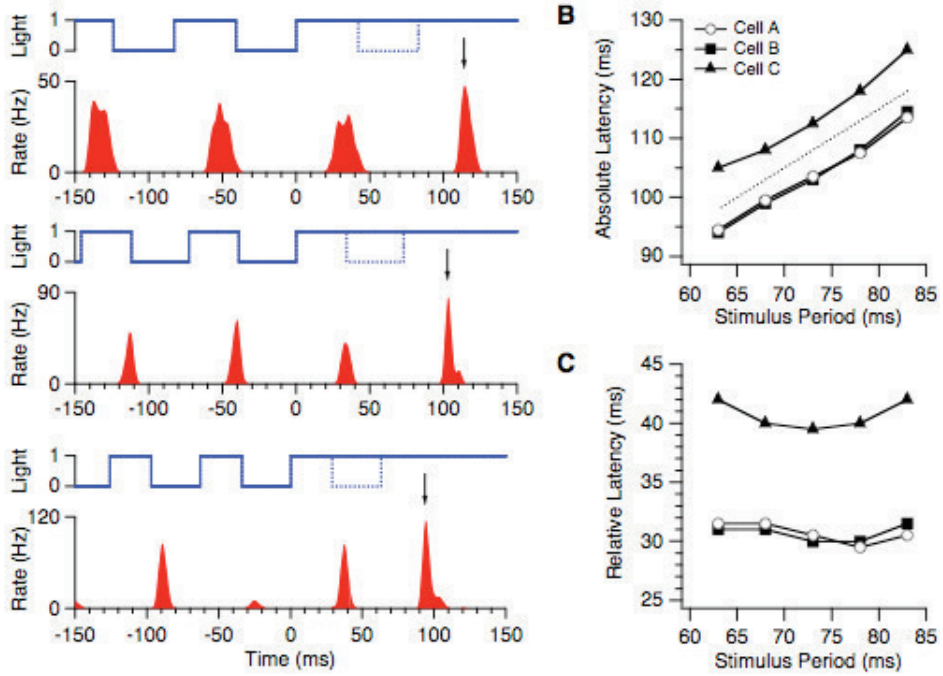
A model for Omitted Stimulus Response, or "How does the retina develop expectations?"

Juan Gao* & Philip Holmes

with Greg Schwartz and Michael J. Berry II (Princeton).

*Now at Dept of Psychology, Stanford University.



Thanks to: NIMH, AFOSR and the Burroughs-Wellcome Foundation.

Dynamical Systems in Biology (Hoppenfest), NYU, April 12-13, 2008.

Motivation

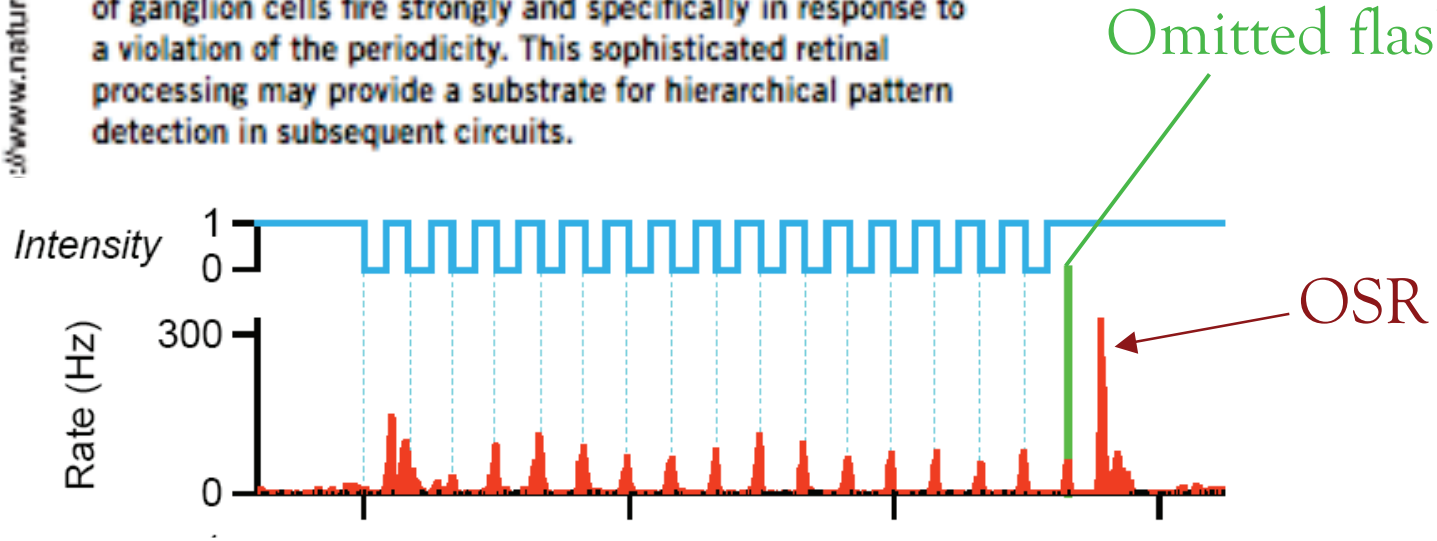
Experimental studies and preliminary modeling in Berry's lab:

nature neuroscience

Detection and prediction of periodic patterns by the retina

Greg Schwartz[1], Rob Harris[2], David Shrom[1] & Michael J Berry II[1]

A fundamental task of the brain is detecting patterns in the environment that enable predictions about the future. Here, we show that the salamander and mouse retinas can recognize a wide class of periodic temporal patterns, such that a subset of ganglion cells fire strongly and specifically in response to a violation of the periodicity. This sophisticated retinal processing may provide a substrate for hierarchical pattern detection in subsequent circuits.

