probability to jump from Si to sPO for a given set of parameters gS, gA as well as the distribution of jumping times ?



D

B

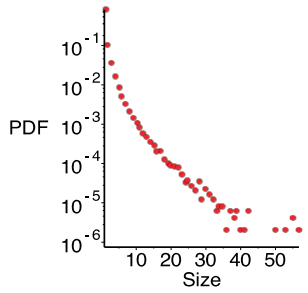


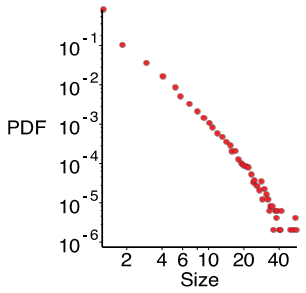
Waves size distribution

lin-log

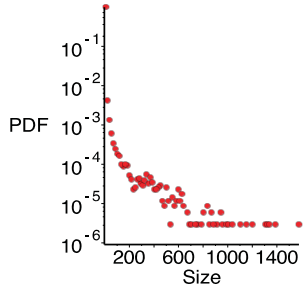
log-log

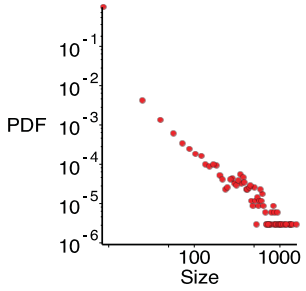
A



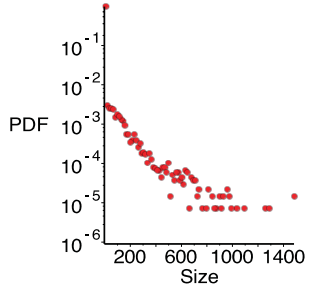


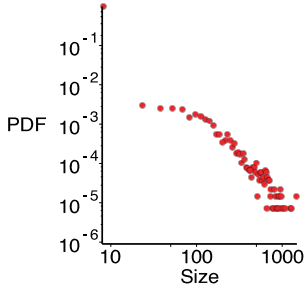
B



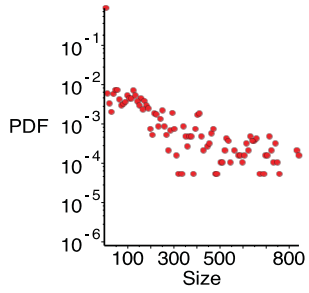


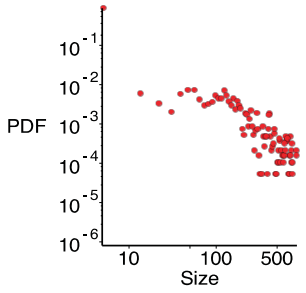
C

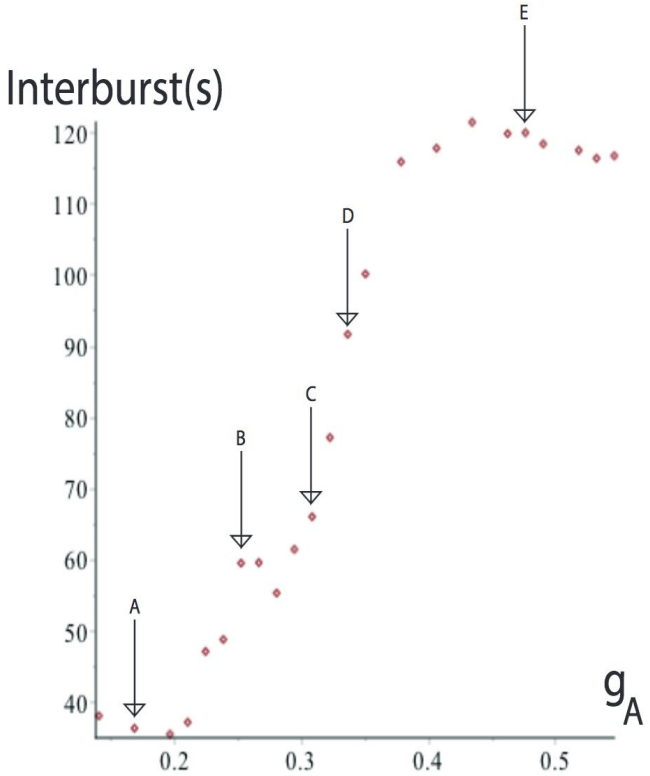




E







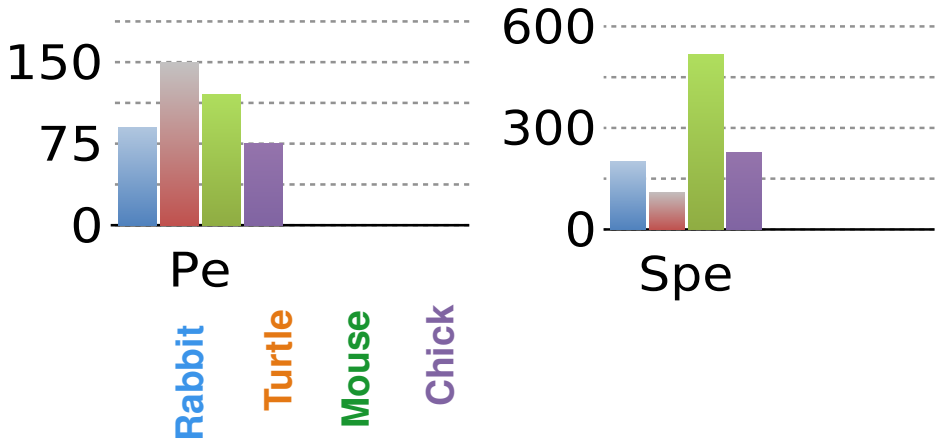
N-neuron model

- There is a **competition** between 2 mechanisms:
  - Period variability which tends to desynchronise
  - Acetylcholine which tends to synchronise
- There is an intermediate regime of coupling, where **variability** is maximum
- Therefore there is a wide repertoire of patterns
  - **Weak coupling** leads to small **localised activity**
  - **Moderate coupling** leads to **propagating patterns**
  - **Strong coupling** leads to **complete synchrony** of neurons

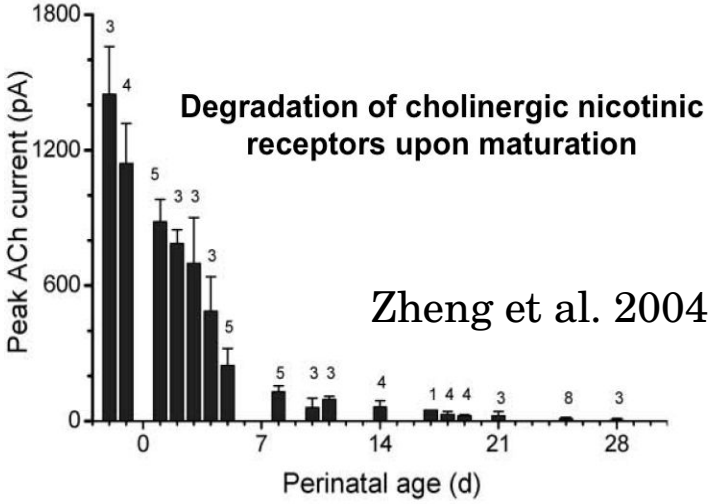
Variability within retinal waves

i) Across species

Godfrey et al. 2007

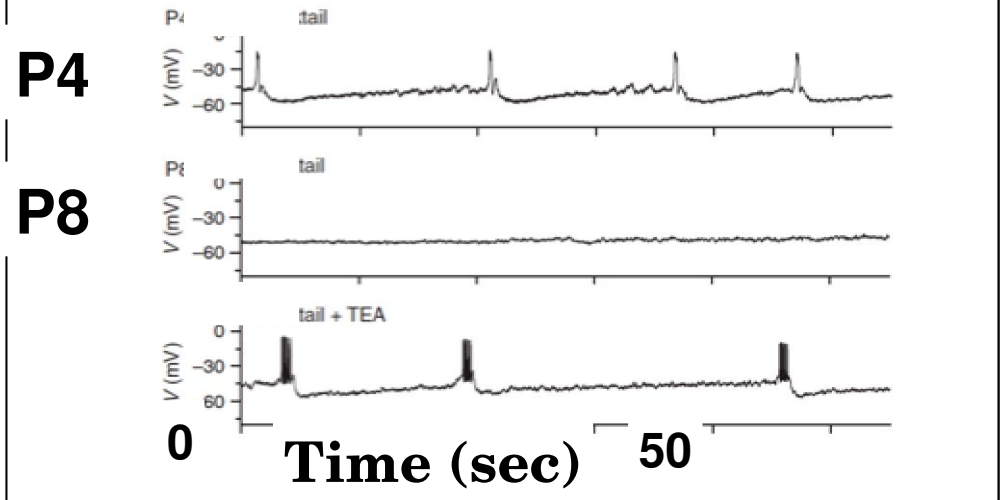


ii) Development



Zheng et al. 2004

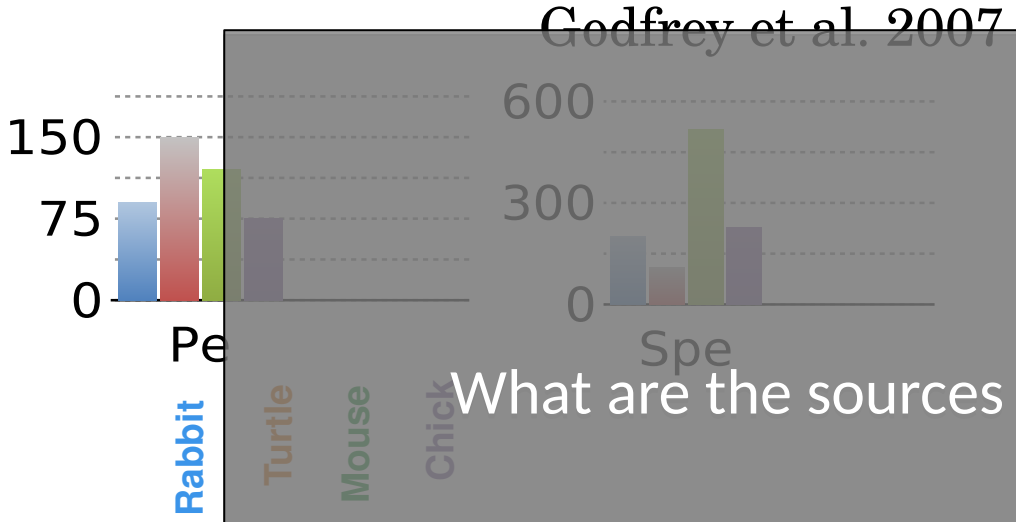
iii) Pharmacology



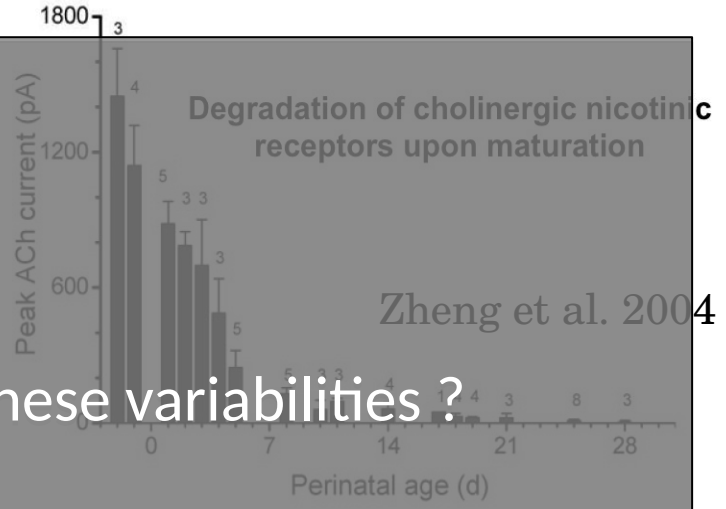
iv) Spatial Variability

Variability within retinal waves

i) Across species



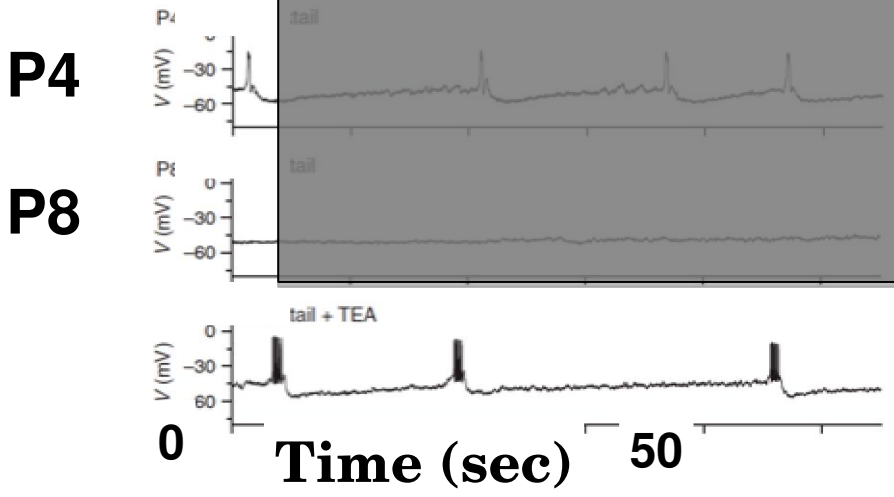
ii) Development



What are the sources of these variabilities ?

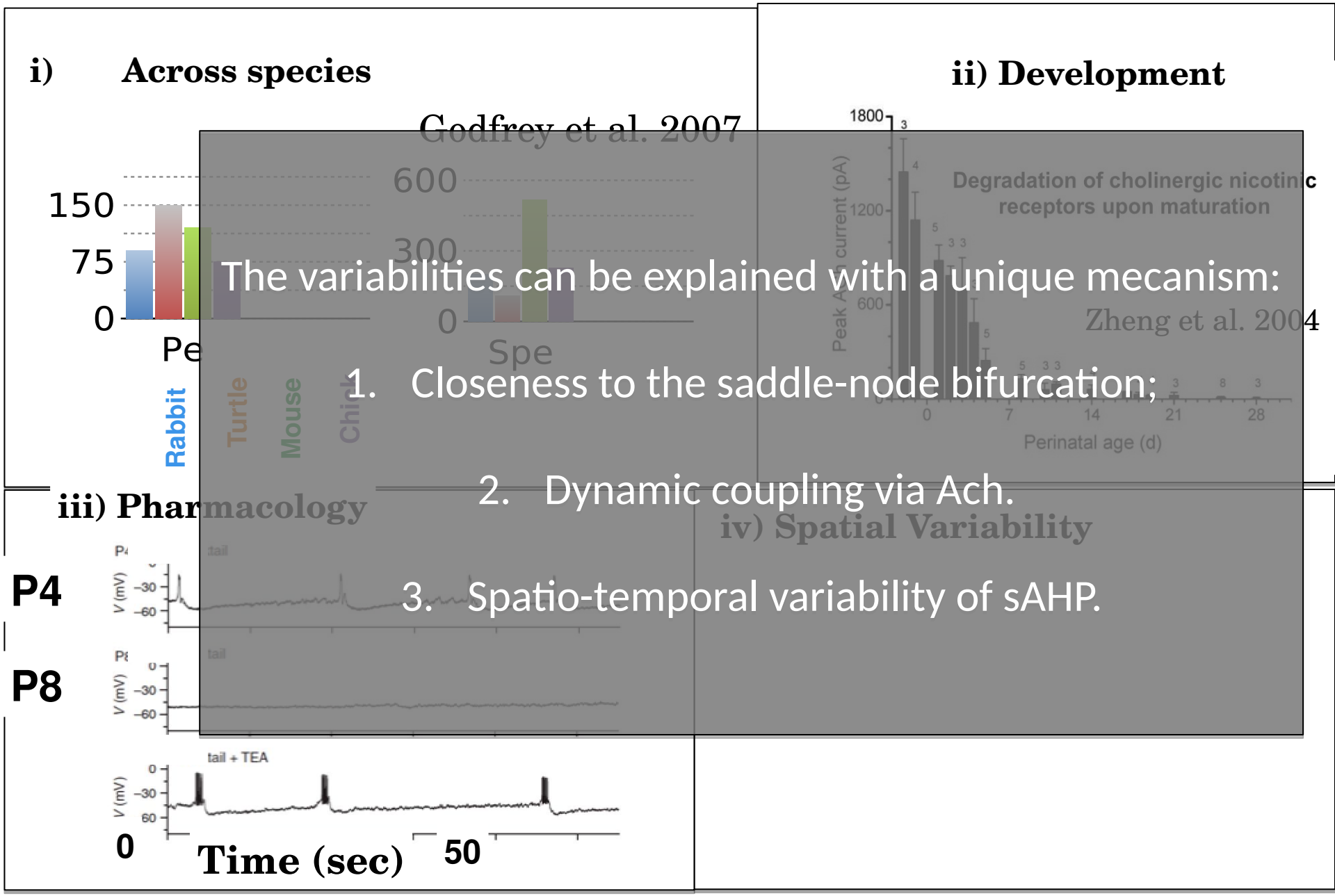
Is there a unique, global, mechanism explaining them ?

iii) Pharmacology



iv) Spatial Variability

Variability within retinal waves

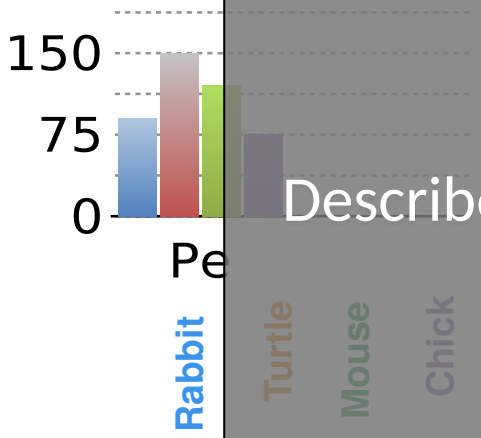


The variabilities can be explained with a unique mecanism:

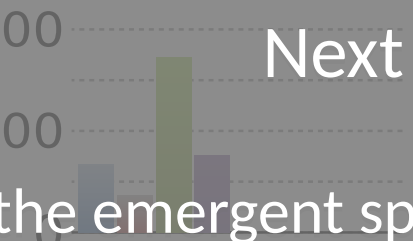
1. Closeness to the saddle-node bifurcation;
2. Dynamic coupling via Ach.
3. Spatio-temporal variability of sAHP.

Variability within retinal waves

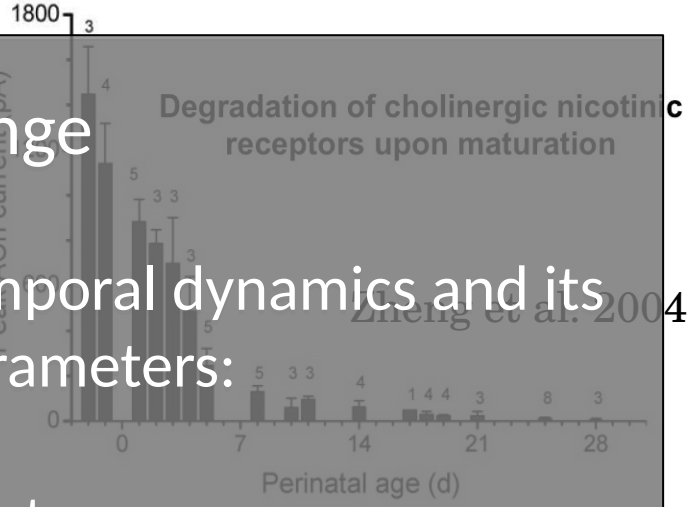
i) Across species



Godfrey et al. 2007



ii) Development



Zheng et al. 2004

Next challenge

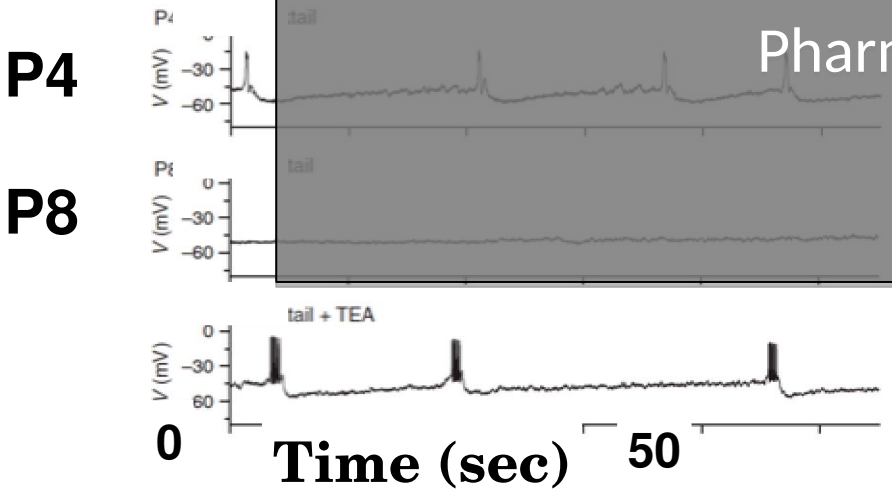
Describe the emergent spatio-temporal dynamics and its dependence on parameters:

Development

Pharmacological control

Pathologies.

