



Modeling the emergence of stage II retinal waves in immature retina

Dora Karvouniari, Lionel Gil, Olivier Marre, Serge Picaud, Bruno Cessac

► To cite this version:

Dora Karvouniari, Lionel Gil, Olivier Marre, Serge Picaud, Bruno Cessac. Modeling the emergence of stage II retinal waves in immature retina. AREADNE 2016 Research in Encoding And Decoding of Neural Ensembles, Jun 2016, Santorini, Greece. . hal-01339875

HAL Id: hal-01339875

<https://inria.hal.science/hal-01339875>

Submitted on 30 Jun 2016

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.

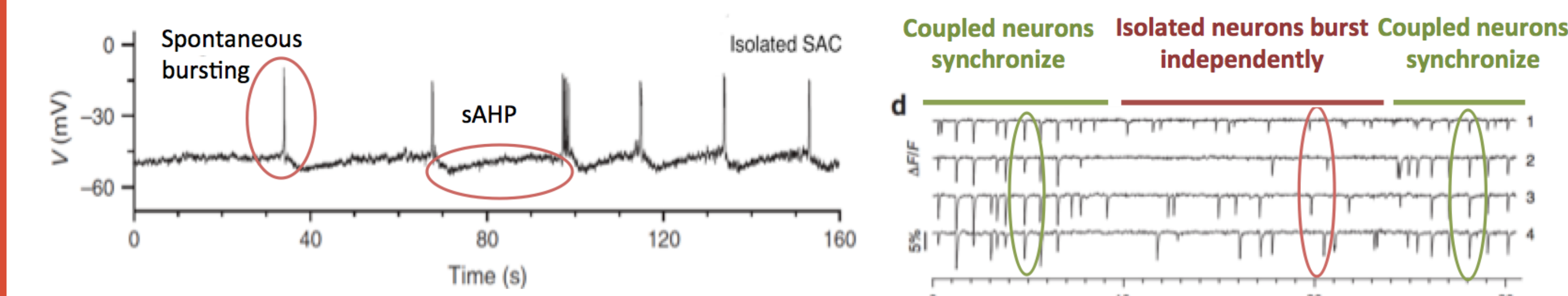
L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

ABSTRACT

Retinal waves are spontaneous bursting activity propagating in the developing retina until vision is functional. In this work we propose a biophysical modelling of the mechanism that generates the spontaneous intrinsic cell-autonomous rhythmic bursting in Starburst Amacrine Cells (SACs), observed experimentally in [1] which is directly linked with the emergence of stage II retinal waves. We analyze this system from the dynamical system and bifurcation theory perspective.

CONTEXT & MOTIVATION

Necessary components for the emergence of retinal waves [1]



Recording of spontaneous cell-autonomous rhythmic bursts in isolated SACs in rabbits [1].

Coupled SACs burst synchronously [1]

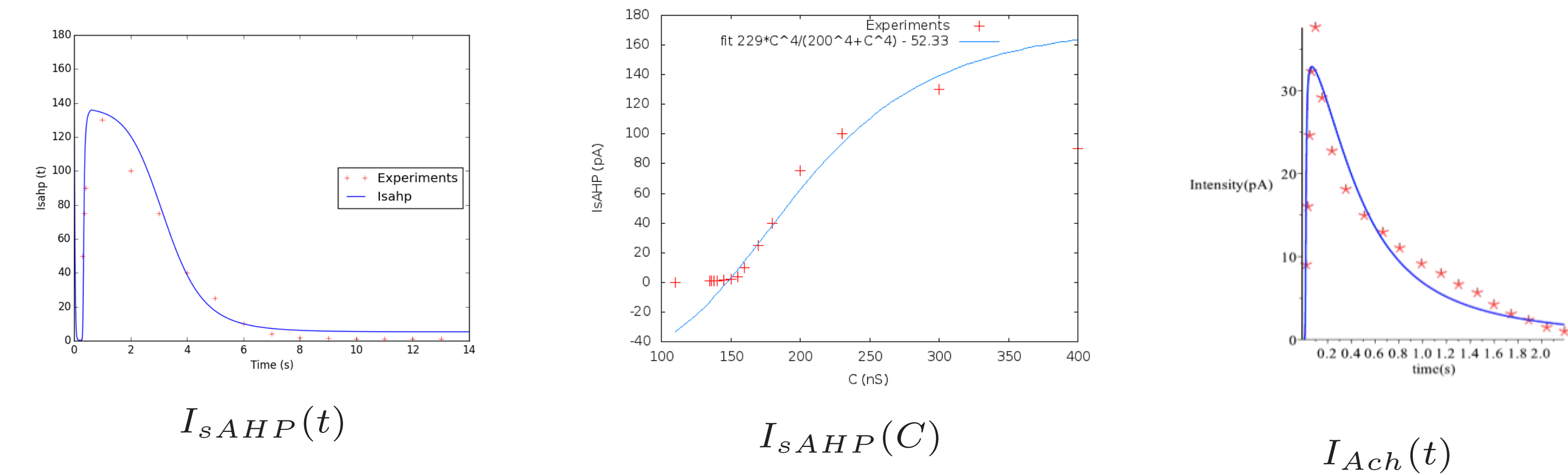
- Spontaneous rhythmic **bursting** activity of isolated SACs
- Refractory mechanism modulating the silent period of the bursting activity (slow After HyperPolarisation current, **sAHP**)
- **Coupling** via cholinergic synapses to ensure the necessary level of synchrony

Motivation & Goals

- Finding a biophysical modelling reproducing these experiments and generating waves by taking into account the biophysical mechanisms and tuning parameters from the biophysical literature.
- Propose a bifurcation analysis in order to extract a generic biophysical mechanism of the spontaneous bursting of isolated SACs.
- Model network interactions to reproduce propagating spatio-temporal patterns with two goals : i) Characterize the conditions for synchronization of neurons ii) Study the effect of the synaptic coupling on spatio-temporal patterns.