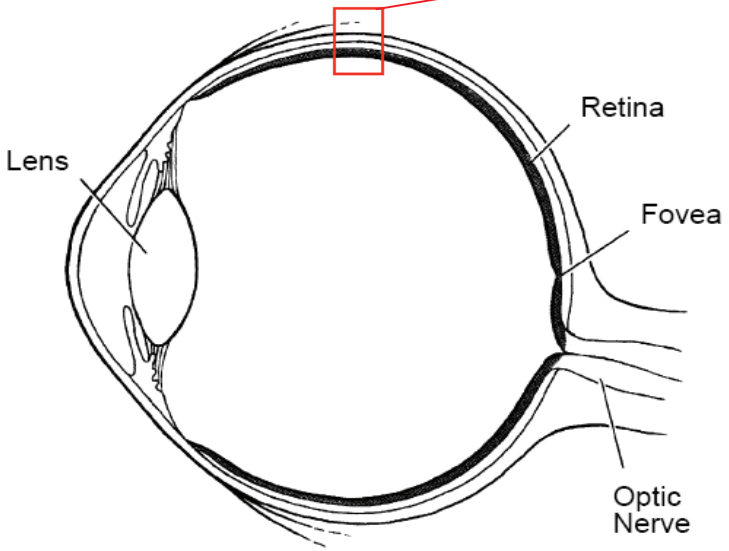


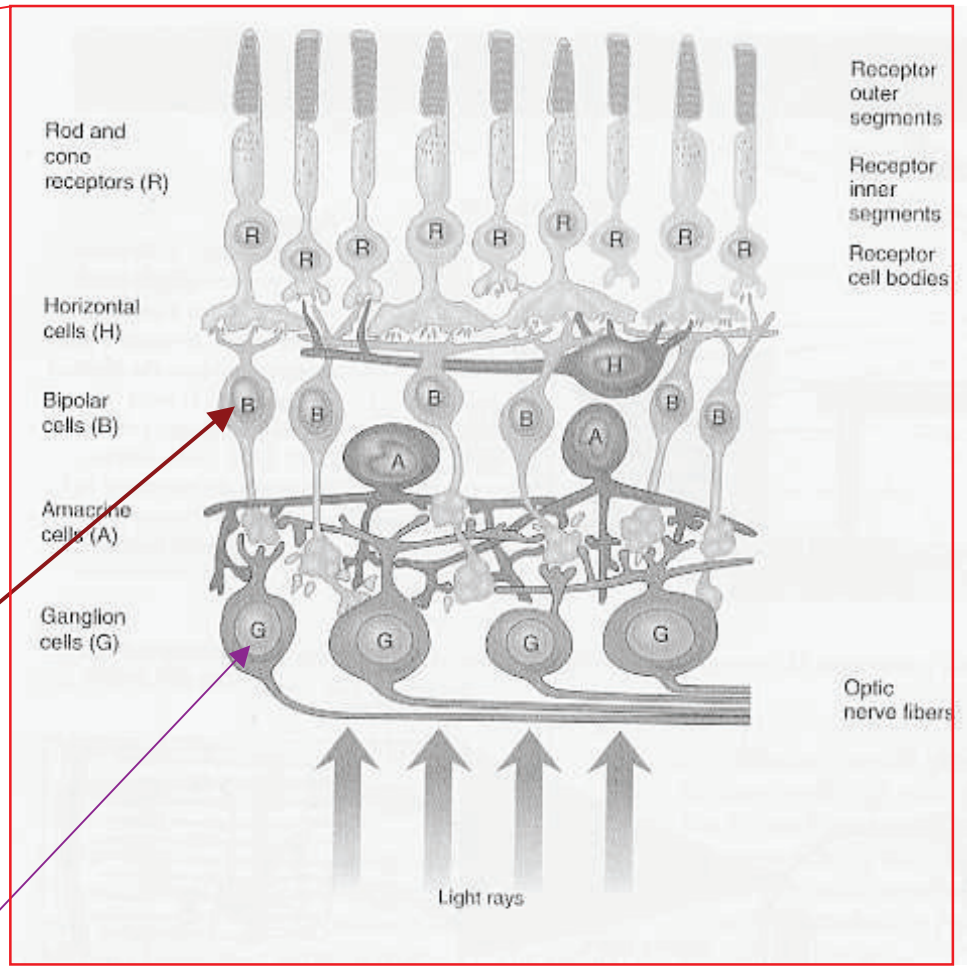
Nature Neuroscience 10 (5): 552-554, 2007;
Schwartz and Berry, J. Neurophysiol. 99, 2008.

Contents:

I. The retinal circuit

Vertebrate retinas (salamanders, mice, humans):



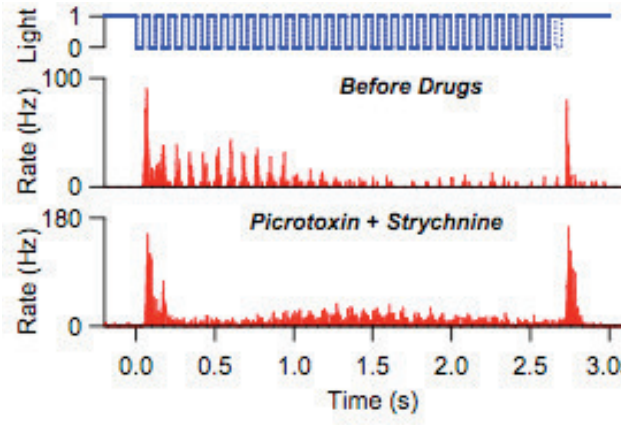


ON and OFF bipolar cells seem to be the major players.

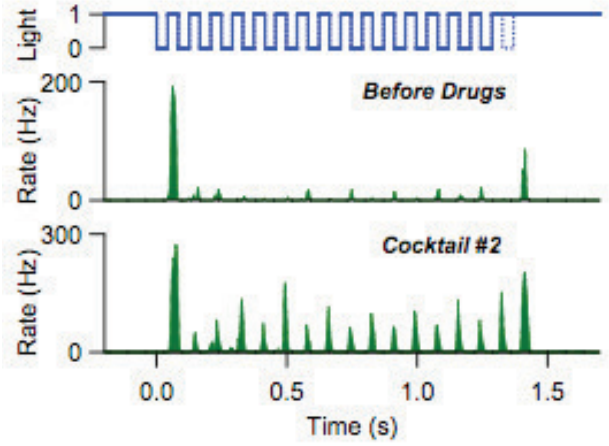
Isolated patch of retina in vitro, record from ganglion cells.

OSR: basic phenomena 1

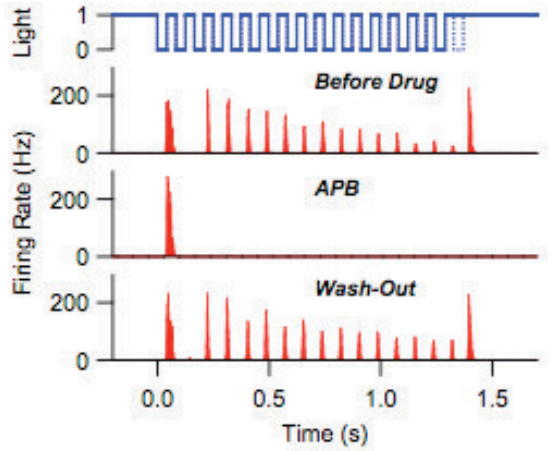
Ganglion cells emit a burst of spikes following an omission in a periodic sequence of stimuli. Blocking ON bipolar cells destroys the pattern; disabling amacrine cells does not do so. OSR is observed from 6 to 20 Hz (but not from same ganglion cell over whole range).