iii) Pharmacology



iv) Spatial Variability

Retinal anticipation

Random connectivity and motion anticipation

S. Souihel (PhD 2016-2019), Biovision team, INRIA, Sophia Antipolis

F. Chavane, INT, Marseille

A. Destexhe, UNIC, Paris

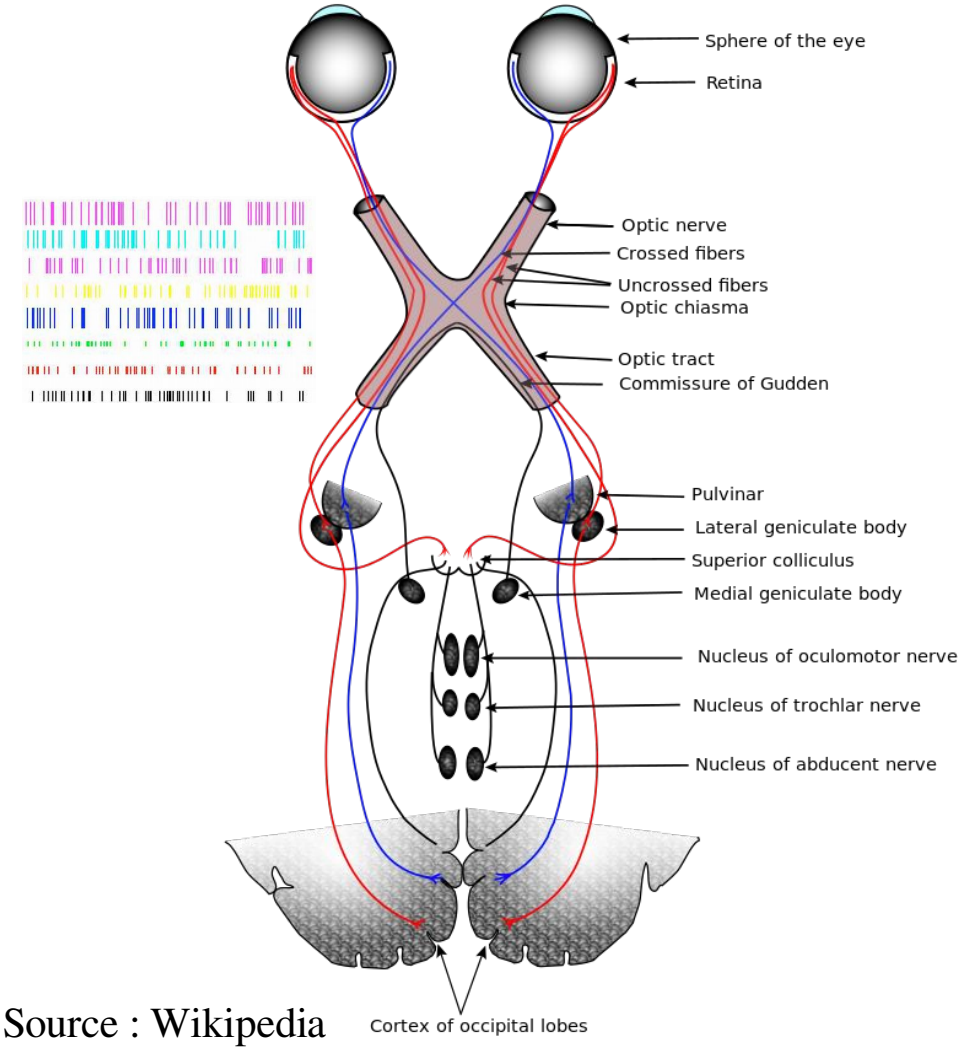
O. Marre, Institut de la Vision, Paris

B. Cessac, Biovision team, INRIA, Sophia Antipolis



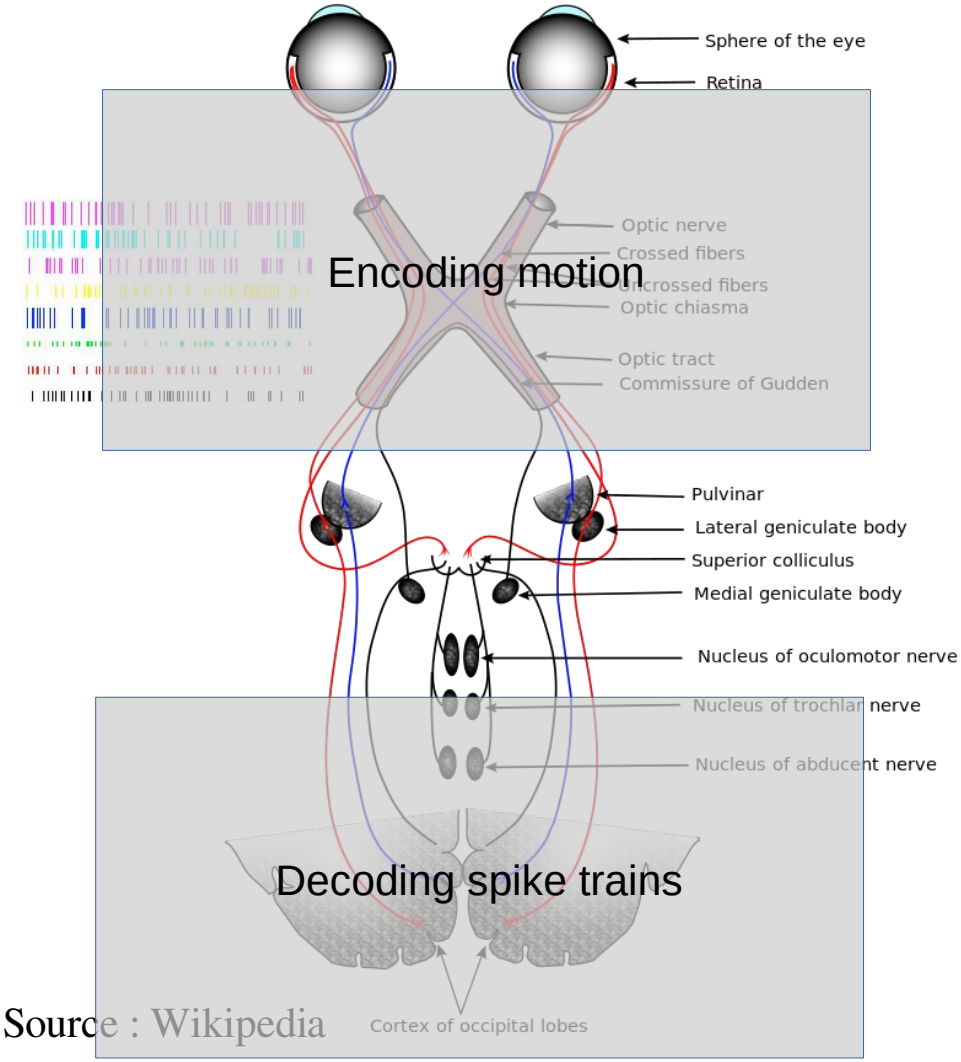
Project : ANR Trajectory.

The visual flow



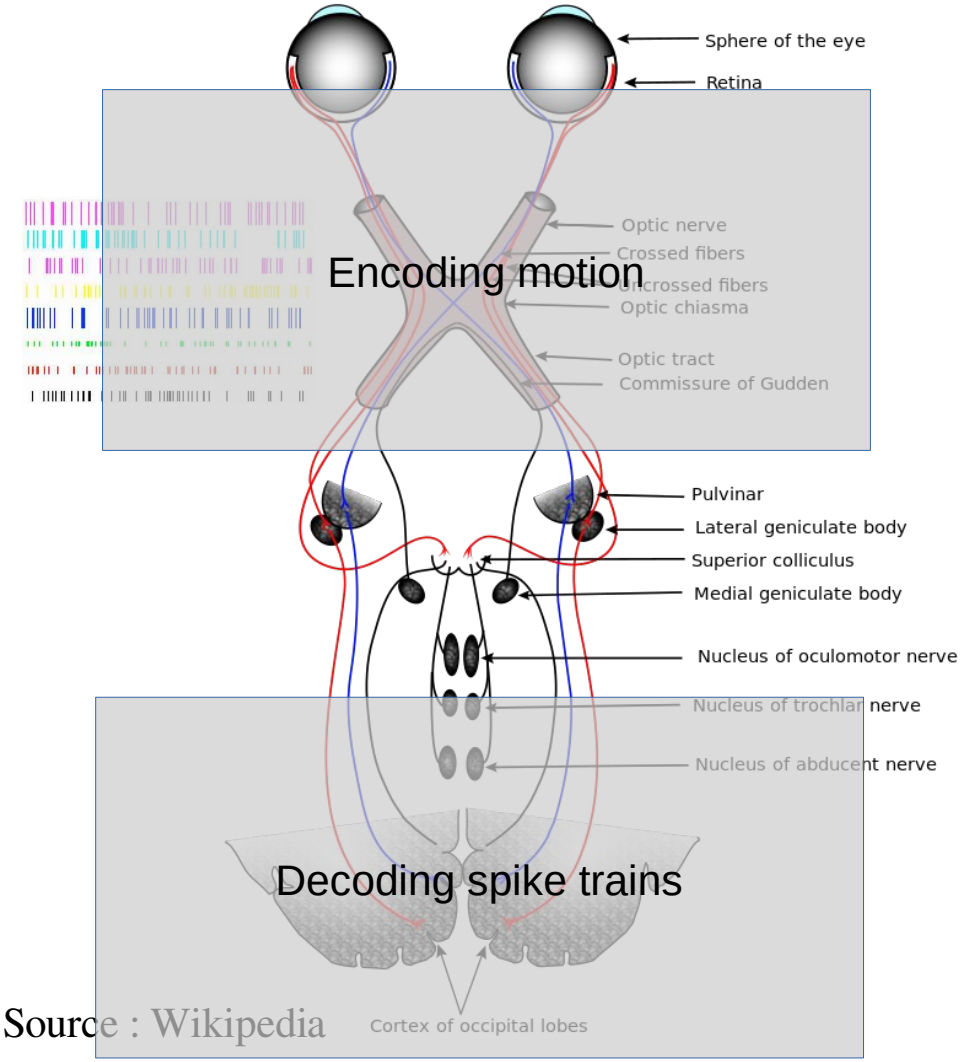
Source : Wikipedia

The visual flow



Source : Wikipedia

The visual flow

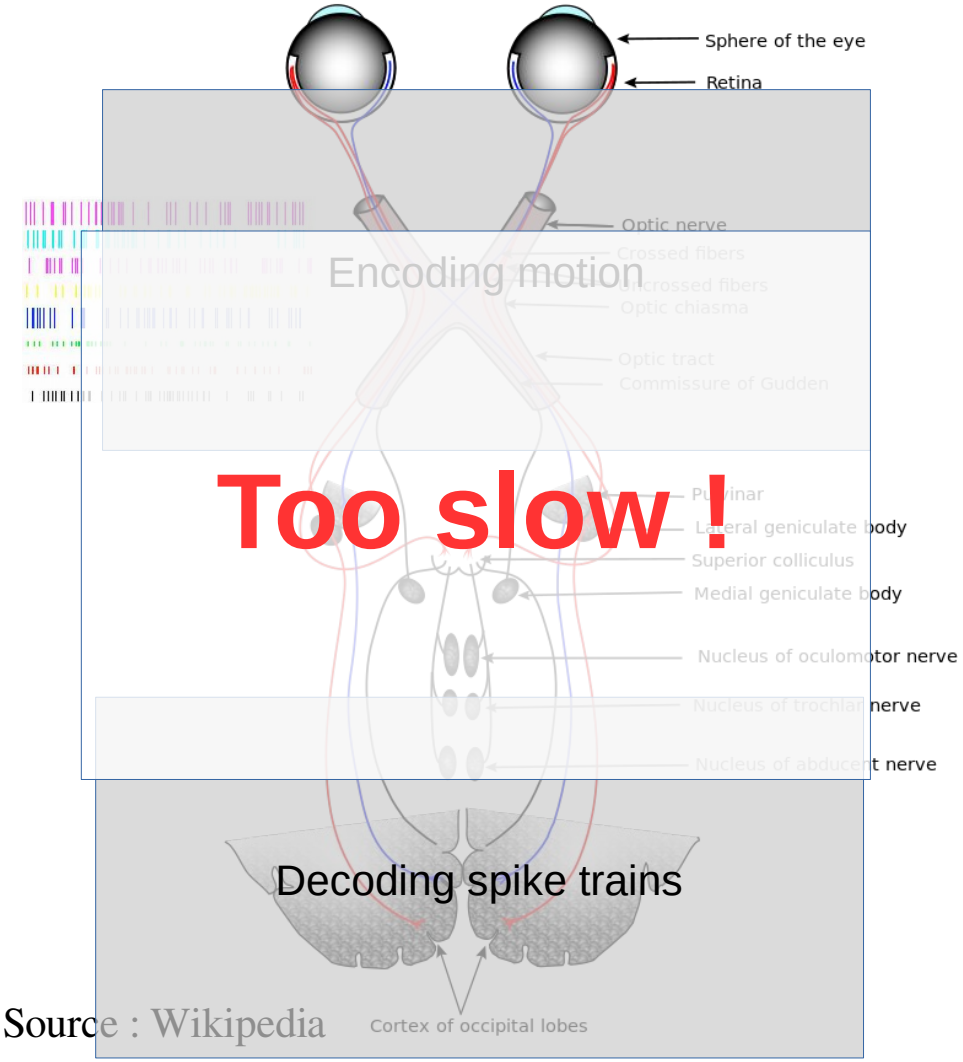


Source : Wikipedia

- **The retina is NOT a camera**

- High transduction rate : 1 photon can trigger a membrane voltage variation of ~1 mV
- Able to detect approaching motion
- Able to detect differential motion
- Sensitive to « surprise » in a visual scene
- Able to perform motion anticipation

The visual flow

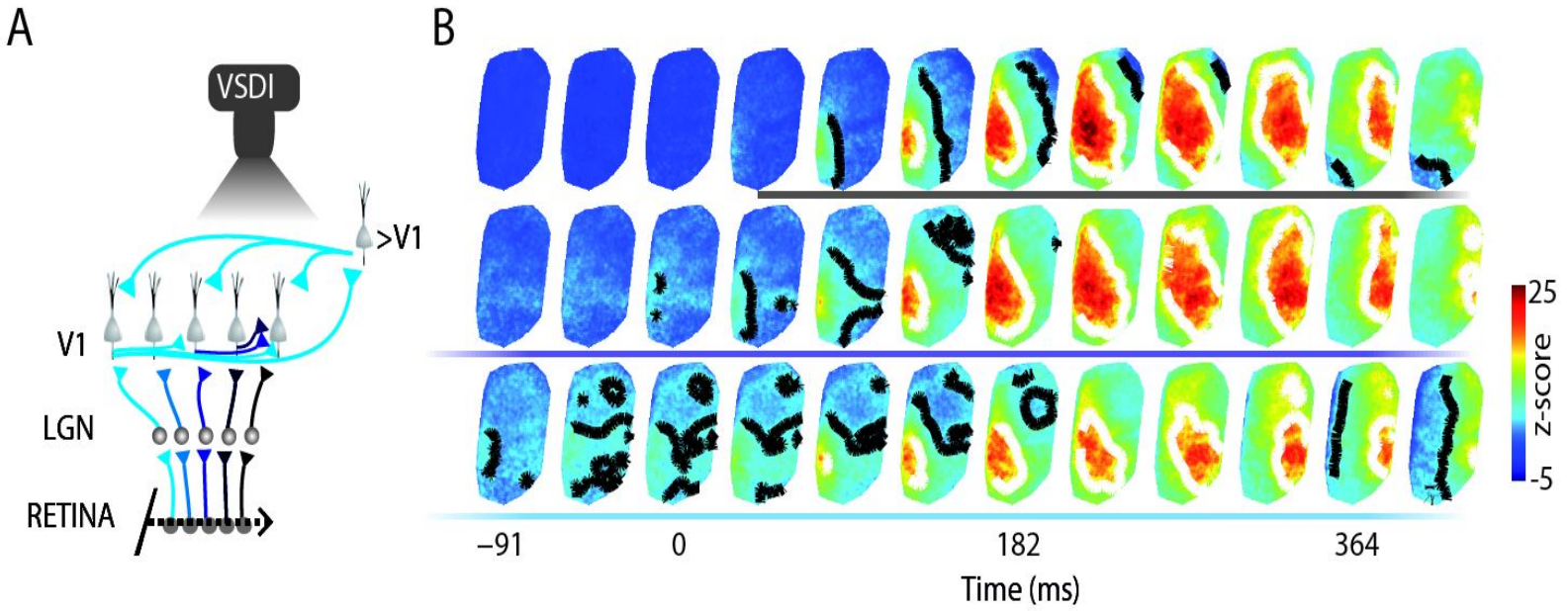


Source : Wikipedia

- **The retina is NOT a camera**

- High transduction rate : 1 photon can trigger a membrane voltage variation of ~1 mV
- Able to detect approaching motion
- Able to detect differential motion
- Sensitive to « surprise » in a visual scene
- Able to perform motion anticipation

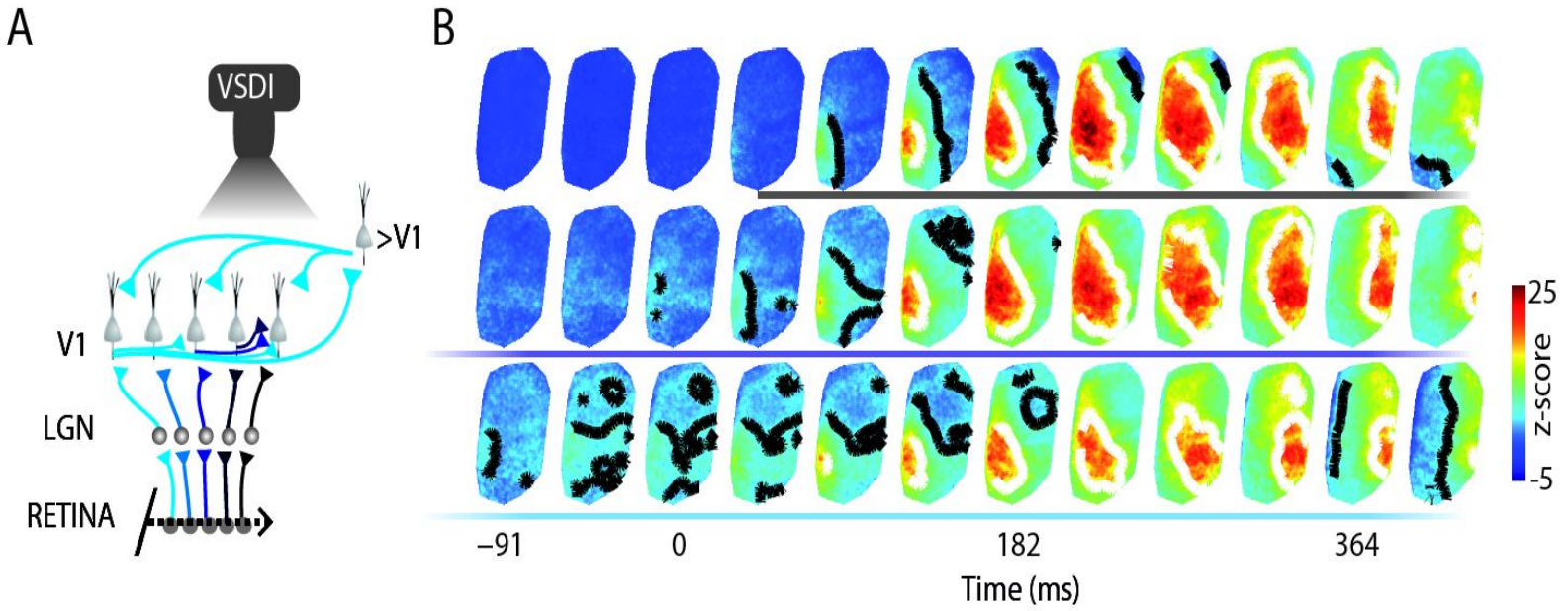
Visual Anticipation



Source : Benvenutti et al. 2015

Visual Anticipation

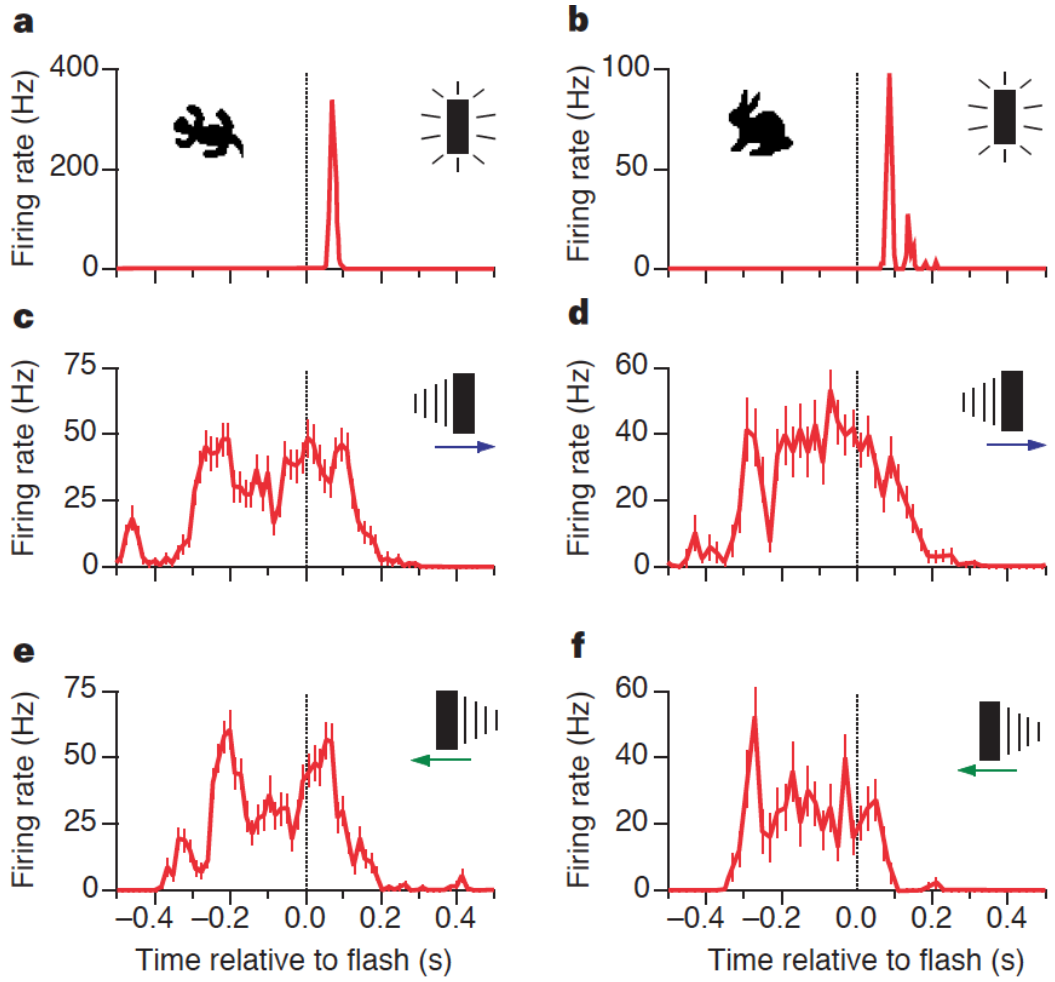
Anticipation is carried out by the primary visual cortex (V1) through an activation wave



