A model of frequency-dependent latency in the thalamocortical response of the rodent somatosensory system

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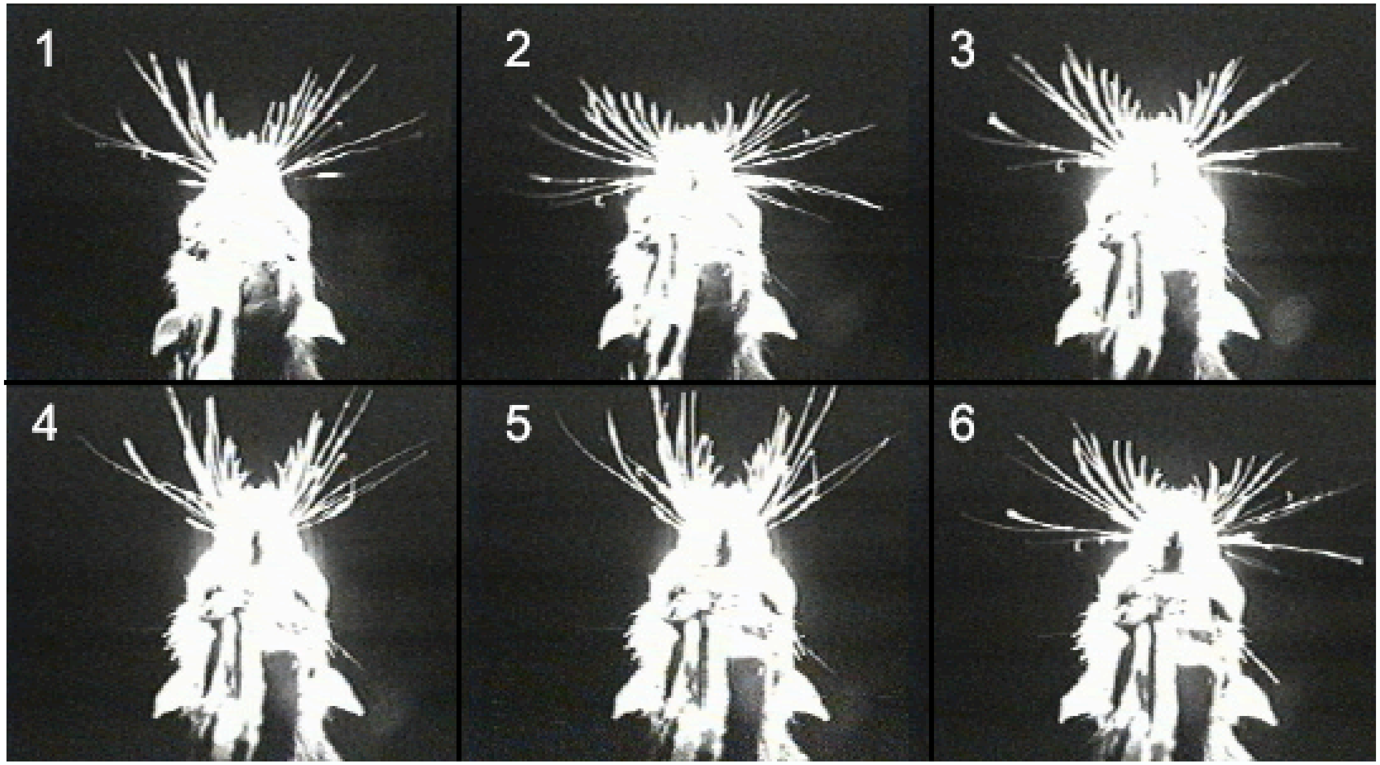
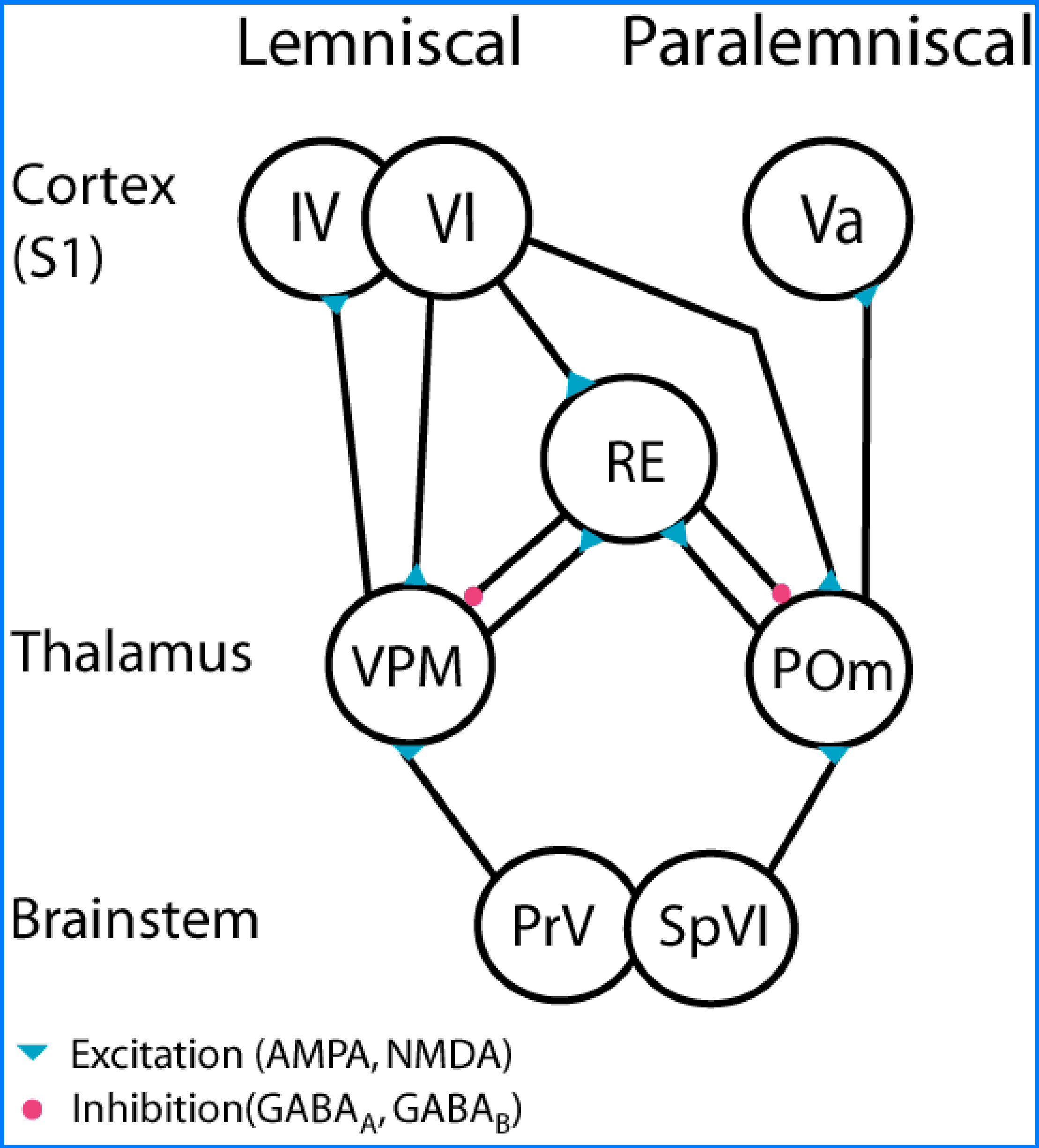
Active Sensation by Rat:
Loop Dynamics in Vibrissa Sensorimotor Control



Free Ranging Rat (Blindfolded) that is Whisking in Air in Search of a Food Tube
Consecutive Video Rate Fields (60 Hz acquisition)

Anatomy of the rat somatosensory system



Crabtree 1999;
Hartings, Temereanca and Simons 2000;
Deschenes et al. 1998;
Steriade 2001.

System physiology: experiments

Ahissar, Sosnik and Haidarliu, Nature (2000); JNP (2001).

