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Hemodynamic correlates of stimulus repetition in the visual and auditory cortices: an fMRI study

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It is also well established that the characteristics of the HDR vary across cortical regions as a function of stimulus properties and experimental parameters. For example, frontal HDRs show late onset and sustained duration of the HDR peak while motor and visual sensory cortices show earlier onset and shorter duration in the HDR to single stimuli (Schacter et al., 1997). Furthermore, the amplitude and latency of the HDR appear to change from cortical to subcortical regions as a function of ISI as well, indicating that the HDR recovers earlier in subcortical regions compared to cortical areas (Pollmann et al., 1998). Evidence of variation between cortical regions in HDR properties and sensitivities to stimulus presentation characteristics also comes from reports indicating that stimulus presentation rate does not alter HDR in bilateral frontal regions for instance, which show a categorical response to the presence of words irrespective of rate, while activation in bilateral occipitotemporal regions increases linearly and the posterior auditory association cortex exhibits a nonlinear (inverted U) relationship with increasing word rate (Buchel et al., 1998; Pollmann et al., 1998). Thus, the latency and amplitude of the HDR waveform vary across brain regions (Aguirre et al., 1998; Buckner, 1998; Buckner et al., 1996; Huettel and McCarthy, 2001; Kim et al., 1997; Miezin et al., 2000; Robson et al., 1998).

HDR varies across *regions*

(plumbing or neuronal?)

superior temporal gyrus (STG) regions (Friston et al., 1998). The finding of nonlinear additivity has also been demonstrated in the visual cortex (VC) using ISIs of 1-, 2-, 4-, and 6-s durations between two consecutive stimuli (Huettel and McCarthy, 2000, 2001). The nonlinear additivity in that study was attributed to the presence of a refractory period following stimulus presentation, which in turn modulated the amplitude of the HDR to subsequent stimuli. Subsequently, numerous studies (Grill-Spector K., 2001; Huettel and McCarthy, 2000, 2001; Kourtzi Z., 2001; Soon and Chee, 2003) have described similar phenomena, such as repetition suppression, repetition priming, or FMR adaptation. Many investigators have used this phenomenon to examine the role of particular cortical regions in processing specific stimulus attributes, with the hypothesis being that if stimulus attributes are processed in overlapping neural spaces, the HDR elicited in those regions by repeated stimulation would show suppression effects consistent with refractory properties (Grill-Spector K., 2001; Kourtzi Z., 2001). Furthermore, previous studies have also demonstrated that the characteristics (such as amplitude and latency) as well as refractory properties of the HDR vary across different cortical regions (Huettel and McCarthy, 2001). Despite numerous studies describing refractory or adaptive properties of the HDR, the exact mechanism and nature of this complex phenomenon remain unclear. Because a combination of multiple physiological changes associated with neuronal activity, such as CBF, $CMRO_2$, and CBV, contributes to the BOLD signal change, it is difficult at this point to distinguish the differential role of these physiological contributors upon changes (linear or not) in the BOLD signal associated with stimulus or task attribute changes. Nevertheless, the "HDR refractory period" (or "repetition priming" or "FMR adaptation") bears significant resemblance to the refractoriness exhibited by neurons in other cortical regions, such as shape adaptation in macaque IT neurons (Sobotka and Ringo, 1993), and hence may reflect a hemodynamic counterpart associated with such a phenomenon.

Can FMR adaptation be at least partially due to hemodynamics?

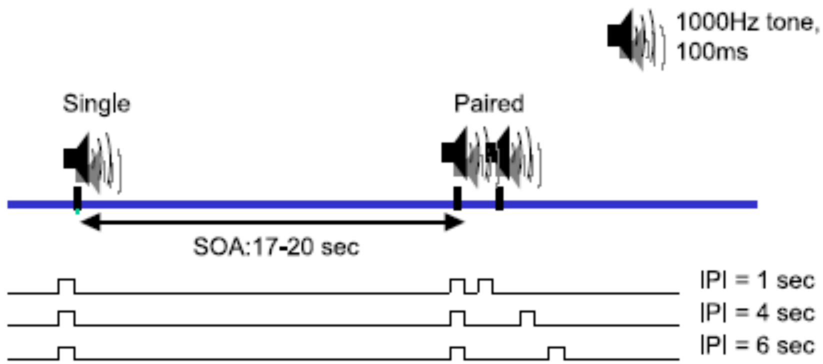


Fig. 1. (Experiment 1) Auditory task design: a brief tone of 1000 Hz presented for 100 ms either singly or in pair. The two stimuli in a pair were separated by a variable intrapair interval of 1, 4, or 6 s. Three types of pair conditions and the single stimulus condition were intermixed randomly during a presentation of 10 runs (3.5 min each). Forty instances of each condition were presented during each session.

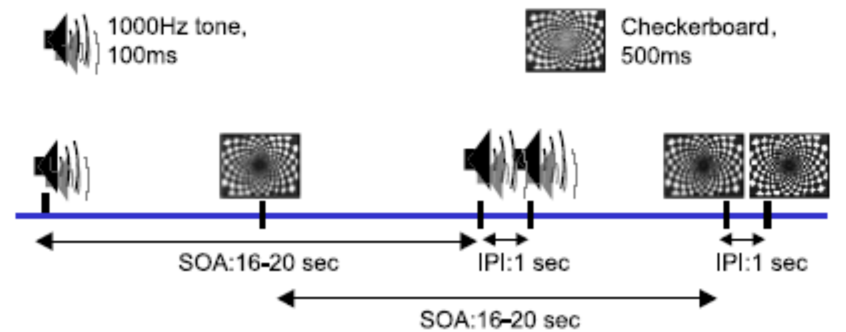


Fig. 2. (Experiment 2) Interleaved auditory and visual task design: single and paired auditory and visual stimuli were presented in an alternating pattern to avoid the overlapping response of the same domain. The time between the two conditions of the same domain varied between 16 and 20 s while two consecutive trials of different modality are separated by 8–10 s. Visual stimuli were checkerboards displayed with a duration of 500 ms, whereas the auditory stimuli were pure tones of 1000 Hz with a duration of 100 ms.

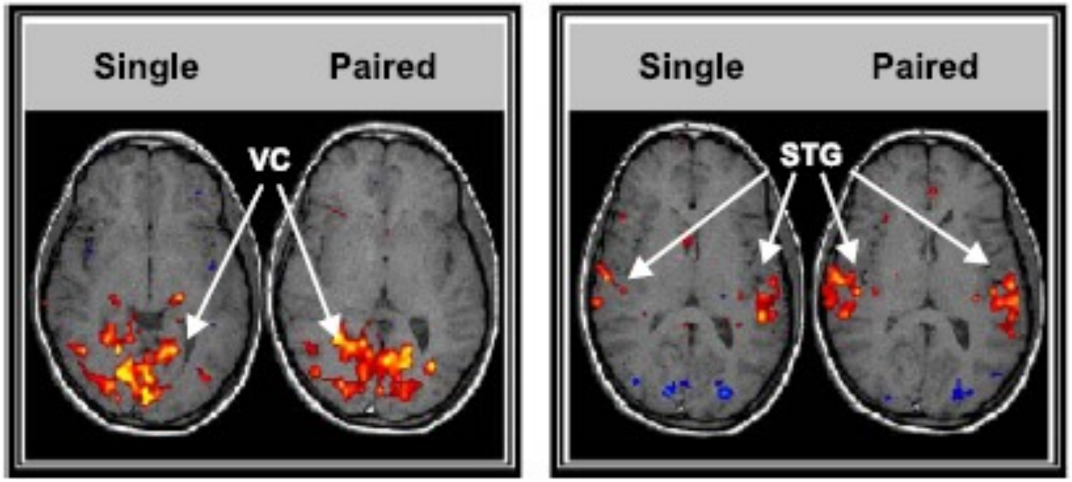


Fig. 4. (Experiment 2) Activation maps in response to single and paired stimulus conditions in both modalities. The response to paired conditions was calculated by averaging the epochs of BOLD signal within the voxels activated by single stimulus presentations. Note that the t-maps in response to single and paired conditions mostly overlap, but do not have the same spatial extent. To eliminate the confounding effects of newly recruited areas, the BOLD signal analysis for both trial types was restricted to voxels that responded to single stimulus presentations.