Source : Benvenutti et al. 2015

Visual Anticipation

Anticipation also takes place in the retina



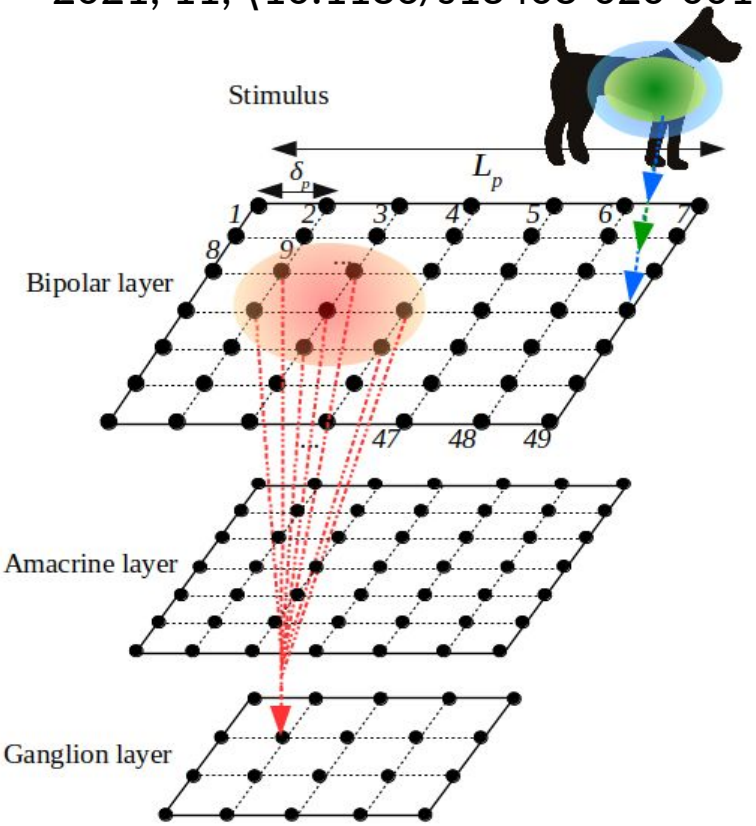
Source : Berry et al. 1999

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

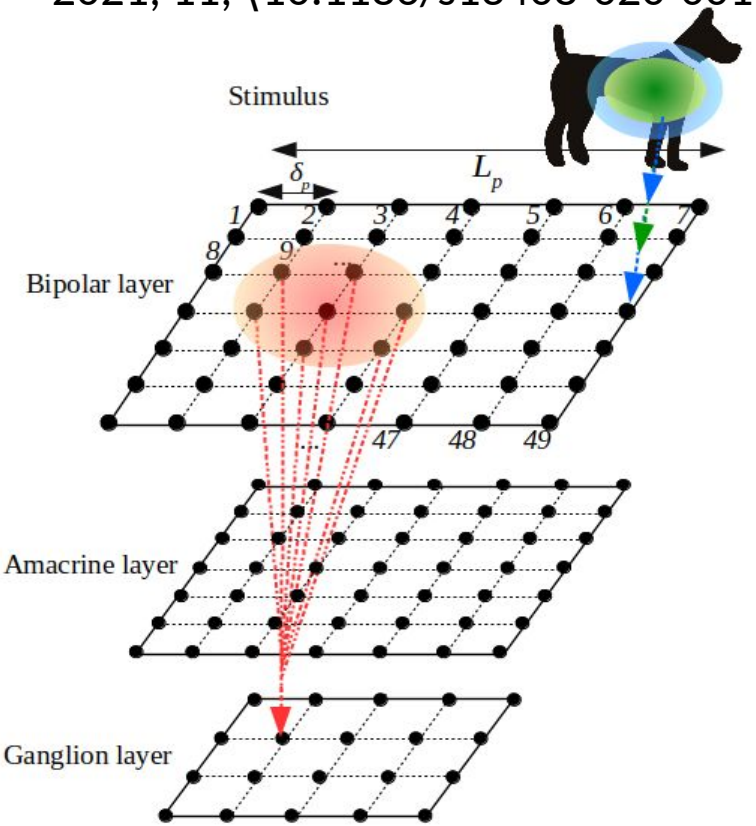
Building a 2D retina model for motion anticipation

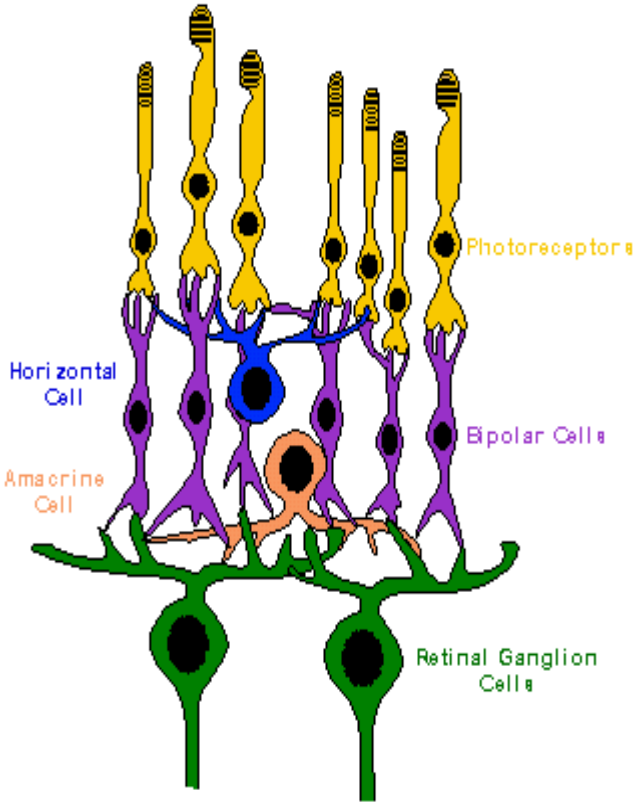
Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



Building a 2D retina model for motion anticipation

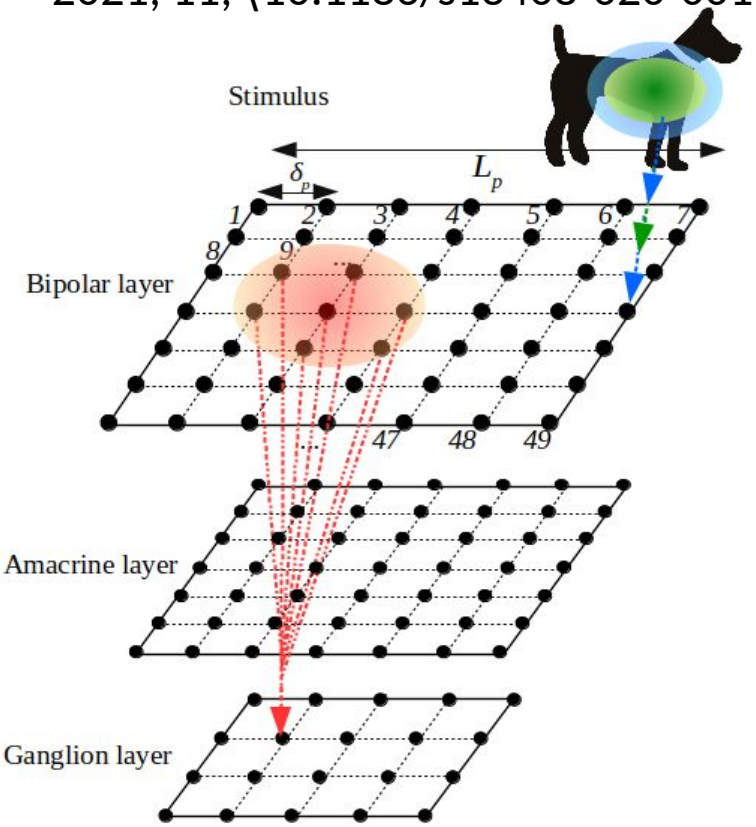
Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



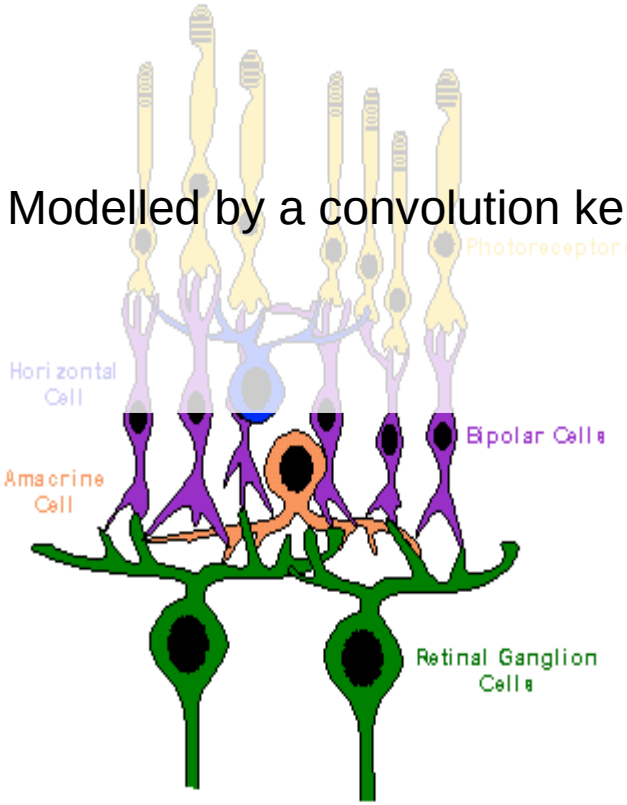


Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

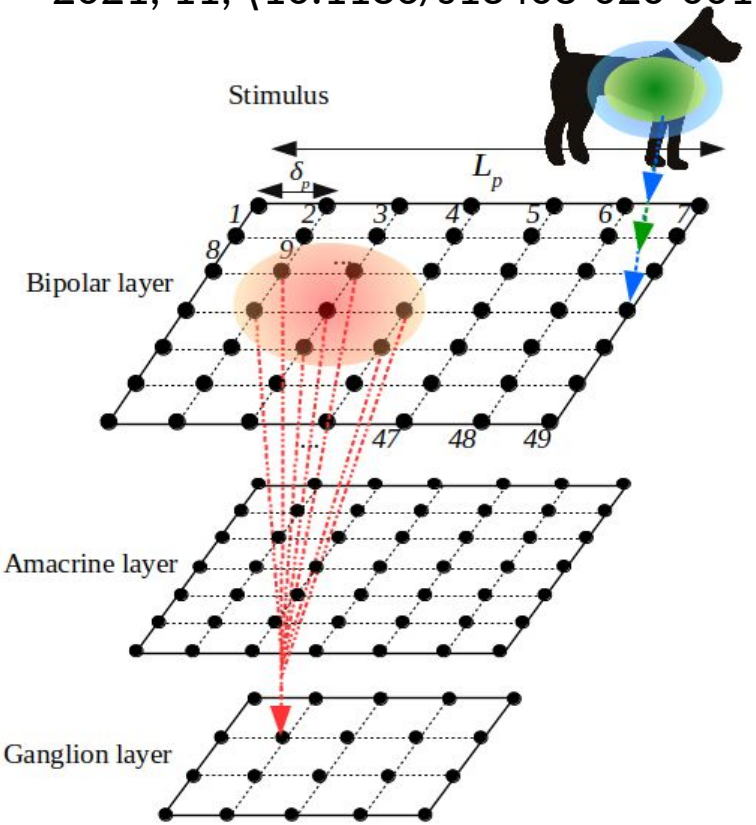


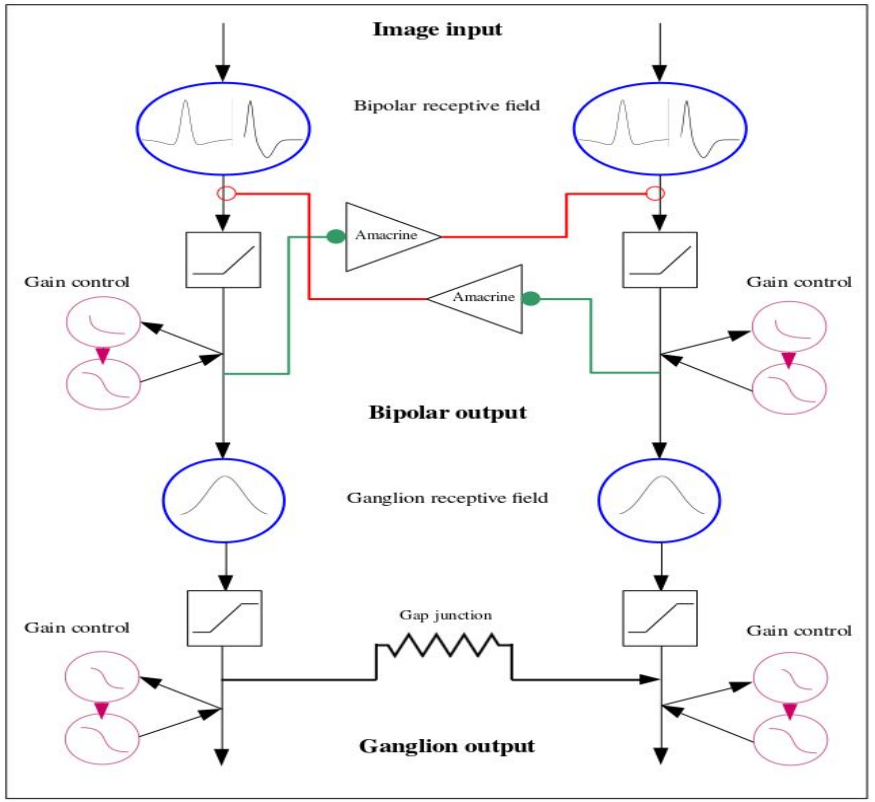
Modelled by a convolution kernel



Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

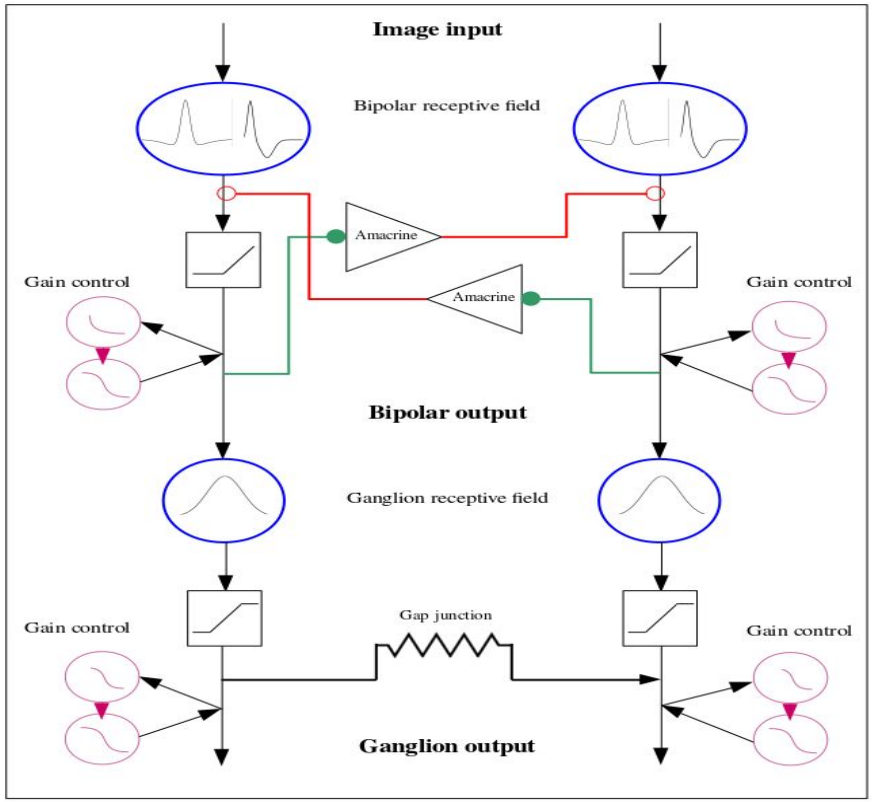




Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

$$\begin{cases} \dfrac{dV_{B_i}}{dt} = -\dfrac{1}{\tau_B} V_{B_i} + \sum_{j=1}^{N_A} W_{B_i}^{A_j} V_{A_j} + F_{B_i}(t), \\ \dfrac{dV_{A_j}}{dt} = -\dfrac{1}{\tau_A} V_{A_j} + \sum_{i=1}^{N_B} W_{A_j}^{B_i} R_{B_i}, \\ \dfrac{dA_{B_i}}{dt} = -\dfrac{A_{B_i}}{\tau_a} + h_B \mathcal{N}(V_{B_i}). \end{cases}$$

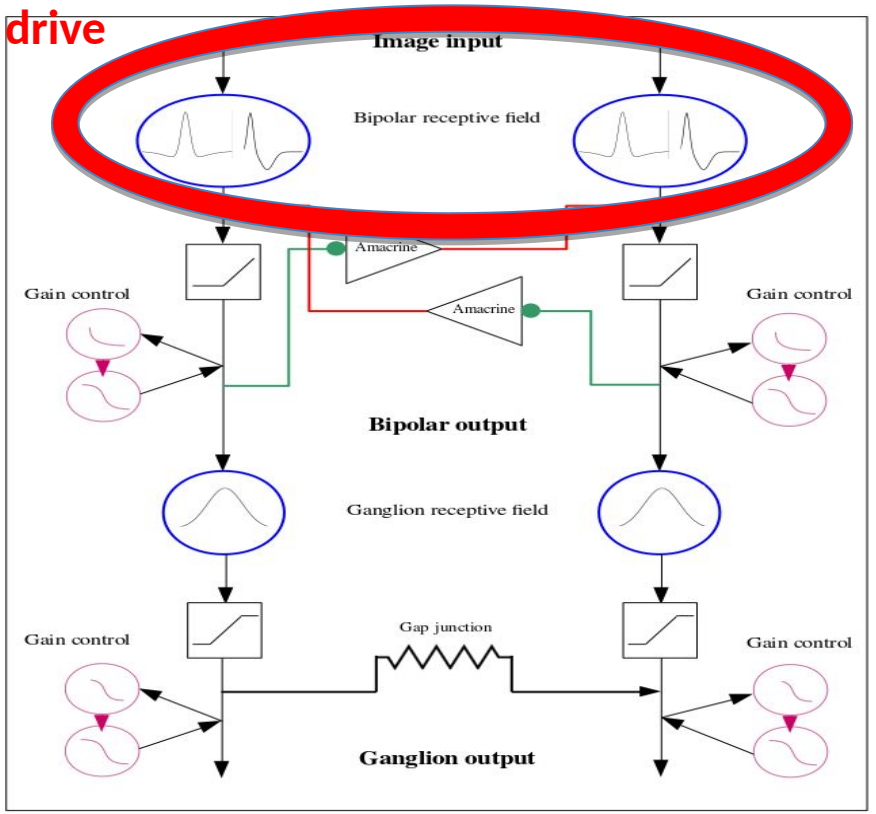


Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

Stimulus dependent drive

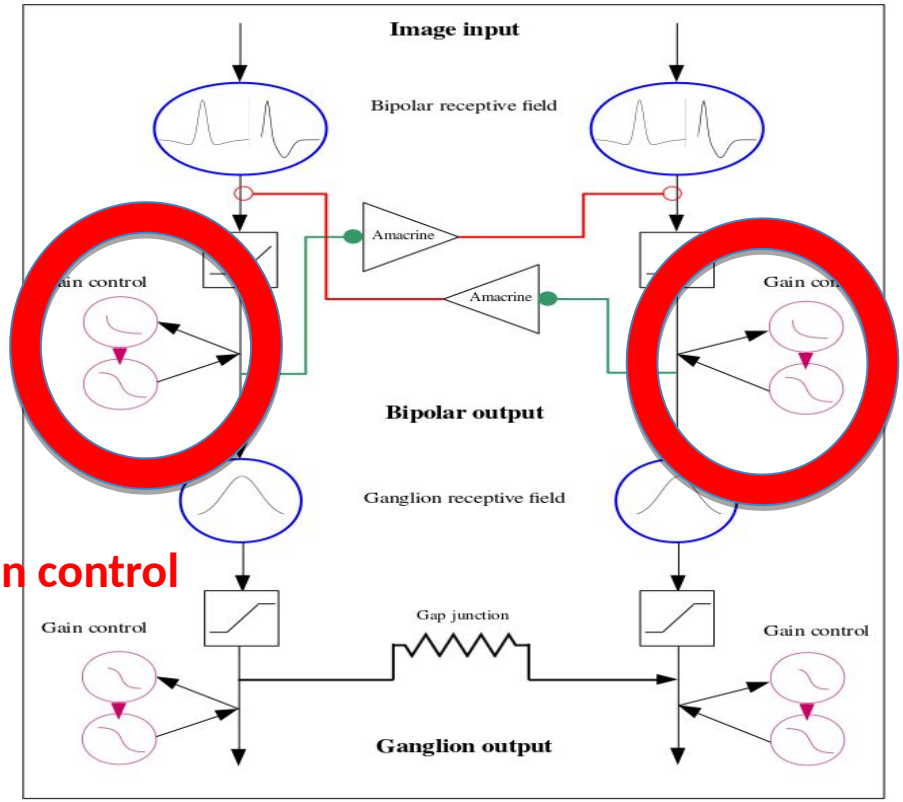
$$\begin{cases} \dfrac{dV_{B_i}}{dt} = -\dfrac{1}{\tau_B} V_{B_i} + \sum_{j=1}^{N_A} W_{B_i}^{A_j} V_{A_j} + F_{B_i}(t), \\ \dfrac{dV_{A_j}}{dt} = -\dfrac{1}{\tau_A} V_{A_j} + \sum_{i=1}^{N_B} W_{A_j}^{B_i} R_{B_i}, \\ \dfrac{dA_{B_i}}{dt} = -\dfrac{A_{B_i}}{\tau_a} + h_B \mathcal{N}(V_{B_i}). \end{cases}$$



Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

$$\begin{cases} \dfrac{dV_{B_i}}{dt} = -\dfrac{1}{\tau_B} V_{B_i} + \sum_{j=1}^{N_A} W_{B_i}^{A_j} V_{A_j} + F_{B_i}(t), \\ \dfrac{dV_{A_j}}{dt} = -\dfrac{1}{\tau_A} V_{A_j} + \sum_{i=1}^{N_B} W_{A_j}^{B_i} R_{B_i}, \\ \dfrac{dA_{B_i}}{dt} = -\dfrac{A_{B_i}}{\tau_a} + h_B \mathcal{N}(V_{B_i}). \end{cases}$$

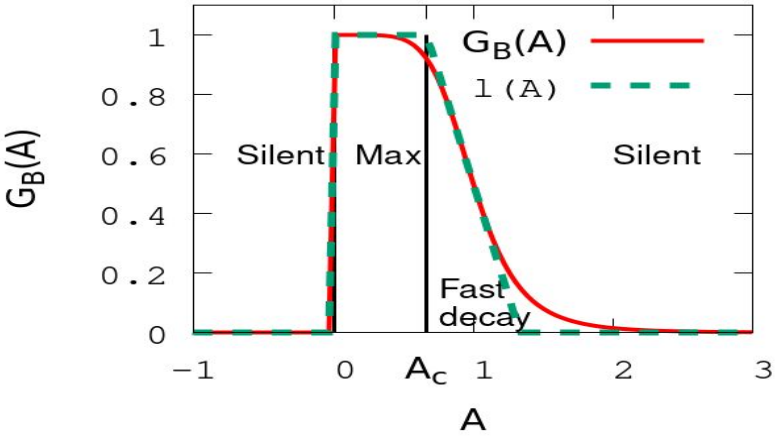


Non linear gain control

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

$$\begin{cases} \dfrac{dV_{B_i}}{dt} = -\dfrac{1}{\tau_B} V_{B_i} + \sum_{j=1}^{N_A} W_{B_i}^{A_j} V_{A_j} + F_{B_i}(t), \\ \dfrac{dV_{A_j}}{dt} = -\dfrac{1}{\tau_A} V_{A_j} + \sum_{i=1}^{N_B} W_{A_j}^{B_i} R_{B_i}, \\ \dfrac{dA_{B_i}}{dt} = -\dfrac{A_{B_i}}{\tau_a} + h_B \mathcal{N}(V_{B_i}). \end{cases}$$



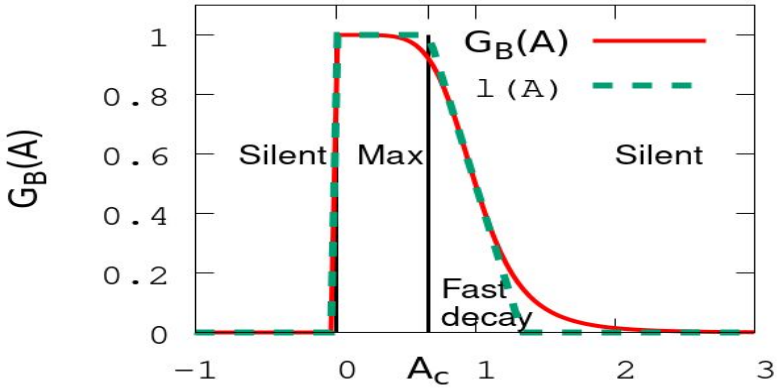
Non linear gain control

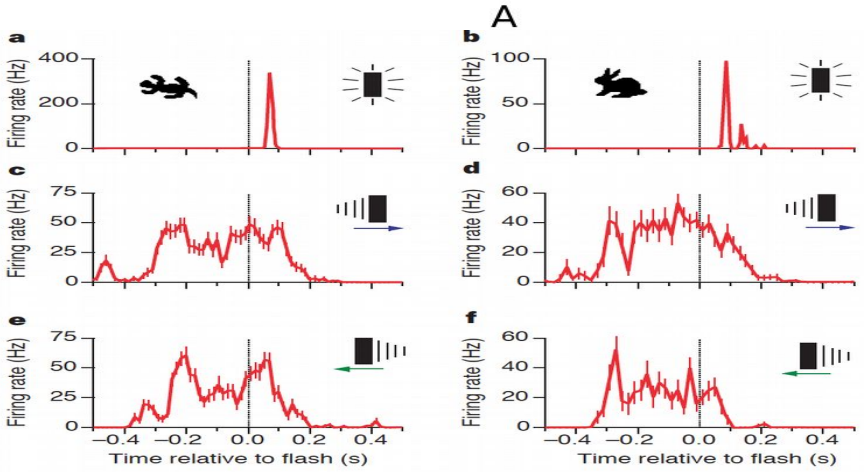
Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

$$\begin{cases} \dfrac{dV_{B_i}}{dt} = -\dfrac{1}{\tau_B} V_{B_i} + \sum_{j=1}^{N_A} W_{B_i}^{A_j} V_{A_j} + F_{B_i}(t), \\ \dfrac{dV_{A_j}}{dt} = -\dfrac{1}{\tau_A} V_{A_j} + \sum_{i=1}^{N_B} W_{A_j}^{B_i} R_{B_i}, \\ \dfrac{dA_{B_i}}{dt} = -\dfrac{A_{B_i}}{\tau_a} + h_B \mathcal{N}(V_{B_i}). \end{cases}$$

Non linear gain control



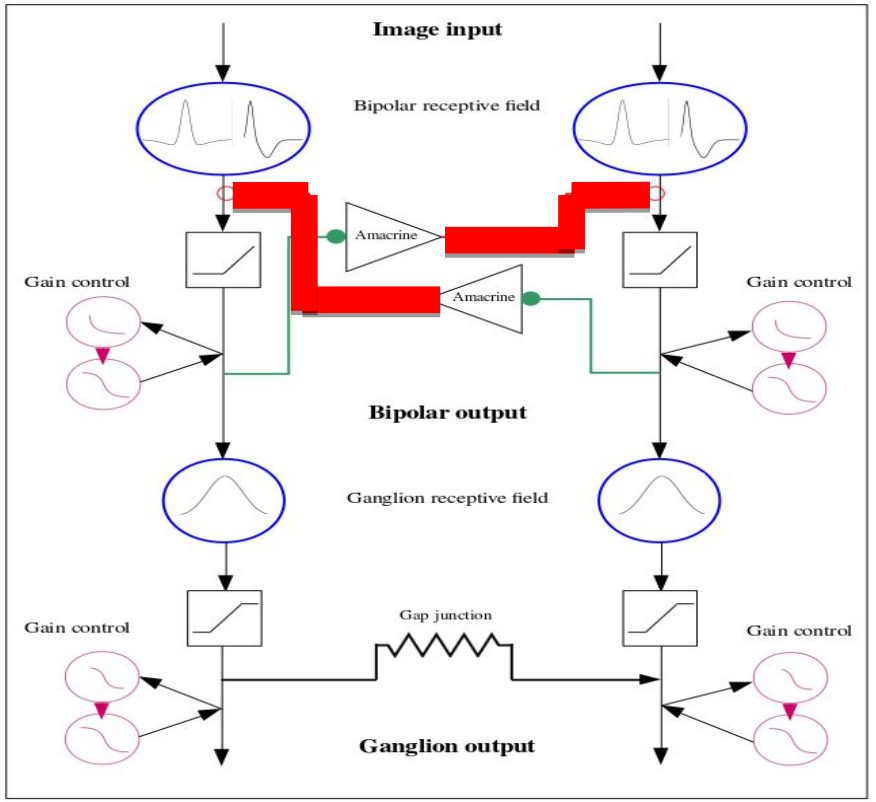


Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

Inhibition

$$\begin{cases} \dfrac{dV_{B_i}}{dt} = -\dfrac{1}{\tau_B} V_{B_i} + \sum_{j=1}^{N_A} W_{B_i}^{A_j} V_{A_j} + F_{B_i}(t), \\ \dfrac{dV_{A_j}}{dt} = -\dfrac{1}{\tau_A} V_{A_j} + \sum_{i=1}^{N_B} W_{A_j}^{B_i} R_{B_i}, \\ \dfrac{dA_{B_i}}{dt} = -\dfrac{A_{B_i}}{\tau_a} + h_B \mathcal{N}(V_{B_i}). \end{cases}$$

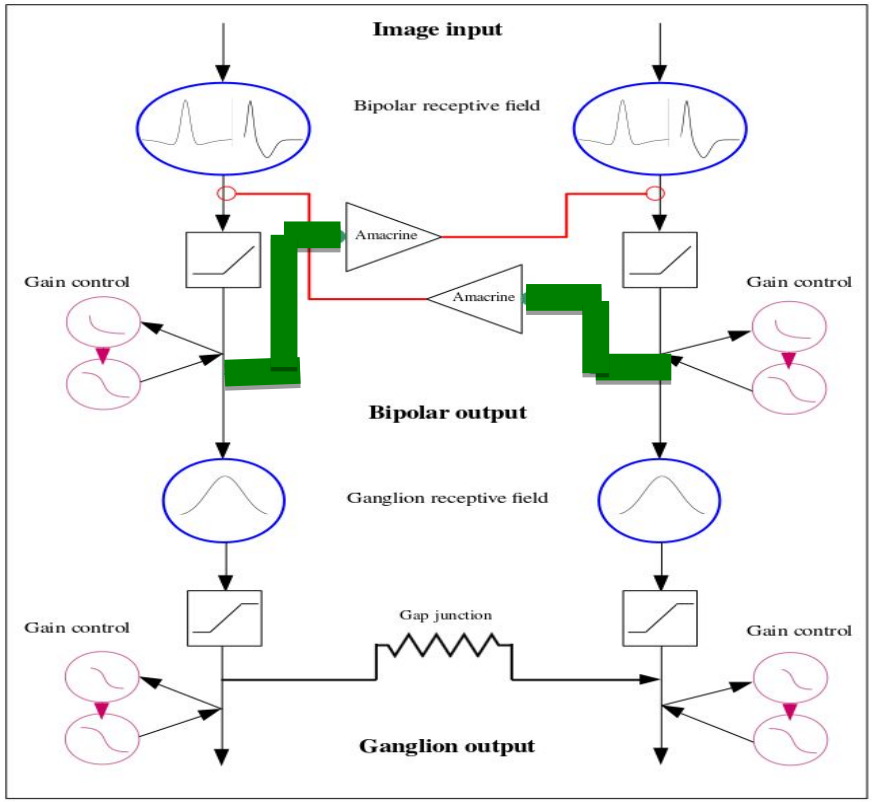


Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

$$\begin{cases} \dfrac{dV_{B_i}}{dt} = -\dfrac{1}{\tau_B} V_{B_i} + \sum_{j=1}^{N_A} W_{B_i}^{A_j} V_{A_j} + F_{B_i}(t), \\ \dfrac{dV_{A_j}}{dt} = -\dfrac{1}{\tau_A} V_{A_j} + \sum_{i=1}^{N_B} W_{A_j}^{B_i} R_{B_i}, \\ \dfrac{dA_{B_i}}{dt} = -\dfrac{A_{B_i}}{\tau_a} + h_B \mathcal{N}(V_{B_i}). \end{cases}$$

Excitation



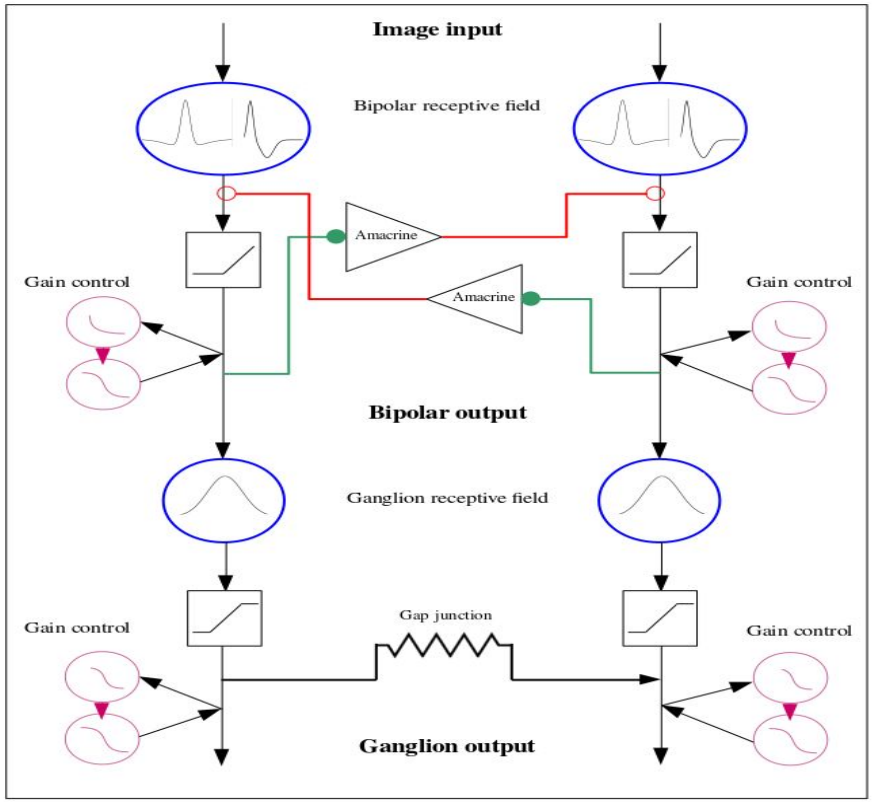
Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

Linear regime

$$\frac{d\vec{\mathcal{X}}}{dt} = \mathcal{L}.\vec{\mathcal{X}} + \vec{\mathcal{F}}(t).$$

$$\mathcal{L} = \begin{pmatrix} -\frac{I_{N,N}}{\tau_B} & W_B^A & 0_{N,N} \\ W_A^B & -\frac{I_{N,N}}{\tau_A} & 0_{N,N} \\ h_B I_{N,N} & 0_{N,N} & -\frac{I_{N,N}}{\tau_a} \end{pmatrix}$$



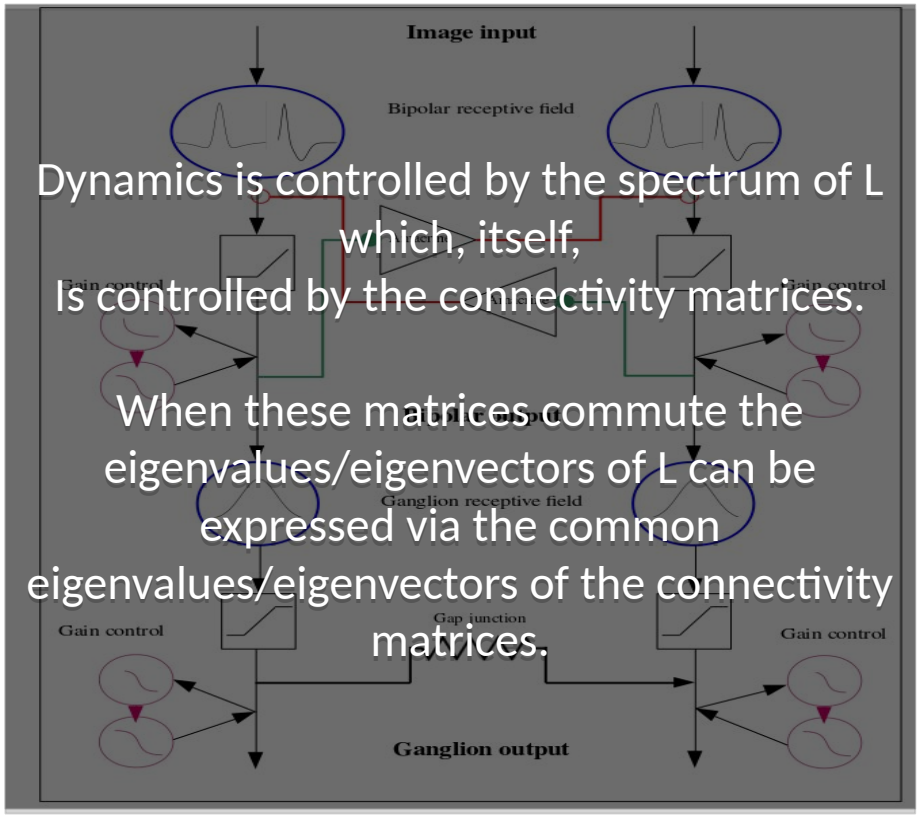
Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

Linear regime

$$\frac{d\vec{\mathcal{X}}}{dt} = \mathcal{L}.\vec{\mathcal{X}} + \vec{\mathcal{F}}(t).$$

$$\mathcal{L} = \begin{pmatrix} -\frac{I_{N,N}}{\tau_B} & W_B^A & 0_{N,N} \\ W_A^B & -\frac{I_{N,N}}{\tau_A} & 0_{N,N} \\ h_B I_{N,N} & 0_{N,N} & -\frac{I_{N,N}}{\tau_a} \end{pmatrix}$$

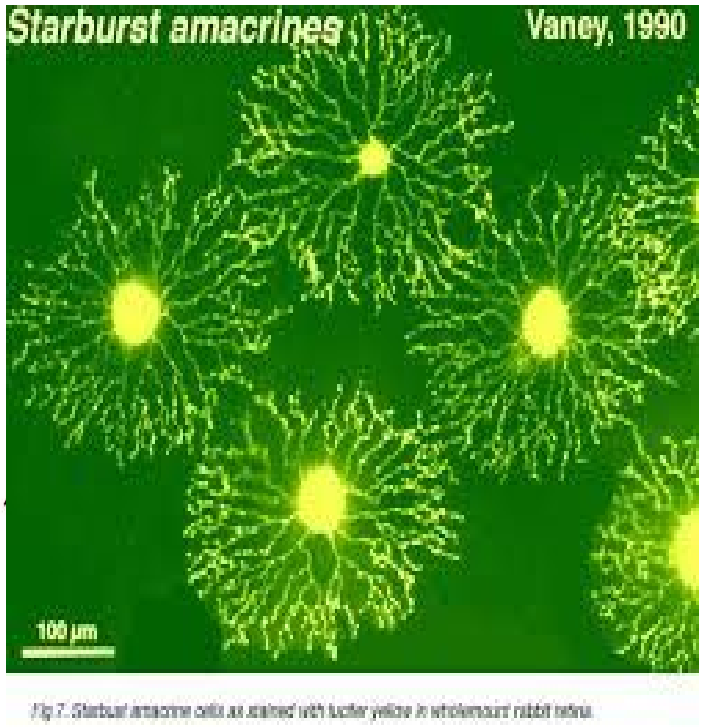


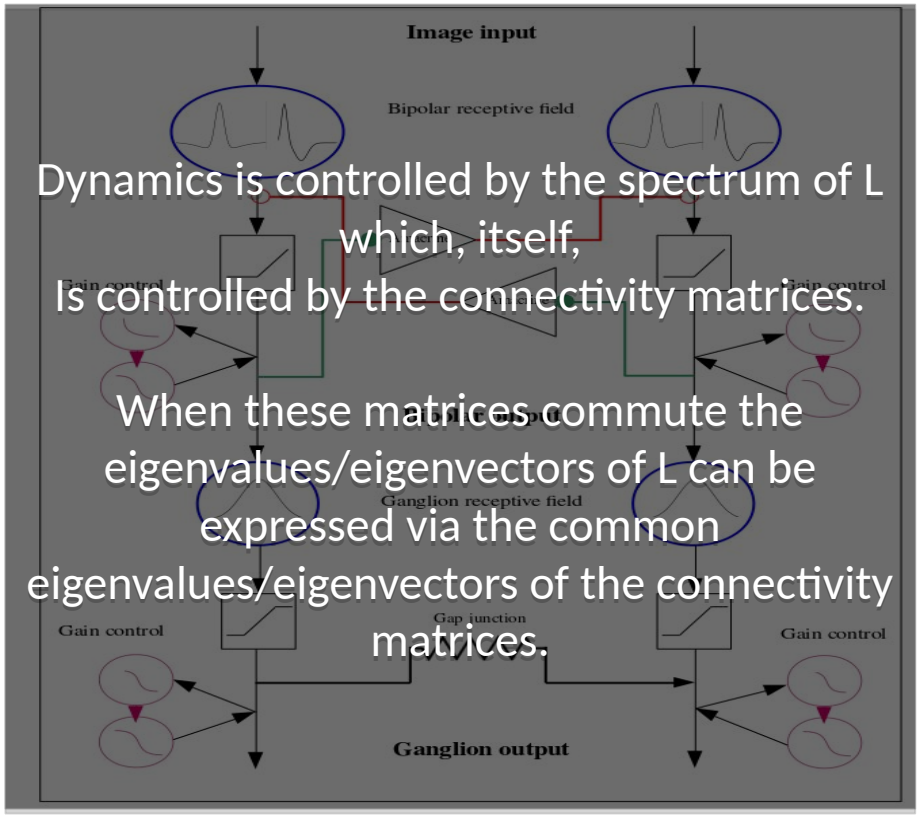
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