Fitting experimental curves

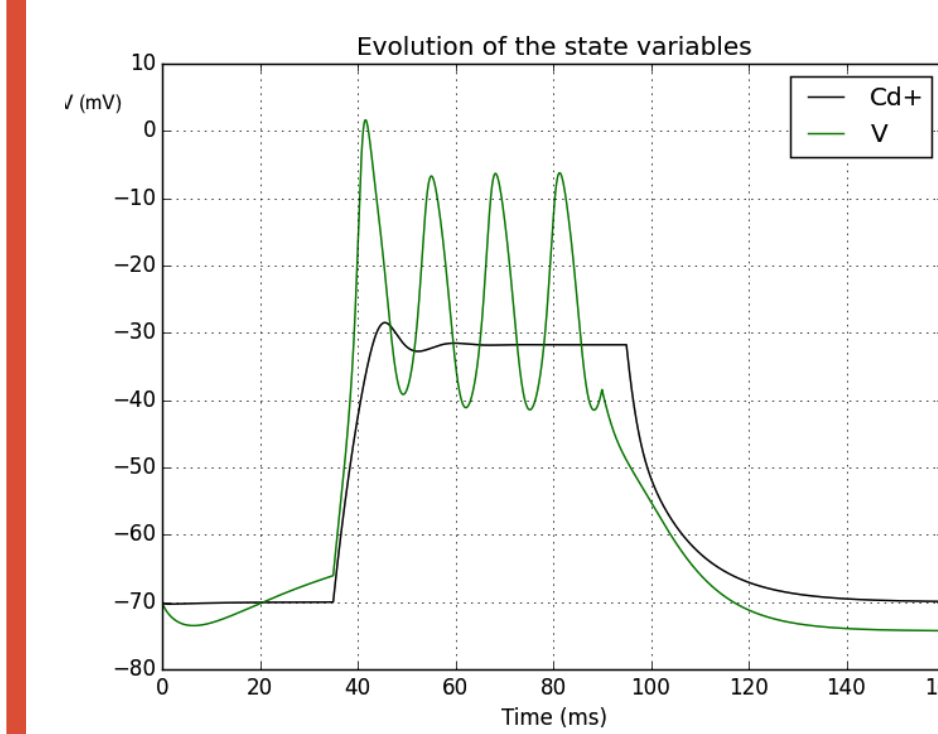
- Model sAHP according to [2] and extract the corresponding parameters by experimental fits and literature.
- For SACs, the kinetics of sAHP are the same as for pyramidal neurons but amplitudes are weaker.
- Extract the parameters for the cholinergic currents by fitting the experimental curves of Zhou et al. 2004.



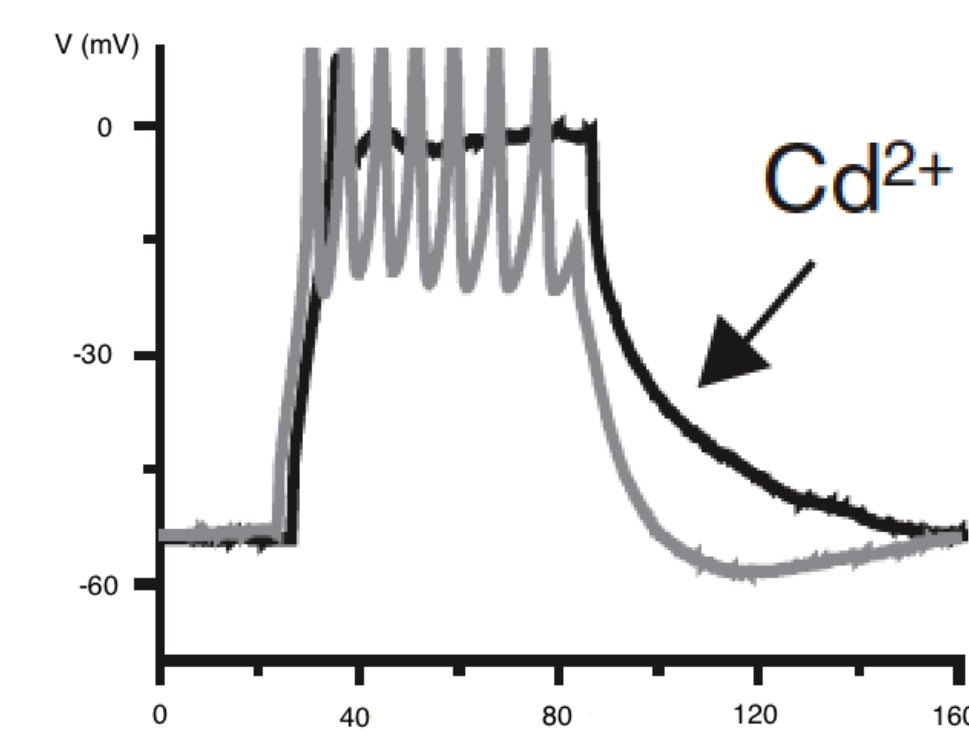
ACKNOWLEDGEMENTS

This work was supported by the French ministry of Research and University of Nice (EDSTIC) and ANR Trajectory. We warmly acknowledge Matthias Hennig and Evelyne Sernagor for their invaluable help.

