

Role of neuron and network properties in MGC neurons synchronisation

H. BEL MABROUK

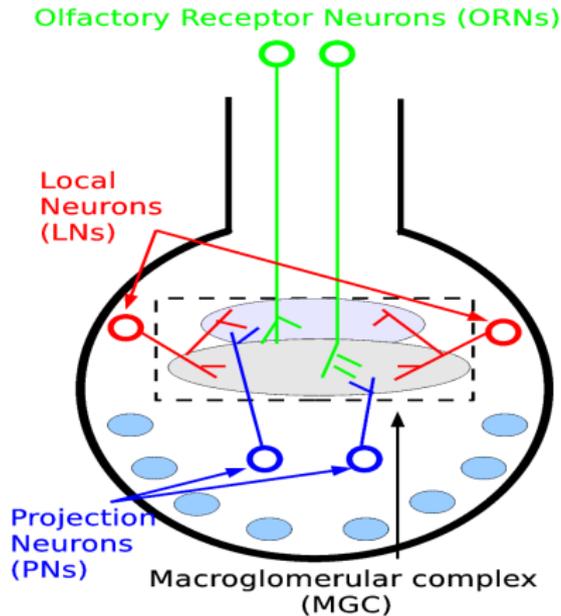
Supervisors : D. MARTINEZ and J.P. ROSPARS

PhD work from March 2008 to March 2011

Funded by ANR-BBSR Pherosys



The antennal lobe morphology of the moth *Manduca sexta*



Plan

- Quick reminder
- The PN model
- The LN model
- The MGC model
- Conclusions

Quick reminder

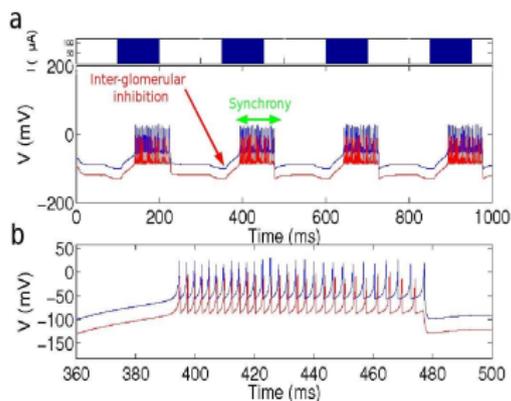


Figure: Response of two PNs connected to the same glomerulus¹.

↻ The - phase coming after the response may be due to the extrinsic (Network) or intrinsic (Channel) properties.

↻ The latency observed may be due to polysynaptic connections (Network) or intrinsic (Channel) properties.

¹H. Lei, T.A. Christensen and J.G. Hildebrand. Nature, 2002

How is the minus phase generated???

↔ Is it due to extrinsic (network) or intrinsic (channel) properties ?

Extrinsic: GABAergic inhibition from LNs.

- *not likely due to GABA-B because the – is abolished by Bicuculline (GABA-A blocker).*
- *not likely due to GABA-A because the – lasts $\sim 400\text{ms}$ (and GABA-A IPSP $\sim 10\text{ms}$) and also it is not disrupted by Picrotoxin (GABA-A blocker).*

How is the minus phase generated???

Intrinsic: small conductance Calcium-dependent Potassium (SK) channel can produce the $-$ phase

- *Bicuculline blocks SK channels (e.g. Khawaled et al., 1999)*
- *Changing extra or intracellular concentration of chloride does not affect the $-$ phase (Christensen et al., 1998)*
- *SK channels produce long after-hyperpolarizations (AHP) and spike frequency adaptation (SFA)*

An SK-like conductance PN model reproduces physiological responses

$$C_m \frac{dV}{dt} = I_{stim} - I_{Na} - I_K - I_L - I_{Ca} - I_A - I_{sk} \quad (1)$$

$$I_{sk} = g_{sk} q_{\infty}^2 (E_{sk} - V) \quad (2)$$

$$q_{\infty} = 1 / (1 + \exp(-1.12 - 2.508 \log((C_{sk} - C_r) / 10))) \quad (3)$$

$$\frac{dC_{sk}}{dt} = \alpha_{sk} I_{Ca} - \frac{C_{sk} - C_r}{\tau_{sk}} \quad (4)$$