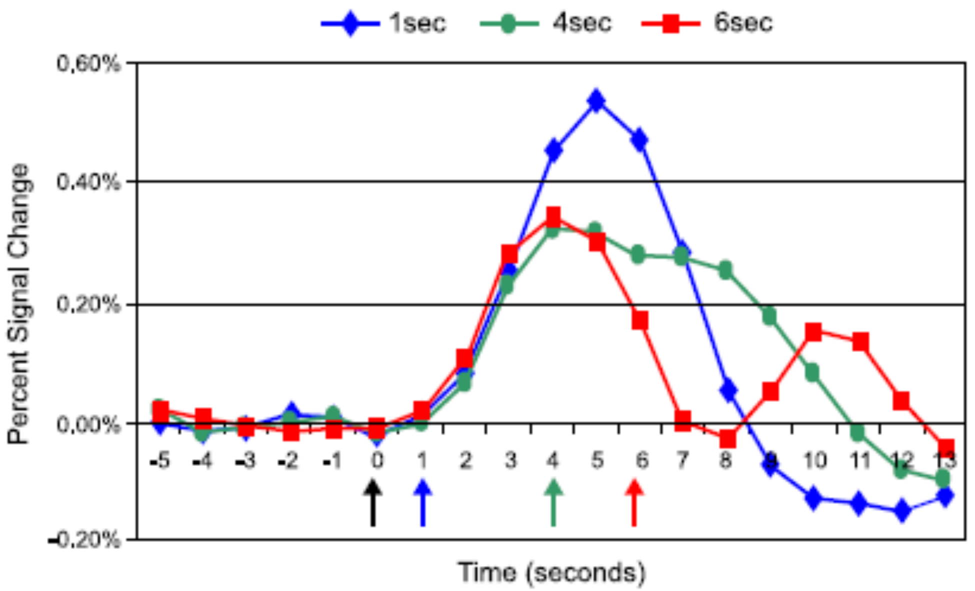


Fig. 5. (Experiment 1) The composite HDRs evoked by the paired conditions aligned to the onset of the first stimulus. Black arrow indicates the onset of first stimulus in all the conditions. Colored arrows indicate the onsets of second stimuli in different IPI conditions (Blue: 1 s IPI; Green: 4 s IPI, Red: 6 s IPI). The HDRs correspond to the matching arrow condition. Legends indicate the time interval between the two stimuli in a pair. This figure demonstrates the separation of two peaks as the time between two stimuli in a pair increases. At the 6 s IPI condition, even though the peaks are separated and the latency to peak from the onset of second stimulus recovers, the peak amplitude still remains suppressed compared to the first peak.

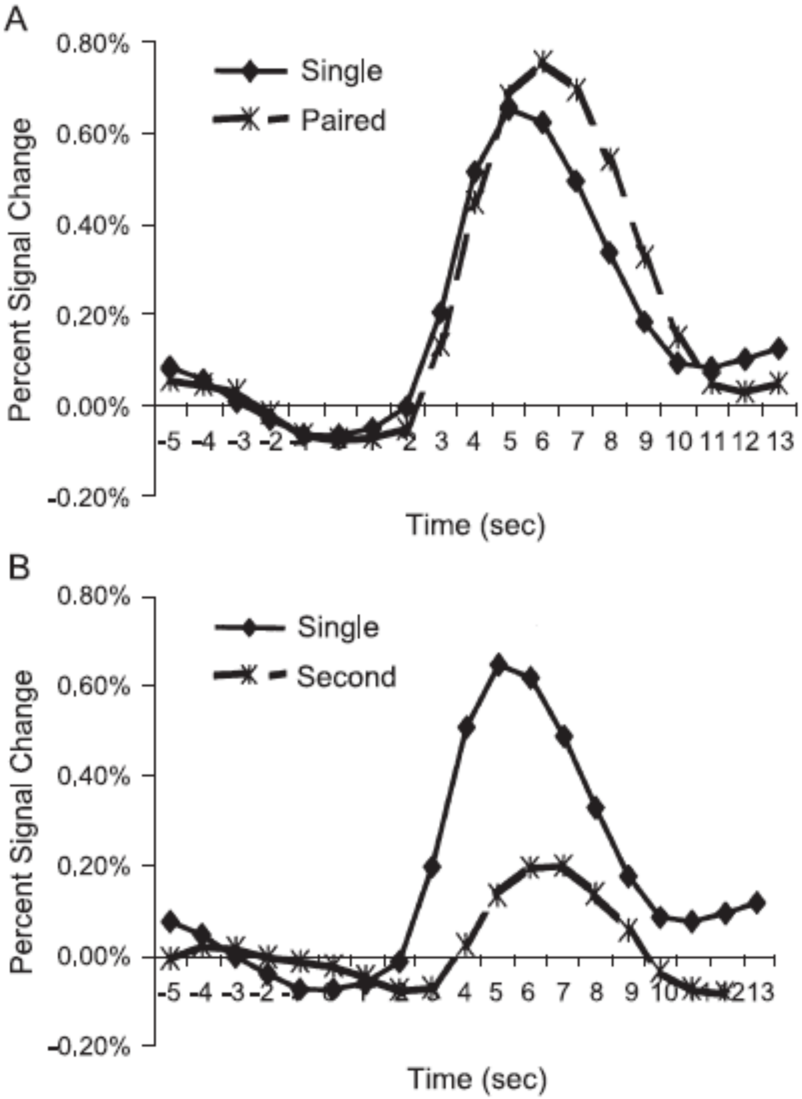


Fig. 6. (Experiment 2) Visual cortex. Average hemodynamic responses in visual cortex. (A) HDRs evoked by single and paired stimulus presentation. Composite HDR to the paired condition shows higher amplitude than the response evoked by single stimulus. (B) To isolate the contribution of the second stimulus in a pair to the composite response, the response to the single stimulus presentation was subtracted from the composite response to the paired condition and shifted by 1 s to realign to the same time onset.

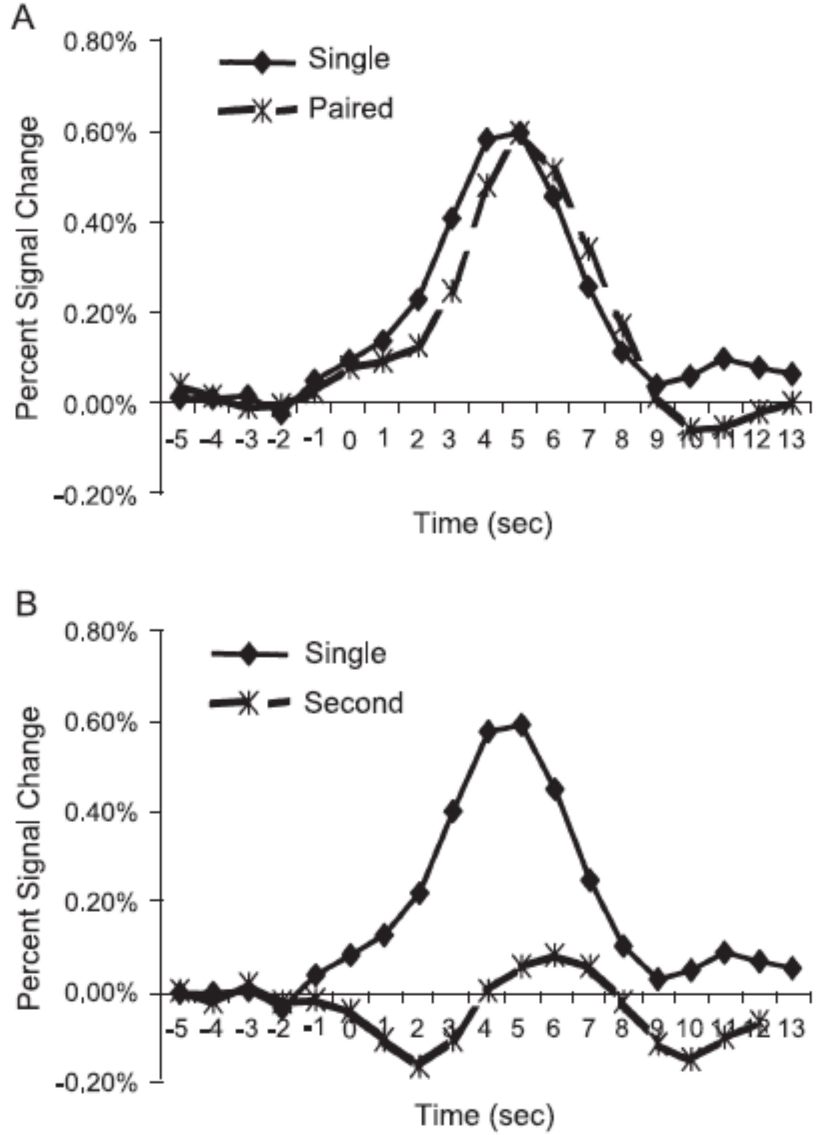


Fig. 7. (Experiment 2) Auditory cortex. Average hemodynamic responses in the auditory cortex. (A) HDRs evoked by single and paired stimuli presentation. (B) To isolate the contribution of the second stimulus in a pair to the composite response, the response to the single stimulus presentation was subtracted from the composite response to the paired condition and shifted by 1 s to realign to the same time onset.