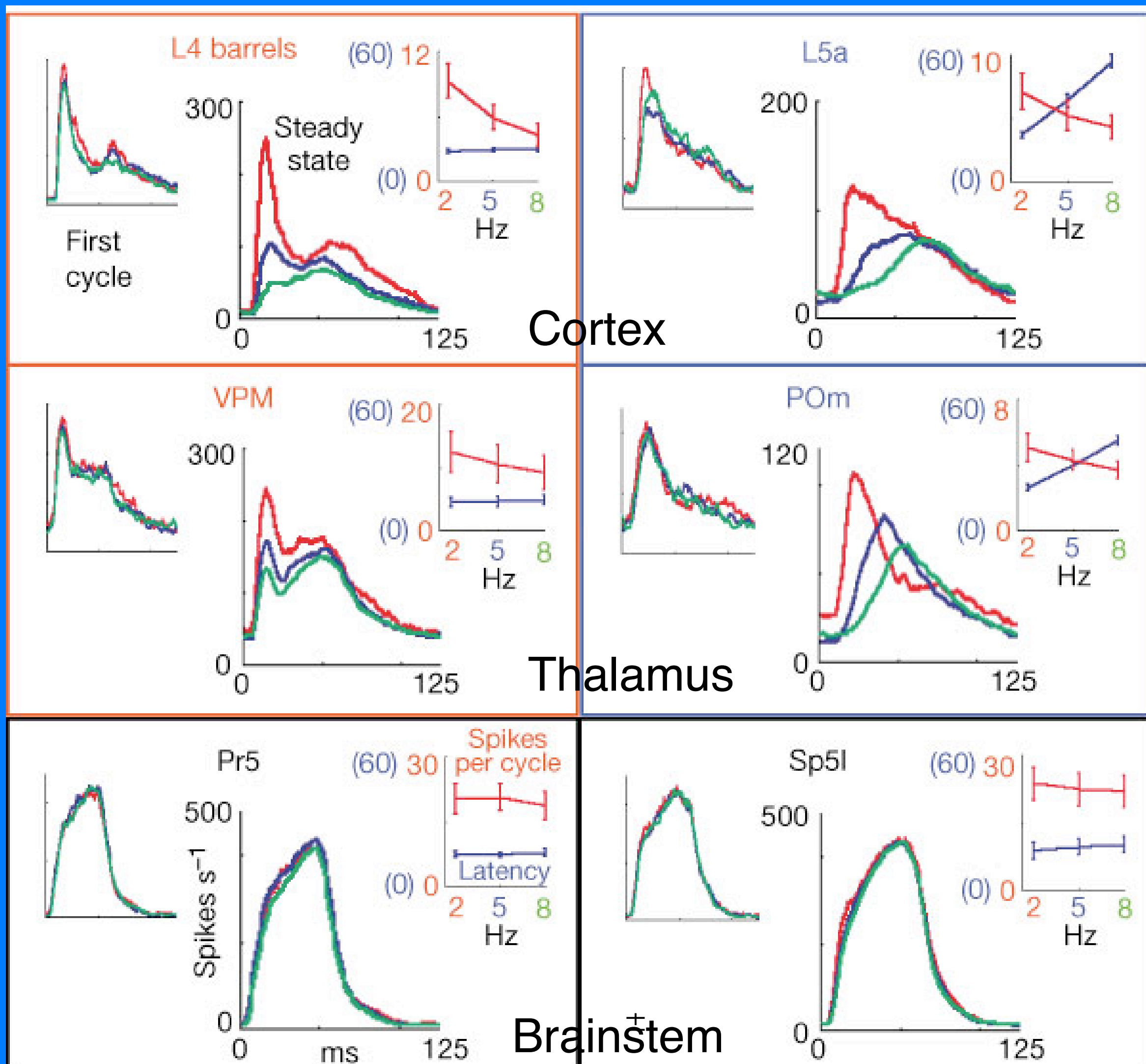
Stimulus: 50 ms air-puff periodic stimulations.
Each train of stimuli lasts for 3 s.
Recording: multi-unit activity.
Computing: peri-stimulus time histograms (PSTHs).

Averaging over:

1. The first response in a train.
2. Steady-state response.

Latency is defined as the time in which the PSTH reaches 50% of its maximal value.

System physiology: experimental results



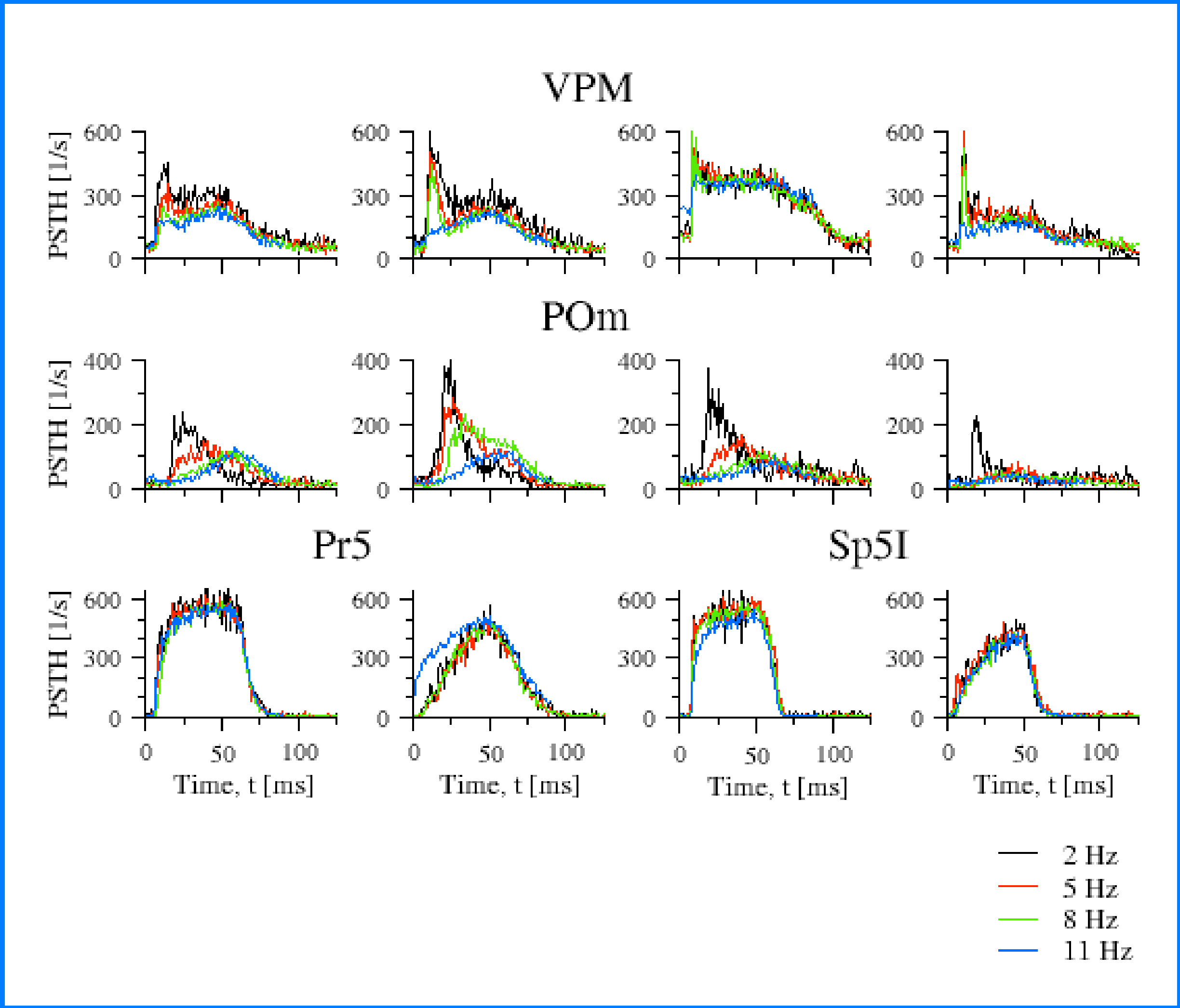
Ahissar, Sosnik and Haidarliu, Nature, 2000.

Almost symmetric architecture, different response!

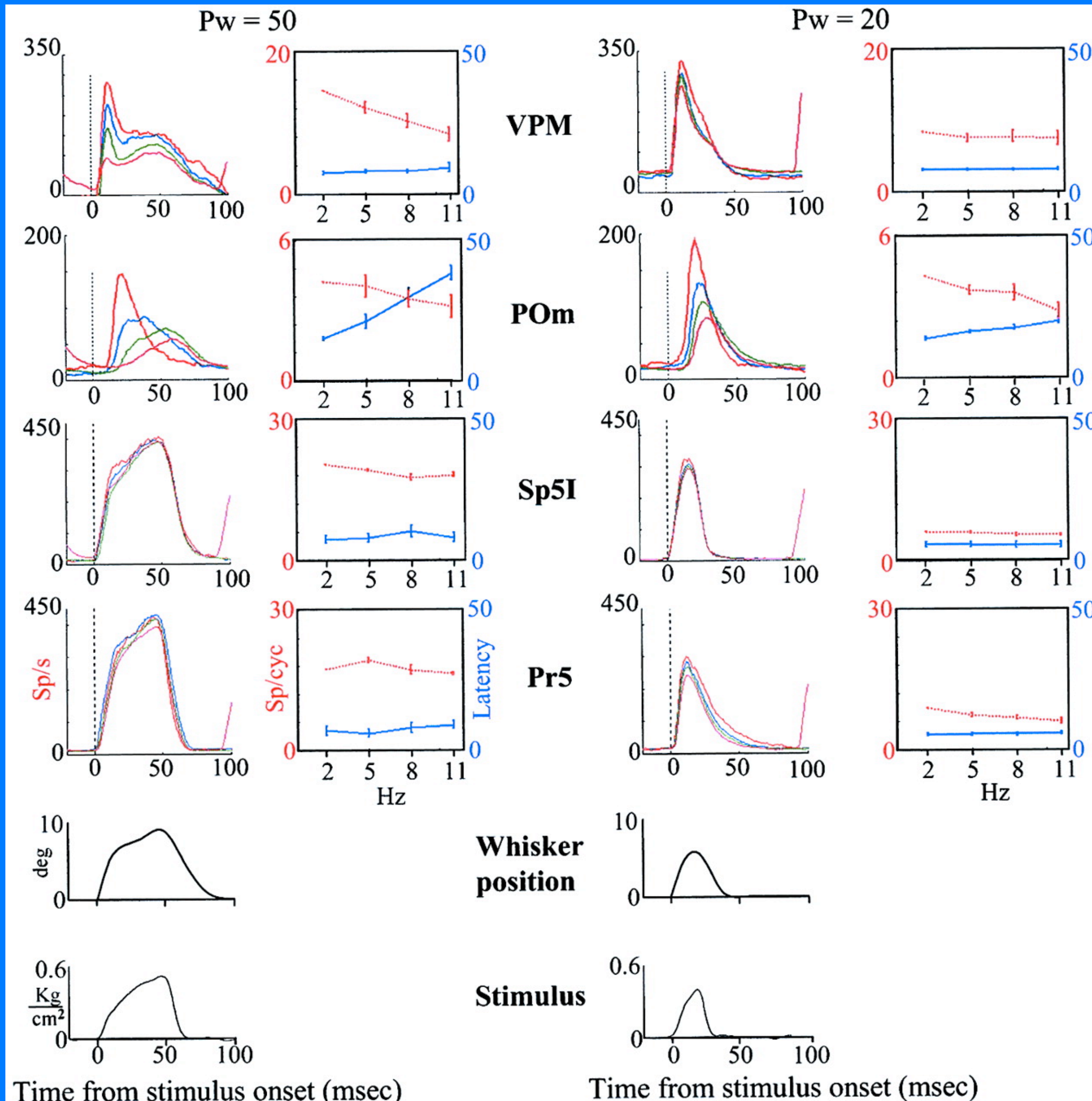
Coding frequency with latency.