$$\frac{dI_{stim}}{dt} = - \frac{I_{stim}}{d\tau_{stim}} \quad (5)$$

An SK-like conductance PN model reproduces physiological responses

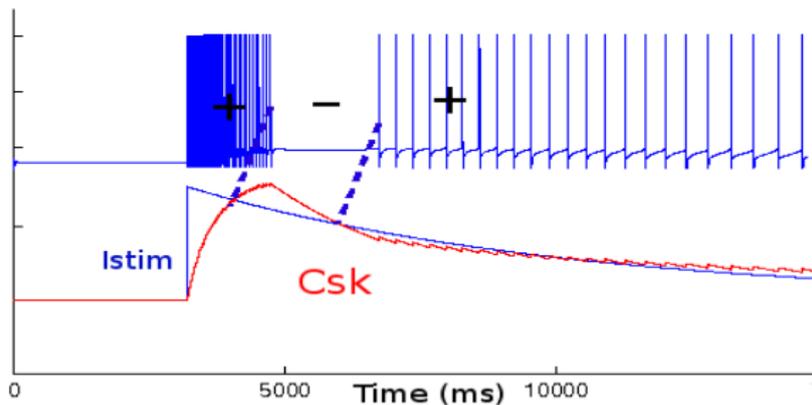


Figure: Response of SK-like conductance PN model.

An SK-like conductance PN model reproduces physiological responses

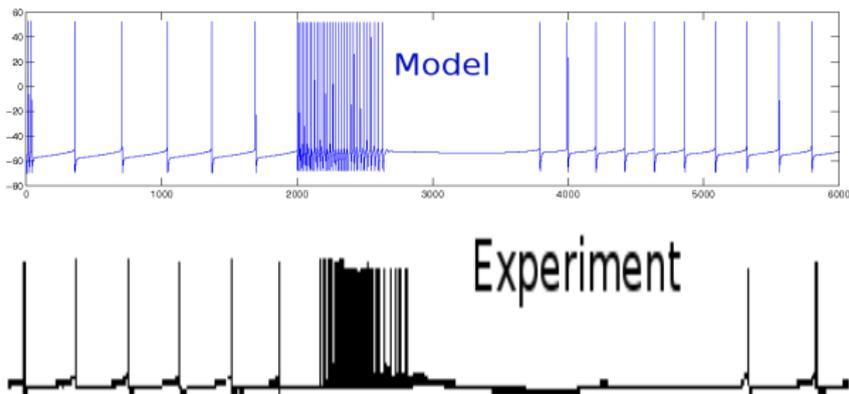


Figure: The response of SK-like conductance PN model have the same shape of the response of real PN (Homberg et.al,1989).

The SK channel is involved in SFA

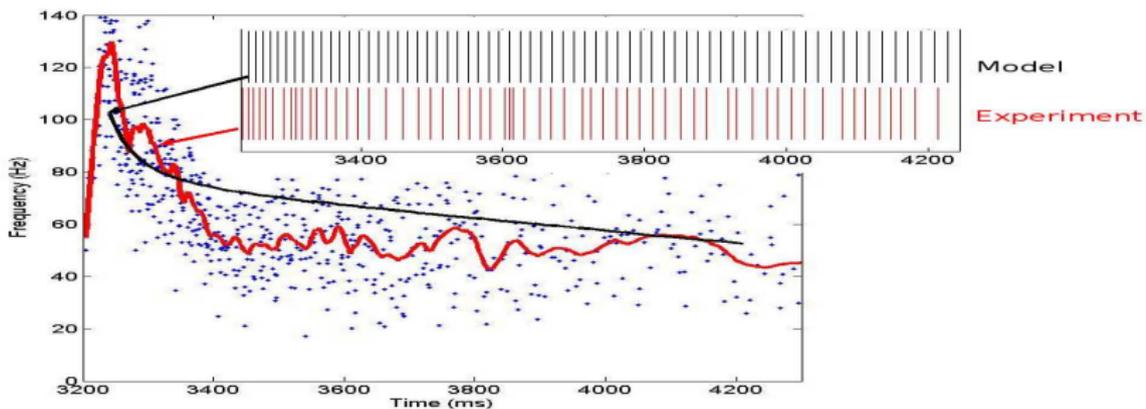


Figure: The spike frequency of the model match with the experimental result.