Table 1

Mean values of the peak amplitude (percent signal change), suppression index based on peak values (SI = [(S2 / S1) 100]), and latency (second) measures of the average HDR evoked in VC and STG

	Peak			Latency	
	Single	Second	SI[a]	Single	Second
Auditory	0.60 (0.18)	0.15 (0.13)	25.9 (24.2)	4.7 (0.4)	5.7 (0.9)
Visual	0.67 (0.13)	0.24 (0.16)	36.4 (26.0)	5.3 (0.6)	6.4 (0.9)

Numbers in parenthesis indicate standard deviation.

[a] SI: suppression index.

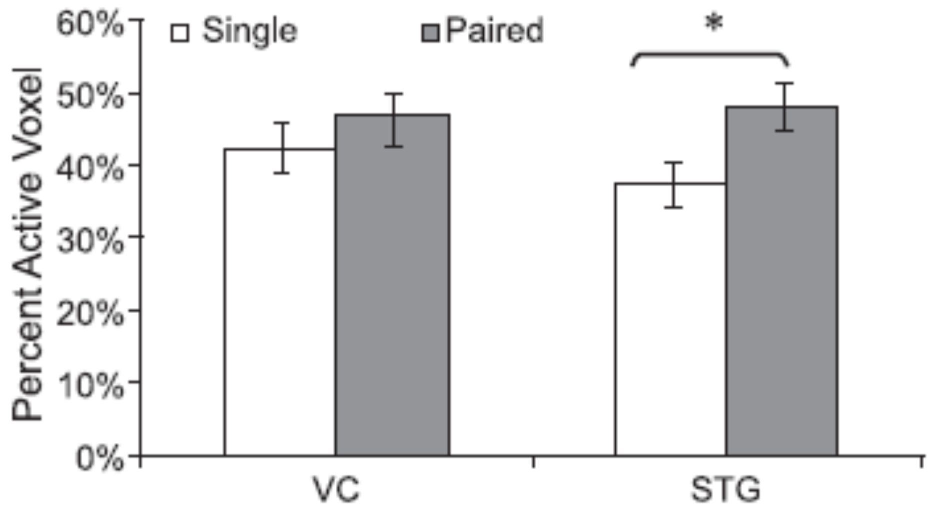


Fig. 8. (Experiment 2) Percent of activated voxels in response to repeated stimuli in visual and auditory cortices (*$P < 0.002$).

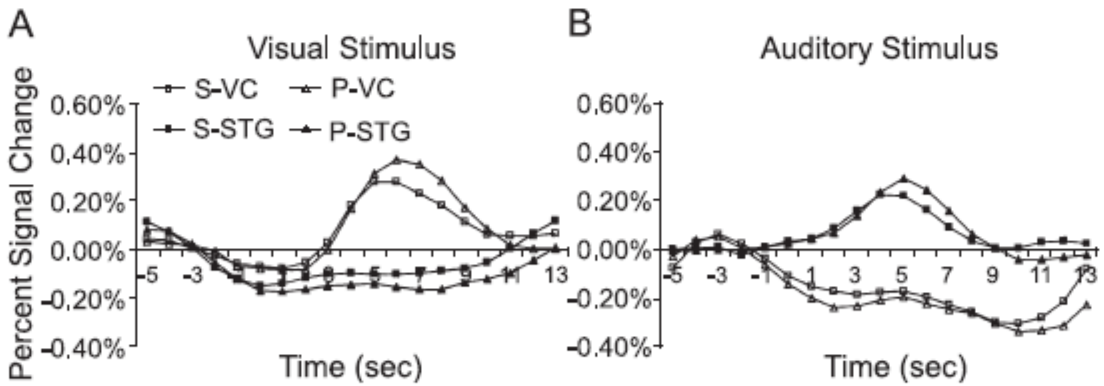


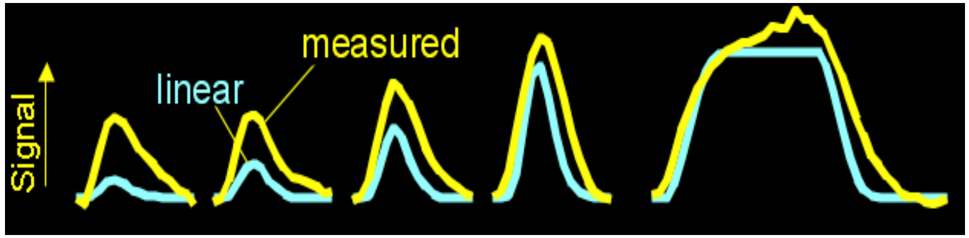
Fig. 9. (A) Percent signal change evoked by single and paired visual stimulus presentations in visual and auditory cortical regions. (B) The HDRs evoked by auditory stimuli in VC and STG (S-VC, single stimulus condition in VC; P-VC, paired stimuli condition in VC; S-STG, single stimulus condition in STG; P-STG, paired stimulus condition in STG).

R. M. Birn, Z. Saad, P. A. Bandettini, Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response. *NeuroImage*, **14**: 817-826, (2001).

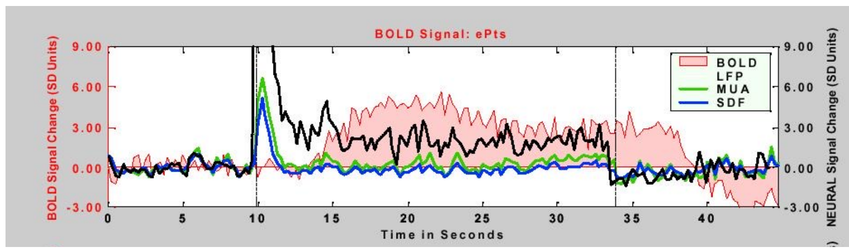
R.M. Birn, P. A. Bandettini, The effect of stimulus duty cycle and "off" duration on BOLD response linearity. *NeuroImage*, **27**, 70-82 (2005)

A. S. Tuan, R. M. Birn, P. A. Bandettini, G. M. Boynton, Differential MEG and fMRI responses to visual stimulation onset rate (in preparation)

Increases: linearity



R. M. Birn, (2001) NeuroImage, 14: 817-826.



Logothetis et al. (2001) Nature, 412, 150-157.