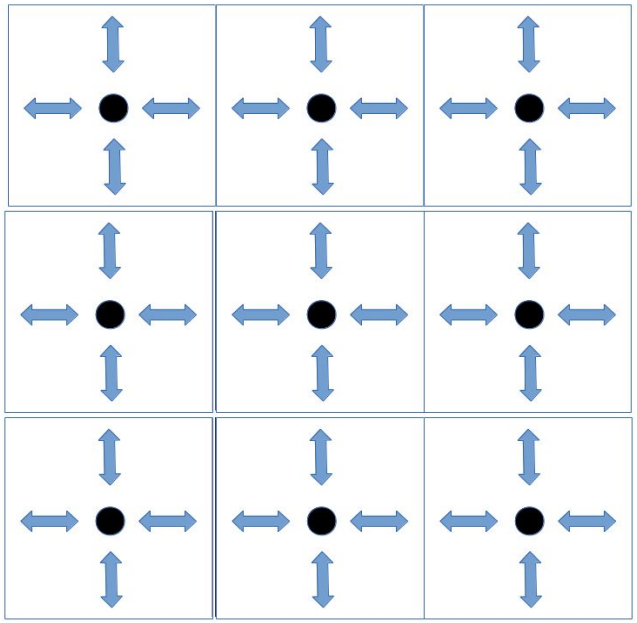


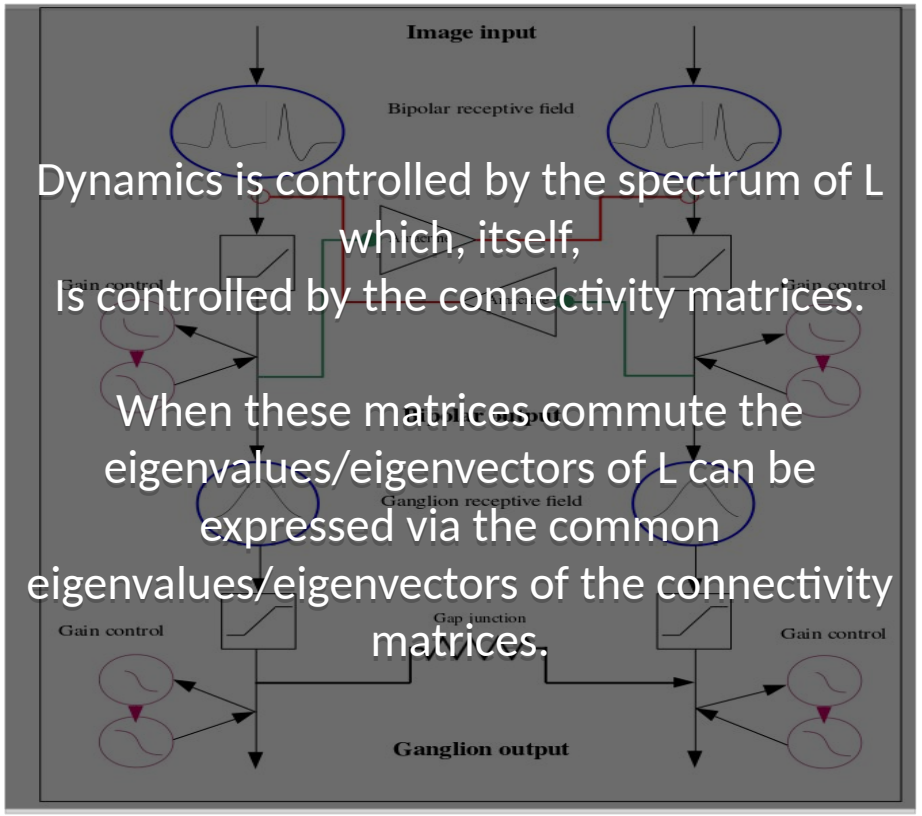
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



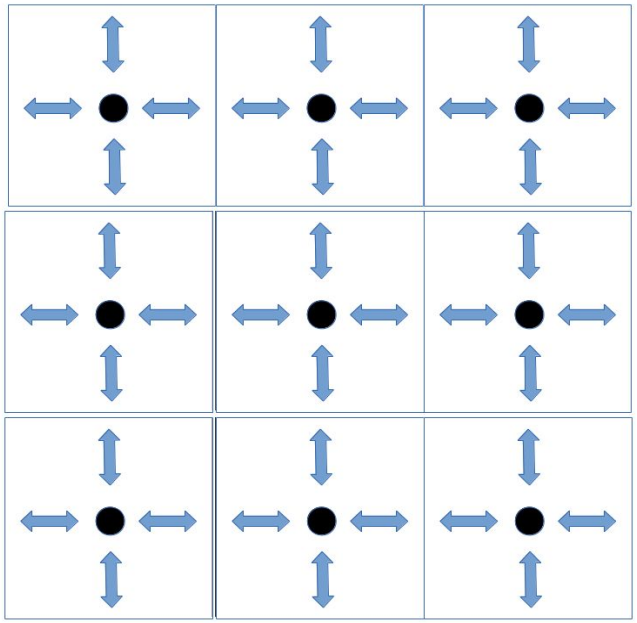


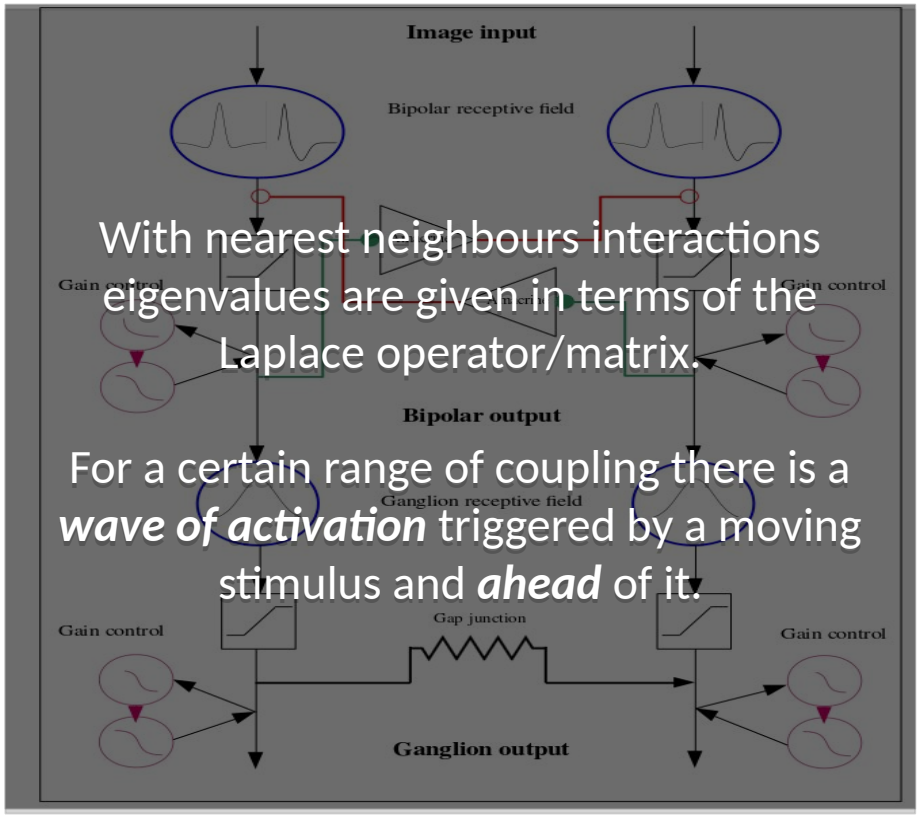
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩





With nearest neighbours interactions eigenvalues are given in terms of the Laplace operator/matrix.

For a certain range of coupling there is a ***wave of activation*** triggered by a moving stimulus and ***ahead*** of it.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

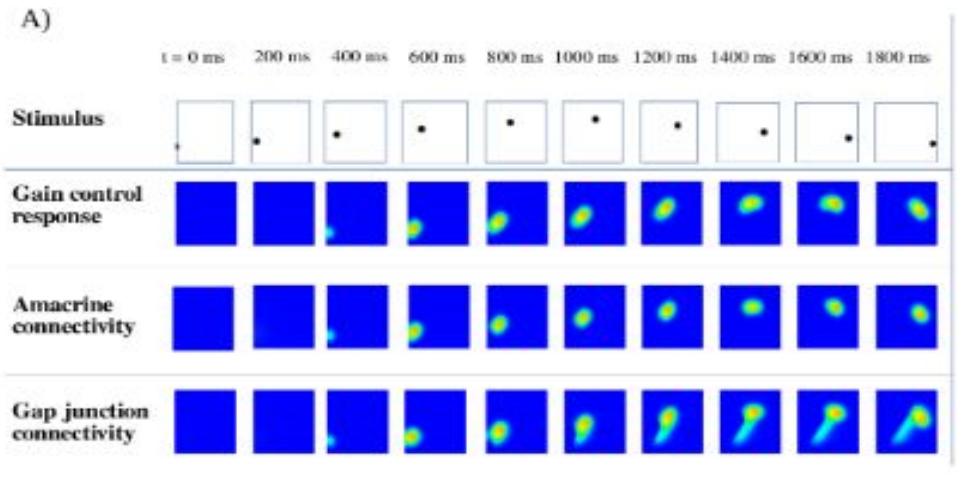
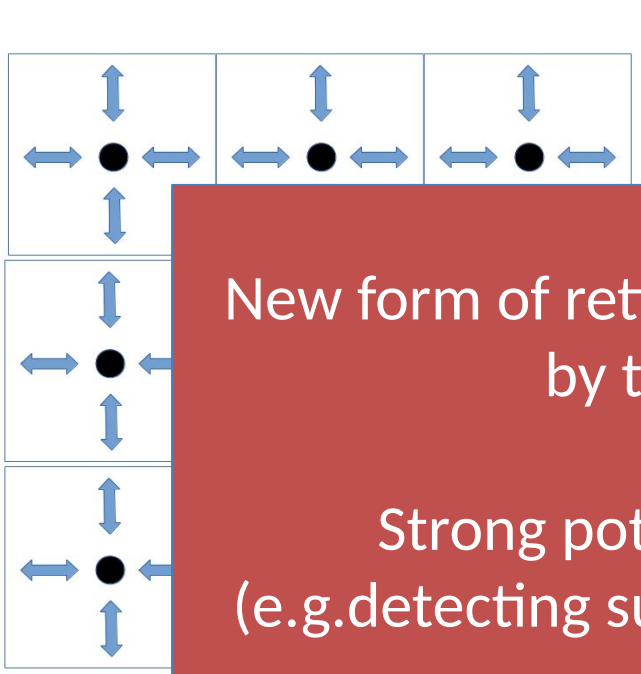
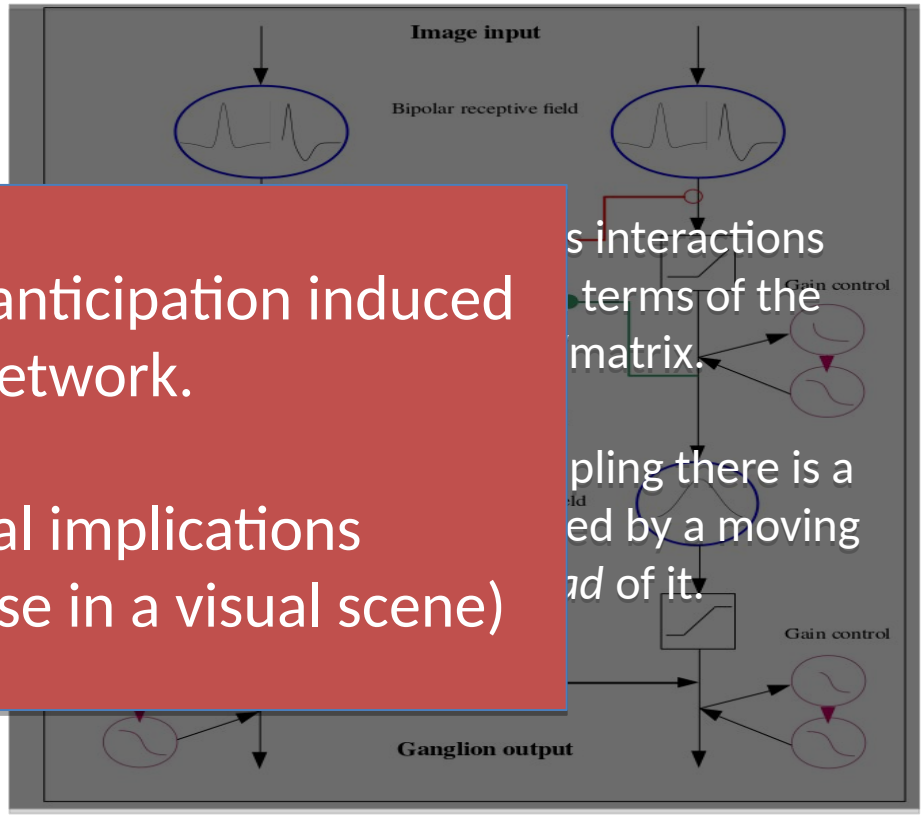


Figure 15: **Effect of anticipatory mechanisms on a parabolic trajectory.** A) Response to a dot moving along a parabolic trajectory. The first line shows the stimulus, the second line shows the GCells response with gain control, the third line presents the effect of lateral ACells connectivity with $w = 0.3\ ms^{-1}$, and the last line shows the effect of asymmetric gap junctions with $v_{gap} = 9\ mm/s$. B) Time course response of a cell responding to the dot near the trajectory turning point. Linear response corresponds to the response to the stimulus without gain control.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



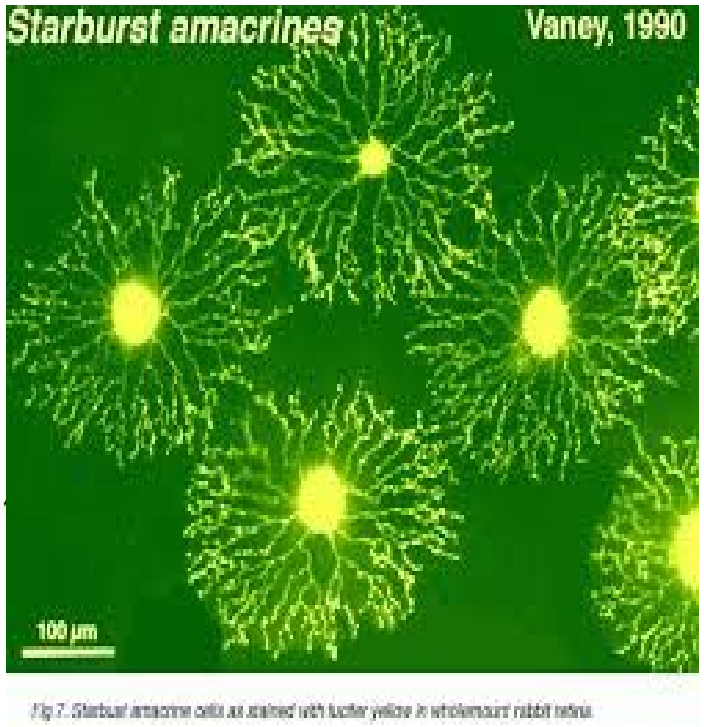


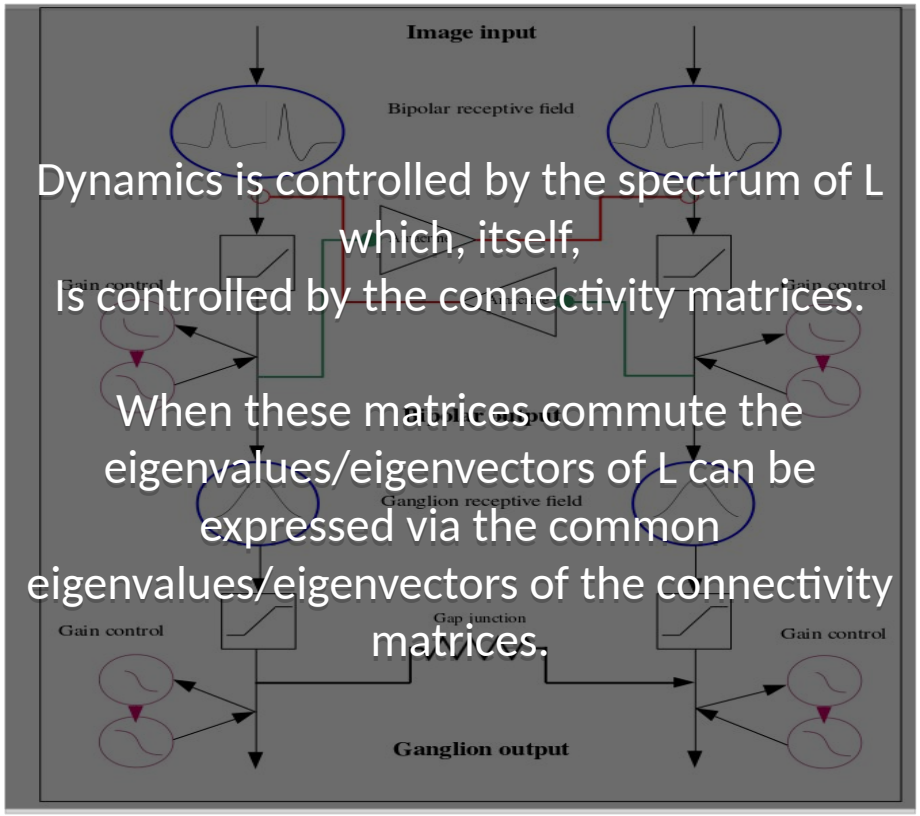
New form of retinal anticipation induced by the network.

Strong potential implications (e.g.detecting surprise in a visual scene)

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



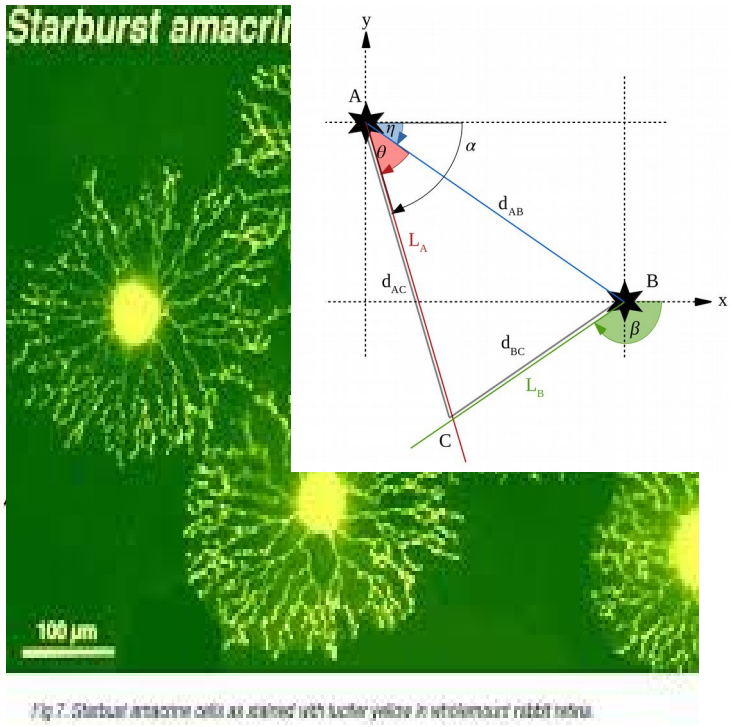


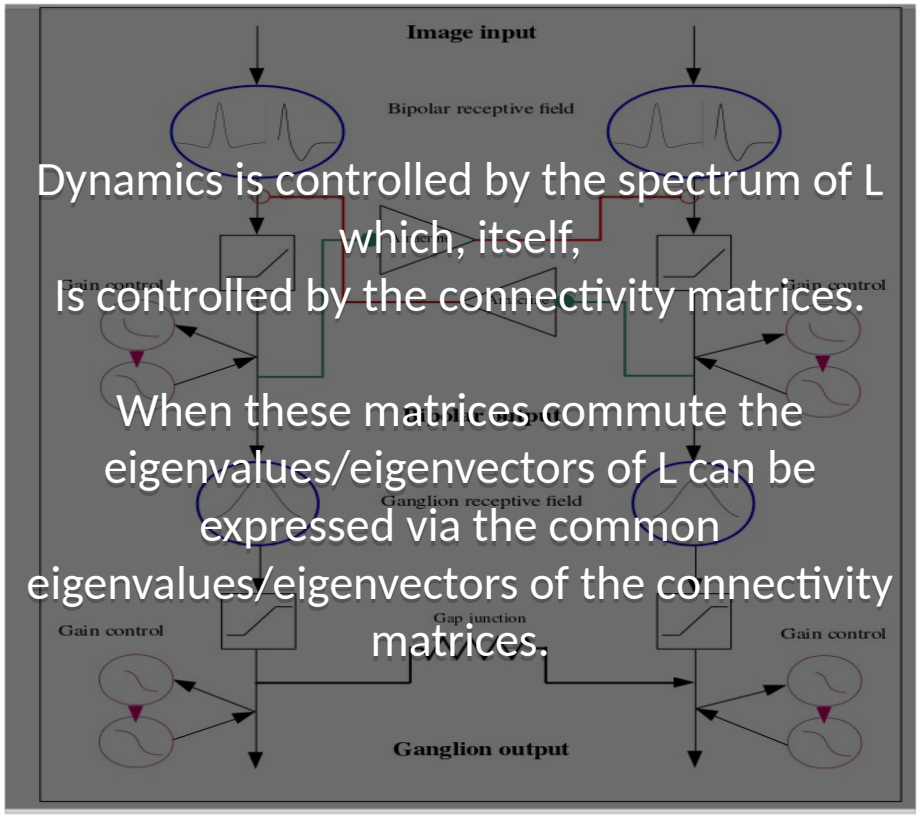
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