MODELLING CELL-AUTONOMOUS BURSTS



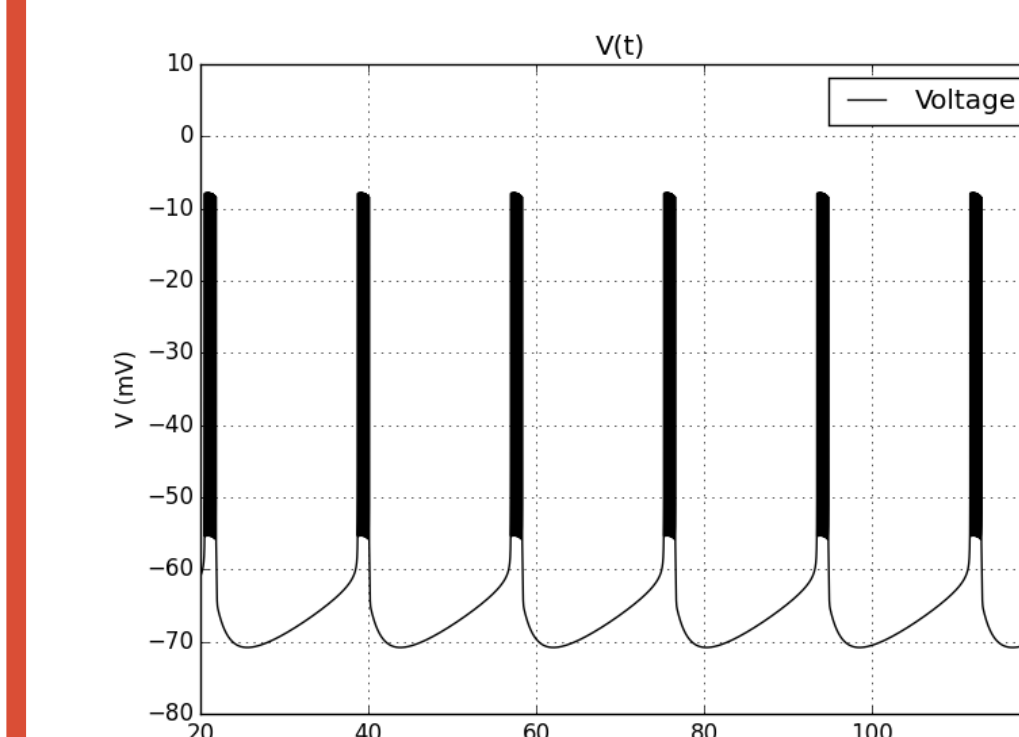
Model



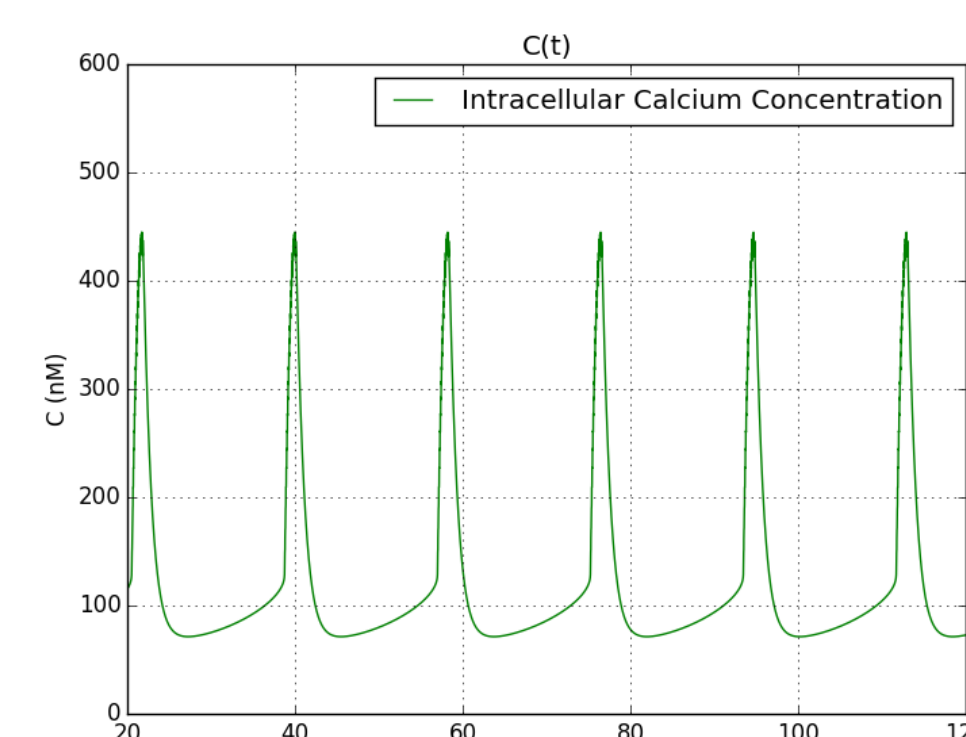
Experiment

- Modeling the ionic mechanism of intrinsic bursts according to [1] based on an extended M-L model.
- Fast oscillations of the voltage while applying an external current pulse of 150 pA followed by a subsequent AHP. Blocking all calcium related currents leads to the vanishing of both fast oscillations and AHP.