Population-average PSTHs.

Examples from multi-unit recording



Response to a briefer (20 ms) stimulus



Sosnik, Haidarliu
And Ahissar,
JNP, 2001

The main issue

Under steady-state conditions, and on average:

The number of spikes fired by neurons in the two pathways decreases with frequency.

However,

Neurons in the paralemniscal pathway (POm thalamus and cortical layer Va), but not in the lemniscal pathway (VPM thalamus, cortical layer IV) exhibit response-latency that increases with frequency.

The effects are prominent for prolonged stimuli and small for brief stimuli.

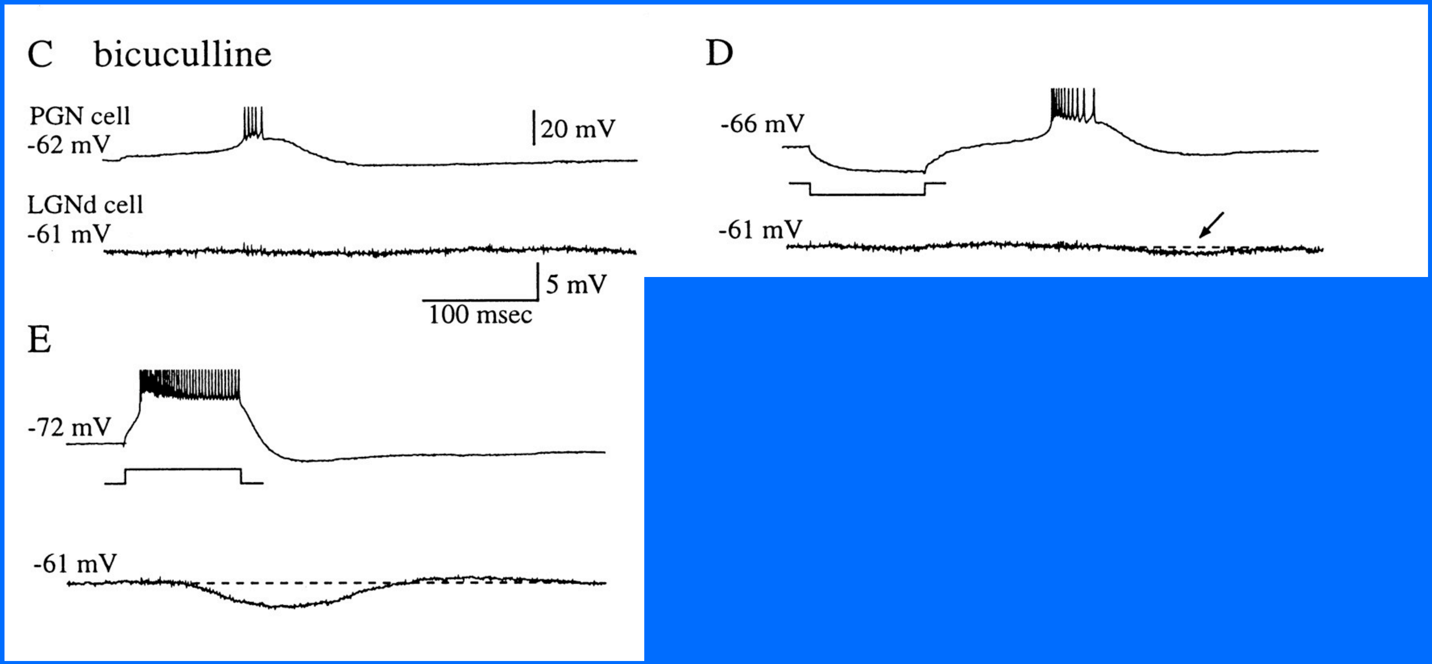
This allows the rat to code the whisking frequency by time (or phase) as well as rate.

What is the neuronal mechanism underlying these effects?

GABA$_B$ Synaptic physiology - facilitation

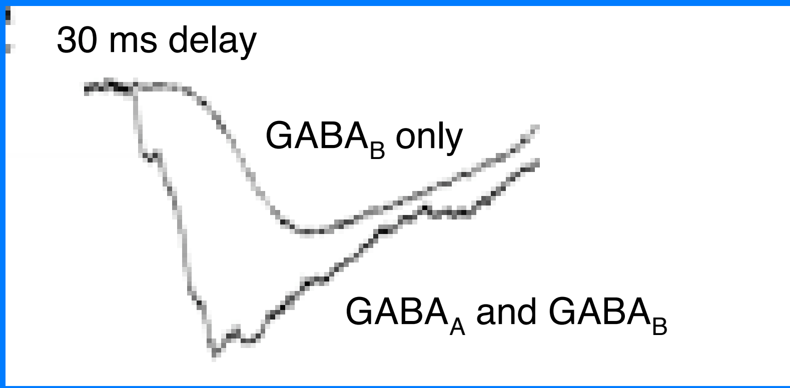
Prediction (Golomb, Wang and Rinzel 1996):
GABA$_B$ receptors strongly facilitate and respond much more strongly to a prolonged burst than to a brief one.

Experimental confirmation (Kim, Sanches-Vives and McCormick, Science, 1997):



GABA$_B$ Synaptic physiology - delay

GABA$_B$ IPSPs in a thalamic cell in response to an RE burst: delayed and prolonged (Kim, Sanchez-Vives and McCormick, Science, 1997).



Focus on the thalamus

The latency effect is not observed in the brainstem. It is observed in the thalamus, and is magnified in the cortex.

Since the thalamus is the first station where the effect is found, we focus on the thalamic level.

Hypotheses

1. Delayed and prolonged $GABA_B$–mediated inhibition from the reticular thalamic nucleus (RE) is responsible for the attenuation of the response with frequency at steady state.

2. The shape of the input from the brainstem is a prominent factor in generating the latency effect.

3. Strong intrinsic adaptation of the neuronal response in the POm causes the attenuation of POm response at later times.

Rate models

Wilson and Cowan 1973; Hopfield 1984; Frankel and Rinzel 1992; Ermentrout 1994; Shriki, Hansel and Sompolinsky 2003.

- Dynamical equations for the population-average fast (AMPA, $GABA_A$) synaptic conductances:

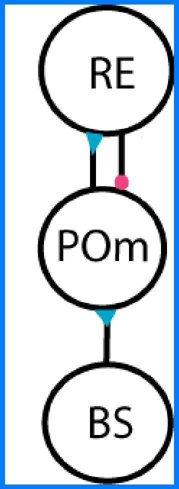
Each brain area is represented by a few equations.

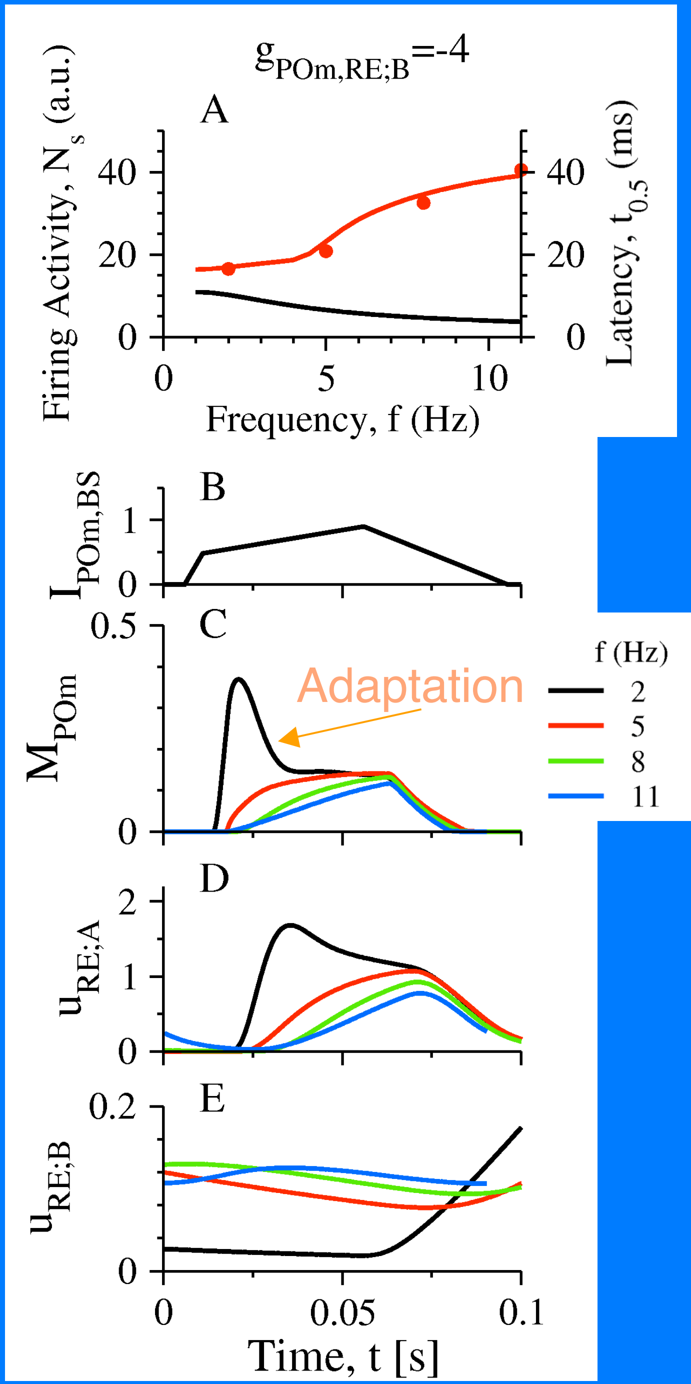
- Strictly justified for:
  - Networks at low levels of synchrony.
  - Weakly non-stationary inputs.
- Our strategy: We use rate models for strongly temporally varying inputs, in order to get an insight about the network dynamics.
- The results will be examined in the framework of a conductance-based model.