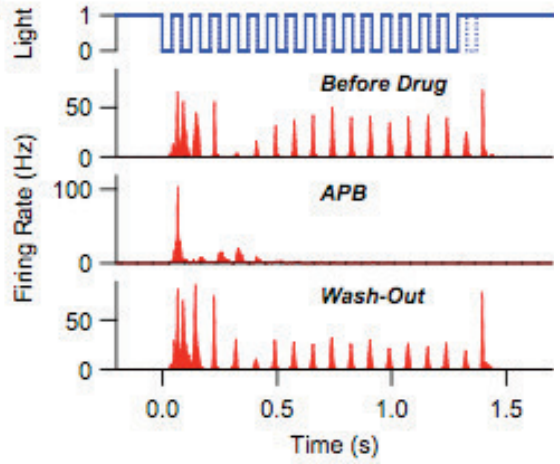


amacrine blocks on left



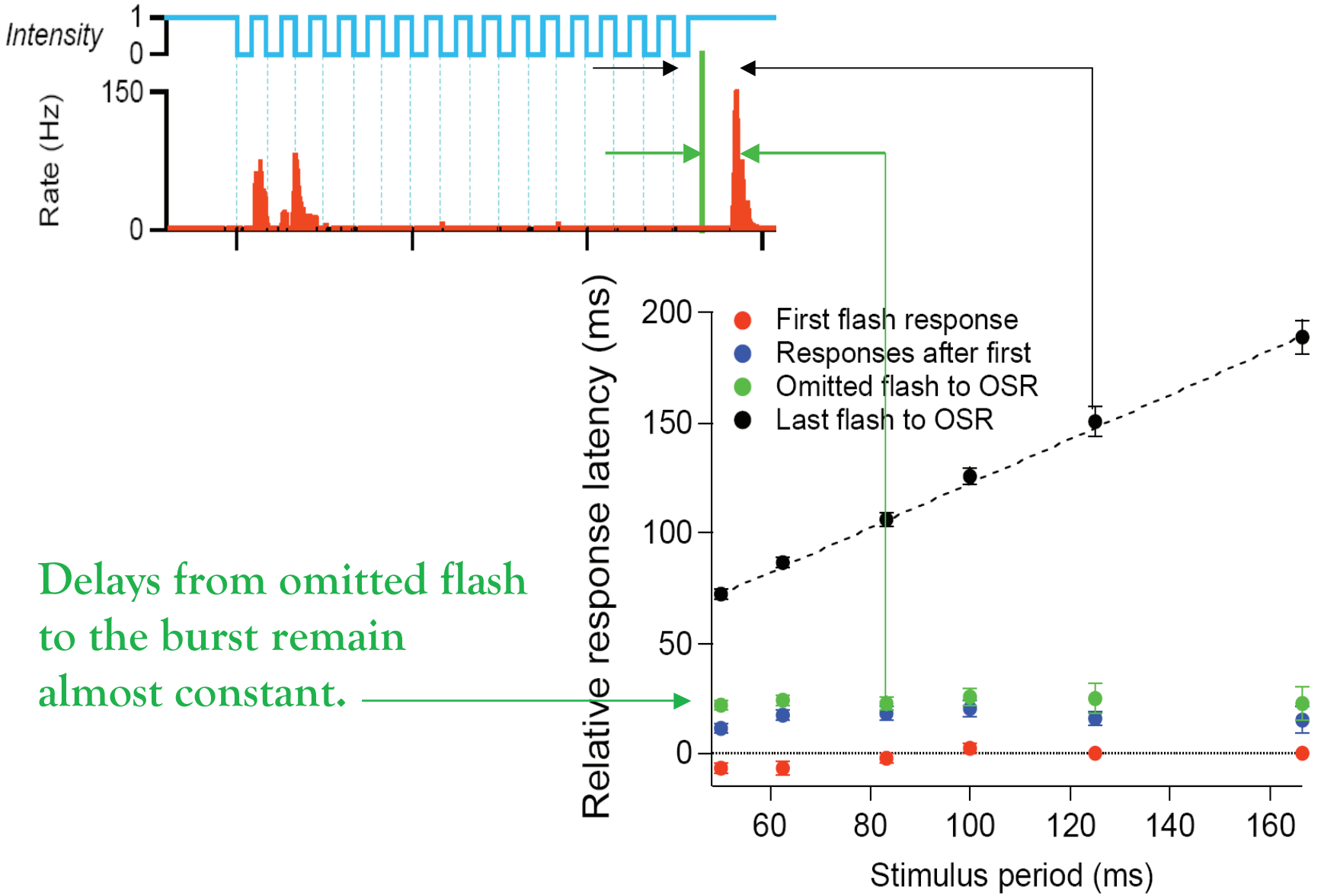
bipolar blocks on right





Schwartz & Berry,
J. Neurophys. 99, 2008.

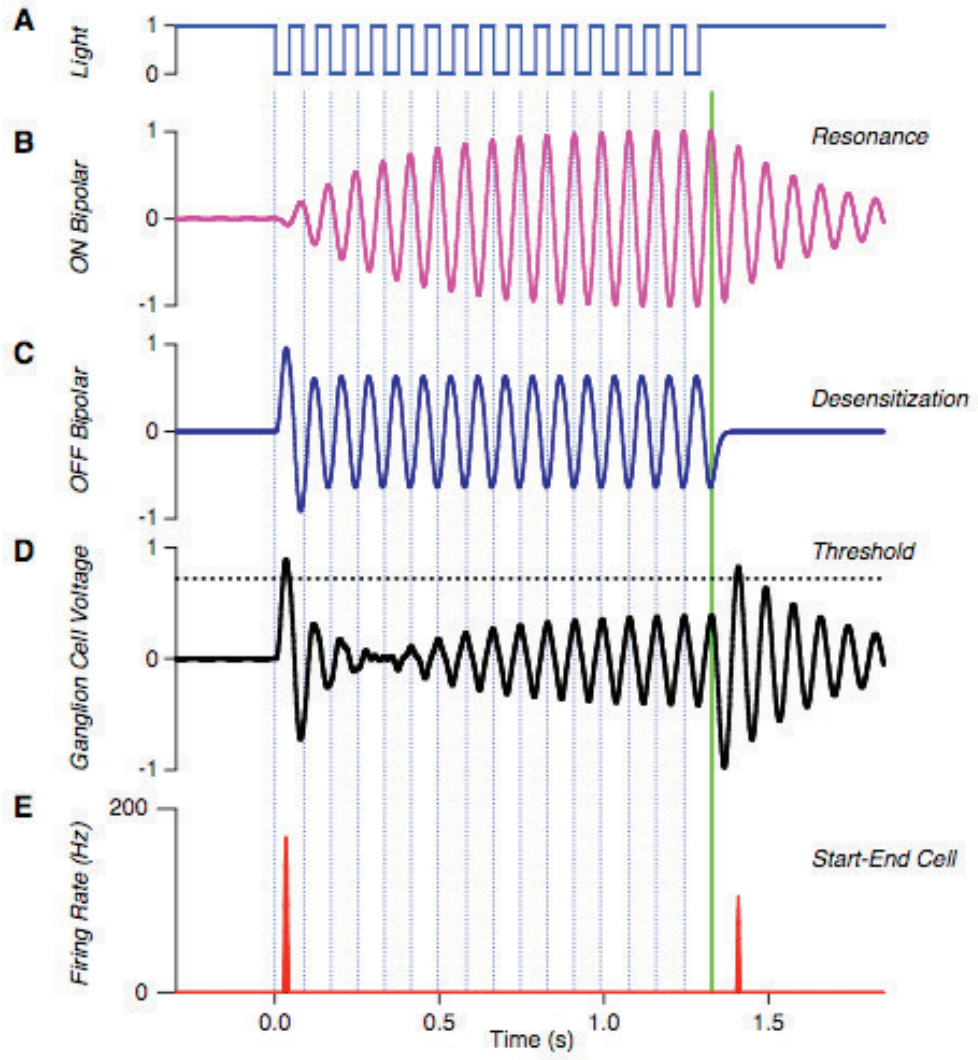
OSR: basic phenomena 2



Delays from omitted flash to the burst remain almost constant.

II. Is OSR a simple linear resonance?

The retinal circuit involves ON and OFF bipolar cells, amacrine cells and horizontal cells. Bipolar cells exhibit nonspiking oscillations.



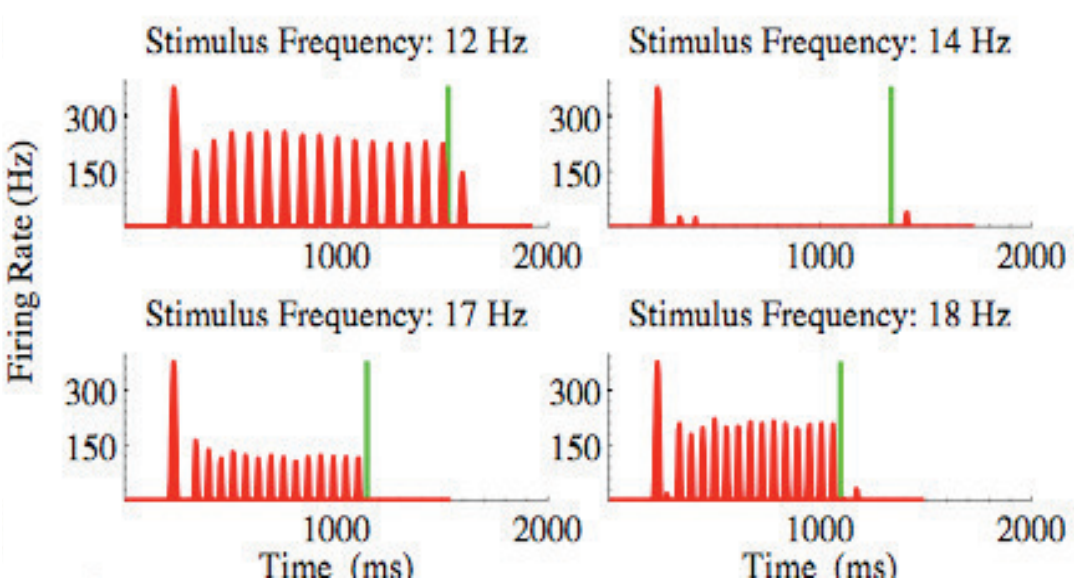
Could ON and OFF outputs from const. coeff. linear oscillators conspire to cancel except at start and end?

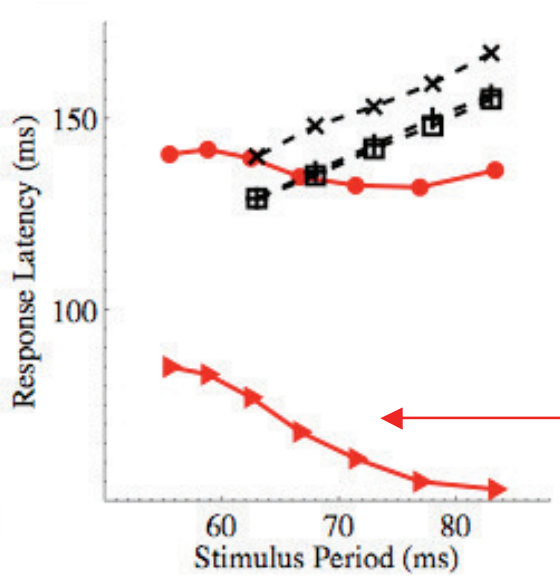
Yes, but only for a single stimulus frequency.

Schwartz and Berry, in review. 2007

A resonator bank model is not robust

Many bipolar cells synapse onto each ganglion cell. This suggests that we might combine a bank of terminal oscillators with a range of natural frequencies and superpose their responses, exploiting phase cancellation. This does works over a limited freq. range, but it requires very careful tuning. It's not robust.





