Classifying the spatiotemporal patterns within stage II retinal waves through dynamical systems analysis

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Dora Karvouniari,[1] Lionel Gil, [2] Olivier Marre, [3] Serge Picaud, [3] Bruno Cessac[1]

(1) Biovision team, Universite Cote d'Azur, INRIA, France, (2) INLN, Sophia-Antipolis, France, (3) Vision Institute, Paris, France

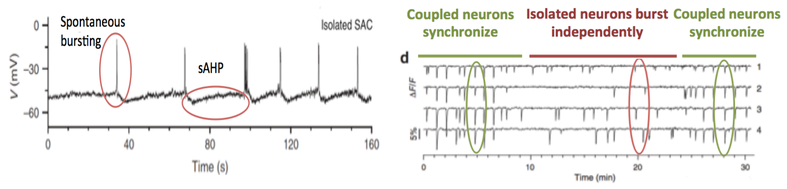
theodora.karvouniari@inria.fr; bruno.cessac@inria.fr

Abstract

Retinal waves are bursts of activity occurring spontaneously in the developing retina of vertebrate species, contributing to the shaping of the visual system organization. They are characterized by localized groups of neurons becoming simultaneously active, initiated at random points. Based on our previous modelling work [1], we now propose a classification of stage II retinal waves patterns as a function of acetylcholine coupling strength and a possible mechanism for waves generation. Our model predicts that spatiotemporal patterns evolve upon maturation or pharmacological manipulation and that there is a regime of cholinergic coupling, only for which, waves are characterized by power-law distributions.

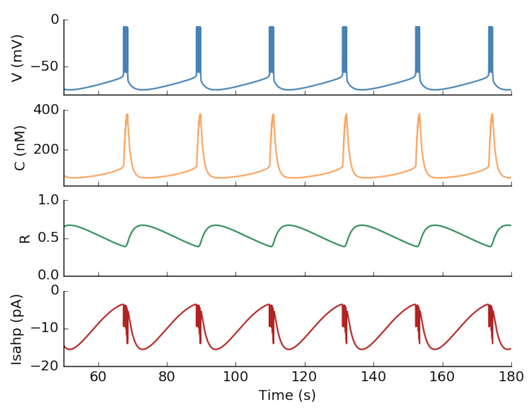
Context & Motivation

Necessary components for the emergence of retinal waves [2]



- 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

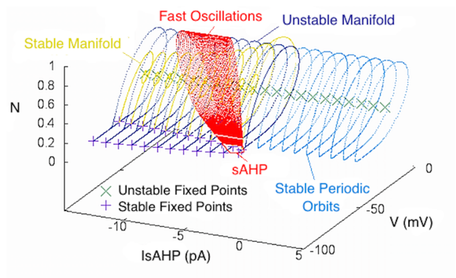
Isolated SACs



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.

Bifurcation Analysis



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

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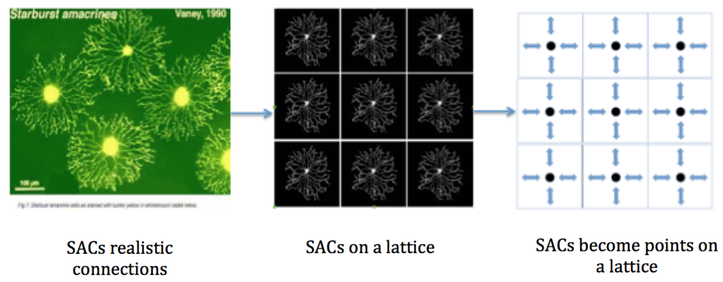
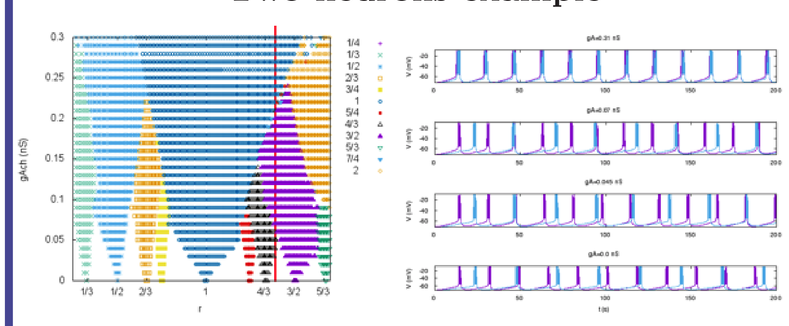
Network interactions



- SACs are placed on a square lattice connected to their four nearest neighbours.
- Synapses are excitatory through cholinergic transmission and their characteristic refractory time follows a Gaussian distribution [4].

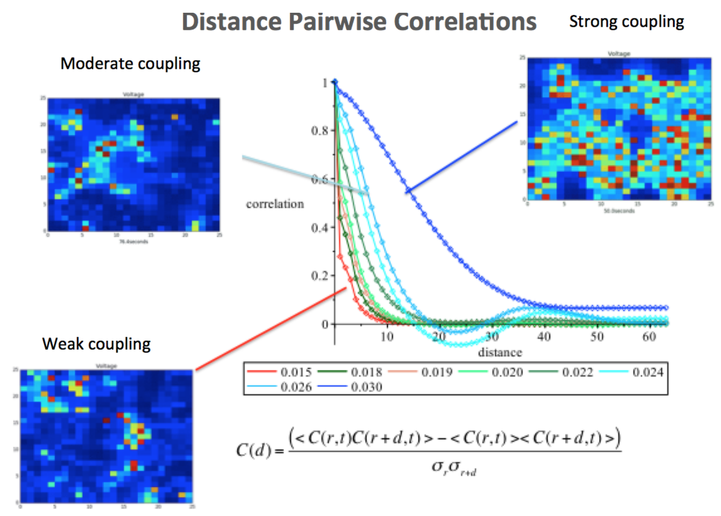
Synchrony

Two-neurons example



- Introducing a variability in the bursting period, we end up with a network of coupled bursters.
- By increasing the coupling, Arnold tongues appear for two neurons.
- We expect therefore to see roughly 3 regimes: weak coupling (disordered phase), moderate coupling (waves), strong coupling (full synchrony).

