Linearity and non-linearity of sensory-evoked neuronal and hemodynamic responses in awake monkey V1.

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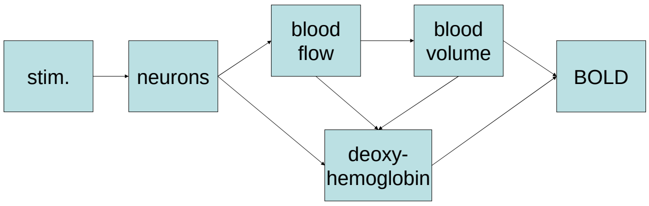
OBJECTIVES

Several functional magnetic resonance imaging (fMRI) studies have found a sub-linear behavior of the activation response with respect to increasing duration of the employed (visual) stimulus. This non-linearity has been often interpreted as a consequence of an adaptative behavior of the neuronal responses to stimuli of longer duration, whereas the link between neuronal and hemodynamic responses has been assumed to be linear. We aimed to test this hypothesis, to determine at which level of the chain rule from stimulation to hemodynamic measures does non-linearity occur, and to use physiological models to predict these non-linearities.

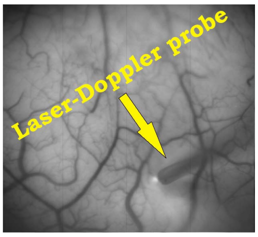
INTRODUCTION



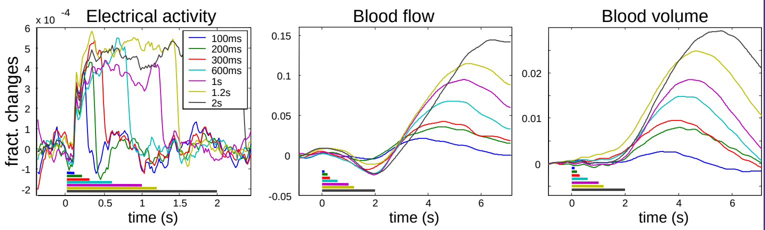
Which link(s) is (are) responsible for the nonlinearities observed in the BOLD signal?

METHODS

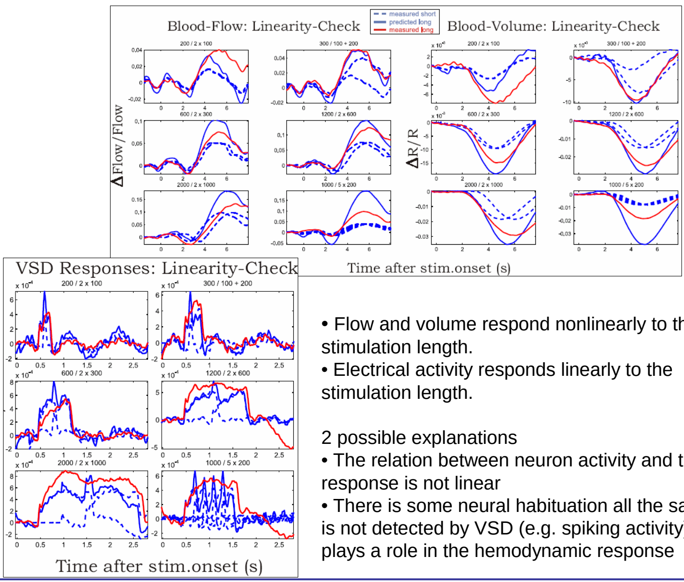
- **Optical Imaging** acquisitions were performed on the **awake macaque** primary visual cortex.
- **Visual stimulations** of different durations were used (100ms, 200ms, 300ms, 600ms, 1s, 1.2s, 2s).
- Sensory-evoked **blood flow** and **blood volume** responses were acquired simultaneously using **Laser-Doppler** measurements and optical imaging of **intrinsic signals** at an isosbestic wavelength (570nm)
- **Electrical activity** of neurons was acquired using optical imaging of **voltage sensitive dyes** (VSD, whose measures are connected to the membrand potential of cells).