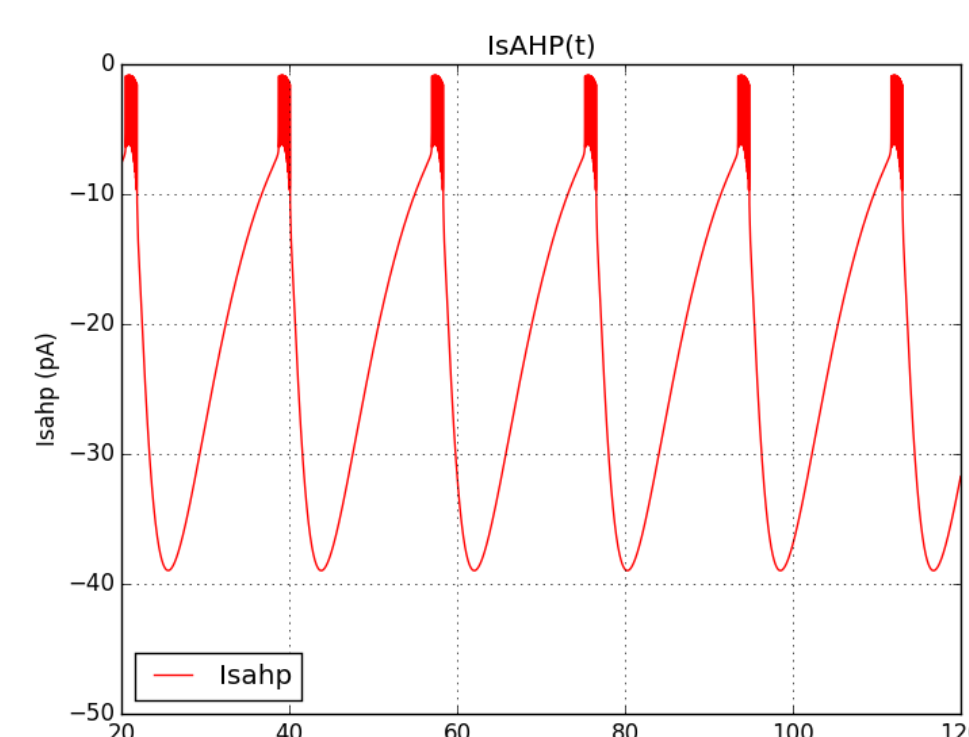
SIMULATIONS OF ISOLATED SACs



$V(t)$

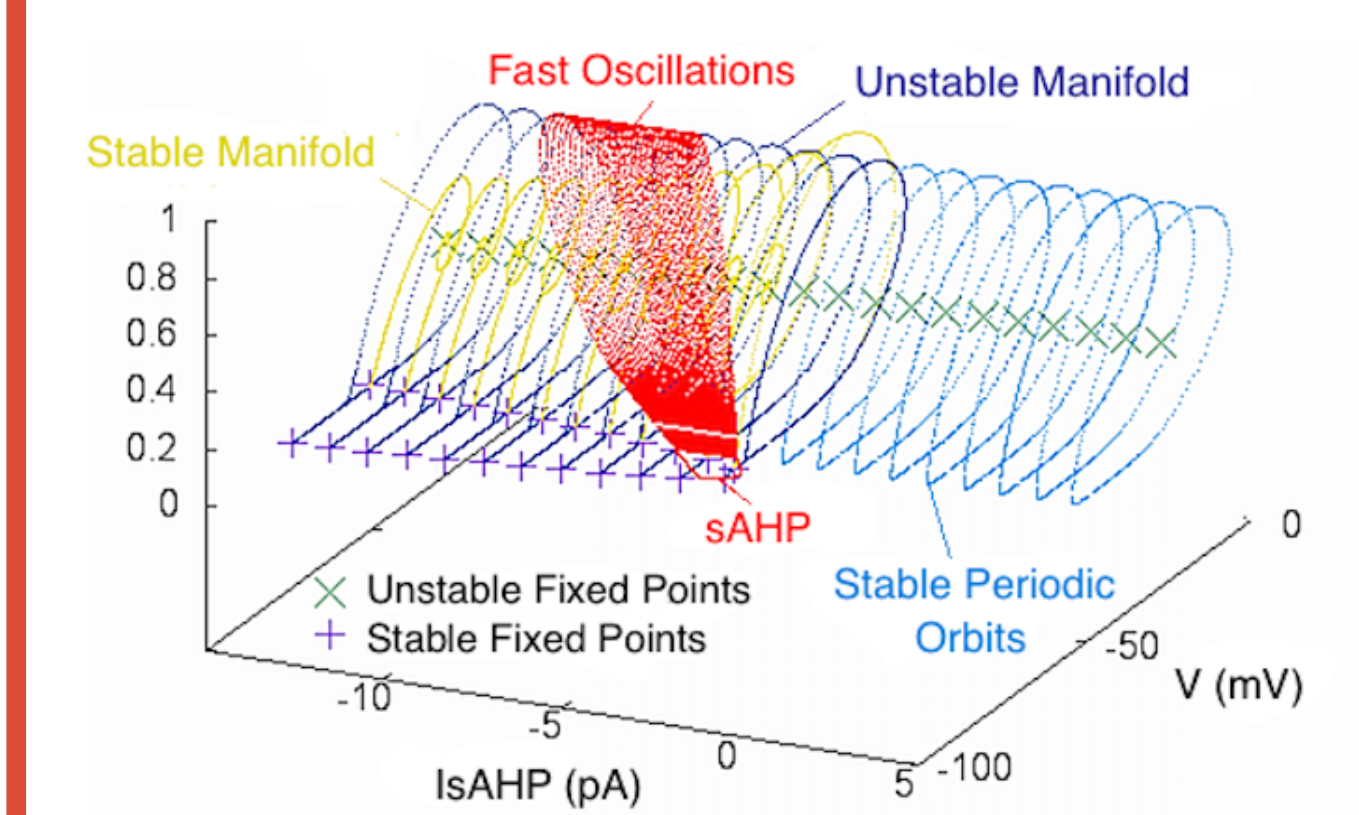


$C(t)$



$I_{sAHP}(t)$

BIFURCATION ANALYSIS FOR ISOLATED SACs

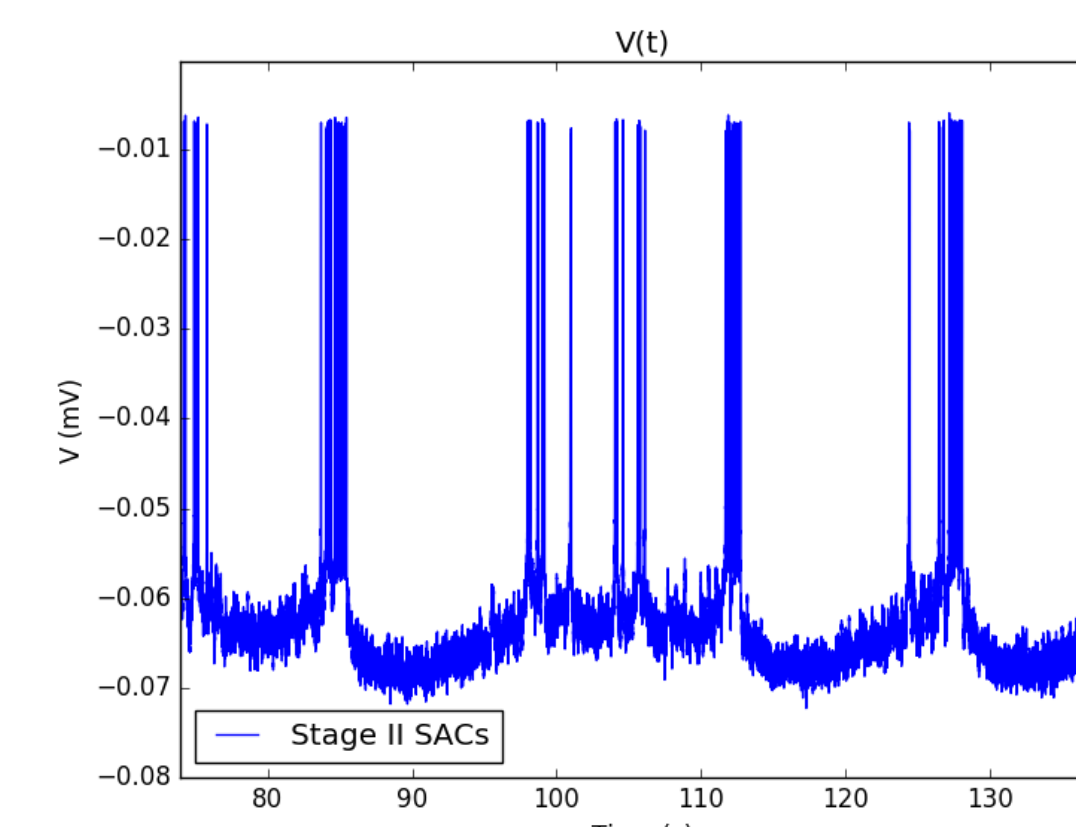


3D Bifurcation diagram of the mechanism generating rhythmic intrinsic bursts in SACs

Proposed biophysical process

- SACs are in a regime where they can oscillate spontaneously.
- As they oscillate, the calcium load increases, so the effect of sAHP increases up to a point where oscillations stop, reaching a steady state where the level of the voltage is quite lower.
- Then, intracellular calcium concentration unloads, I_{sAHP} decreases, until the effect of sAHP is small and oscillations start again.