Blocking the SK channel disrupts the –

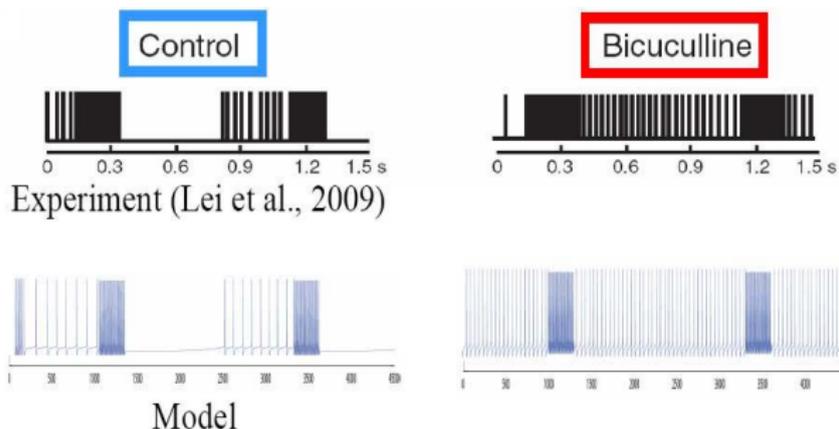
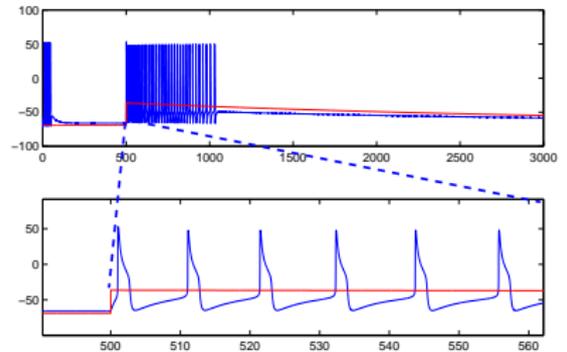
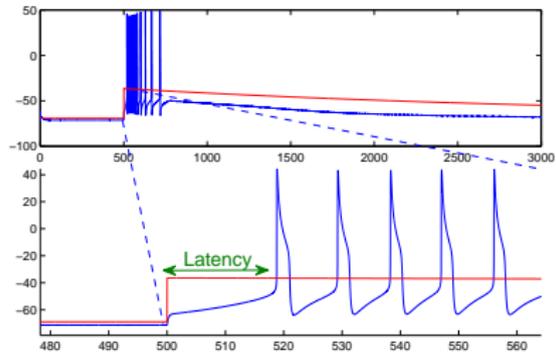


Figure: Simulated Bicuculline vs. experiments.

The Latency can be due to an I_A current



The I_A current introduces a latency of the response. If we block it, the PN responds immediately after it receives excitation.

Local neuron (LN) model

$$C_m \frac{dV}{dt} = I_{stim} - I_{Na} - I_K - I_L - I_{Ca} - I_A - I_{sk} \quad (6)$$

↪ Not the same parameter for the sk channel and the I_A current.

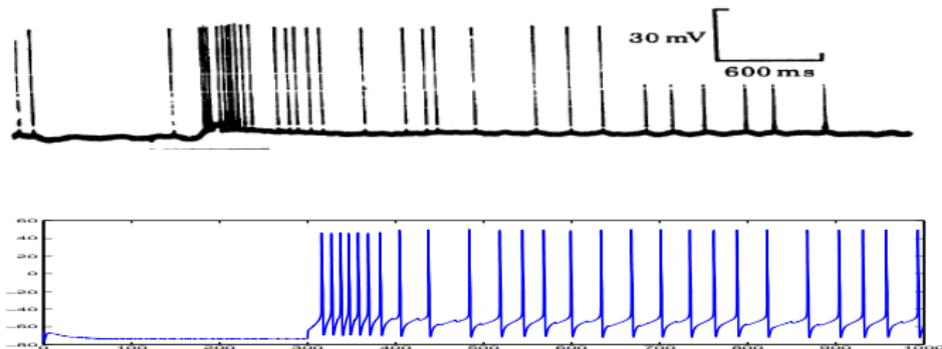


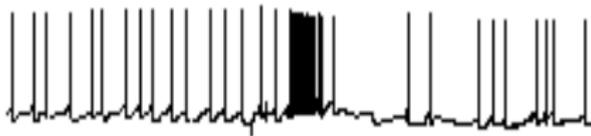
Figure: The LN have a long response with adaptation of the frequency (Matsumoto and Hildebrand, 1981).