- Slow $GABA_B$ inhibition (Golomb et al. 1996)

- Adaptation:
  Multiplicative.
  Two time scales for activation and deactivation.

The extreme case of only the paralemniscal pathway





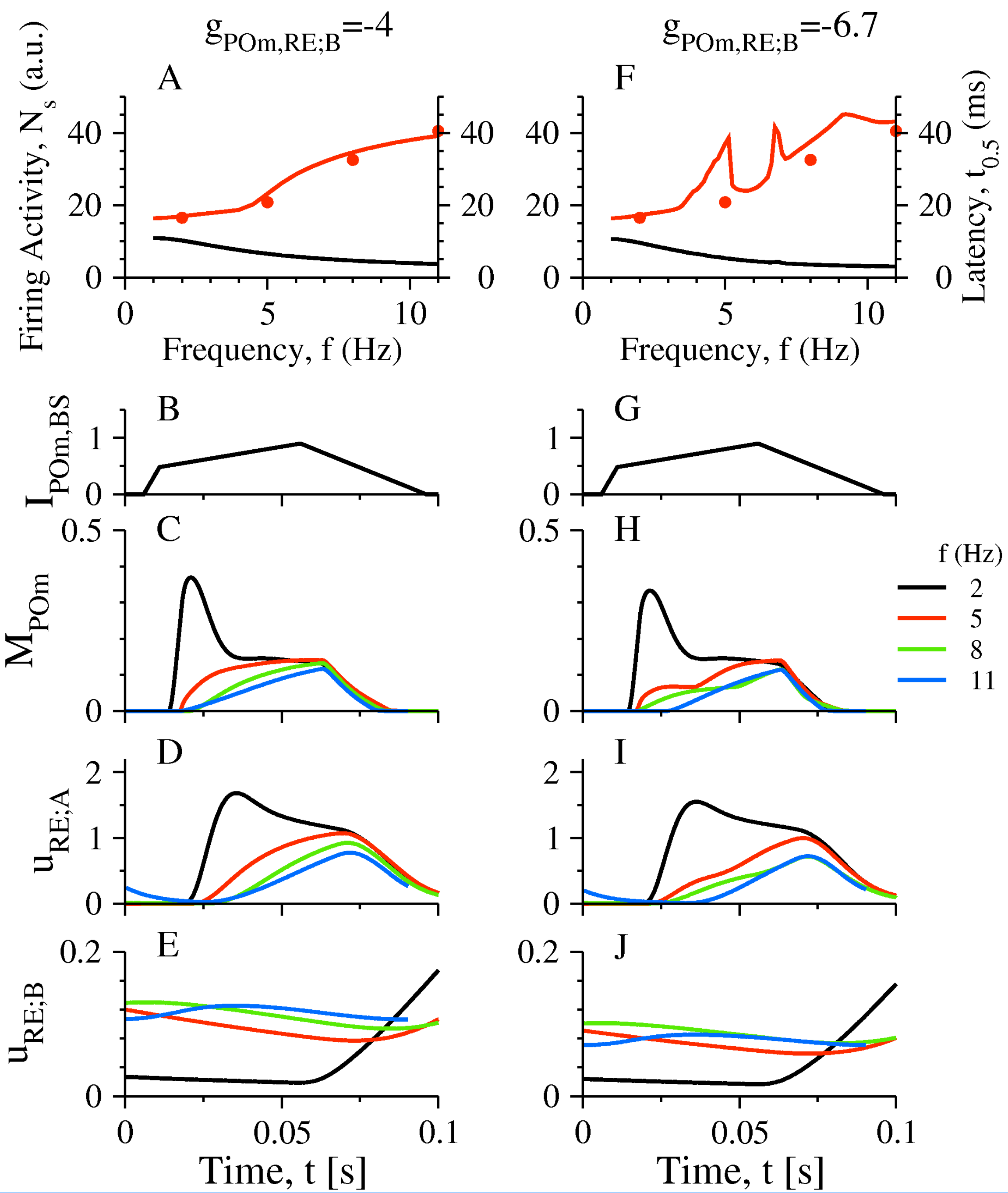
Moderate $GABA_B$ levels, moderately:

- increase the latency in the POm
- Decrease the firing rate.

The latency value obtained from The model fit the experimental results.

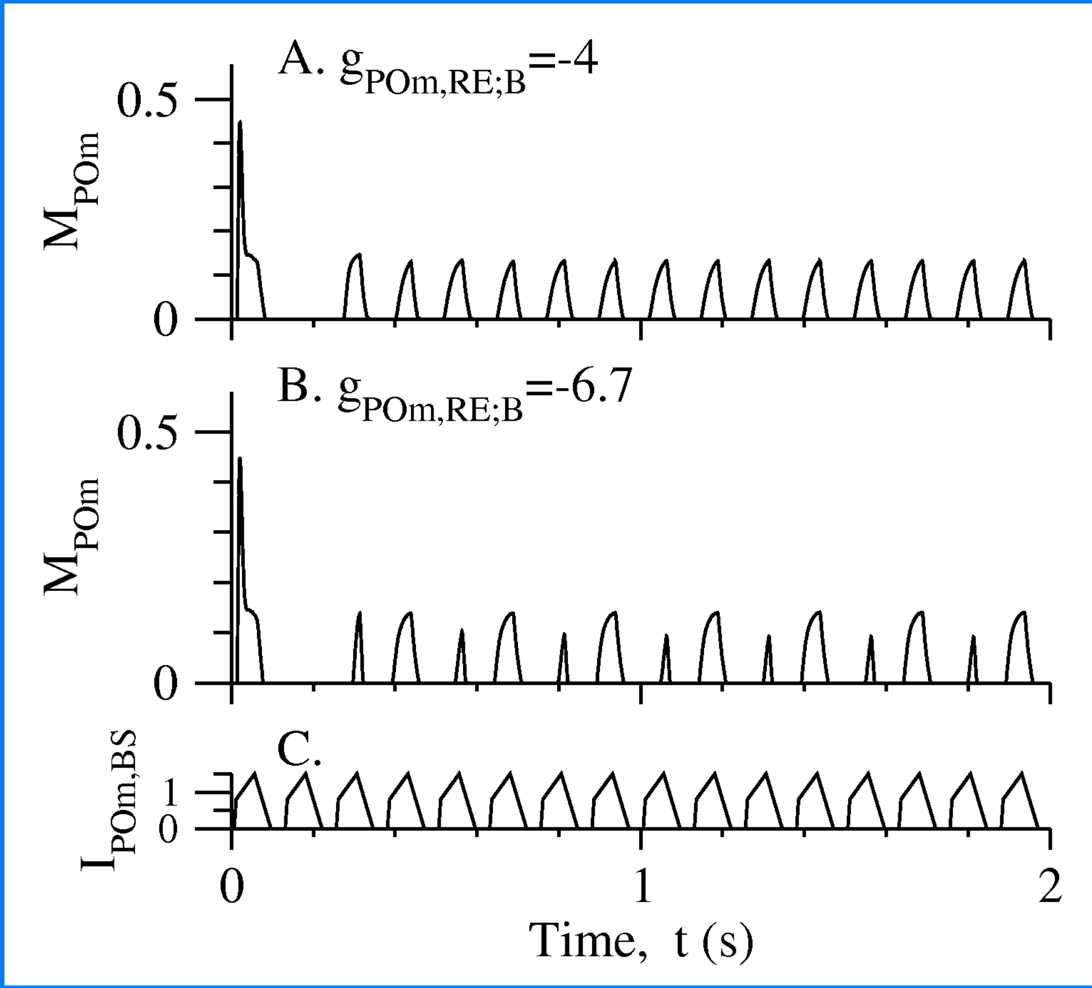
M and *u*'s are averaged over the Last 2s.

Is it possible to increase the Effect by increasing $g_{GABA\text{-}B}$?



$g_{POm,RE;B}$=-4
$g_{POm,RE;B}$=-6.7
A
F
Firing Activity, N_s (a.u.)
Latency, $t_{0.5}$ (ms)
Frequency, f (Hz)
Frequency, f (Hz)
B
G
$I_{POm,BS}$
C
H
M_{POm}
f (Hz)
2
5
8
11
D
I
$u_{RE;A}$
E
J
$u_{RE;B}$
Time, t [s]
Time, t [s]

Period doubling



- 8 Hz stimulus
- Strong $GABA_B$ conductance _ 2:1 firing mode at high frequencies.