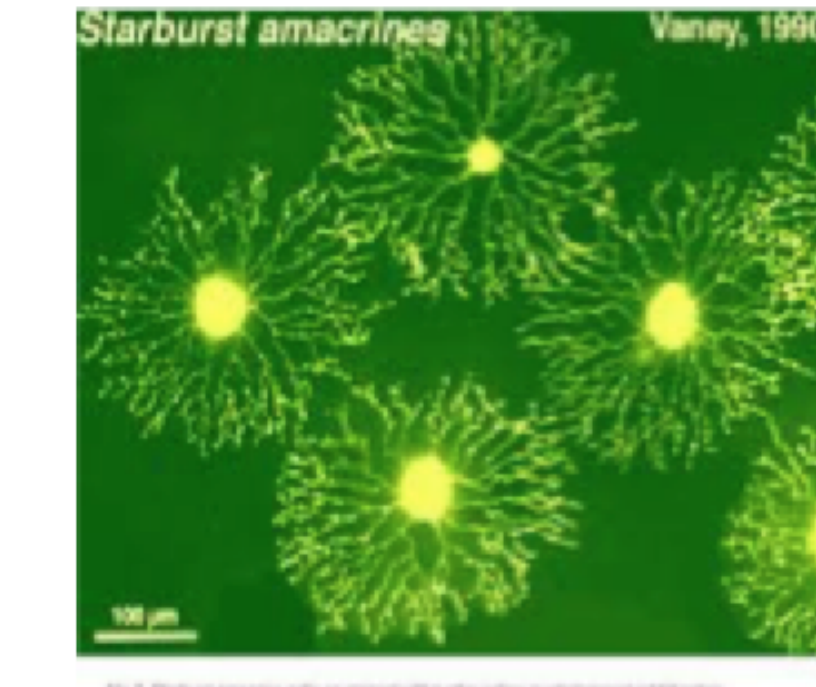
ADDING NOISE



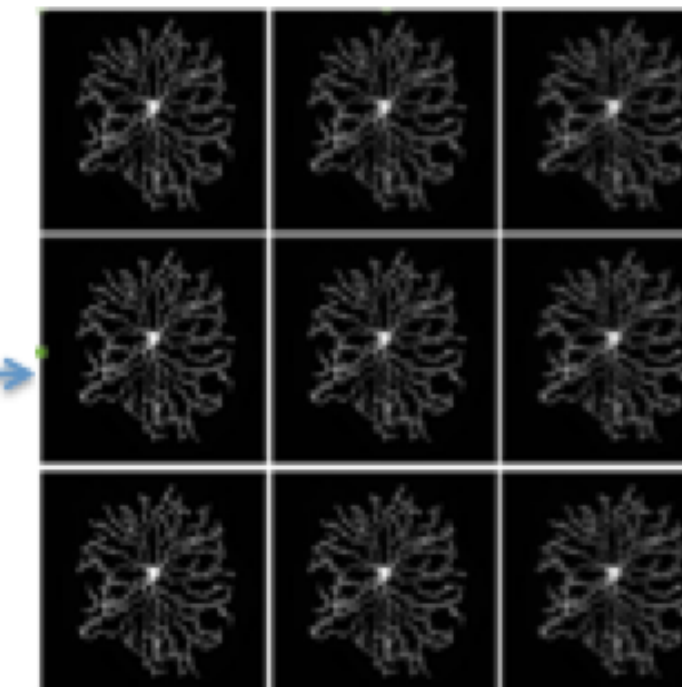
Simulation adding Gaussian noise

- Our model is deterministic and bursting period is regular.
- In order to break the regularity, we add a zero-mean Gaussian noise of $\sigma = 10pA$.
- Increasing the standard deviation of the noise we observed that bursting period decreases.