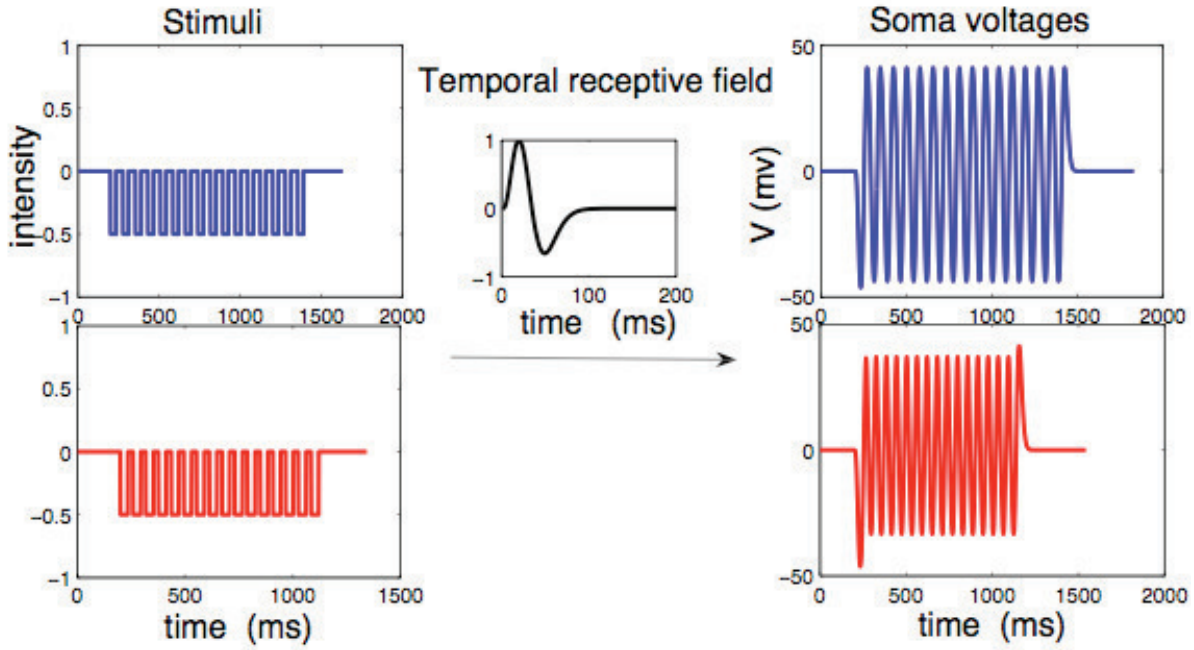
OSR is typically too small or has multiple peaks (ringing) or is absent, and delays from the missing flash to OSR are **not constant.**

III. Oscillator model 1

We develop a self-tuning oscillator model of the ON bipolar cell. The ON and OFF bipolar cell somas respond to light changes with subthreshold non-spiking voltage, modeled by linear filters.

$$V_{\mathrm{ON}}(t) = \bar{V} \int_0^{\tau} s(\tau) D_{\mathrm{ON}}(t-\tau)\, d\tau$$

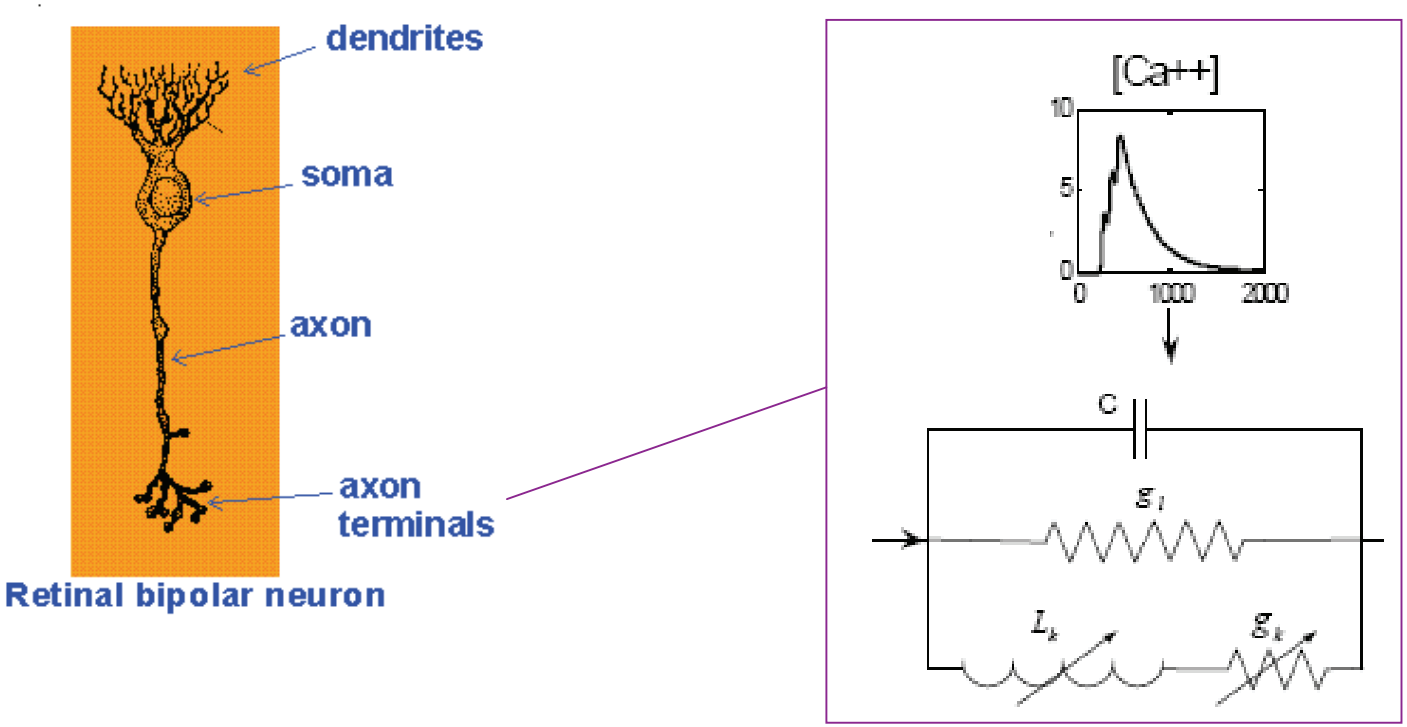
ON bipolar cell responses



OFF cells additionally desensitize, although this is not critical.

Oscillator model 2

We now focus on the large synaptic terminals of ON bipolar cells. These are capable of oscillatory behavior, although the bipolar cells do not spike. The terminals contain Ca^{2+} activated K^{+} channels, modeled as LRC circuits. Ca^{2+} release is driven by the ON cell's soma voltage.

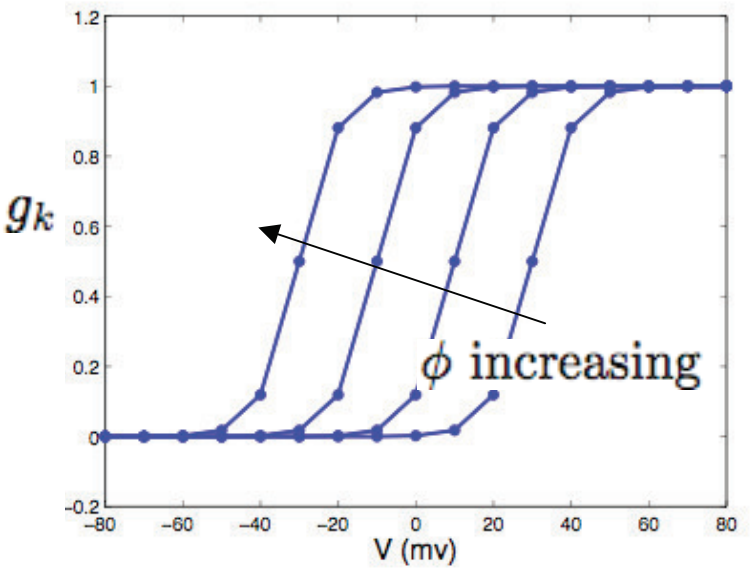


Oscillator model 3

Ca^{2+} release is driven by ON cell's soma voltage $V_{ON}(t)$:

$$\tau_{Ca}\,\dot{\phi} + \phi = \beta_v \max\{V_{ON}, 0\}$$

This tunes the resistor and inductor in the terminal:



$$g_k = \bar{g}\frac{1}{1+e^{-4d(V-V_b)}},$$

$$L_k = \frac{\bar{L}(1+e^{-4d(V-V_b)})^2}{4de^{-4d(V-V_b)}}$$

$$V_b = V_{b0} - \alpha\phi$$

$$b = V_{b0} - V$$

$$g_k = \bar{g}\frac{1}{1+e^{-4d(\phi-b)}},$$

$$L_k = \frac{\bar{L}(1+e^{-4d(\phi-b)})^2}{4de^{-4d(\phi-b)}}$$

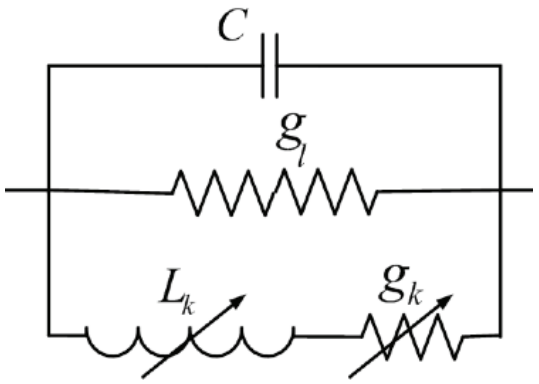
Ca^{++} dominates the behavior,
So we may drop $V_{ON}(t)$.

Jones, Gray-Keller & Fettiplace, J. Physiol. 1999.

Oscillator model 4

So, Ca^{2+} release ϕ tunes the terminal's resonant frequency:

$$C\frac{d^2U}{dt^2}+\left[\frac{C}{L_k(t)g_k(t)}+g_l\right]\frac{dU}{dt}+\left[\frac{g_k(t)+g_l}{L_k(t)g_k(t)}\right]U=\frac{dI(t)}{dt}+\frac{I(t)}{L_k(t)g_k(t)}$$



$$g_k = \bar{g}\frac{1}{1+e^{-4d(\phi-b)}},$$

$$L_k = \frac{\bar{L}(1+e^{-4d(\phi-b)})^2}{4de^{-4d(\phi-b)}}$$

$$f_0=\sqrt{\frac{de^{-4d(\phi-b)}\left[1+\frac{g_l}{\bar{g}}(1+e^{-4d(\phi-b)})\right]}{\pi^2C\bar{L}(1+e^{-4d(\phi-b)})^2}}$$

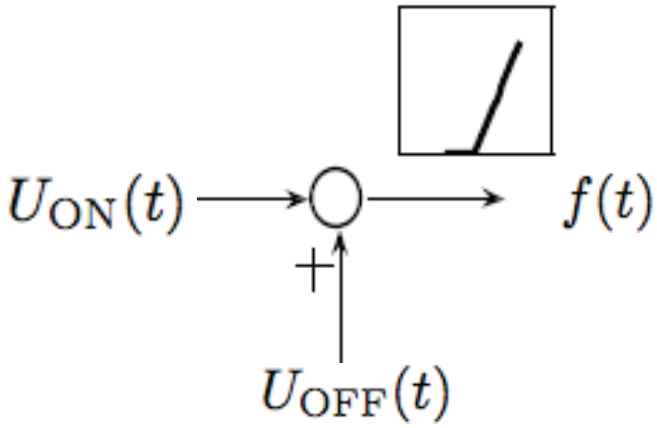
f_0 decreases with ϕ for $\phi > b$

Oscillator model 5

Finally, the ON bipolar terminal voltages and OFF bipolar soma voltages are summed and fed into ganglion cells, whose resulting firing rates are modeled by a simple piecewise linear ramp:

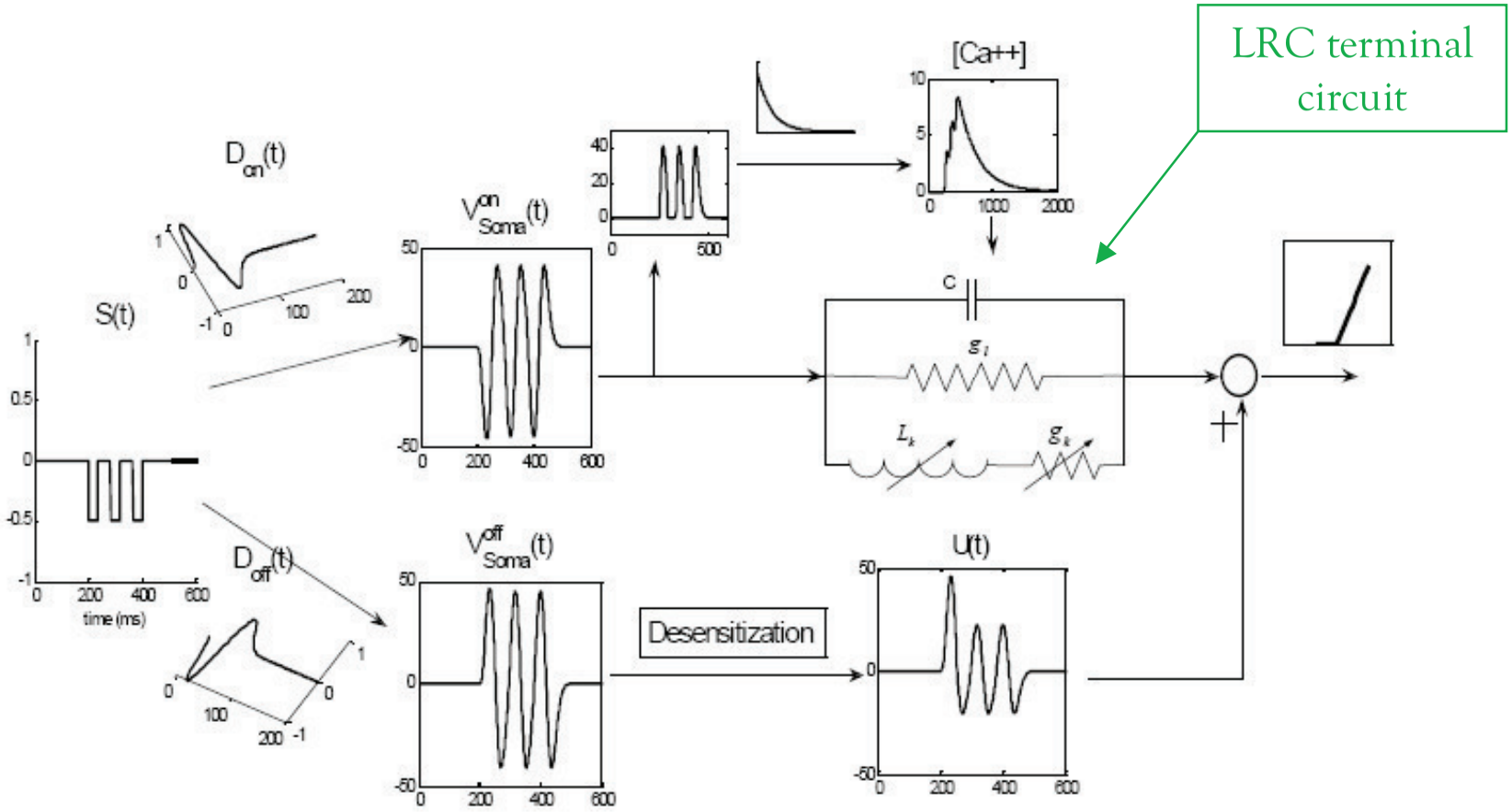
$$U_{\text{sum}}(t) = U_{\text{ON}}(t) + U_{\text{OFF}}(t)$$

$$f(t) = \begin{cases} \bar{f}(U_{\text{sum}}(t) - U_\theta), & U_{\text{sum}} \geq U_\theta \\ 0, & U_{\text{sum}} < U_\theta \end{cases}$$