Questions:

- Why is the period-1 state unstable at high frequencies?
- Is period doubling a generic behavior of the model?
- Under which condition does it appear?

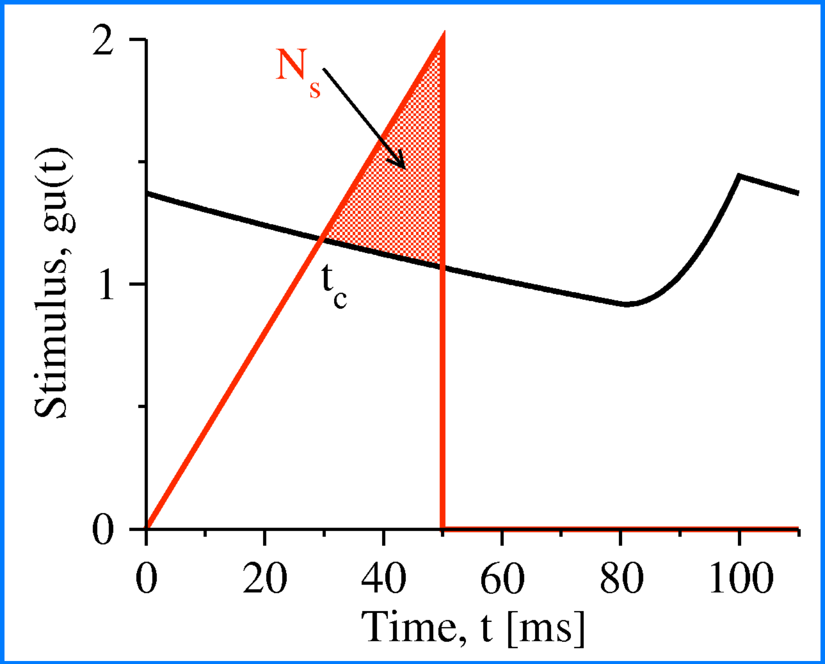
Analytically-solvable model

Linear equation

Instantaneous fast synapses

Triangular stimulus with a width *d*

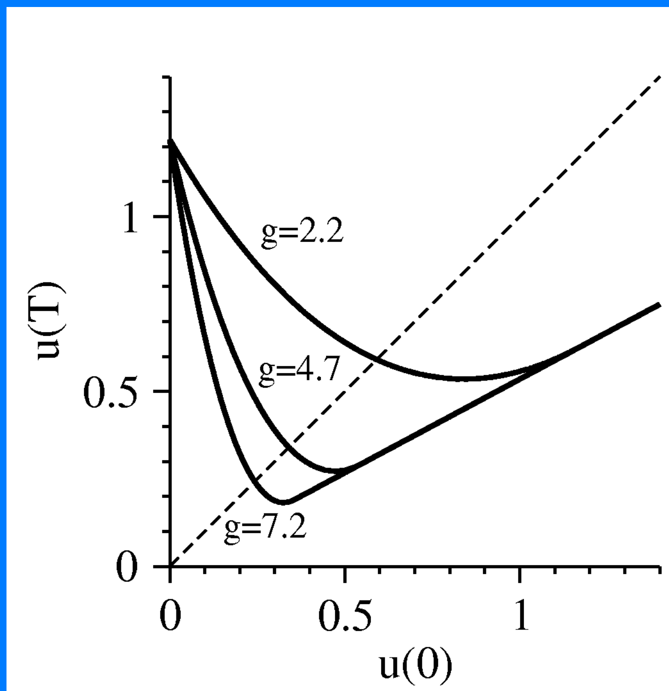
Analysis for *T*>2*d*.



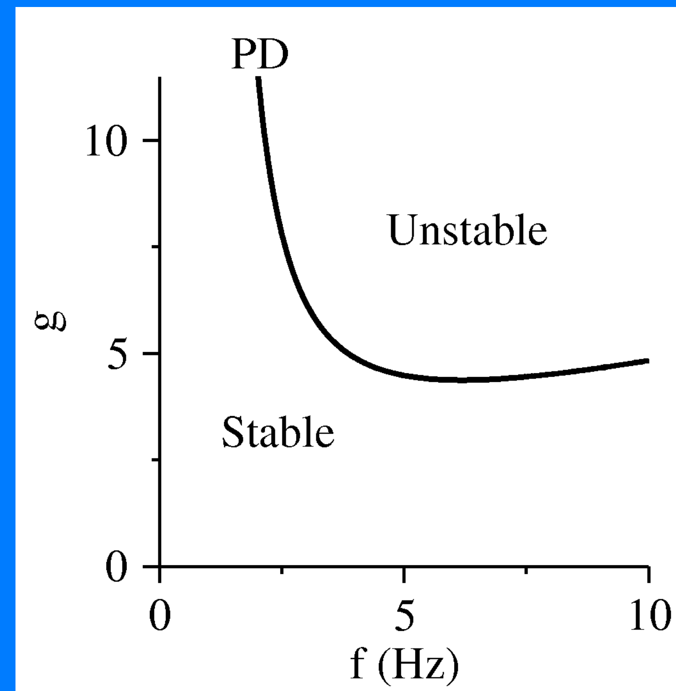
For *d*«

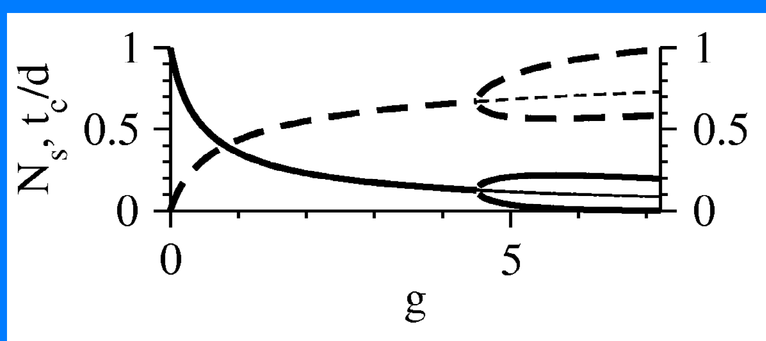
Logistic map: leads to period doubling, chaos…

Map



d=50, □=200

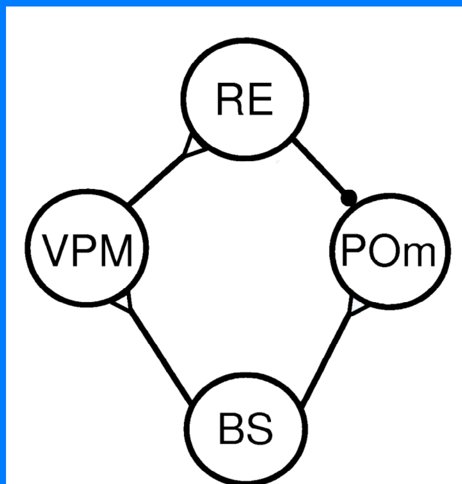


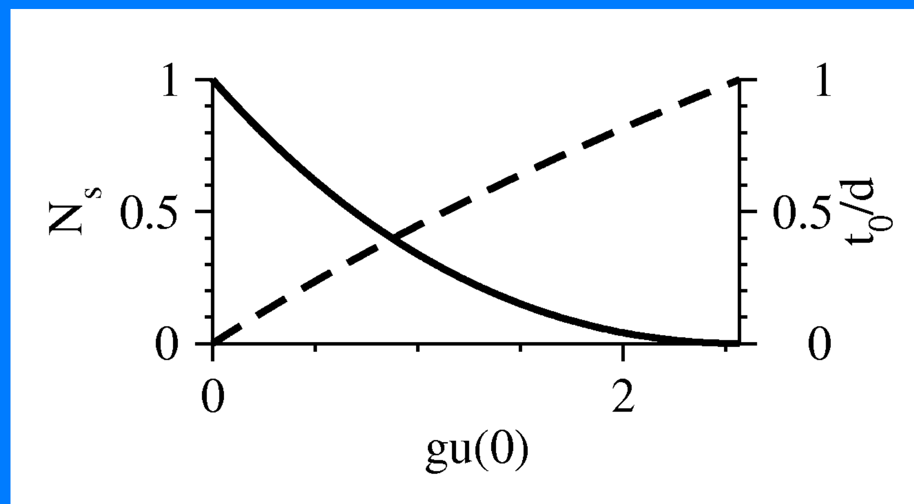


PD is a generic type of behavior that appears for large enough *g* and frequencies that are not too low.

No doublet behavior was observed
In analysis of experimental data.