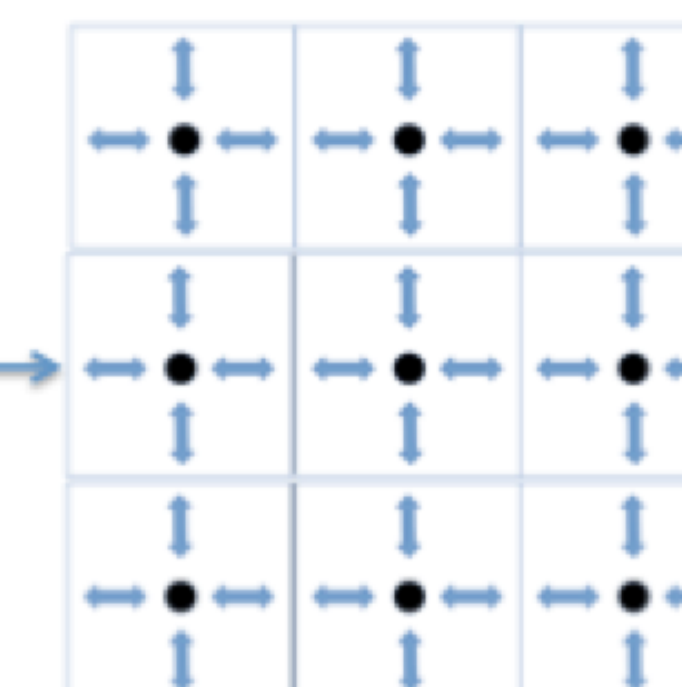
MODELING NETWORK INTERACTIONS



SACs realistic connections

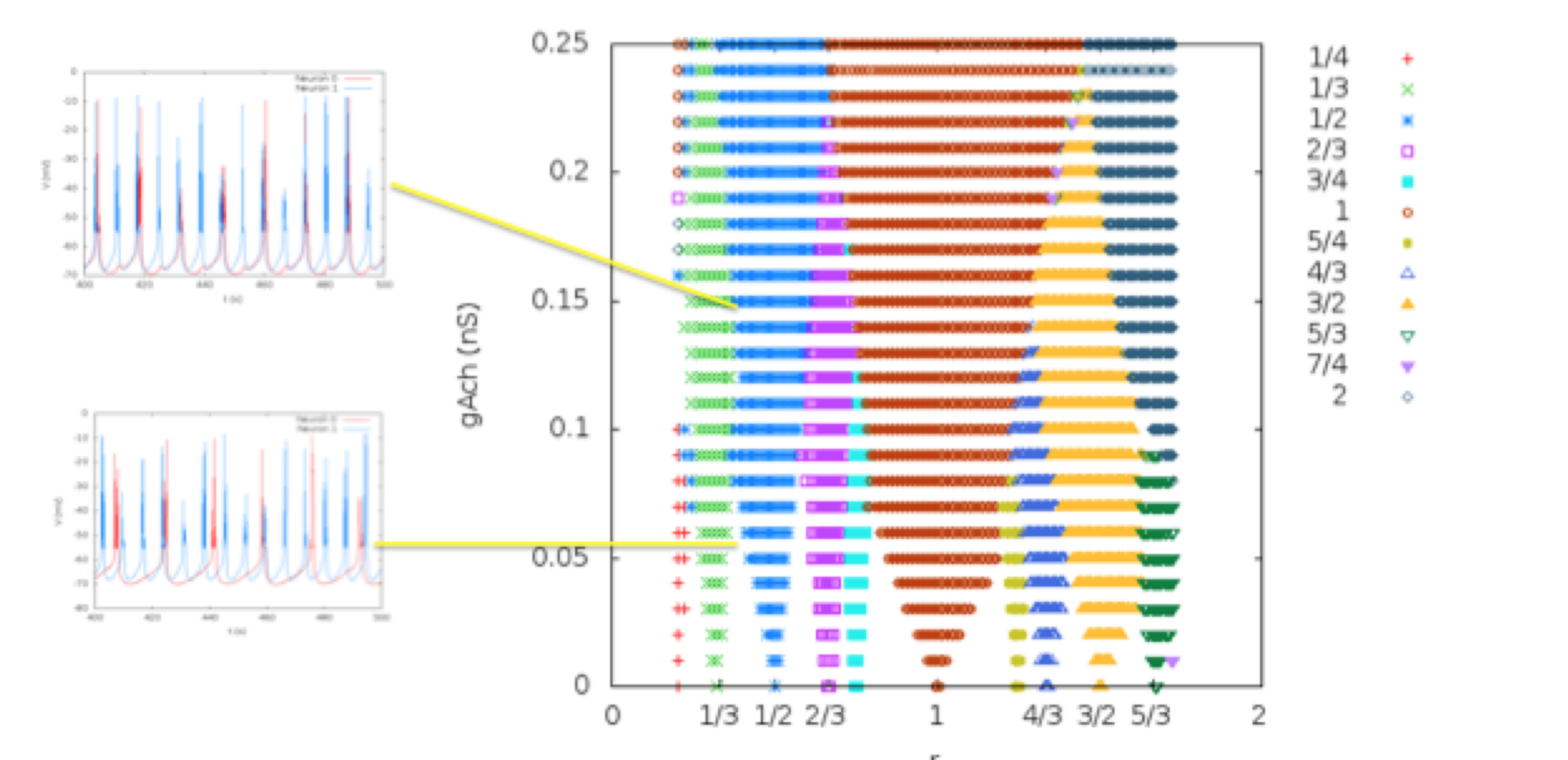


SACs on a lattice



SACs become points on a lattice

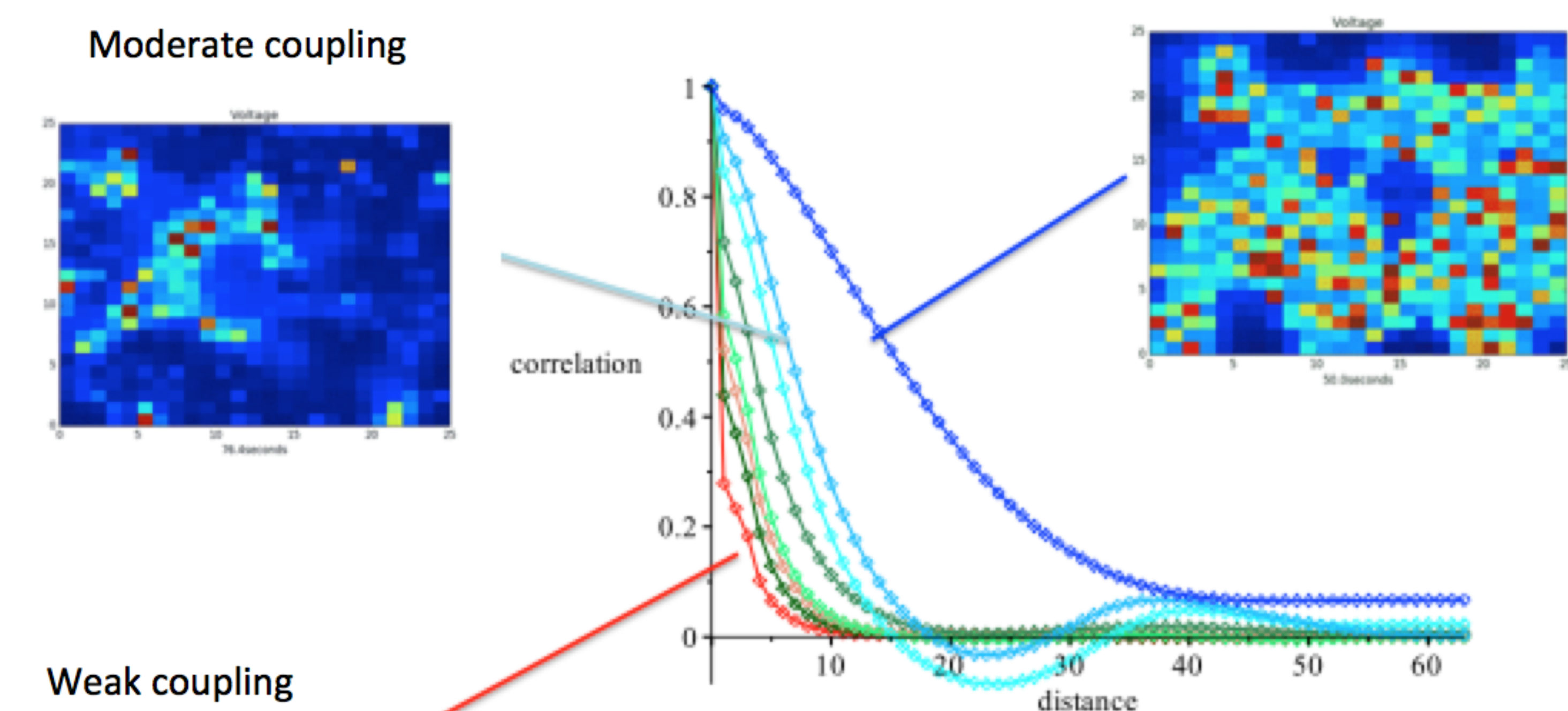
- SACs are placed on a square lattice connected to their four nearest neighbours.
- Synapses are excitatory through cholinergic transmission.
- It is found experimentally that SACs are not identical, i.e. their characteristic refractory time follows a Gaussian distribution.