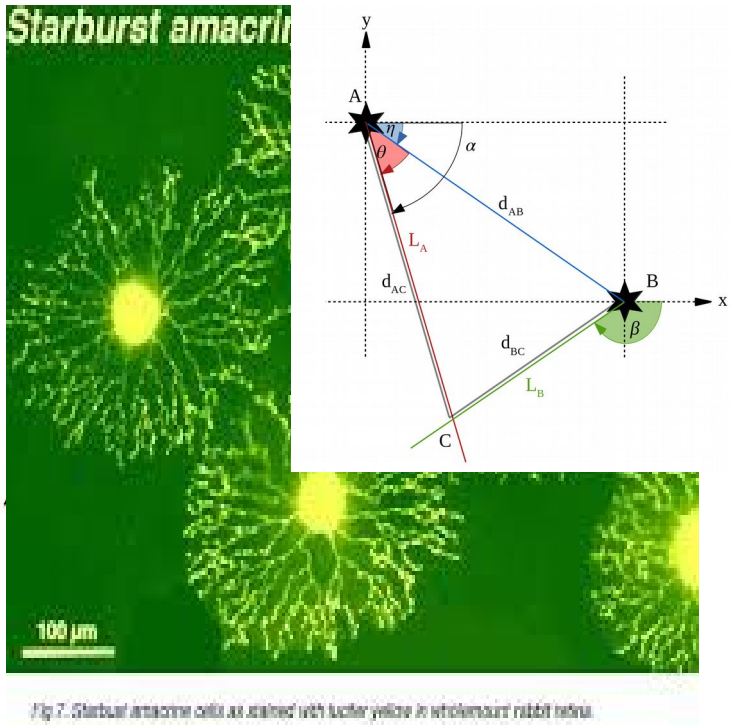


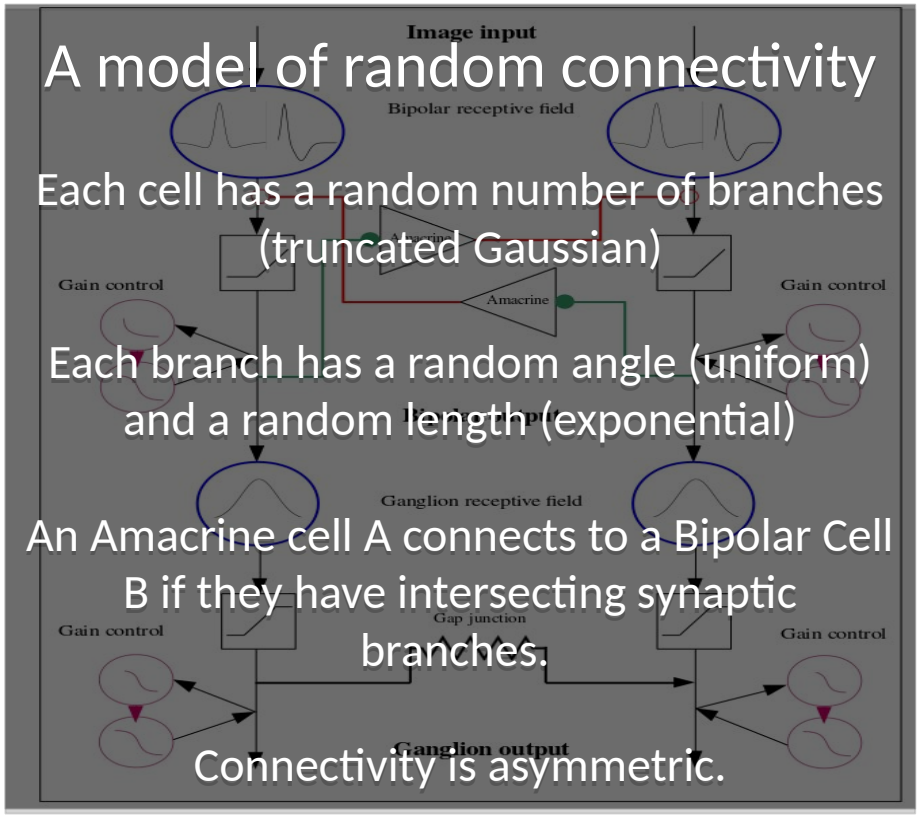
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩





A model of random connectivity

Each cell has a random number of branches (truncated Gaussian)

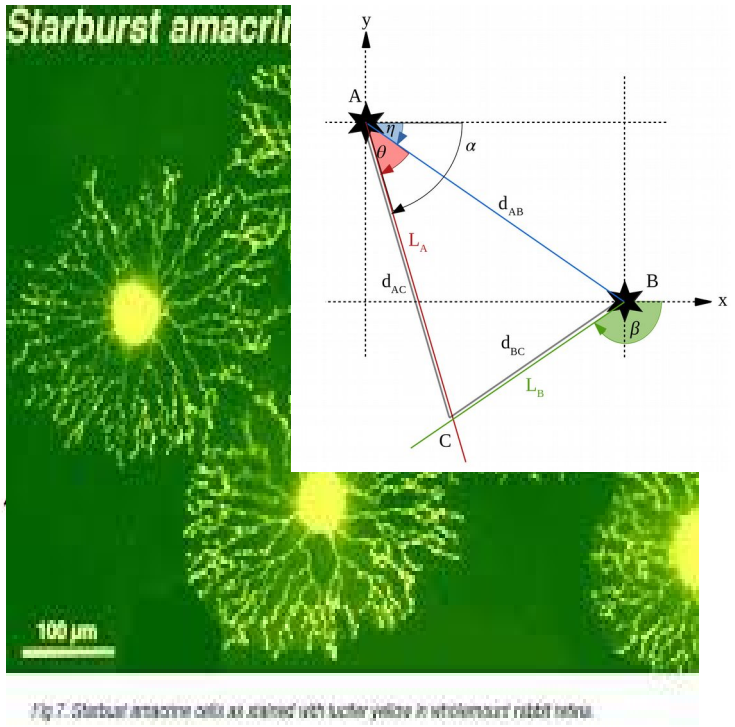
Each branch has a random angle (uniform) and a random length (exponential)

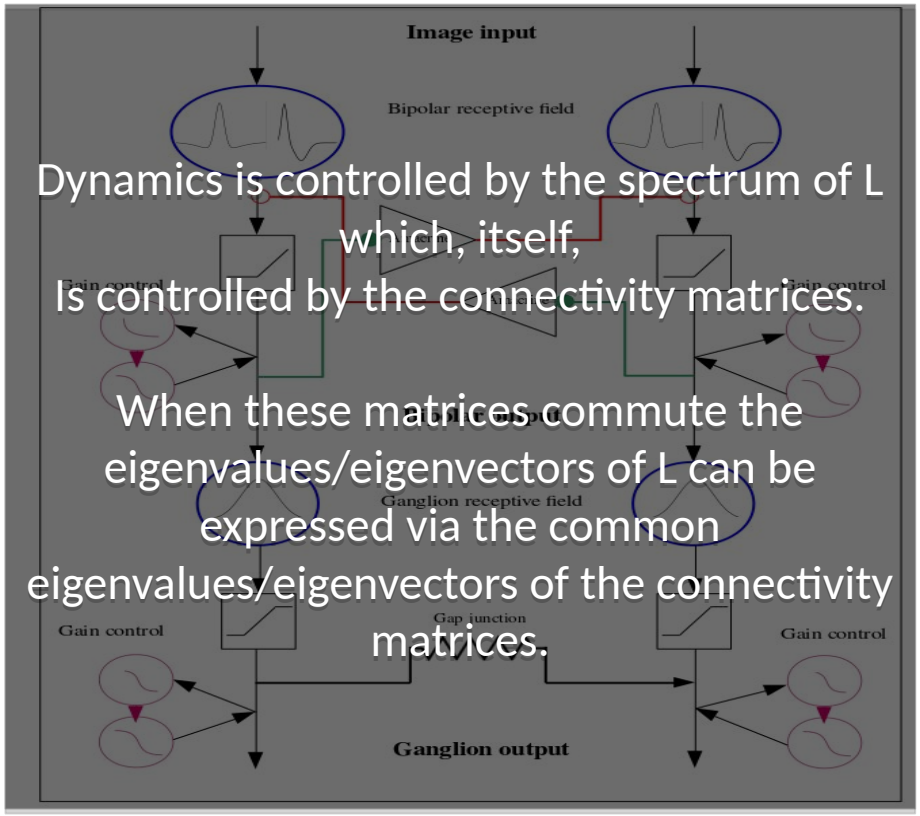
An Amacrine cell A connects to a Bipolar Cell B if they have intersecting synaptic branches.

Connectivity is asymmetric.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



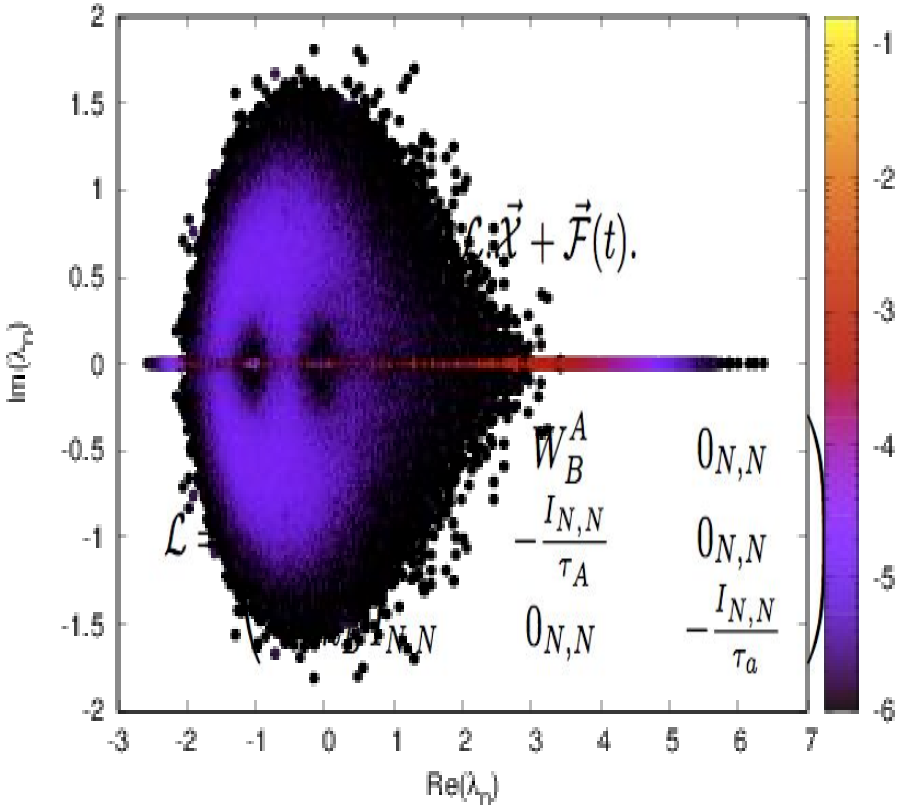


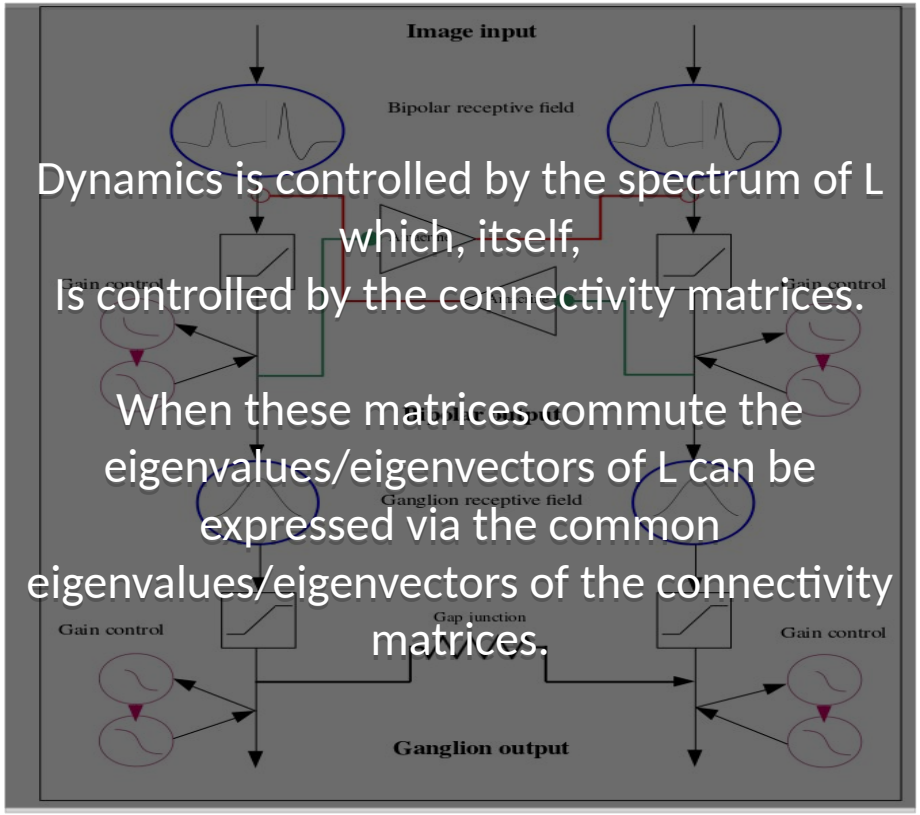
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩





Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

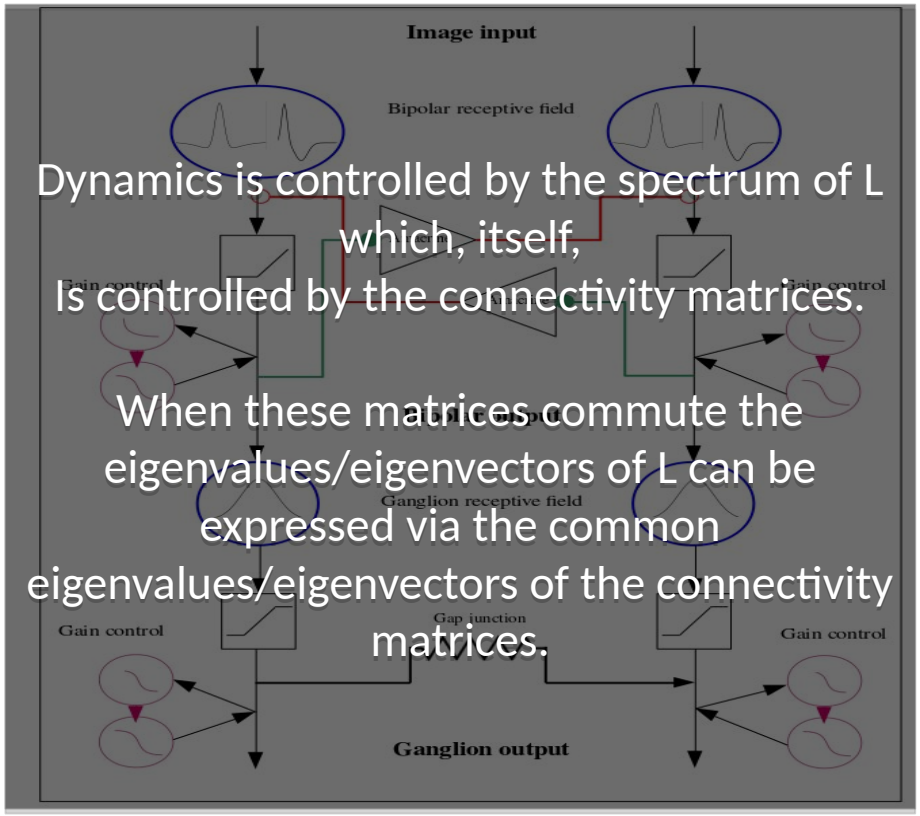
When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩

$$\frac{d\vec{\mathcal{X}}}{dt} = \mathcal{L}.\vec{\mathcal{X}} + \vec{\mathcal{F}}(t).$$

$$\mathcal{L} = \begin{pmatrix} -\frac{I_{N,N}}{\tau_B} & W_B^A & 0_{N,N} \\ W_A^B & -\frac{I_{N,N}}{\tau_A} & 0_{N,N} \\ h_B I_{N,N} & 0_{N,N} & -\frac{I_{N,N}}{\tau_a} \end{pmatrix}$$

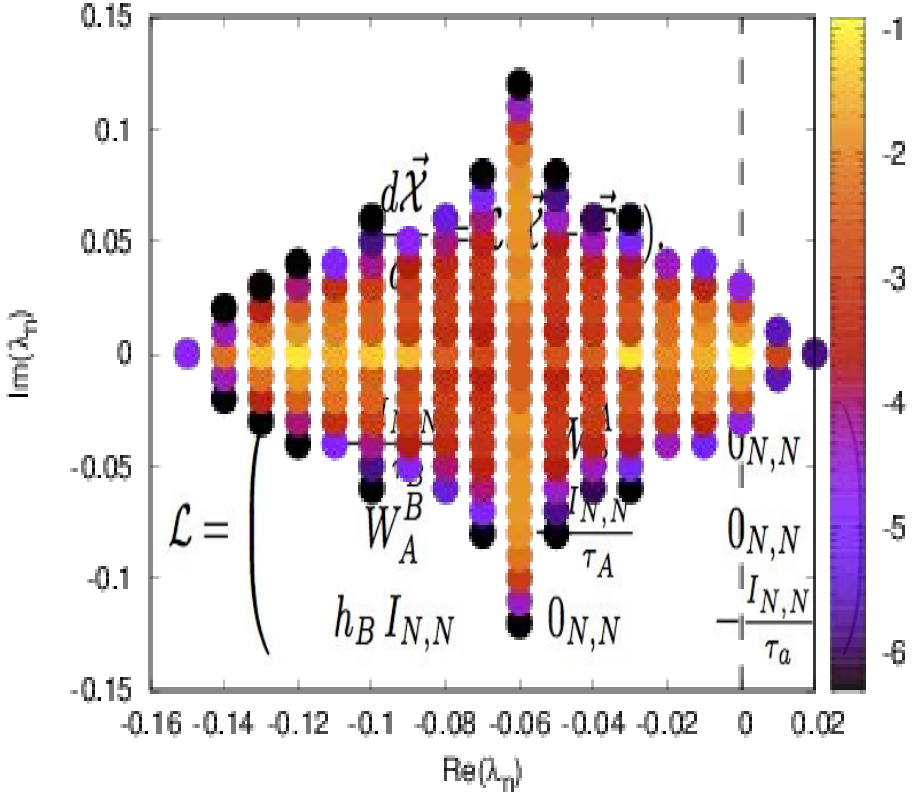


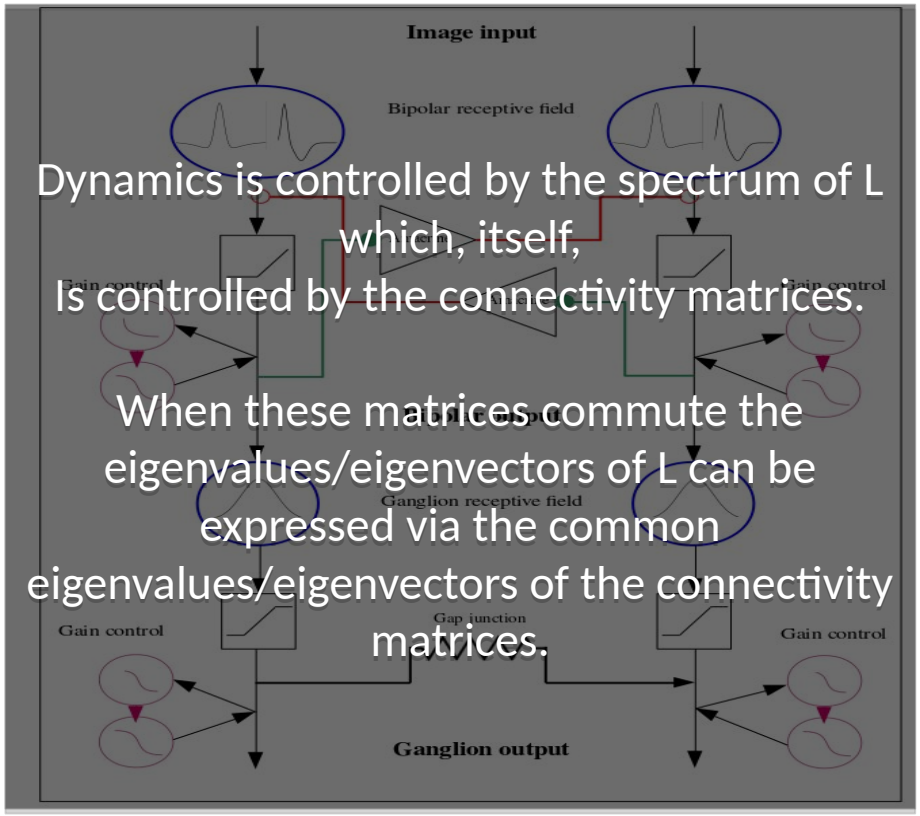
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