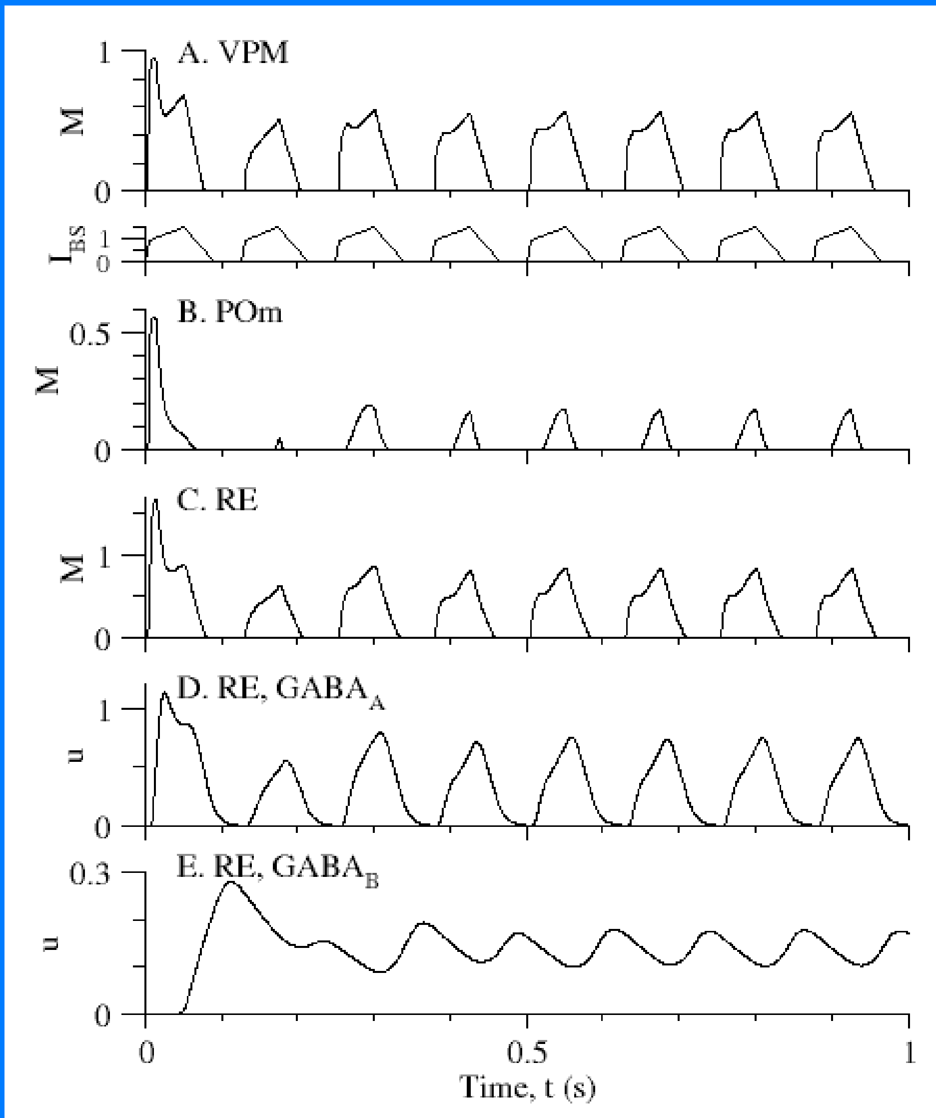
The extreme case of the feed-forward model

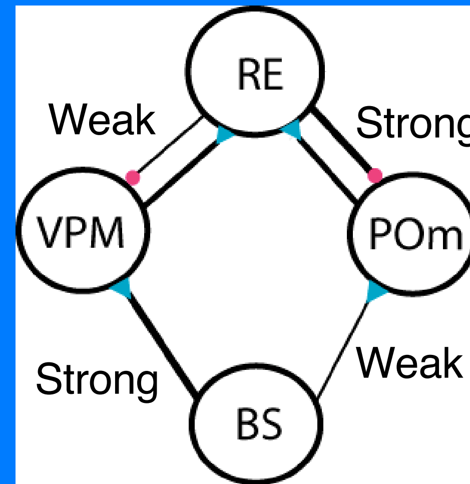




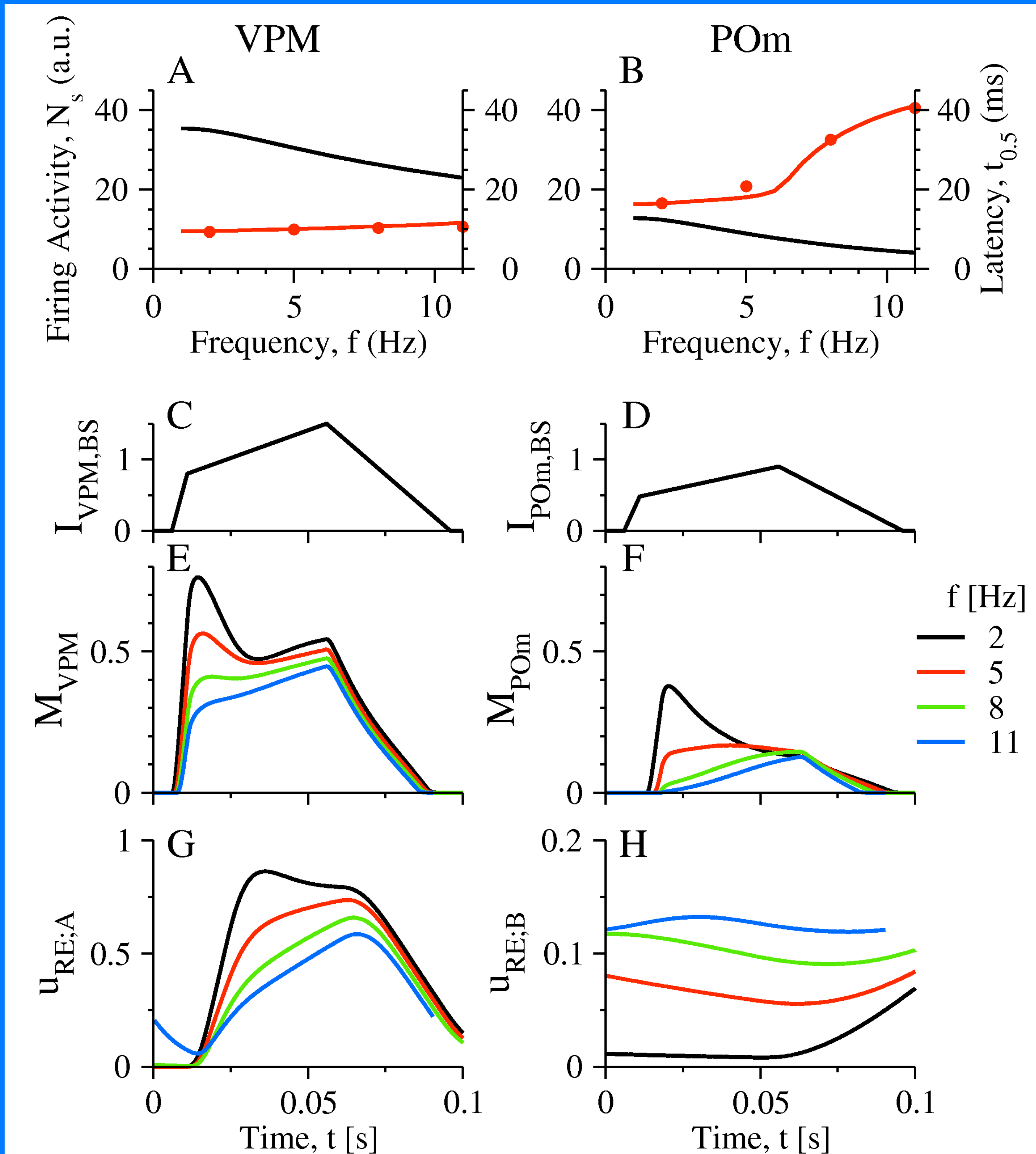
- No period doubling.
- The activity is 0 for large *g*.

Results from the full thalamic model





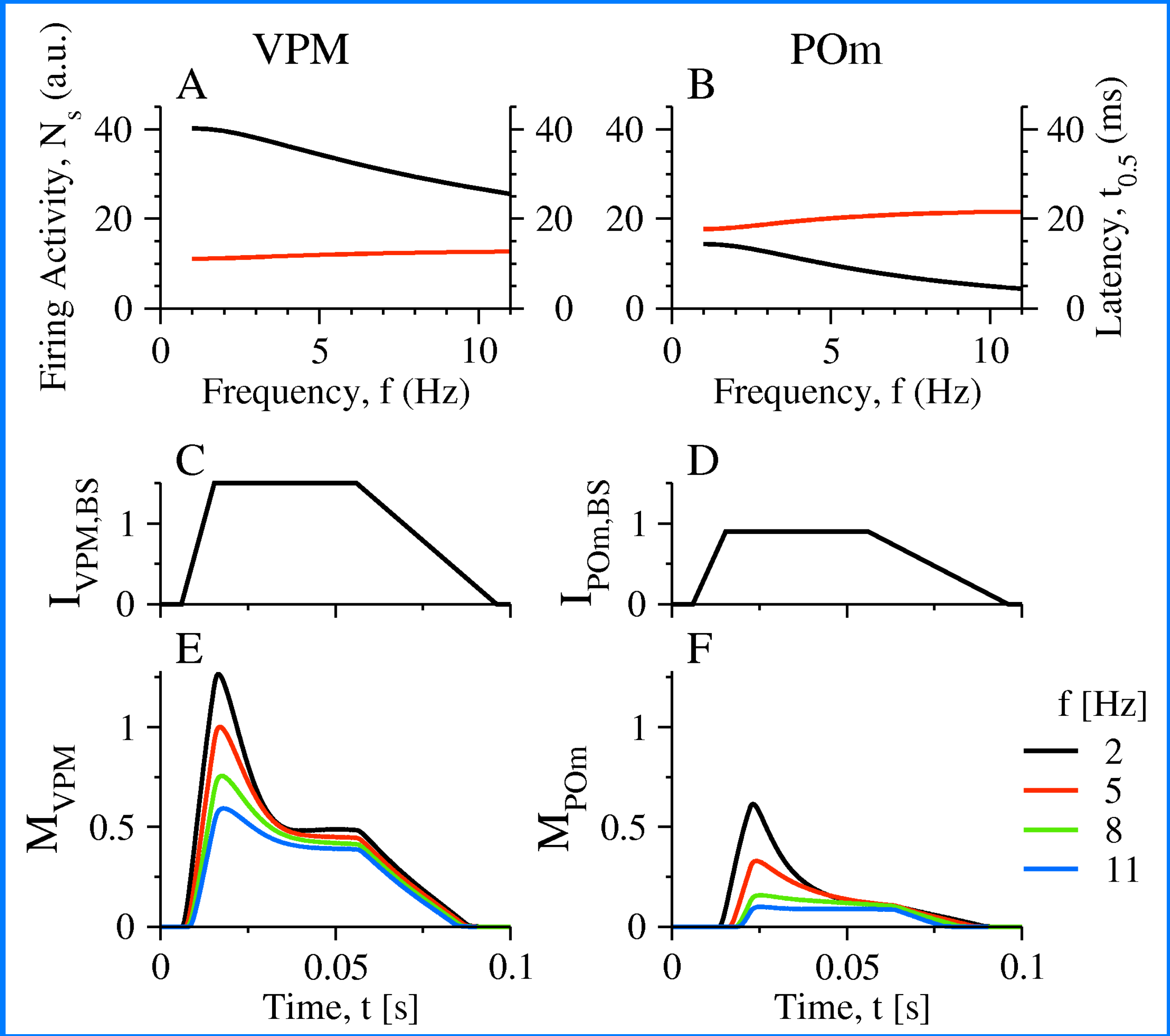
- POm gets more $GABA_B$ inhibition than VPM, and a weaker input from the brainstem.
- The full model is effectively a feedforward model because the VPM activity is considerably Stronger than the POm activiry.