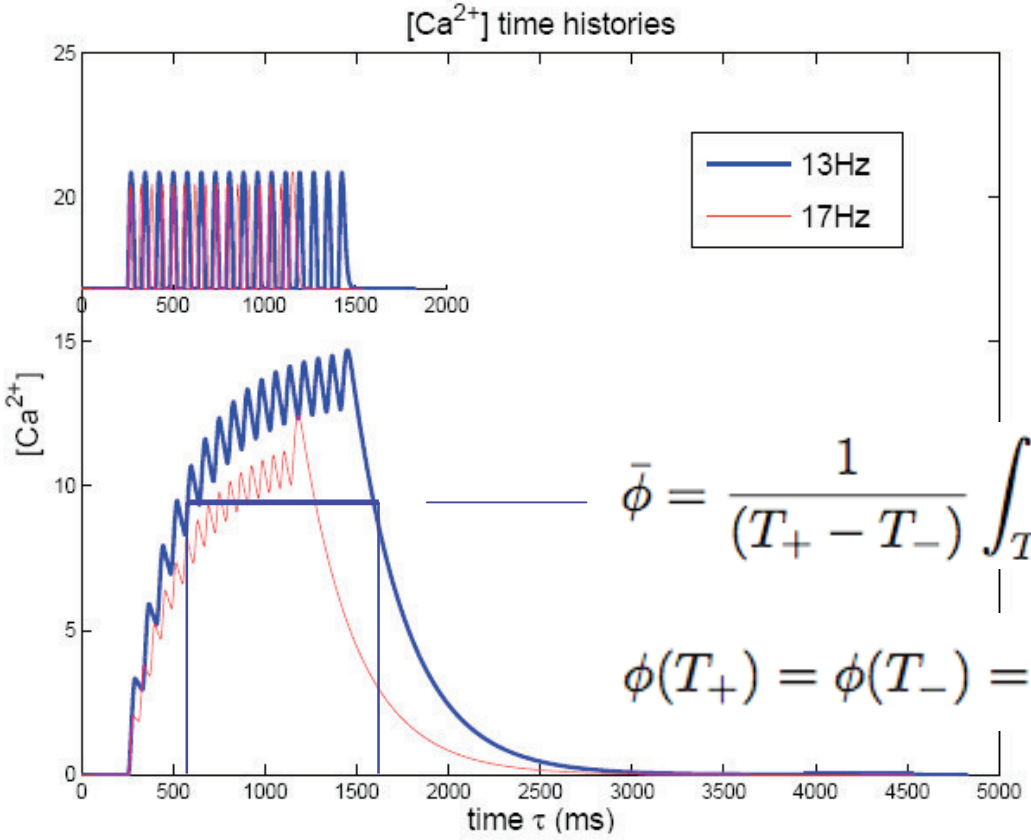
[Can also rectify $U_{\text{OFF}}(t)$prior to summation.]

Review: A self-tuning oscillator model



IV. Calcium dynamics is relatively slow

ON bipolar soma voltage determines [Ca++] levels, and we may approximate [Ca++](t) by short-term average.



$$\bar{\phi} = \frac{1}{(T_+ - T_-)} \int_{T_-}^{T_+} \phi(t)\, dt$$

$$\phi(T_+) = \phi(T_-) = \frac{3\phi(T_{\max})}{4}$$

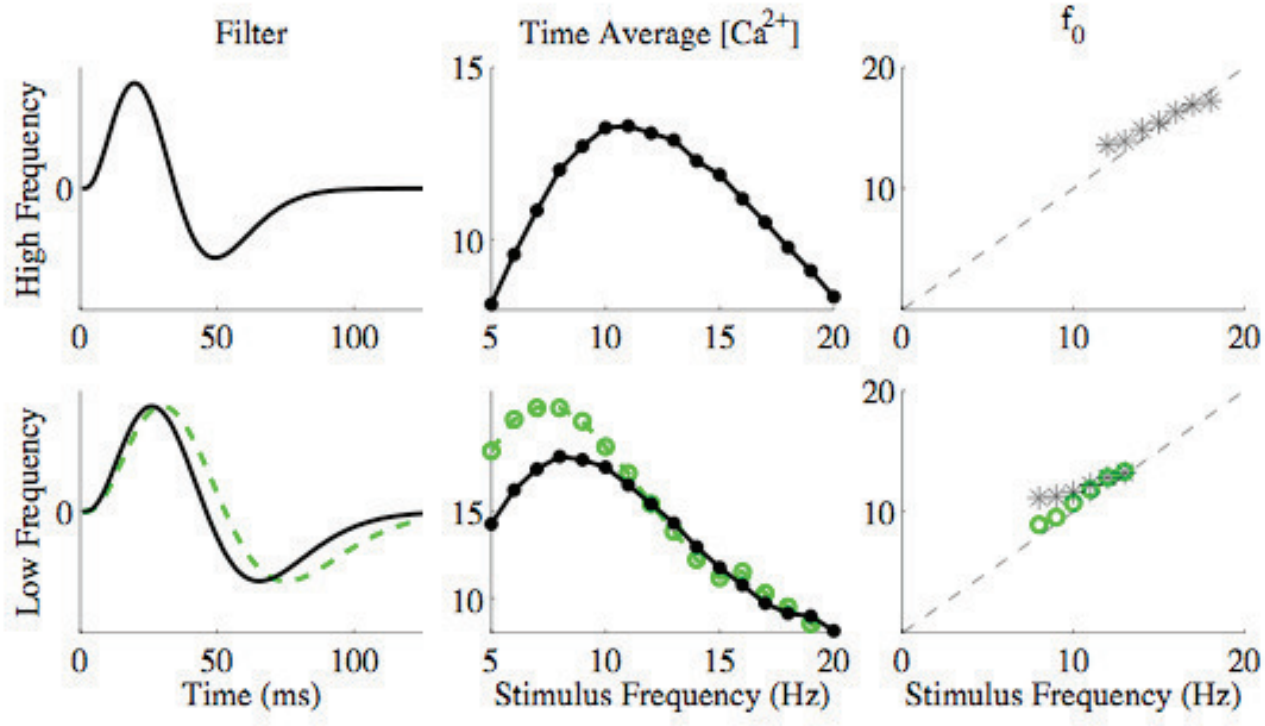
Different bipolar cells respond in different frequency ranges:

Stimulus frequency tunes $[Ca^{2+}]$ level ϕ → resonant frequency can adapt to stimulus:

$$f_0 = \sqrt{\frac{de^{-4d(\phi-b)}\left[1+\frac{g_l}{\bar{g}}(1+e^{-4d(\phi-b)})\right]}{\pi^2 C\bar{L}(1+e^{-4d(\phi-b)})^2}}$$

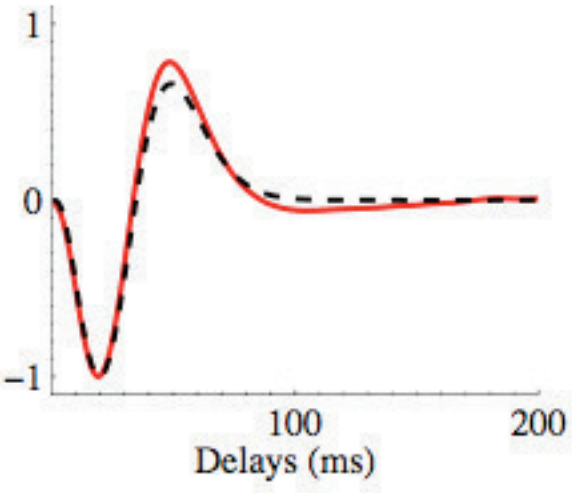
Faster filter

Slower filter

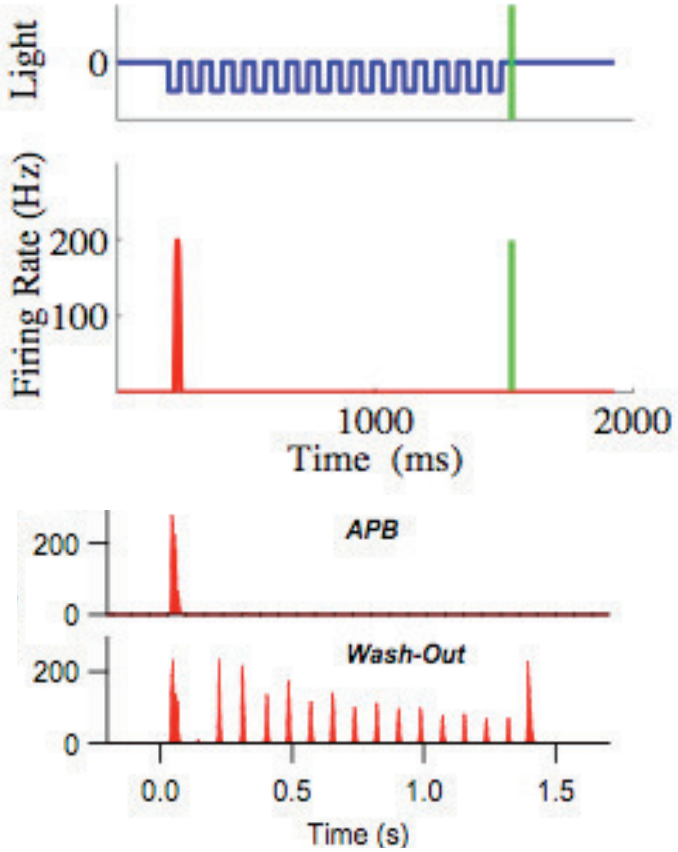


The average $[Ca^{2+}]$ level analysis guides parameter selection to cover the 6-20 Hz range. Only 4 parameters are critical: $C\bar{L}$, d, b .