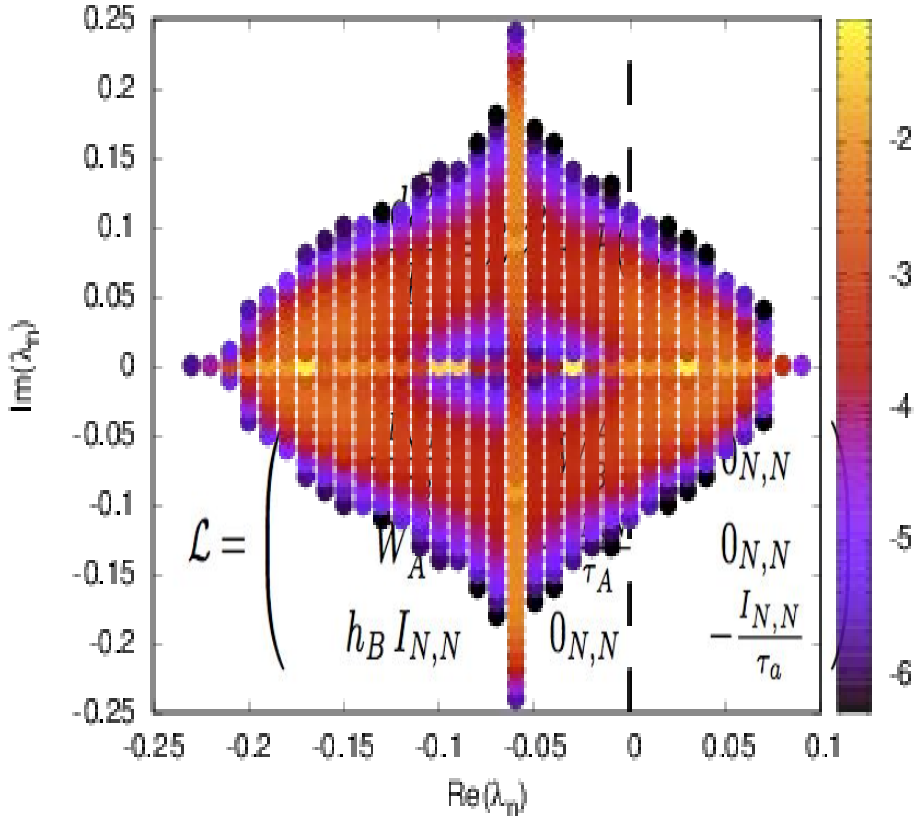


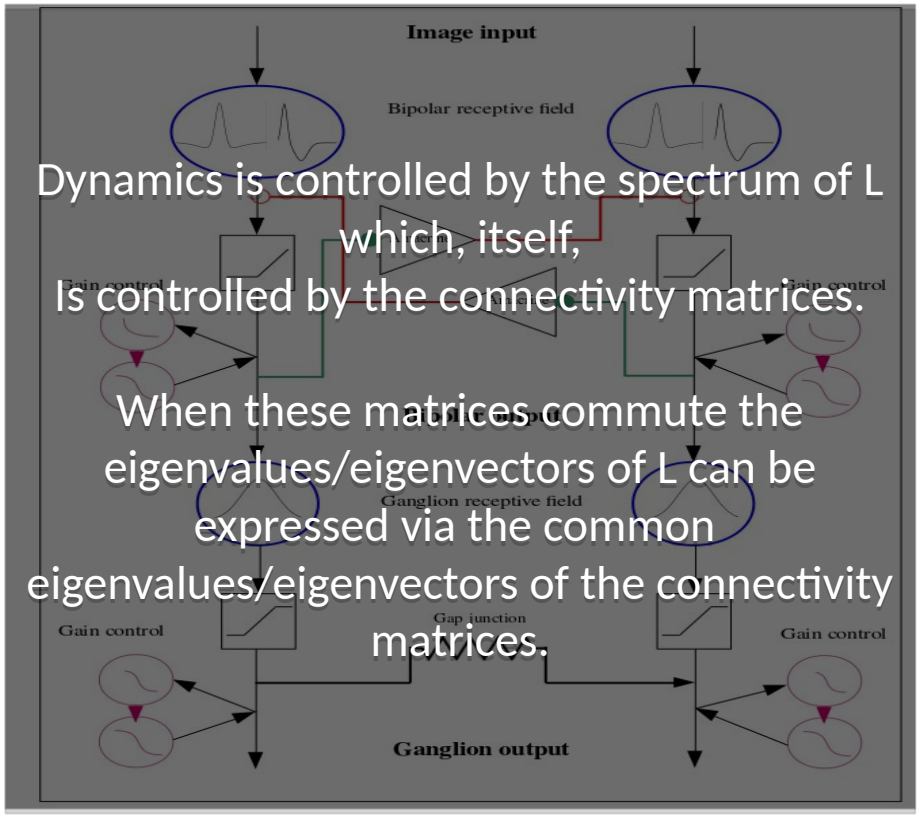
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



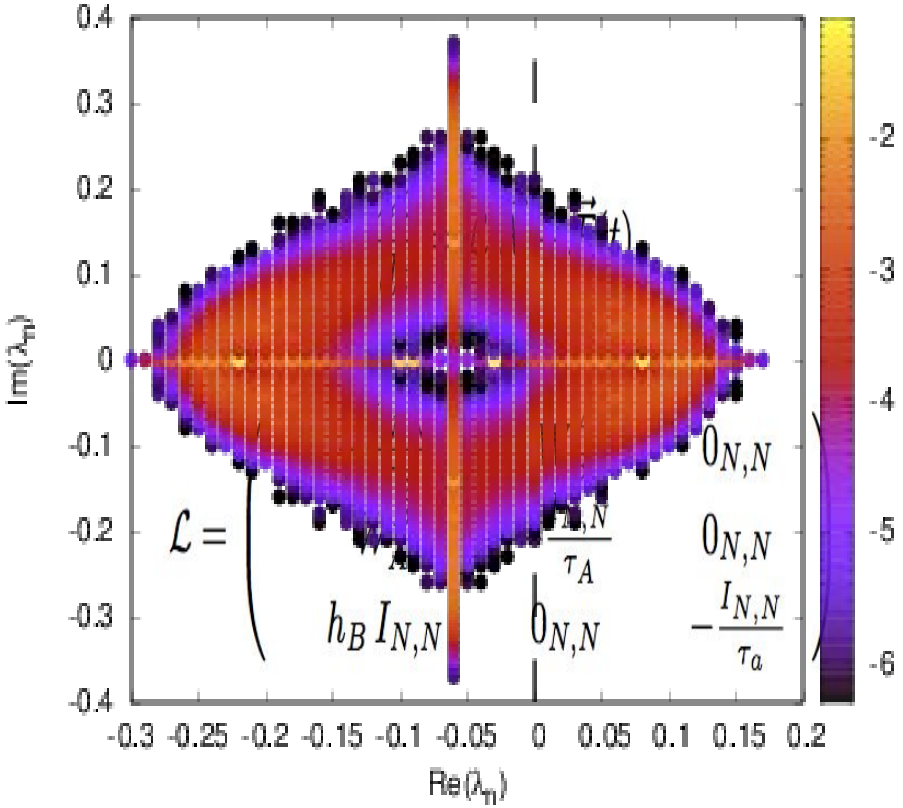


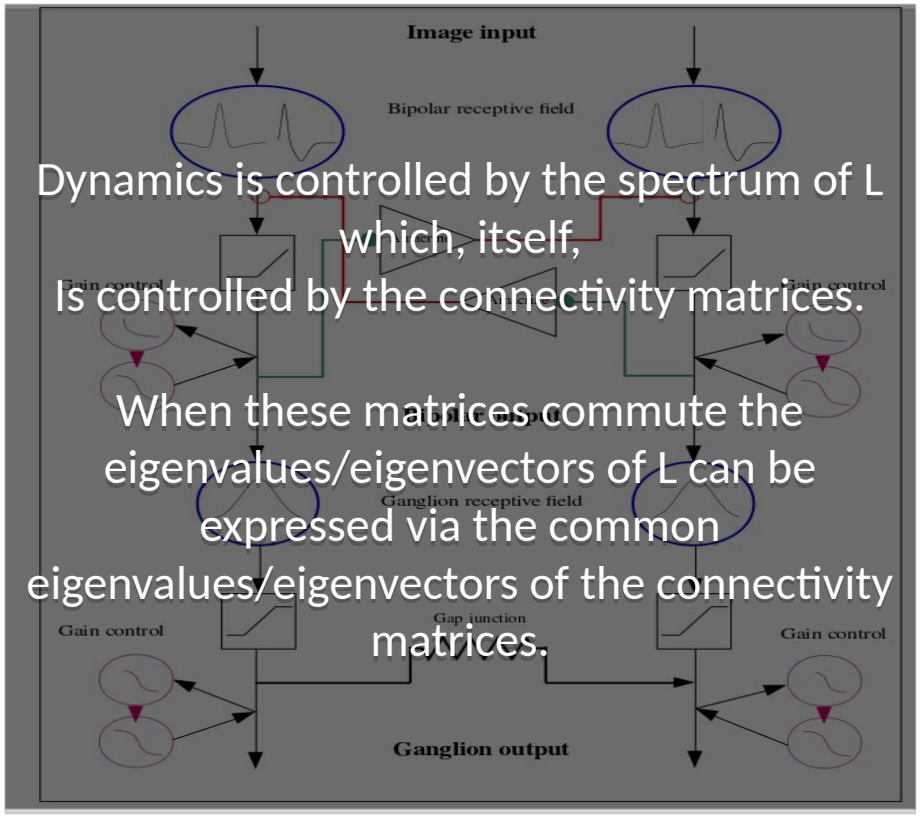
Dynamics is controlled by the spectrum of L which, itself,
Is controlled by the connectivity matrices.

When these matrices commute the eigenvalues/eigenvectors of L can be expressed via the common eigenvalues/eigenvectors of the connectivity matrices.

Building a 2D retina model for motion anticipation

Souihel S., Cessac B., “On the potential role of lateral connectivity in retinalanticipation”, Journal of Mathematical Neuroscience, BioMed Central, 2021, 11, ⟨10.1186/s13408-020-00101-z⟩



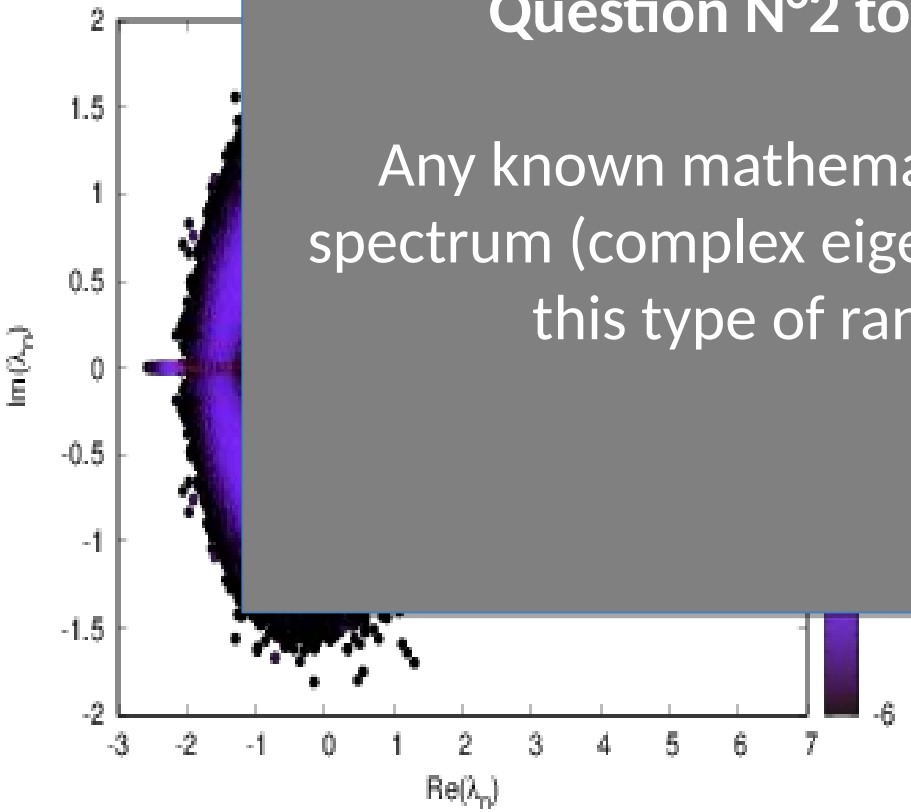


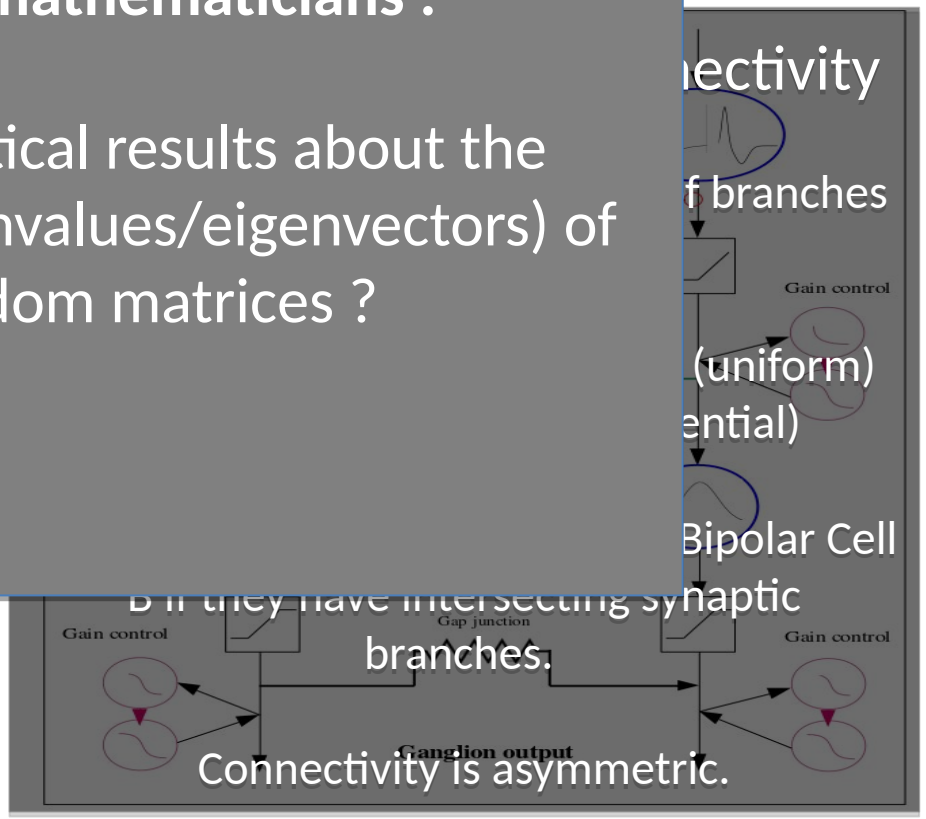
Building a 2D retina model for motion anticipation

Soui
retin

Question N°2 to mathematicians :

Any known mathematical results about the spectrum (complex eigenvalues/eigenvectors) of this type of random matrices ?





Perspectives

- A retino-cortical (V1) model of anticipation (with F. Chavane, S. Chemla, A. Destexhe, S. Souihel, M. Di Volo.

Perspectives

- A retino-cortical (V1) model of anticipation (with F. Chavane, S. Chemla, A. Destexhe, S. Souihel, M. Di Volo.

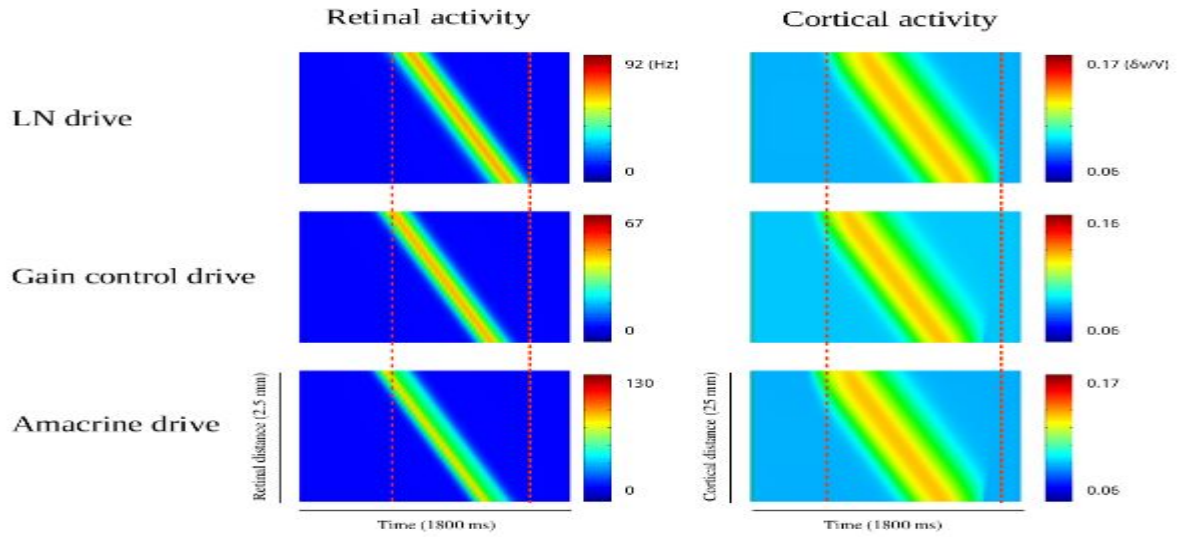


Figure 11: Comparing the spatio-temporal activity with the different drives. Left column figures display the spatio-temporal retinal activity with different anticipatory mechanisms, and the right column displays the corresponding spatio-temporal cortical activity. The red dashed lines denote the start and the end times of the LN retinal and cortical activities, as a reference base.

Perspectives

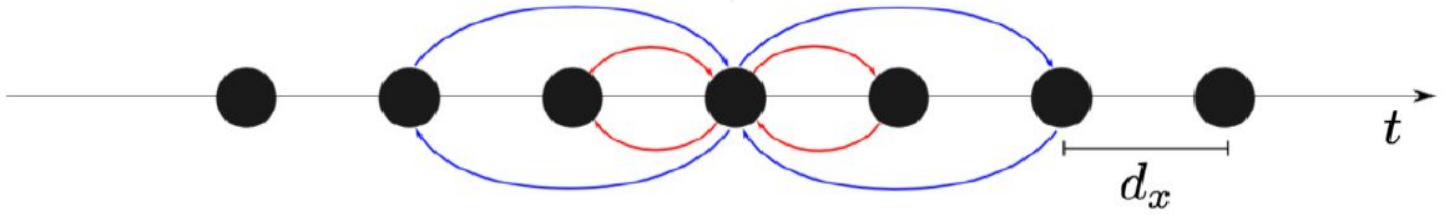
- A retino-cortical (V1) model of anticipation (with F. Chavane, S. Chemla, A. Destexhe, S. Souihel, M. Di Volo.
- Is our model able to anticipate more complex trajectories, with accelerations for instance ?
- How to calibrate connectivity using biology ?
- How does anticipation affect higher order correlations ?
- Would it be possible to design psycho-physical tests clearly showing the role of the retina in visual anticipation ?

Linear response for spiking neuronal networks with unbounded memory

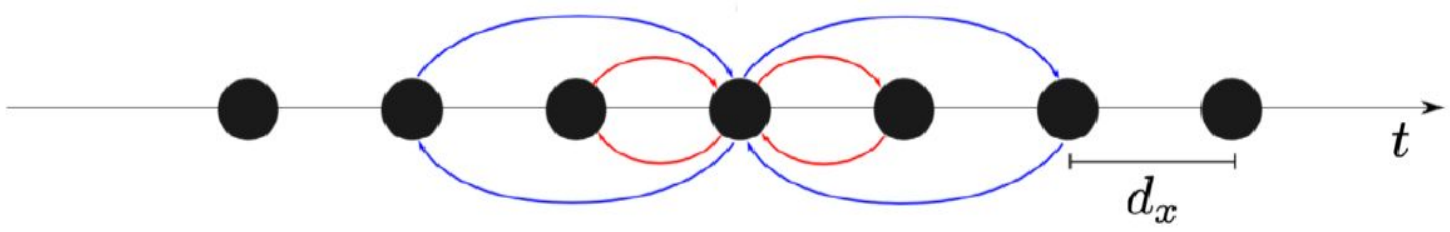
R. Cofré, CIMFAV, Facultad de Ingenieria,
Universidad de Valparaiso, Valparaiso, Chile

Ignacio Ampuero, Departamento de Informatica,
Universidad Tecnica Federico Santa Maria,
Valparaiso, Chile