- Introducing a variability in the bursting period, we end up with a network of coupled bursters. In order to study the conditions for synchrony we start from the simpler case of two coupled neurons.
- As in the case of coupled oscillators, in our case we observe Arnold tongues.
- Starting from isolated neurons with a random ratio of bursting period, we observe that as we increase the strength of the coupling we obtain resonances at the closest rational numbers. Strong coupling would give 1:1 synchrony.

NETWORK SIMULATIONS

Distance Pairwise Correlations Strong coupling

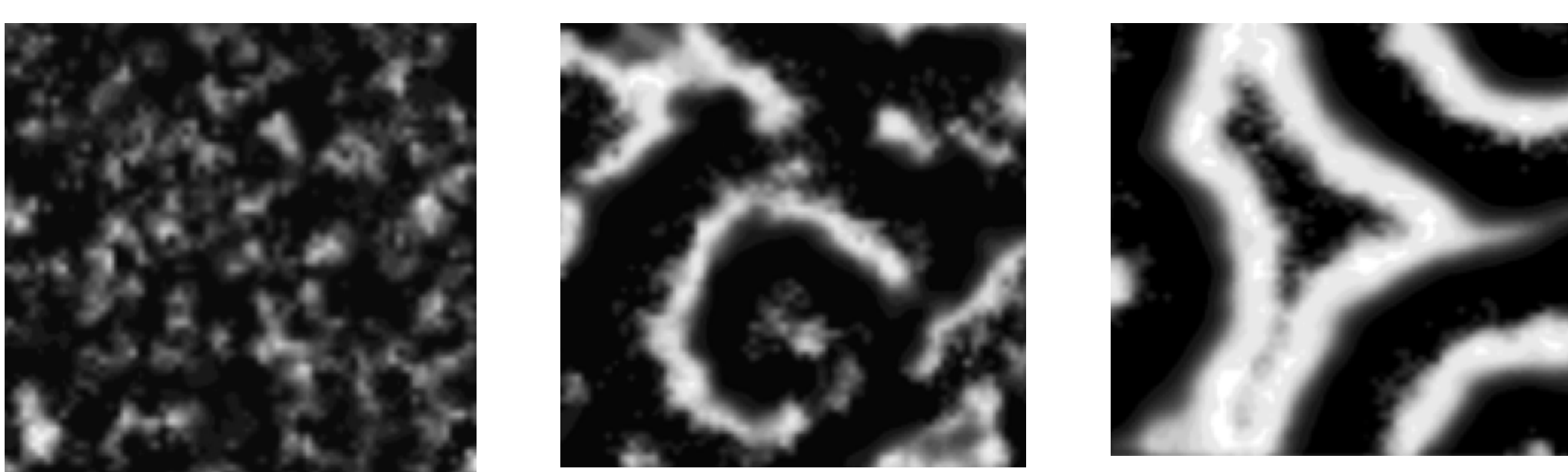


Weak coupling

$$C(d) = \frac{\langle C(r,t)C(r+d,t) \rangle - \langle C(r,t) \rangle \langle C(r+d,t) \rangle}{\sigma_r \sigma_{rd}}$$

- Top: Network simulations for the Voltage of 625 neurons on a square lattice. Blue and red colours correspond to low and high activity respectively. Also, we compute the correlations with respect to the distance of cells.
- Bottom: Network simulations for the Calcium of 4096 neurons on a square lattice. Black and white colours correspond to low and high activity respectively.
- Weak coupling leads to localised bumps of activity. Strong coupling leads to complete synchrony. Moderate coupling leads to propagating patterns.
- We study pairwise correlations with respect to distance. There is an intermediate regime where we observe anticorrelations. Anticorrelation corresponds to a region of hyperpolarization corresponding to the boundary of the wave.

Calcium Waves



Weak

Moderate

Strong

CONCLUSIONS & FUTURE PERSPECTIVES

- We proposed a biophysical modelling of the spontaneous intrinsic cell-autonomous rhythmic bursting in Starburst Amacrine Cells during stage II retinal waves, directly extracted from experimental and biophysical data.
- Our model is able to generate spontaneously the observed rhythmic bursting, without the need of any external excitation to trigger the system, as opposed to [3] and [4].
- With our model we are able to explain biophysically and dynamically how the slow oscillations are generated and sustained in developing SACs.
- We have shown by our modelling the network effect: there is a necessary level of synchrony to be achieved between neighbouring SACs to generate propagating waves.

REFERENCES

1. Zheng J., Lee S., J.Zhou, A transient network of intrinsically bursting starburst cells underlies the generation of retinal waves, Nature Neuroscience, Volume 9, 2006
2. H. J. Abel, J. C. F. Lee, J.C. Callaway, R. C. Foehring, Relationships between Intracellular calcium and Afterhyperpolarizations in Neocortical Pyramidal Neurons, JNeurophysiol:91, 324-335, 2004
3. M.Hennig, C. Adams, D. Willshaw, E.Sernagor, Early-Stage Waves in the Retinal Network Emerge Close to a Critical State Transition between Local and Global Functional Connectivity, JNeuroscience, 2009
4. Lansdell B., Ford K., Kutz N., A Reaction-Diffusion Model of Cholinergic Retinal Waves, PLOS Computational Biology, 2014