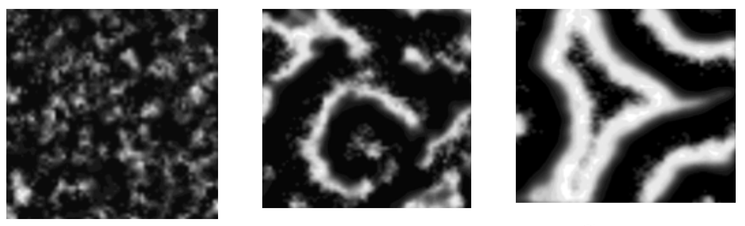
Network Simulations



Simulated local Voltage of 625 neurons on a square lattice. Blue and red colours correspond to low and high activity respectively.

- Weak coupling: localised bumps of activity. Strong coupling: complete synchrony standing waves. Moderate coupling: propagating patterns.
- Pairwise correlations with respect to distance show an intermediate regime where we observe anticorrelations. Anticorrelations correspond to a region of hyperpolarization linked to the boundary of the wave.

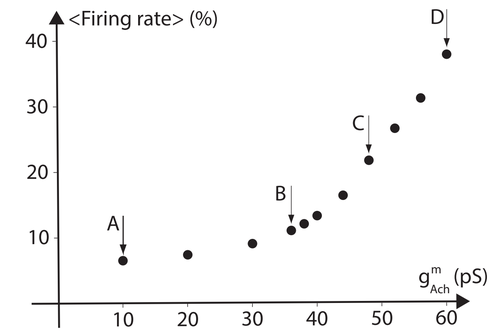
Calcium Waves



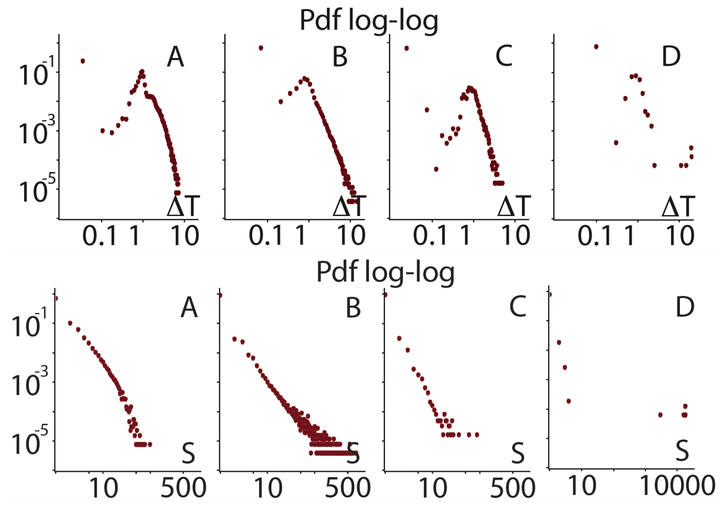
Simulated Calcium waves of 4096 neurons on a square lattice. Black and white colours correspond to low and high activity respectively.

Characterizing Waves

Average Population Bursting Rate

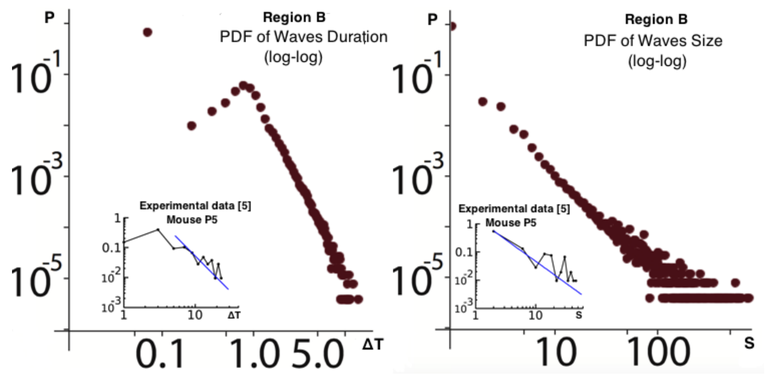


Distribution of the waves characteristics



Distribution of waves duration (top) and size (bottom) for weak, moderate and strong coupling.

- Low coupling: exponential distribution. Moderate coupling: power-law distributions. Strong coupling: large waves.



Distribution of waves duration and size moderate coupling (region B).

- For region B, in all cases, we observe power-law distributions of wave characteristics (duration, size).
- This type of distribution, has been primarily observed in [5] in experimental data of stage II retinal waves for different species.

Conclusion

- Cholinergic coupling evolves upon maturation. According to our model, spatiotemporal dynamics depends on Ach coupling. This suggests that, **within stage II**, there may exist different periods of spatio temporal activity, with possible consequences on visual system development.
- In our model, there is a regime of cholinergic coupling where waves are power-law distributed.
- Biophysical parameters (e.g. conductances) could vary upon maturation or pharmacological manipulations, affecting the characterstics of emerging waves.

References

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