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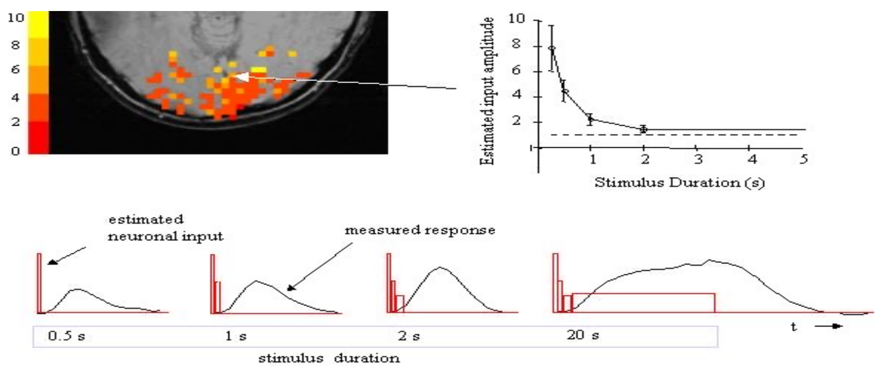
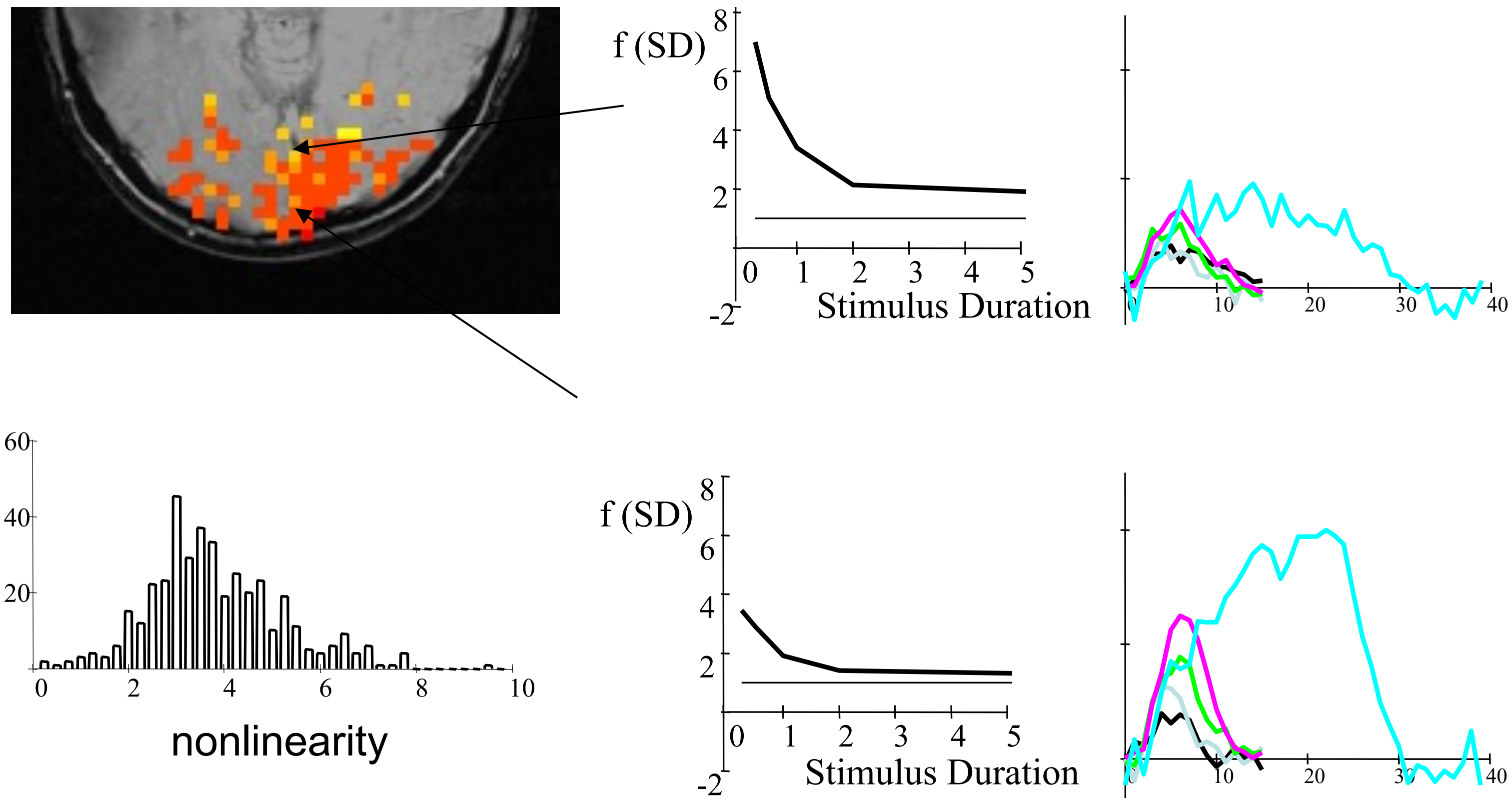


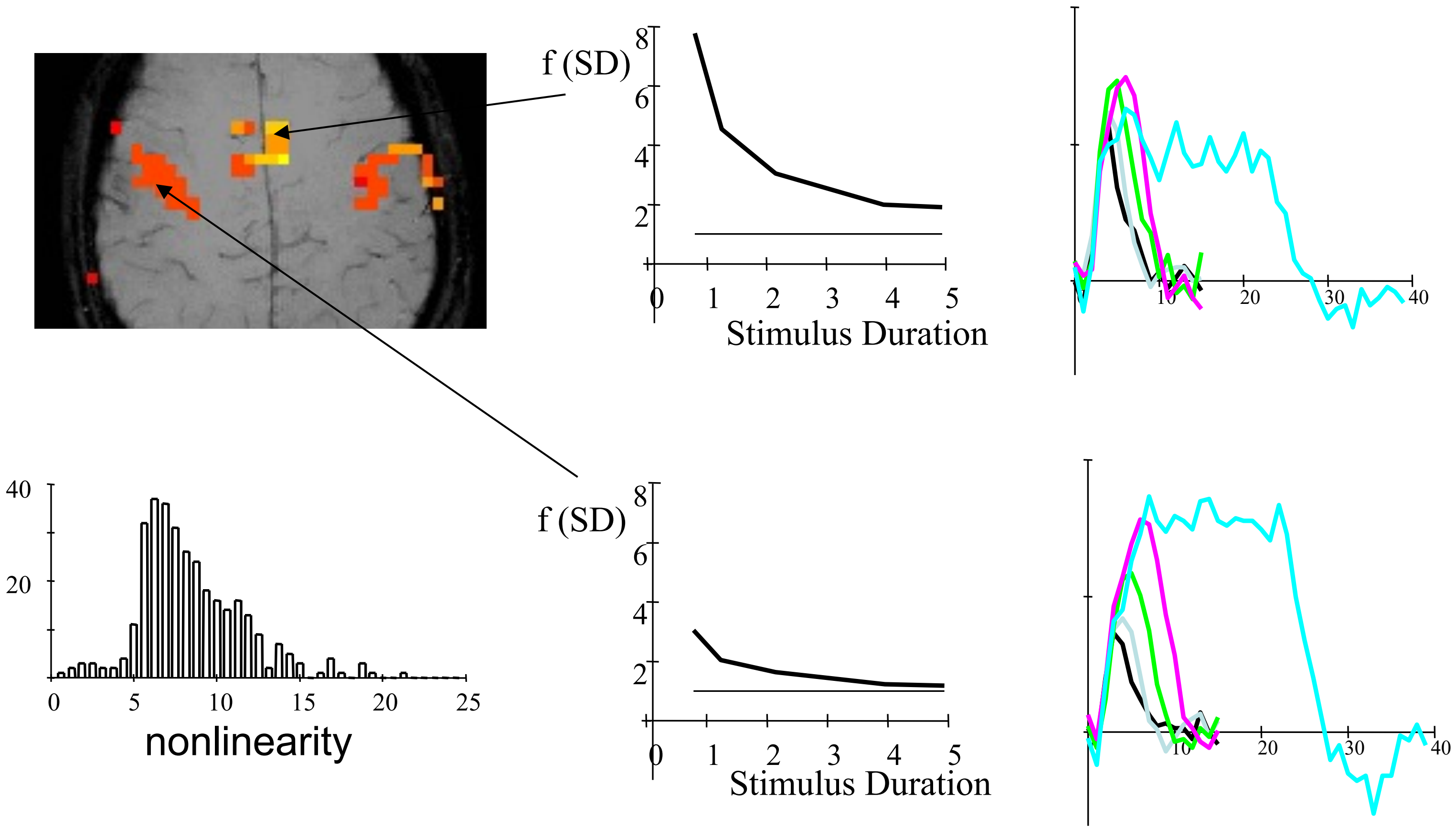
P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