Different type of response of the PNs (Homberg et al, 1989)

- The Bal + response



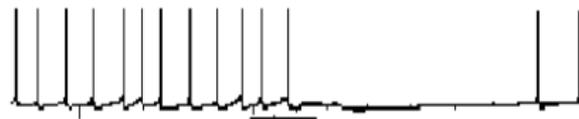
- The C15+ and Bal+ response



- The C15 + response



- The Bal- (or C15-) response



- The blend - / + / - response



Indirect MGC model (Last year)

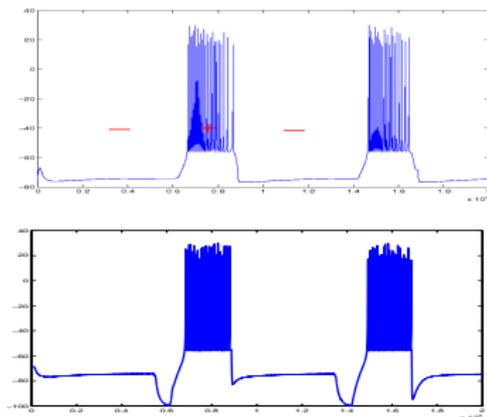
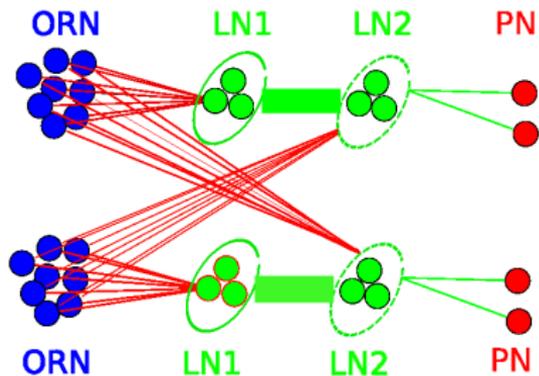


Figure: Indirect MGC model: PNs respond by desinhibition

Figure: Response reproduced by MGC model

- ↔ Does NOT reproduce all type of response
- ↔ We propose a direct MGC Model.

Hypothesis for new model

Hypothesis

LNs are MULTIGLOMERULAR (connected to all ORNs)

Hypothesis

PNs are UNIGLOMERULAR (connected directly to one population of ORNs)

Hypothesis

LNs respond faster than PNs (S. Krofczik et al, 2009).

Hypothesis

The LNs \rightarrow LNs, the PNs \rightarrow LNs, the LNs \rightarrow PNs and the PNs \rightarrow PNs connections are generated with a probability p .

Direct MGC model

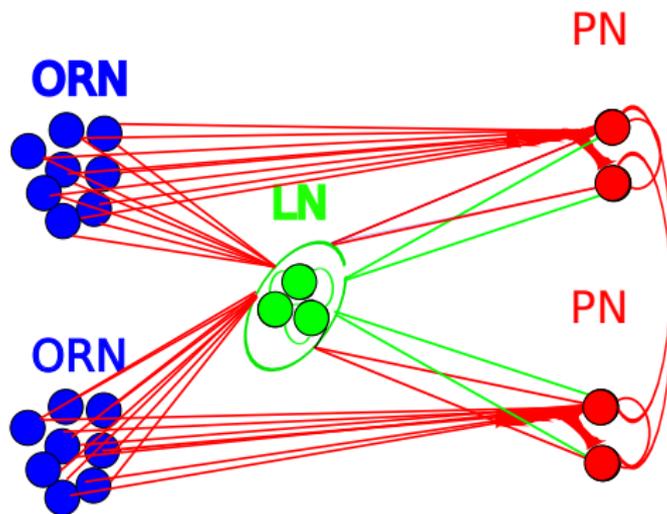


Figure: Direct MGC model: PNs are directly connected to the ORNs. The other connections have a probability p .