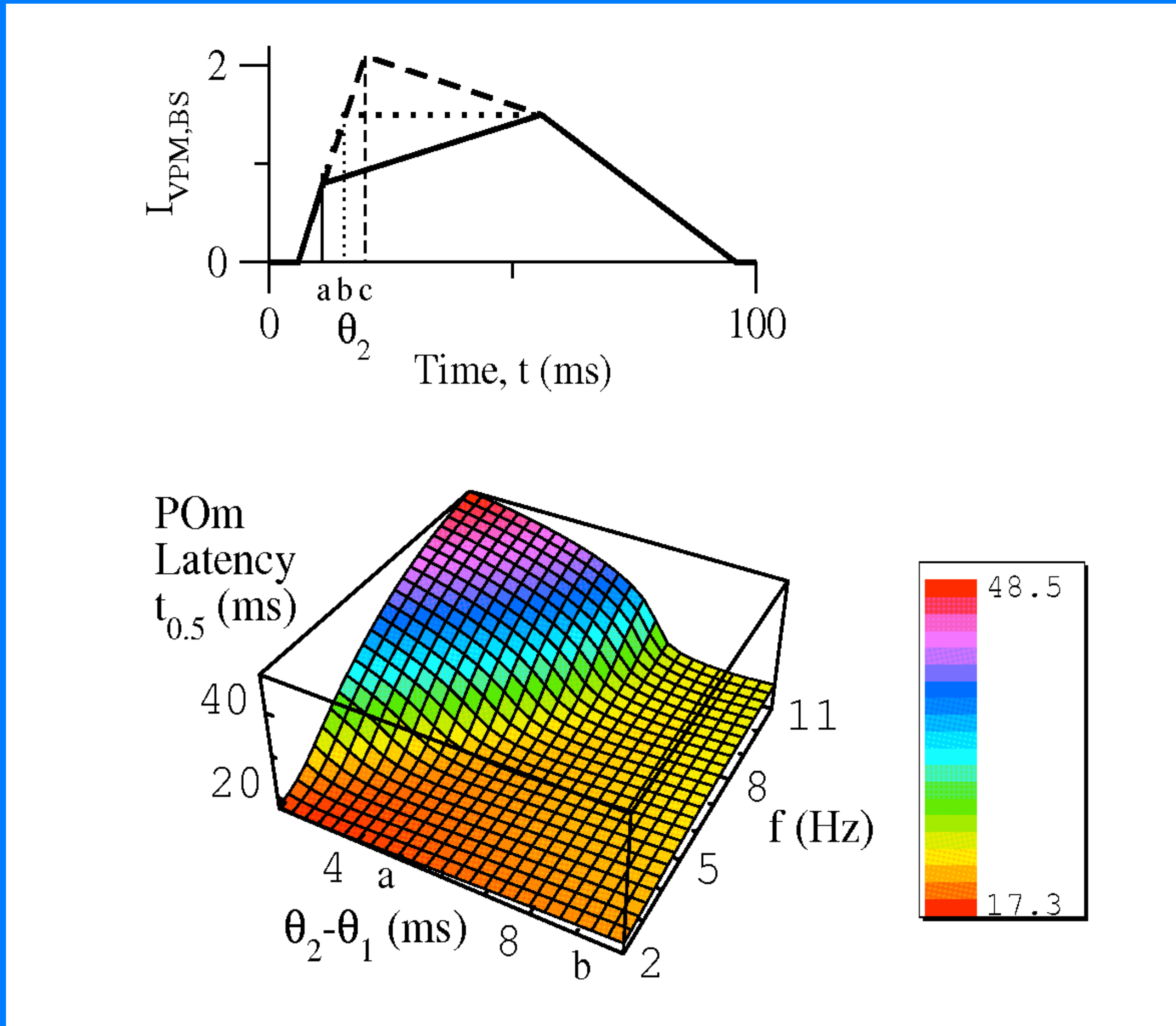
"Iceberg effect": POm cells receive less input and/or more $GABA_B$ inhibition.
At high frequencies, only the "tip of the iceberg" is seen in the PSTHs.

The latency effect is a consequence of the two-ramp stimulus shape (mostly)+ decreasing $GABA_B$ inhibition at intermediate frequencies.

Effects of stimulus shape

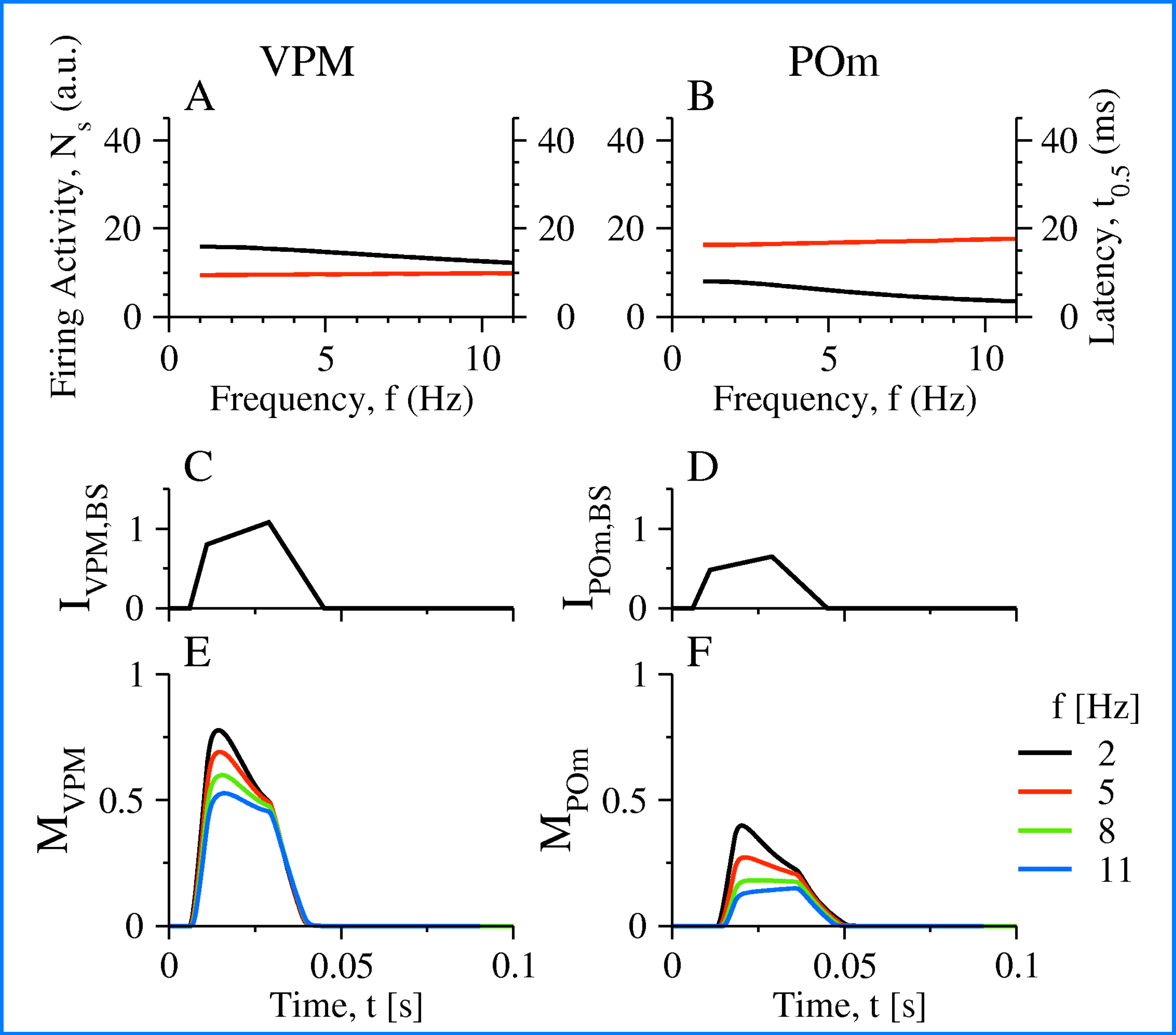


The latency effect in the POm exists only weakly for a trapezoid stimulus with the same height as before.