Nonlinearity – visual task



R.M. Birn, et al. Neuroimage 14, 817-26, 2001

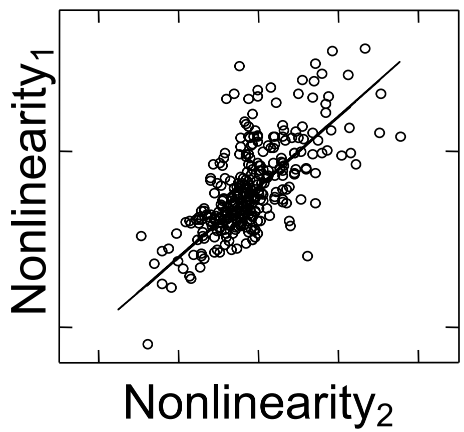
Nonlinearity – motor task

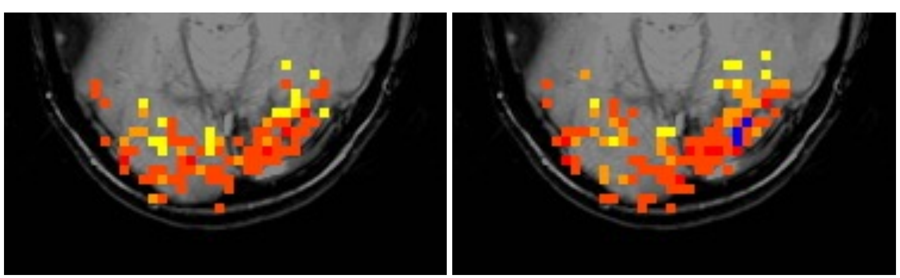


R.M. Birn, et al. Neuroimage 14, 817-26, 2001

Reproducibility

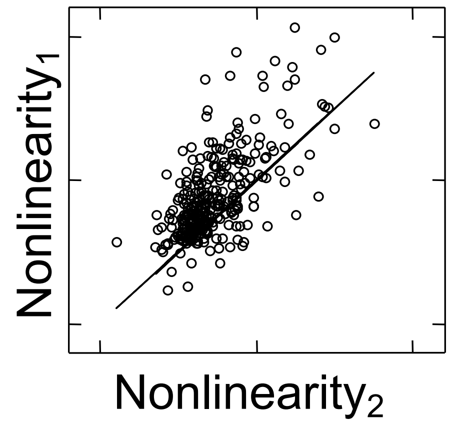
Visual task

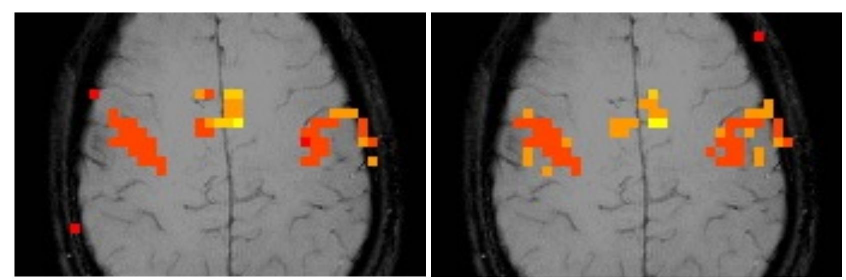




Experiment 1 Experiment 2

Motor task





Experiment 1 Experiment 2

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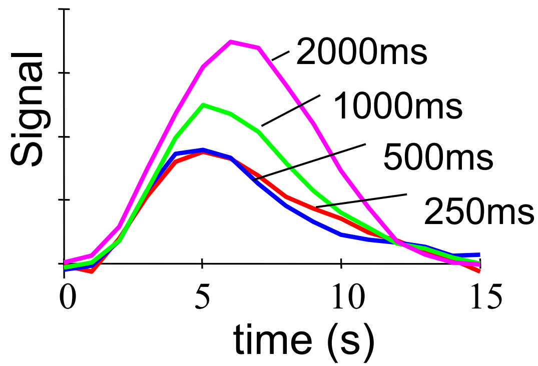
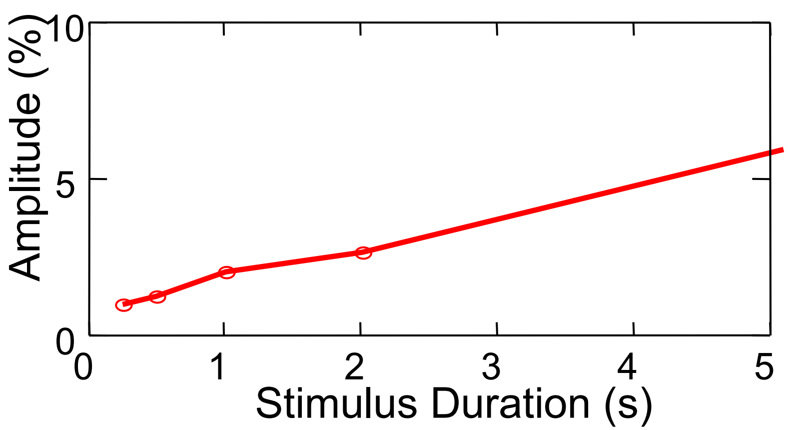
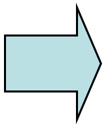
Estimated neuronal input