Reality checks on model:



Spike-triggered average of entire circuit, light input to ganglion cell, matches typical filter shape.
black: STA red: recept. field

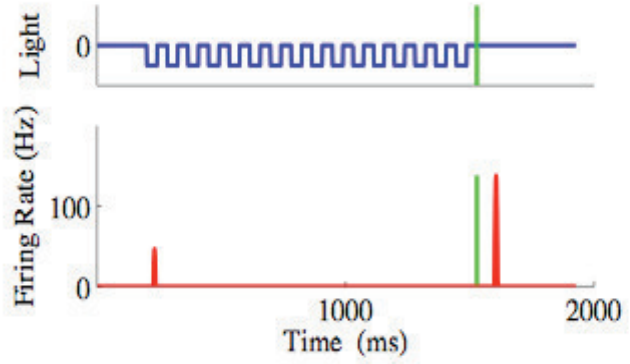


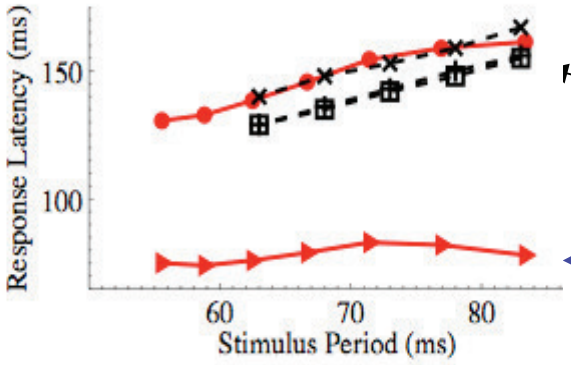
Disabling the ON bipolar cell pathway abolishes the OSR as well as all intermediate spikes (expt data below).

V. Model predictions 1

12 Hz stimuli

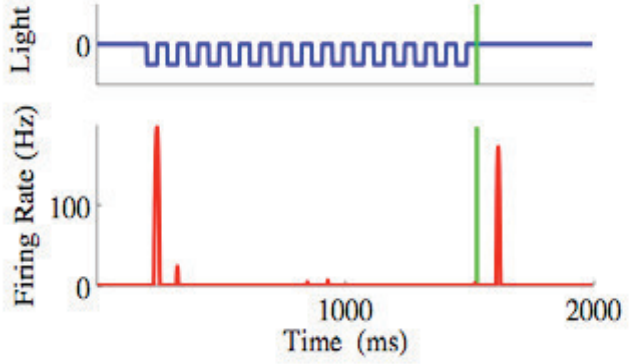
Fast cell: 12-18 Hz range

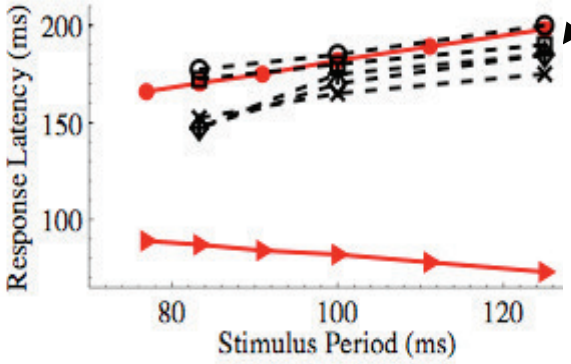




data

Slow cell: 8-13 Hz range





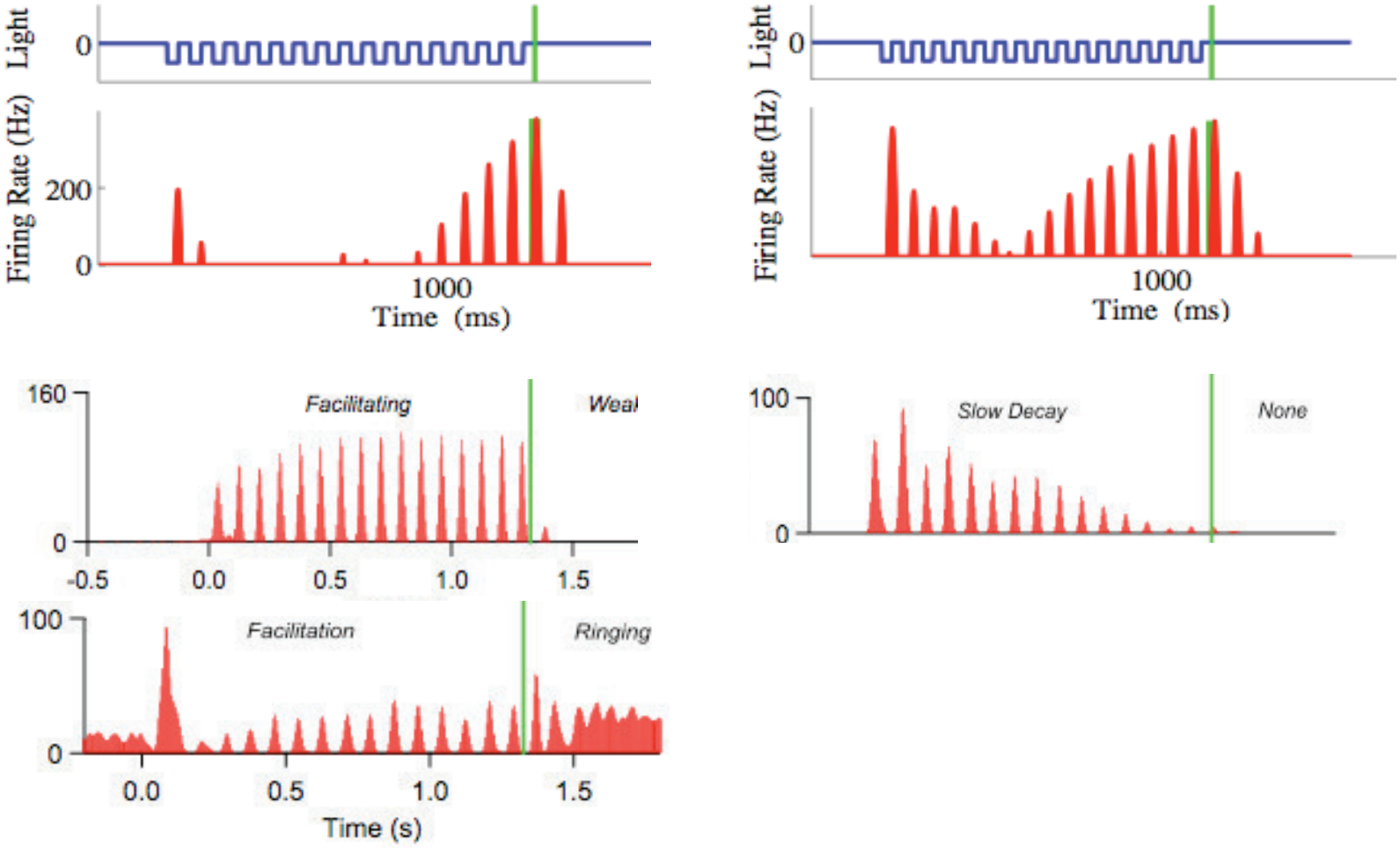
Black: data.

Red: model

Approx. constant omitted flash to OSR latencies.