Direct MGC model

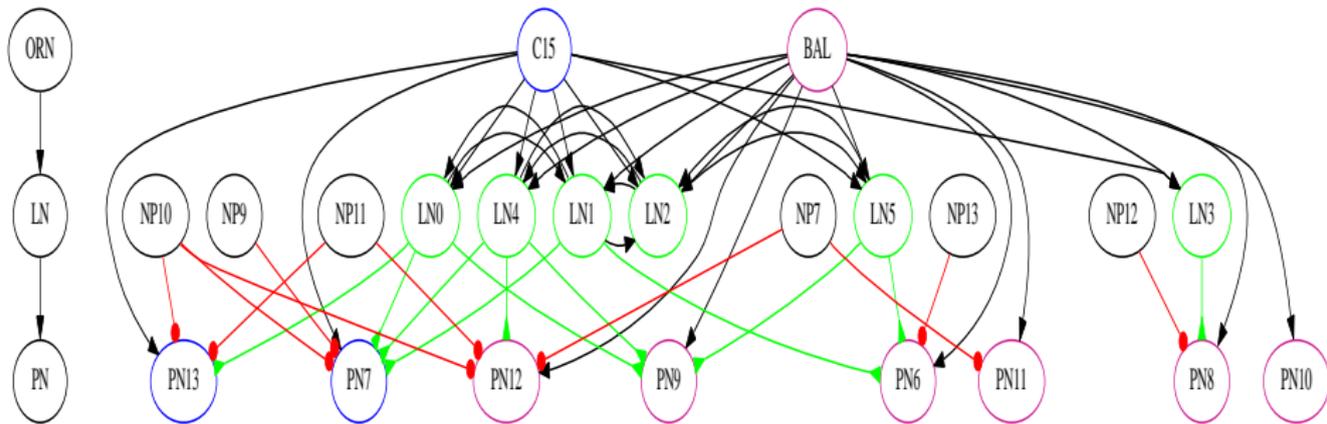
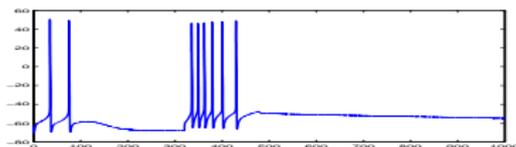


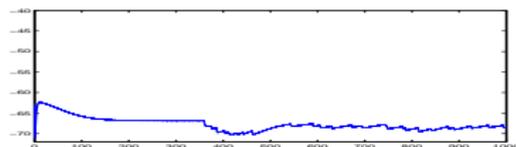
Figure: Exemple of a generated network with $p = 0.3$

Different type of response of the PNs

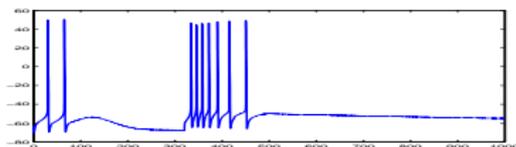
- The Bal + (or C15+) response



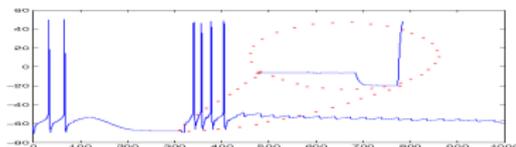
- The Bal- (or C15-) response



- The C15+ and Bal+ response



- The blend -/ + /- response



Synchronisation and inhibition

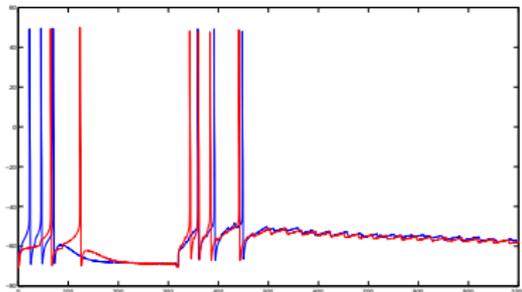


Figure: response of two PN to blend (Bal+C15)

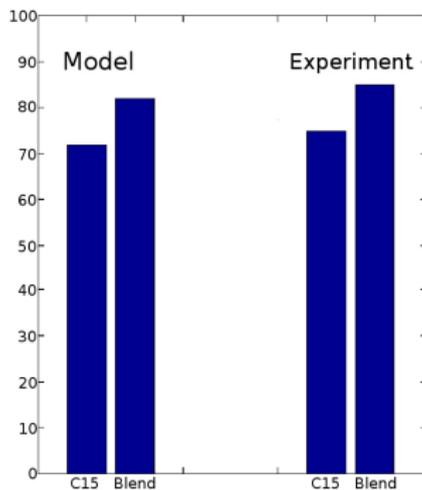


Figure: rate of synchronisation between PNs receiving inhibition Vs PNs does not receive inhibition

Conclusions

- We developed a detailed model of PN and of LN.
- We developed a new MGC model.

Perspectives

- Make a quantitative study of synchronisation rate.