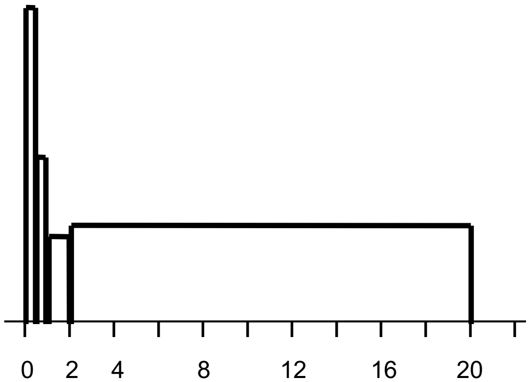
Contrast Reversing Checkerboard





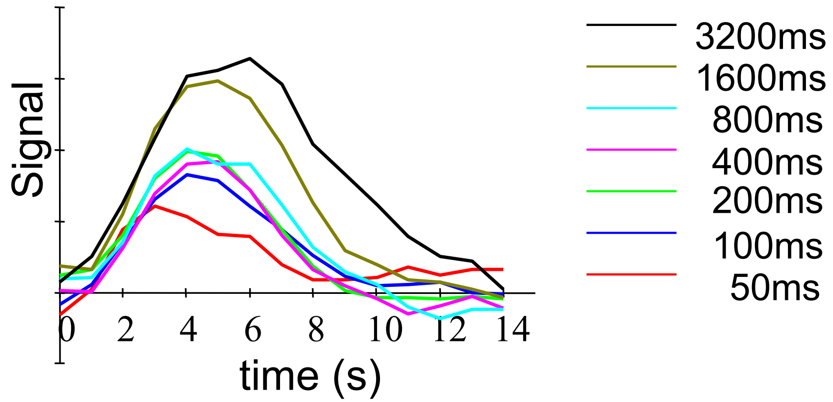


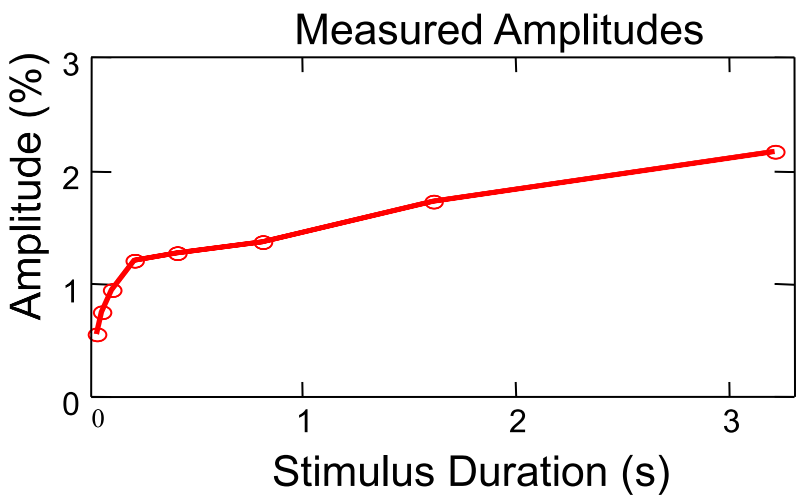
Estimated Neuronal Activity

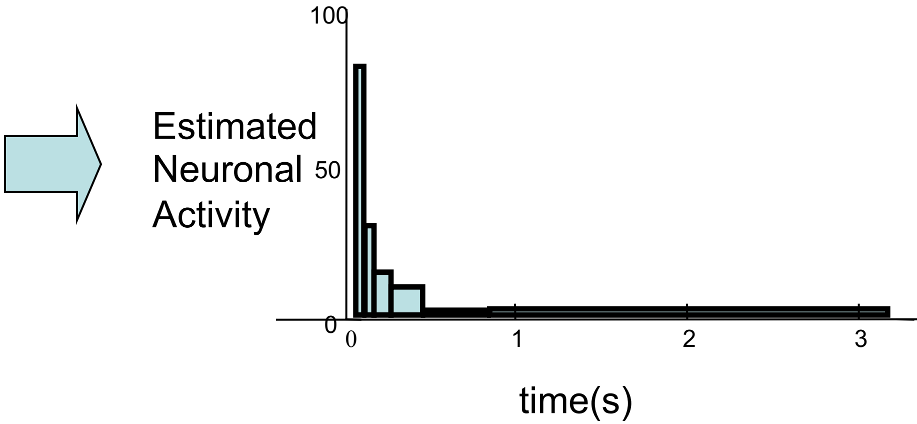


Estimated neuronal input

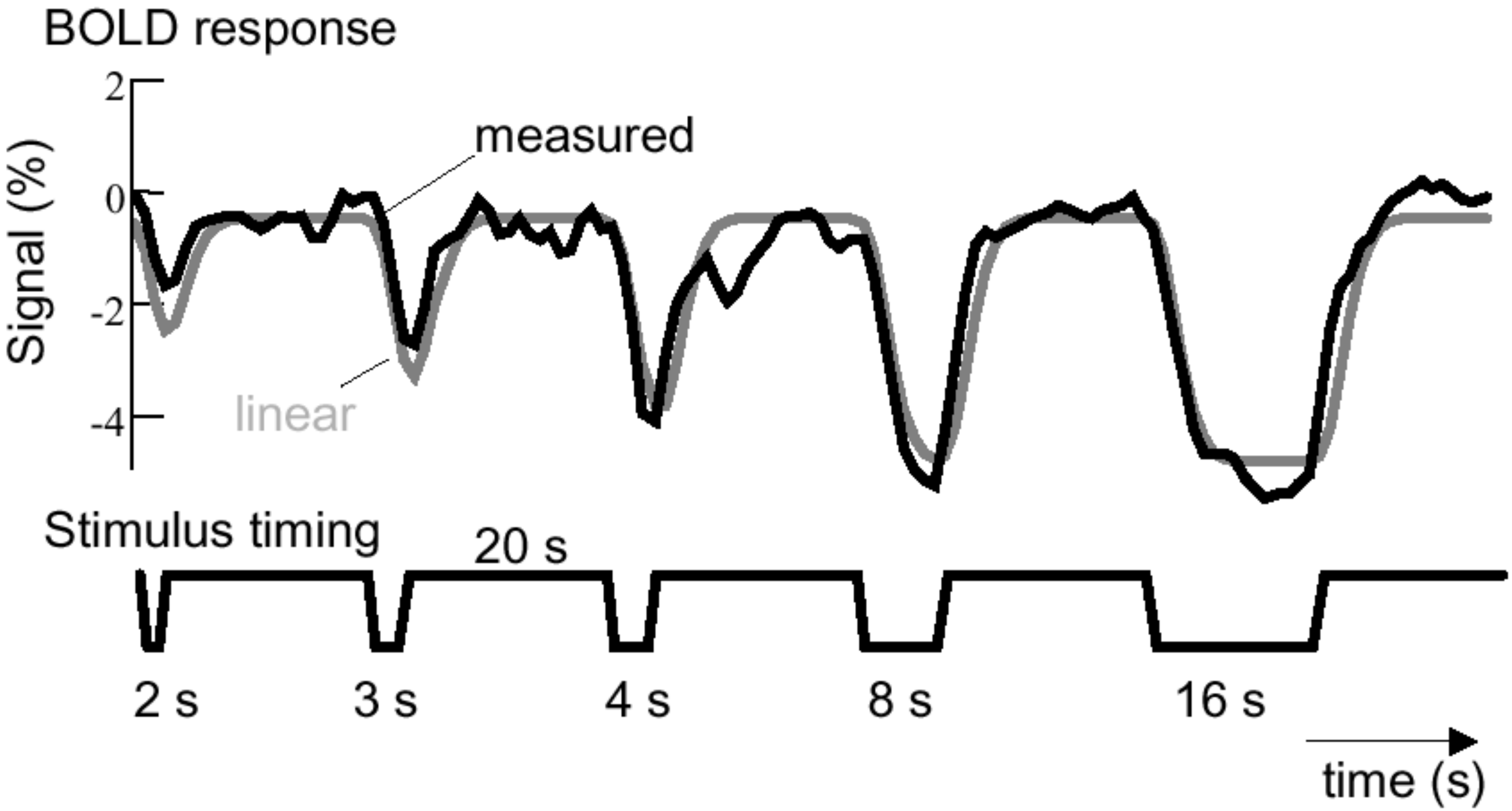
Static Grating



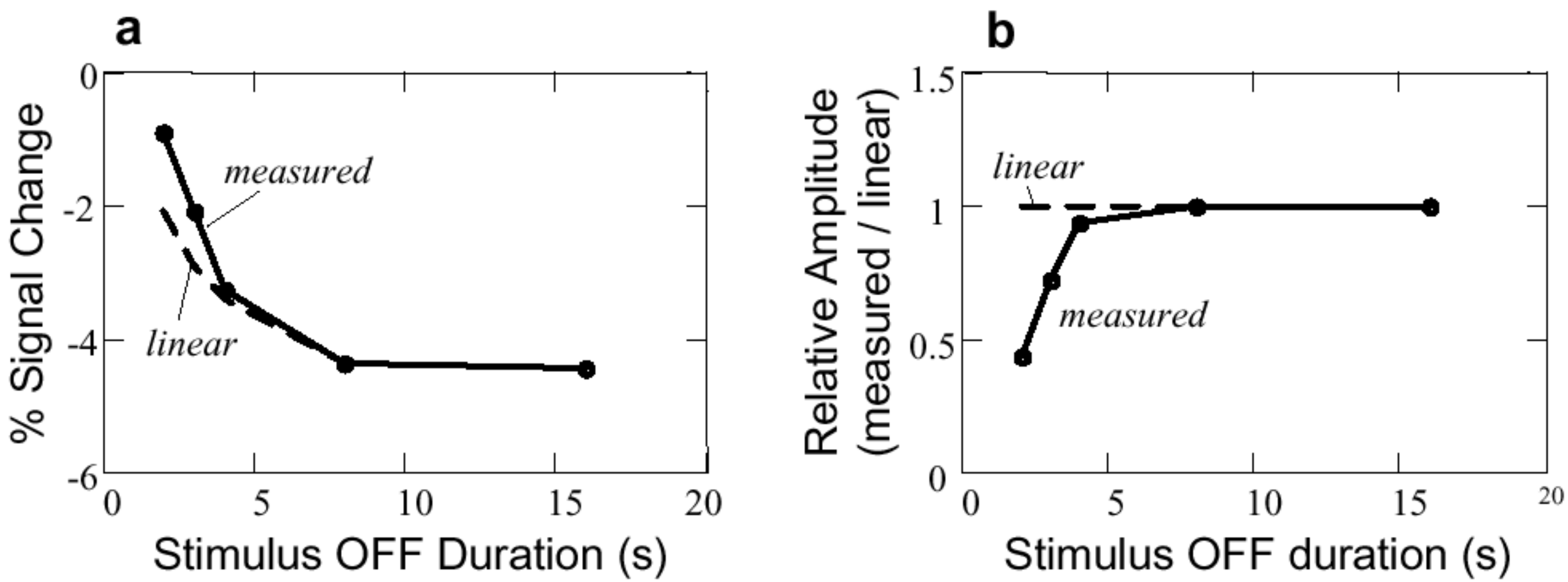




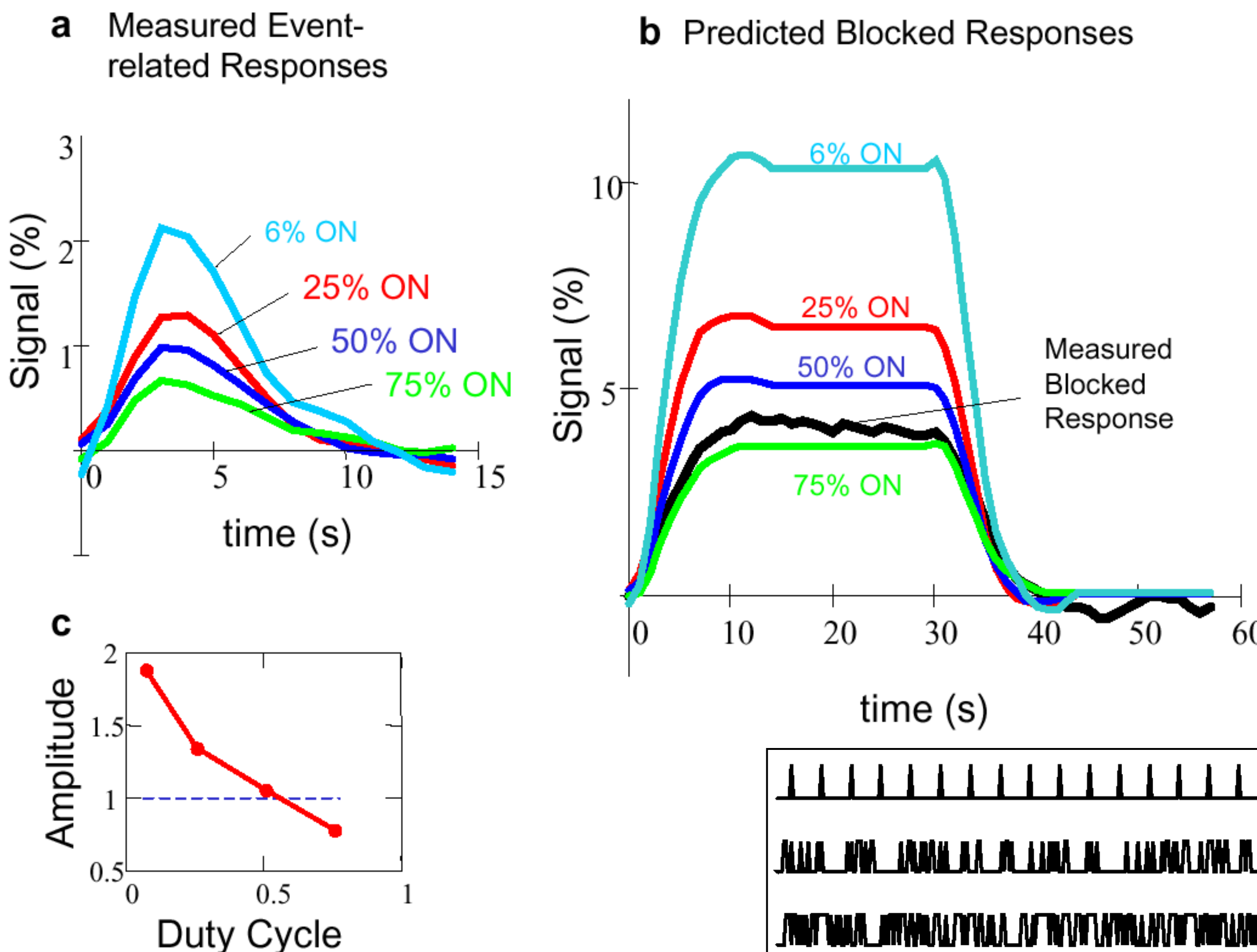
Decreases: linearity

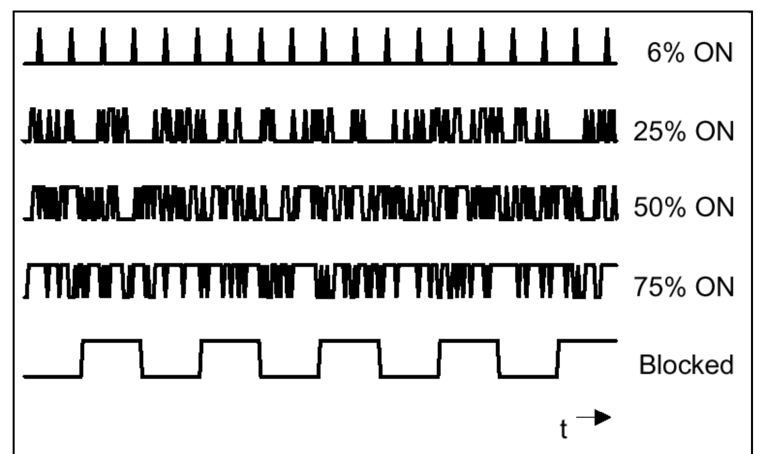