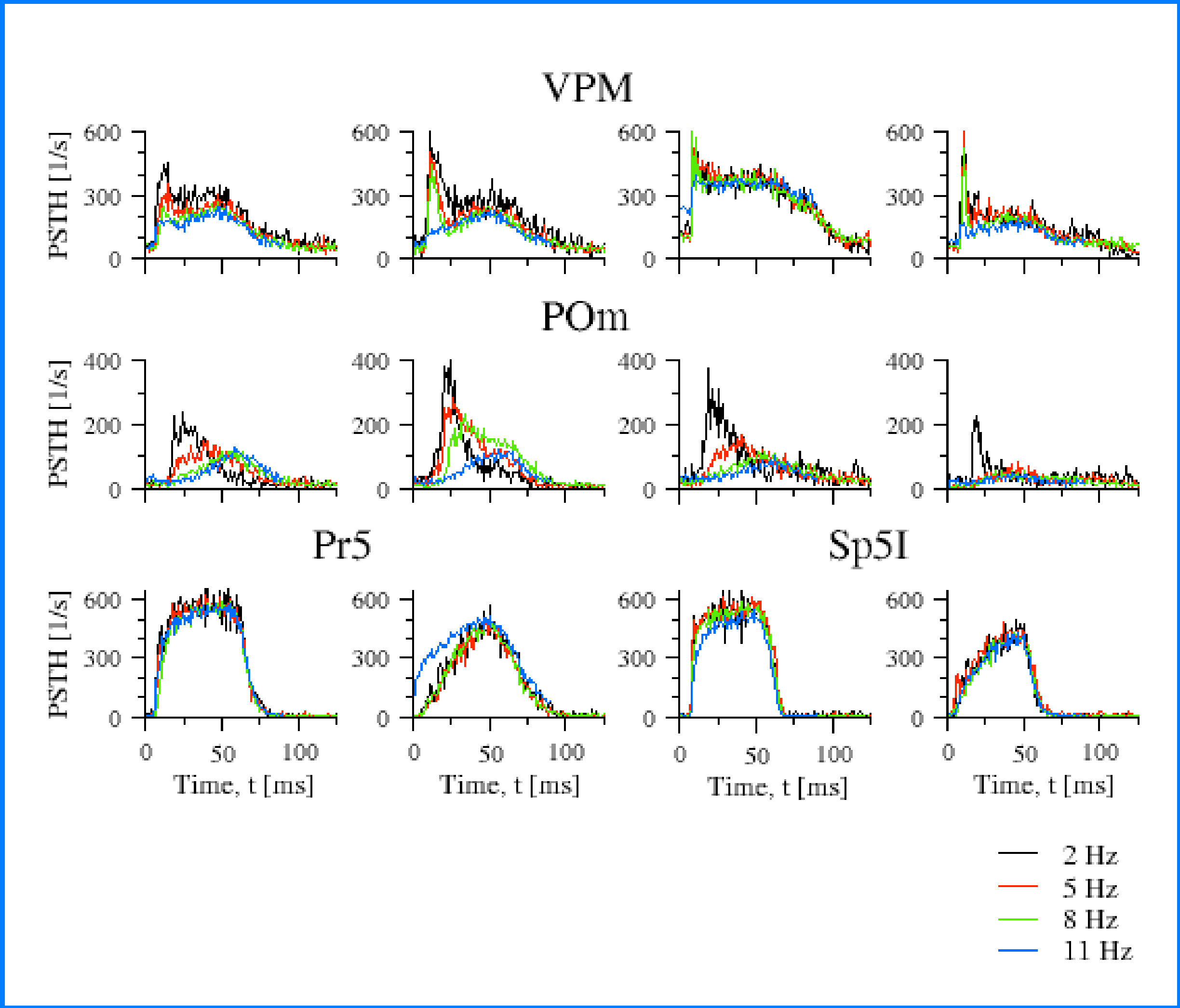
Large latency is obtained in the POm at high stimulus frequencies if the second ramp of the stimulus is steep enough.

Response to a briefer (20 ms) stimulus



Briefer stimulus _ smaller $GABA_B$ inhibition _ reduced effect.

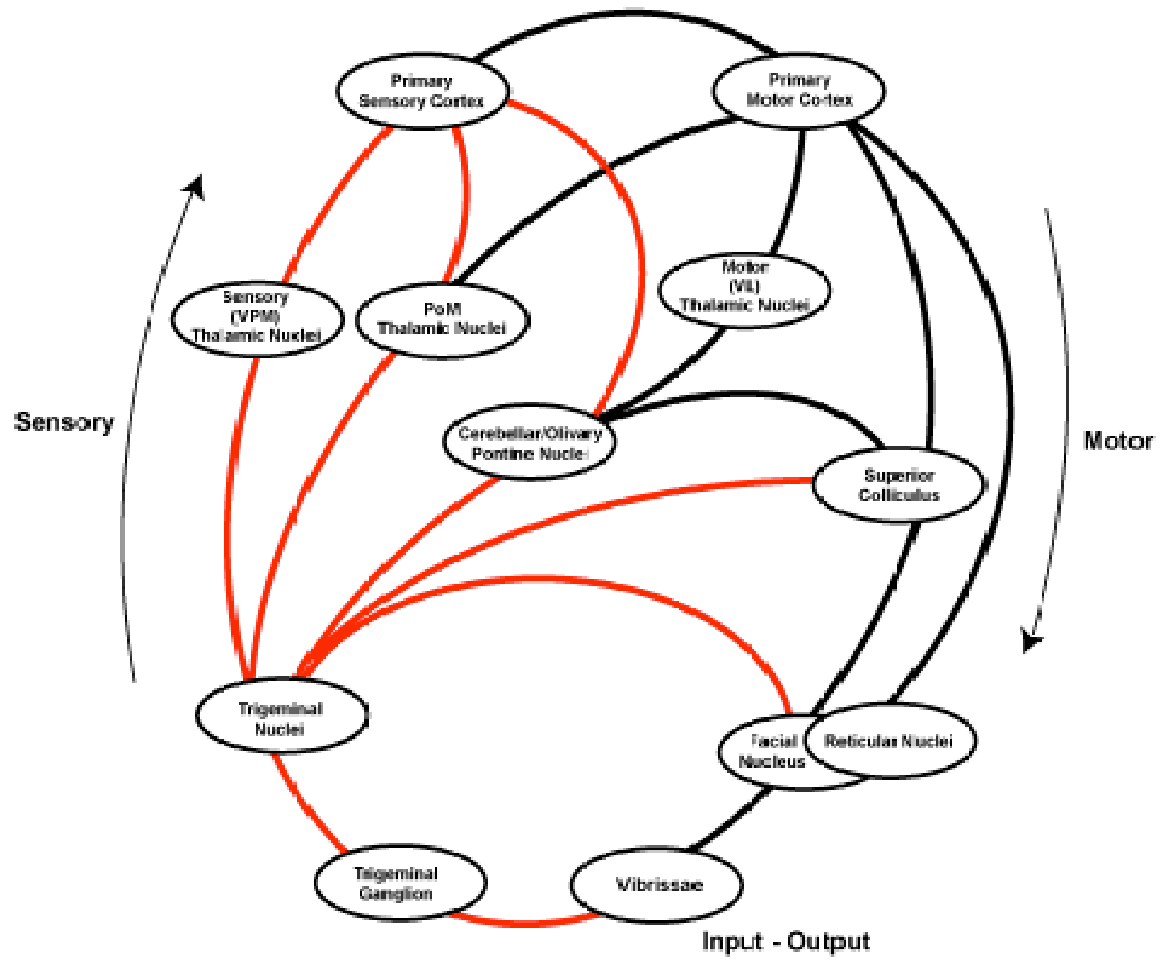
Examples from multi-unit recording



Conclusions

- System physiology (Ahissar *et al.* 2000) is explained by:
  Anatomy (Crabtree 1999, Steriade 2001) + stimulus shape (Ahissar *et al.* 2000) +
  cellular physiology (Kim *et al.* 1997) + rate modeling (Ermentrout 1994, Shriki *et al.* 2003).
- A model of POm-RE only exhibit period doubling at high stimulus frequencies and large $GABA_B$ conductance. No 2:1 firing mode is found in experiments at high stimulus frequencies.
- At high frequency, the POm (and cortical layer Va) activity can be controlled by the inhibitory interaction between the two pathways without period doubling.
- Predictions:
  - Complete $GABA_B$ blockade _
    - No frequency-dependent effect (VPM: Castro-Almancos, 2002).
  - Partial $GABA_B$ blockade _
    - Smaller amplitude effect, almost no latency effect.
  - Generating sharply rising stimuli _
    - Smaller amplitude effect, almost no latency effect.

The Vibrissa Sensorimotor System is Comprised of Nested Loops



Is there period doubling in experiments?

For each unit and each frequency, we:

1. Consider a train of responses r_j (numbers of spikes) to the jth stimulus, after omitting a 1s transient.
2. Compute S_1 and S_2 for each trace
3. Define Z as:
4. Plot the standard deviation of Z as a function of its average value.

Conclusion: no period doubling is observed experimentally.