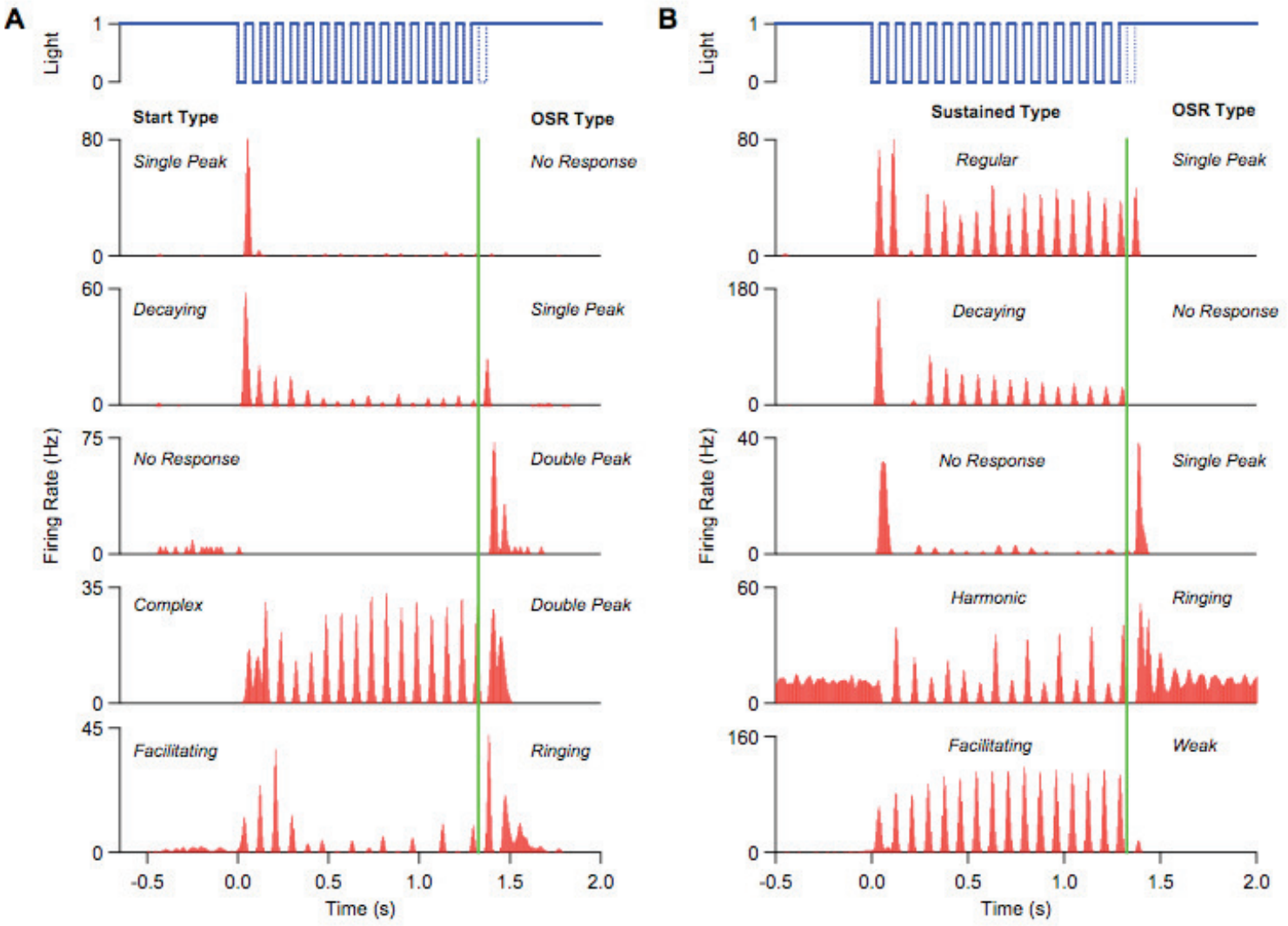
Model predictions 2

The model also works with OFF channel rectified before summation with ON channel



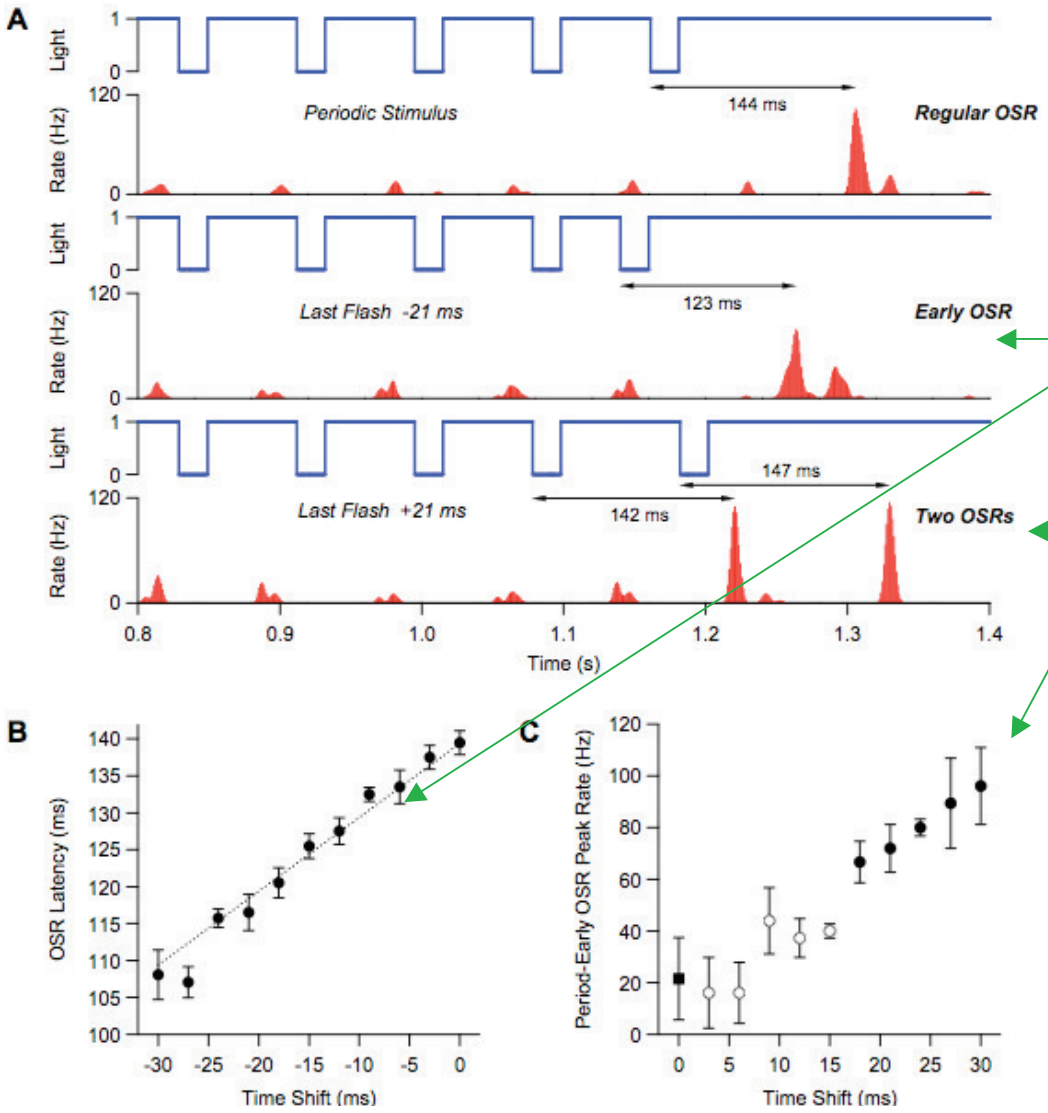
Top traces: model; bottom traces: data.

OSR: second order phenomena 1: a zoo of cell types!



Schwartz and Berry, J. Neurophysiol. 99, 2008.

OSR: second order phenomena 2



Instead of dropping a flash, we can advance or delay it:

early flash

late flash

So, there's plenty more to do!

Schwartz and Berry, J. Neurophysiol. 99, 2008.

VI. Summary, and some questions

- Omitted stimulus response occurs in a 'low level' sensory circuit: data processing at the periphery.
- A simple, passive, self-tuning linear oscillator can reproduce the phenomenon: it detects pattern violations.
- Q1: Could an intrinsic (limit cycle? excitable?) oscillator model describe the subharmonic and time-shifted responses?
- Q2: How might the diversity of ganglion cell responses be used in subsequent image processing?

Thanks for your attention.