RESULTS



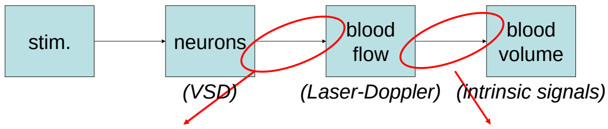
NON-LINEARITIES



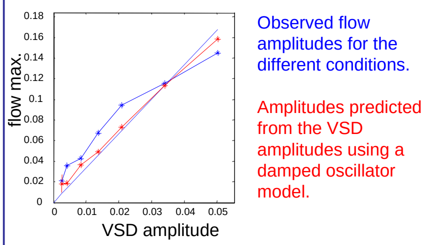
- Flow and volume respond nonlinearly to the stimulation length.
- Electrical activity responds linearly to the stimulation length.

2 possible explanations
- The relation between neuron activity and the flow response is not linear
- There is some neural habituation all the same that is not detected by VSD (e.g. spiking activity) and plays a role in the hemodynamic response

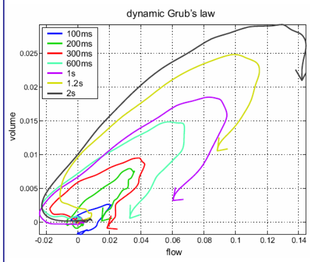
CONTRADICTIONS WITH EXISTING MODELS



Models proposed by Friston et al. [2000] (a damped oscillator) and by Buxton et al. [2004] (a convolution with a gamma-variate function) both suppose a linear relationship here, but we observed a nonlinear one.

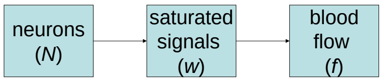


The Balloon Model proposed by Buxton et al. [1998,2004] supposes that volume is delayed with respect to flow, but we observed the contrary.



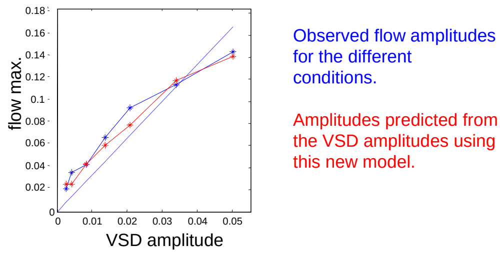
PROPOSITION FOR A NEW MODEL OF THE FLOW

We propose a signal saturation model (which is actually constructed on the same equations as the neural habituation model in [Buxton et al., 2004]) previous to the damped oscillator.



$$\left\{\begin{array}{lcl} \ddot{f} & = & \epsilon w(t-\delta_t) - \kappa_s \dot{f} - \kappa_f (f-1) \\ w & = & \max(h_w * N, 0) \\ h_w(t) & = & D(t) - \frac{\kappa_w}{\tau_w} e^{-\frac{\kappa_w + 1}{\tau_w} t} \end{array}\right.$$

- ϵ neural efficiency
- δ_t time delay
- $\kappa_s \kappa_f$ flow decay and feedback time constants
- $\kappa_w \tau_w$ saturation time constants
- D Dirac's function



CONCLUSION

Our data indicates a nonlinear dependency of the blood flow and volume responses to neural activity. This nonlinearity is probably due to saturation effects in the flow response, and could be described by a simple saturation model.

This nonlinearity should be taken into account in hemodynamical response models, otherwise the analysis of BOLD signals using dynamical models where the flow response is supposed linear with respect to neural activity could conclude abusively that there is neural habituation in the data.

We observed also other contradiction between our data and the Balloon Model proposed by Buxton et al., in terms of delays between the flow and volume response. In fact, more precise models should not consider the flow and volume variations in the venous compartment, but also in the arterial and capillaries compartments.

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