R.M. Birn, P. A. Bandettini. *NeuroImage*,


a
0
-2
-4
-6
% Signal Change
measured
linear
0
5
10
15
20
Stimulus OFF Duration (s)
b
1.5
1
0.5
0
Relative Amplitude
(measured / linear)
linear
measured
0
5
10
15
20
Stimulus OFF duration (s)

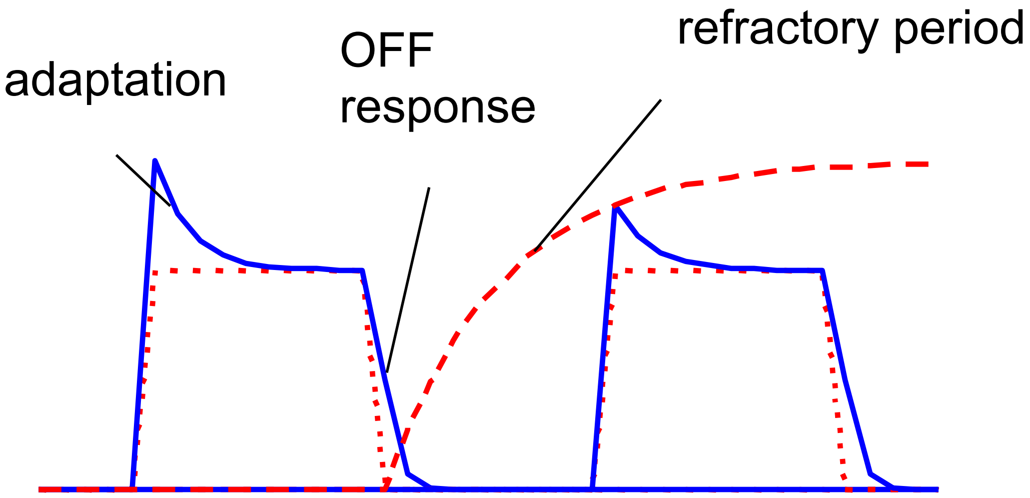
Increases: duty cycle



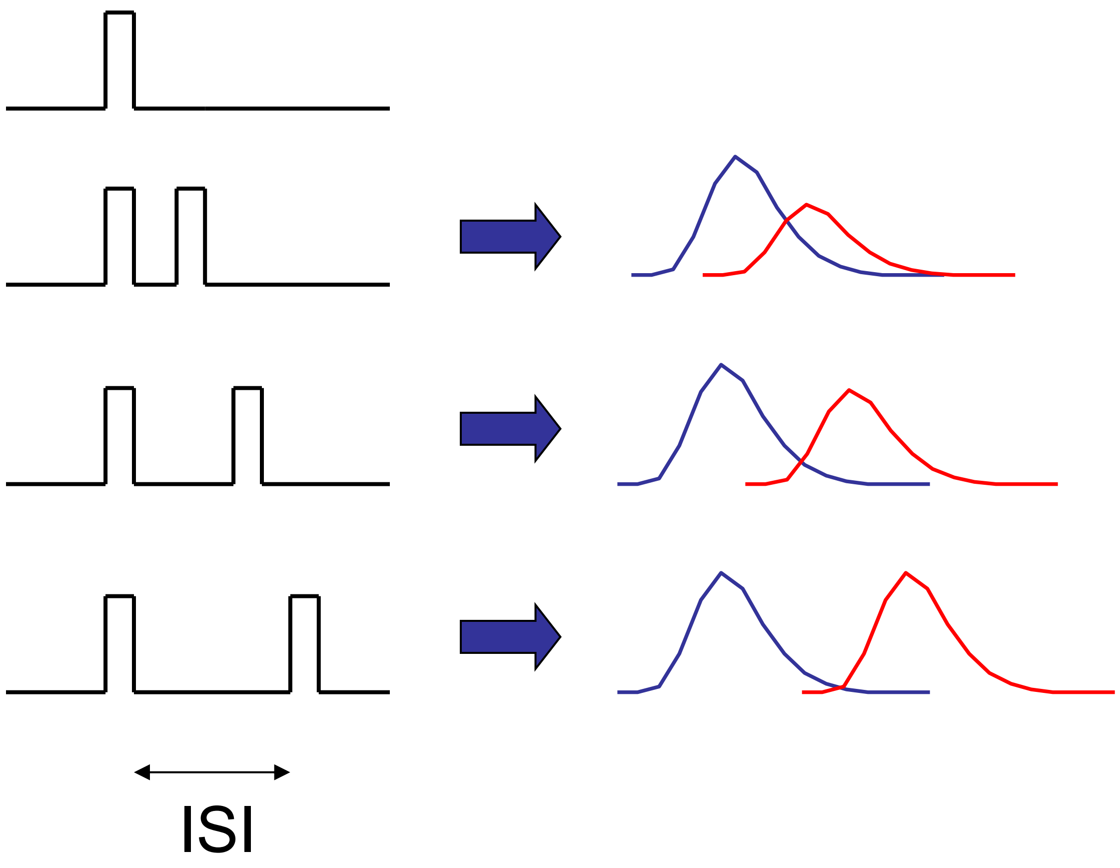


R.M. Birn, P. A. Bandettini, The effect of stimulus duty cycle and "off" duration on BOLD response linearity. *NeuroImage*, **27**, 70-82 (2005)