Spontaneous spiking activity

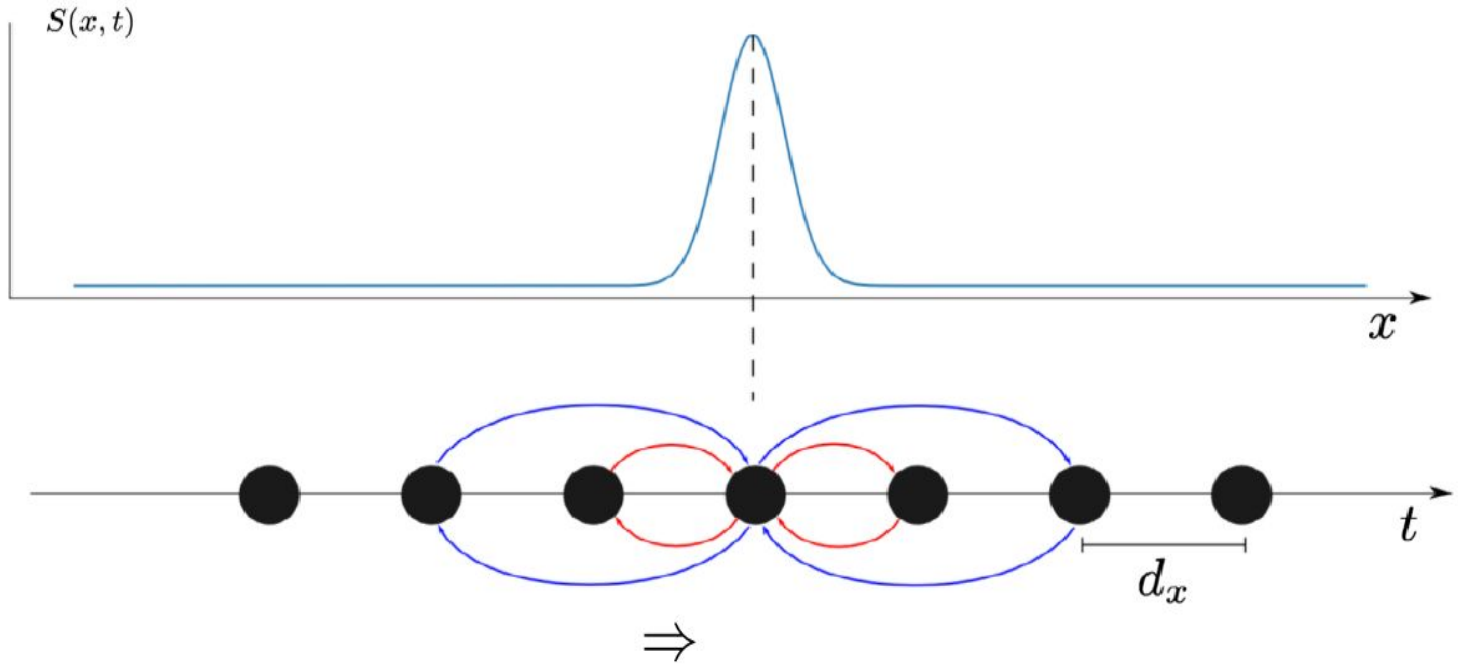


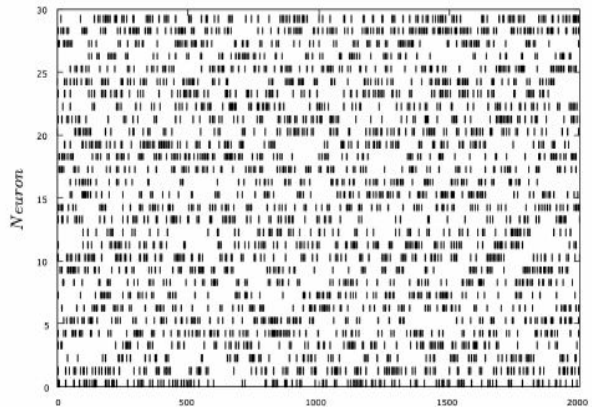
Spontaneous spiking activity



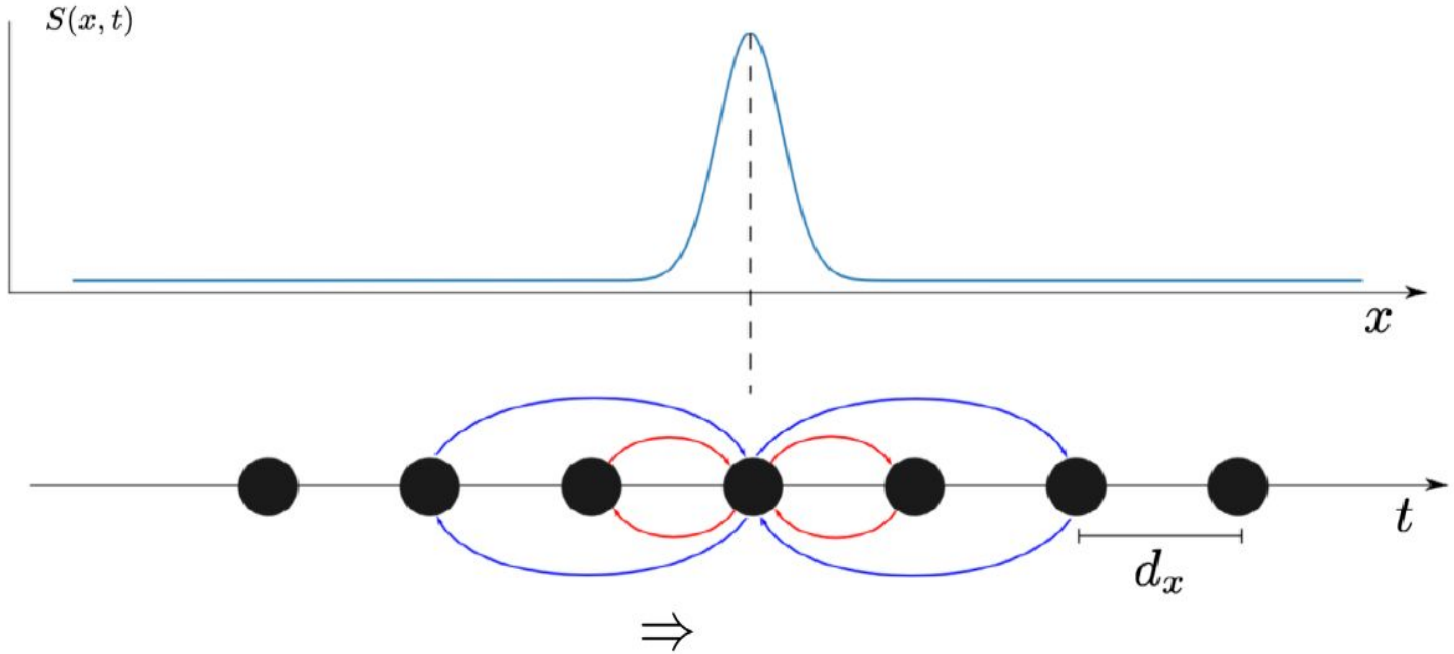


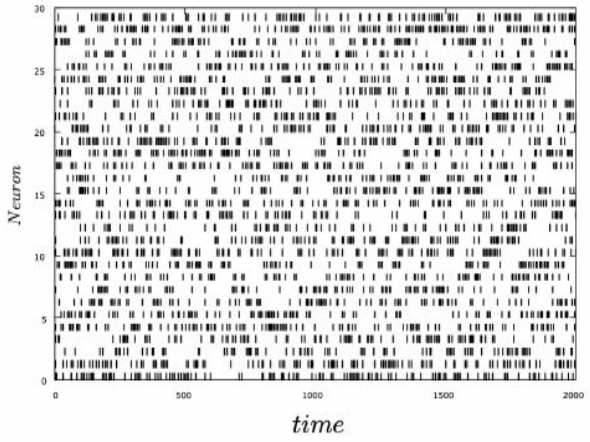
Spontaneous spiking activity

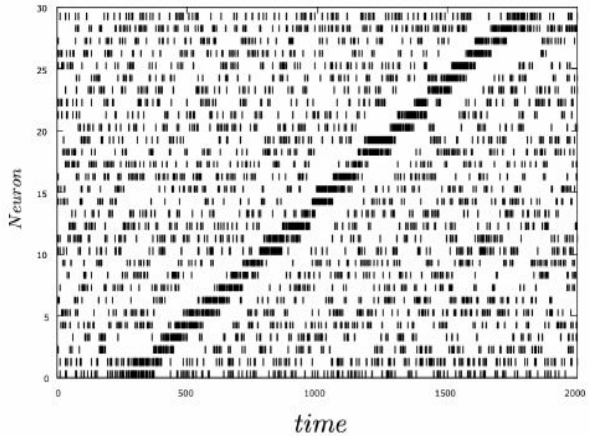




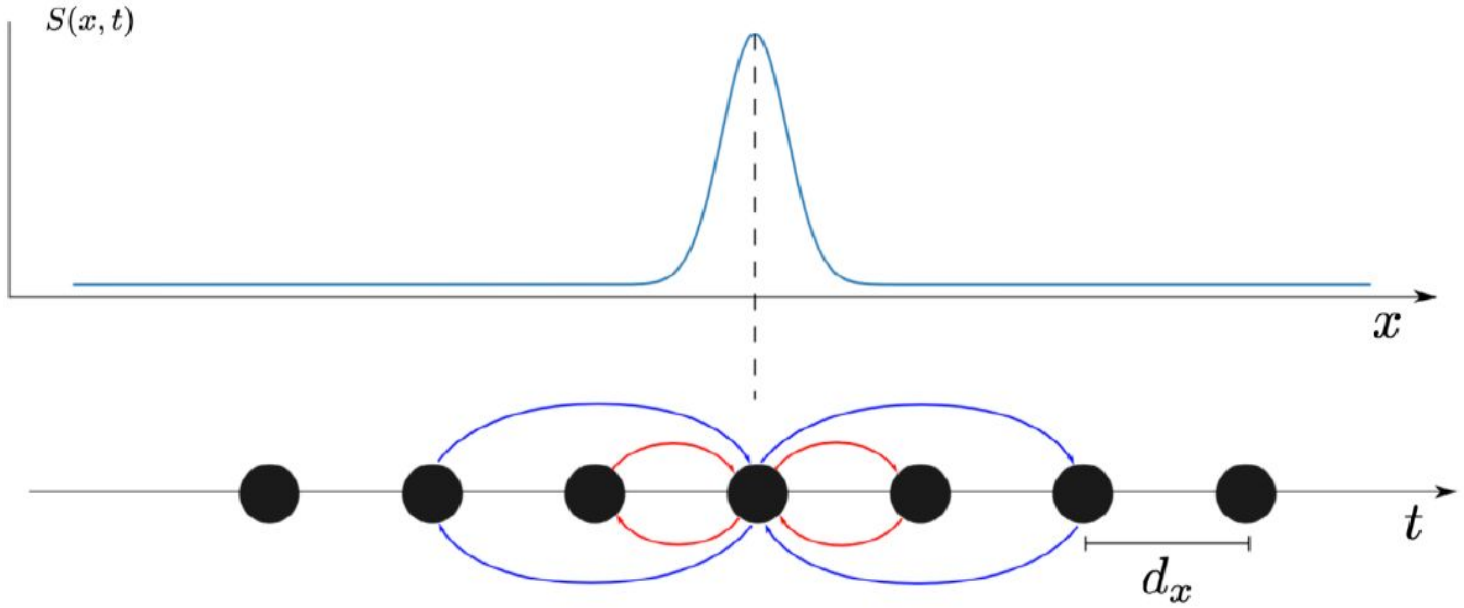
Spontaneous spiking activity

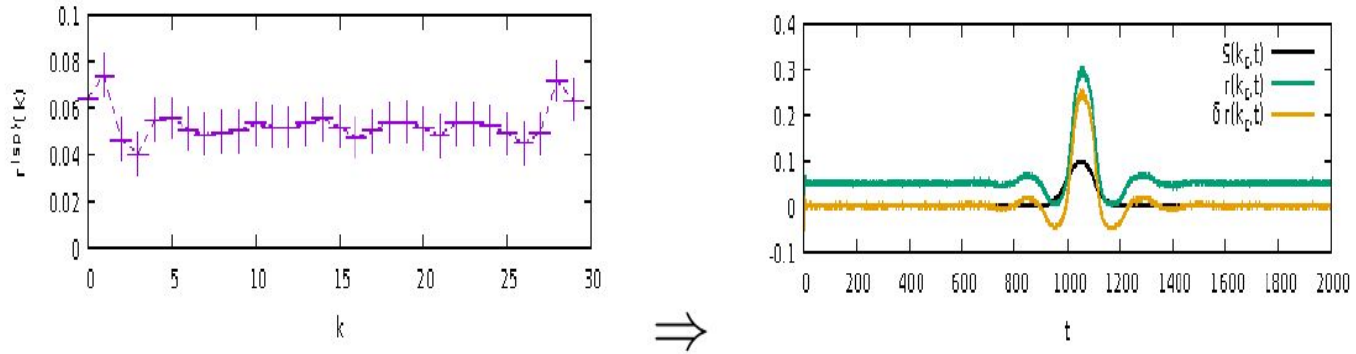






Spontaneous spiking activity

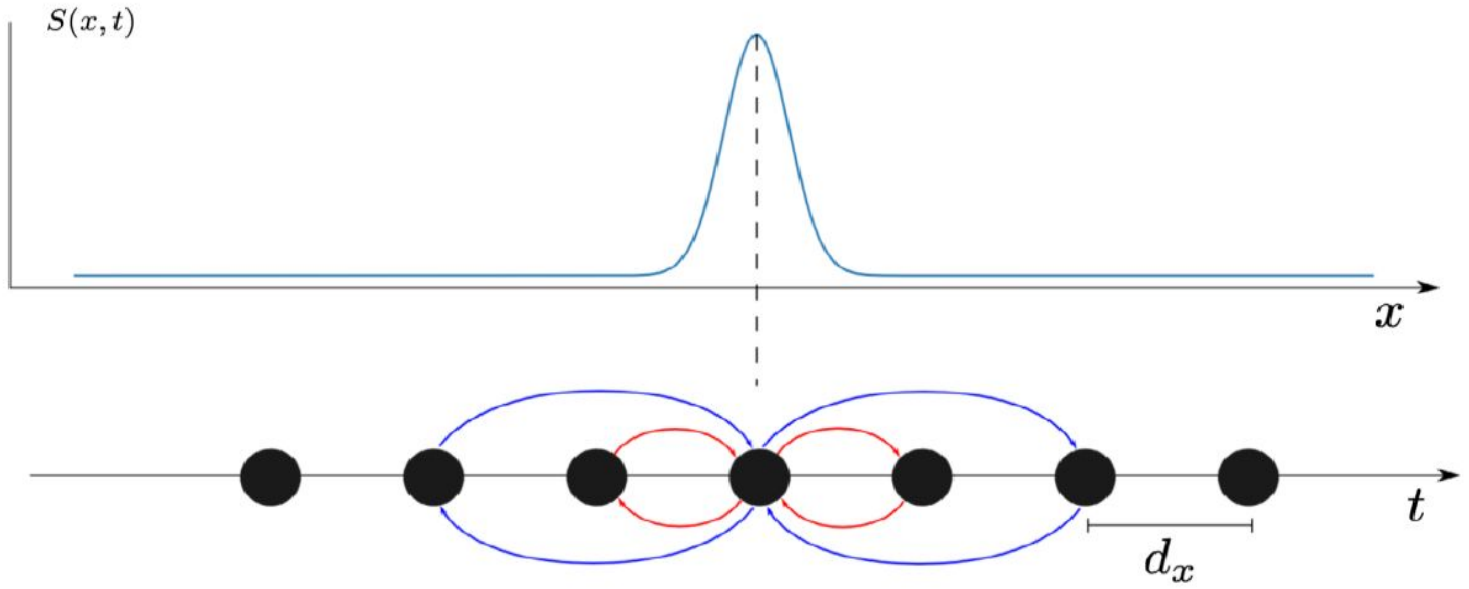


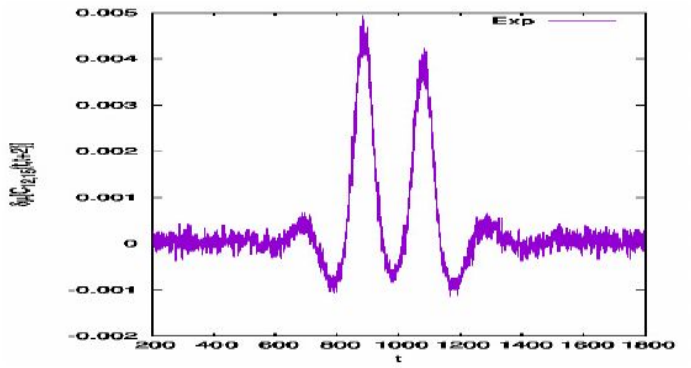


$\Rightarrow$

Sample averaging (non stationary)

Spontaneous spiking activity





Variation in the correlation $C_{12,15}(t, t+2)$

Correlation variations are triggered by the stimulus, but they are constrained by the network dynamics.

Question

How to compute the spatio-temporal response of a neuronal network to a time dependent stimulus ?

Can we compute the time variation of spike-observables as a function of the stimulus and spontaneous dynamics ?

B. Cessac, I. Ampuero, R. Cofre, Linear response for spiking neuronal networks with unbounded memory. Entropy, MDPI, 2021, 23 (2), pp.155.

Response to stimuli

B. Cessac, I. Ampuero, R. Cofre, Linear response for spiking neuronal networks with unbounded memory. Entropy, MDPI, 2021, 23 (2), pp.155.

GIF model without stimulus $\Rightarrow$*stationary Gibbs distribution*.

time-dependent stimulus $S(t) \Rightarrow$*non stationary Gibbs distribution*.

How is the average of an observable $f(\omega, t)$ affected by the stimulus ?

If S is weak enough: $\delta\mu[f(t)] = [\kappa_f * S](t)$, (linear response).

$$\kappa_{k,f}(t - t_1) = \frac{1}{C_k} \sum_{r=-\infty}^{n=[t]} \mathcal{C}^{(sp)} \left[f(t,\cdot), \frac{\mathcal{H}_k^{(1)}(r,\cdot)}{\sigma_k(r-1,\cdot)} \int_{\tau_k(r-1,.)}^{r-1} S_k(t_1)\Gamma_k(t_1, r-1, \cdot)dt_1 \right]$$

Firing rates

Computations have been done using the INRIA Pranas software, B. Cessac et al, Frontiers in Neuroinformatics, Vol 11, page 49, (2017).

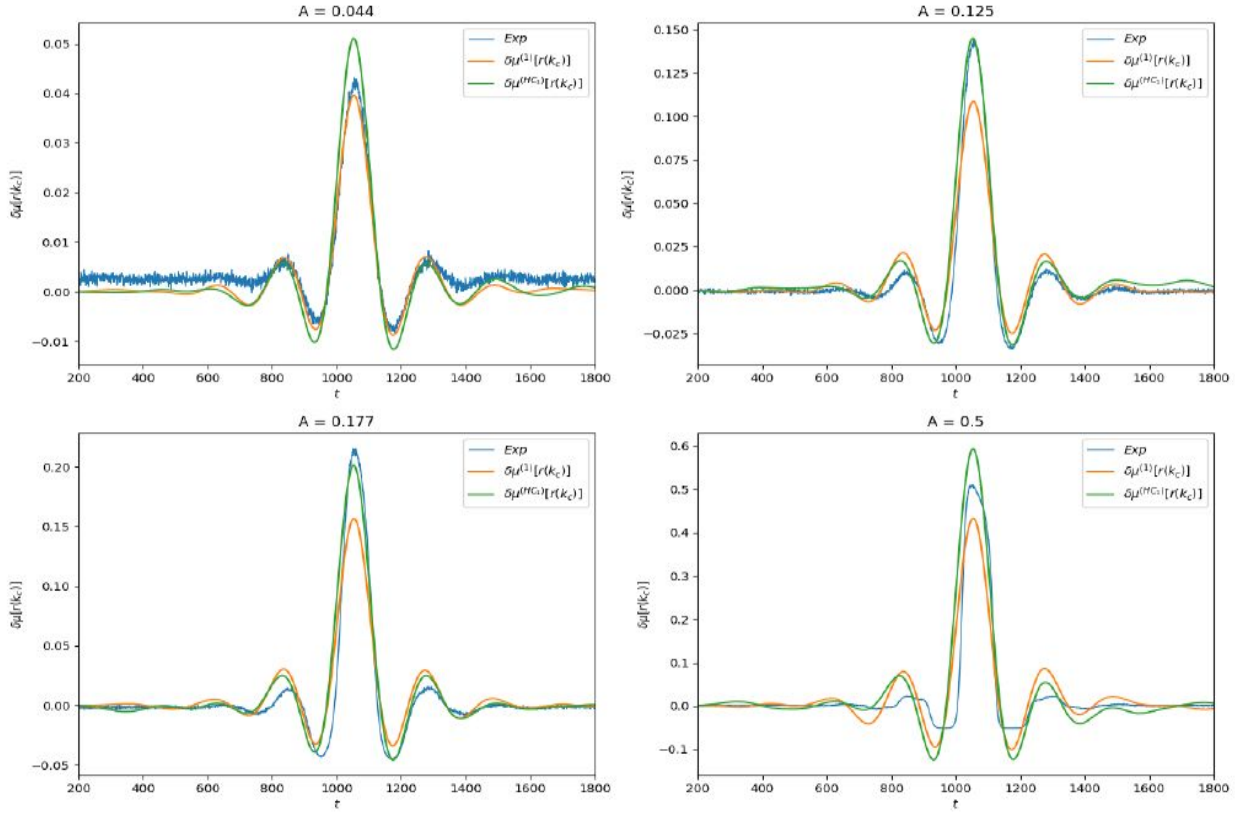


Figure: Linear response of $f(\omega, n) = \omega_{k_c}(n)$ for different values of stimulus amplitude A.

Higher order observable

Computations have been done using the INRIA Pranas software, B. Cessac et al, Frontiers in Neuroinformatics, Vol 11, page 49, (2017).

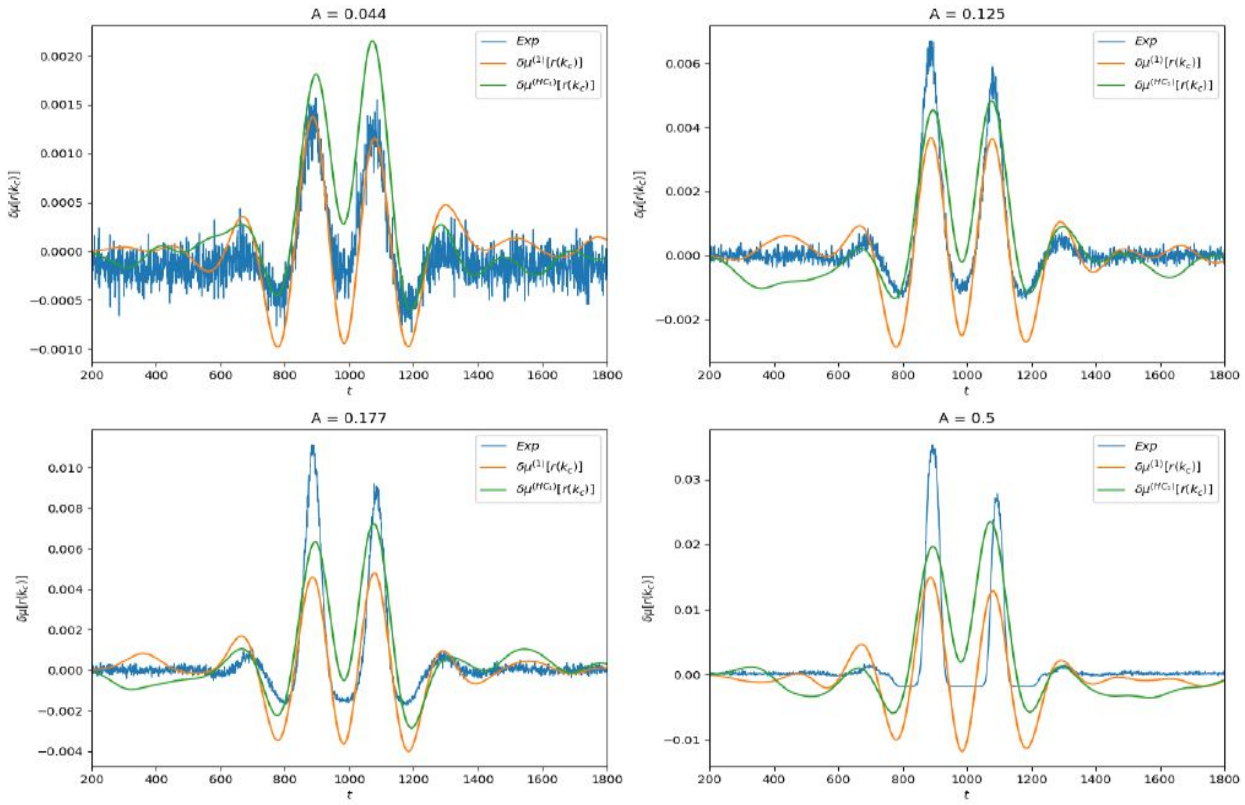


Figure: Linear response of the observable $f(n,\omega) = \omega_{k_c-2}(n-3)\omega_{k_c}(n)$.

Higher order observable

Computations have been done using the INRIA Pranas software, B. Cessac et al, Frontiers in Neuroinformatics, Vol 11, page 49, (2017).

Question N°3 to mathematicians :

Would it be possible to extend this linear response in a more general context (Hawkes processes, Galves-Löcherbach model) ?



Figure: Linear response of the observable $f(n, \omega) = \omega_{k_c-2}(n-3)\omega_{k_c}(n)$.

Thanks ⏪