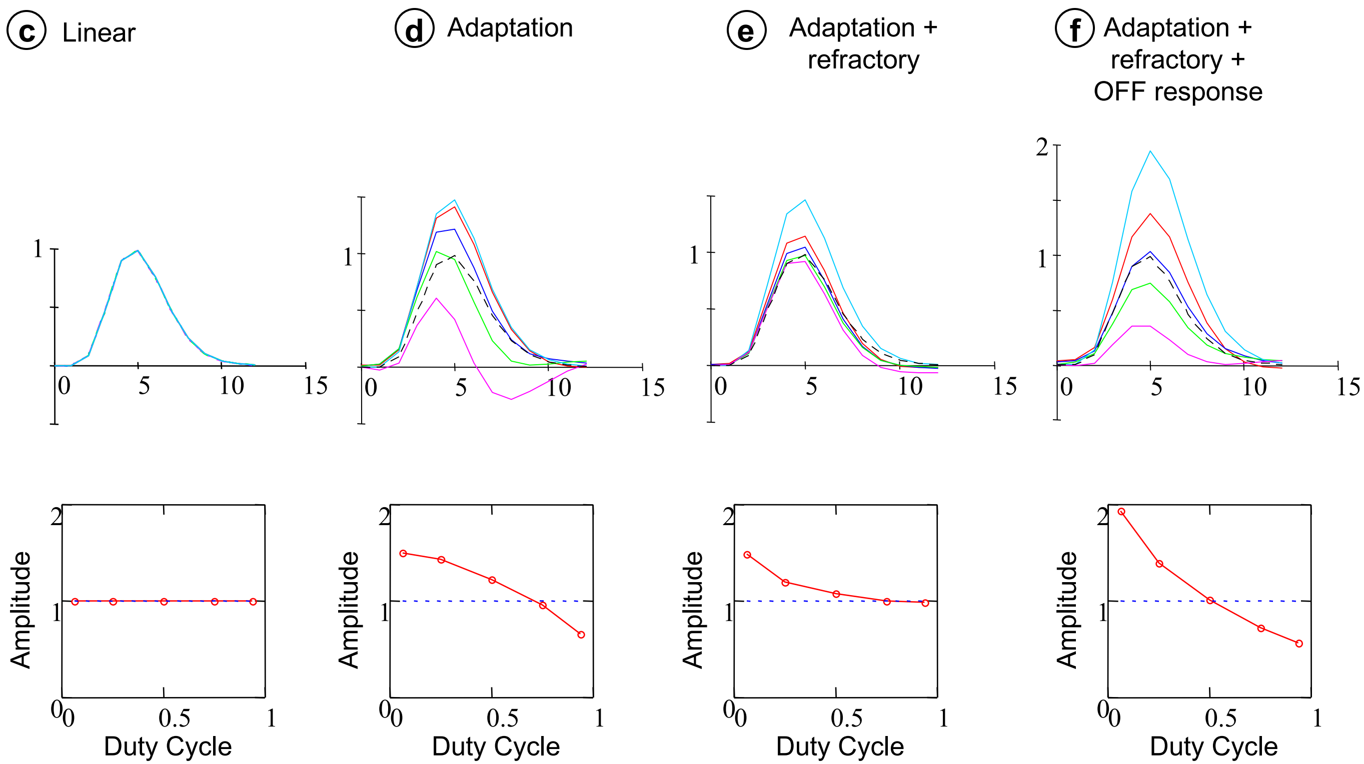
Model – Neuronal effects

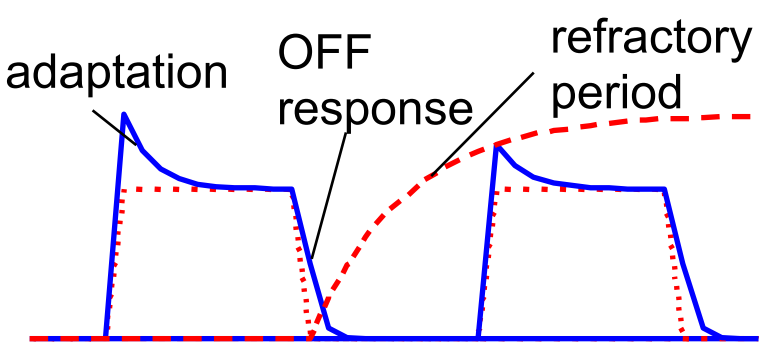


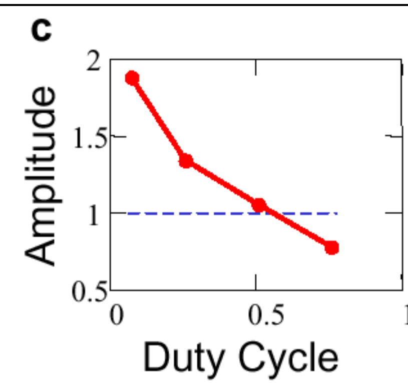
Refractory effect

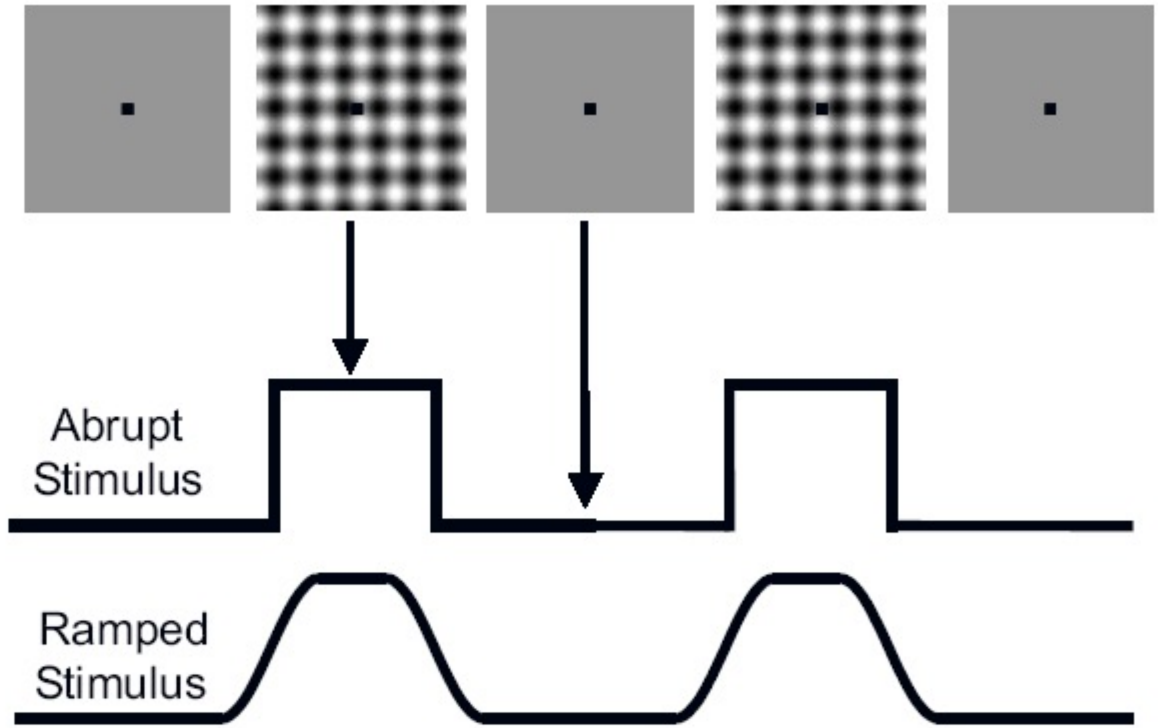


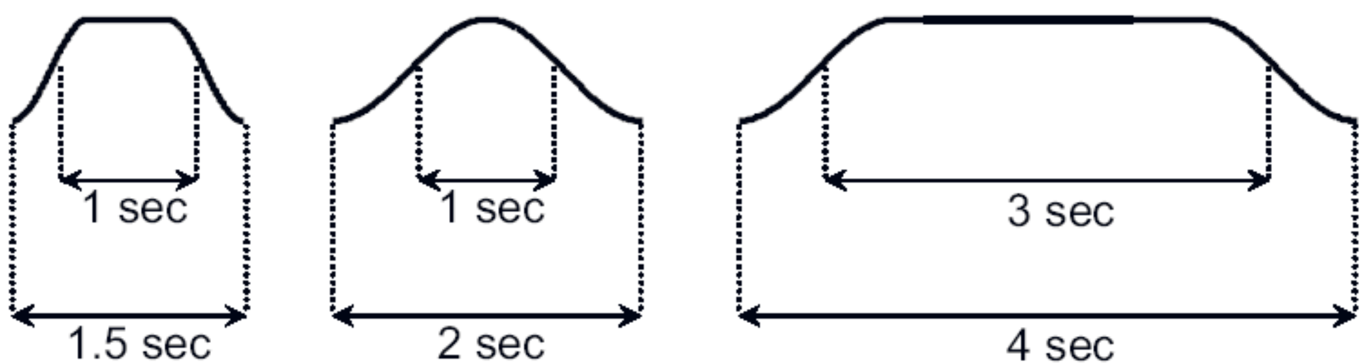
Simulation results – Neuronal effects

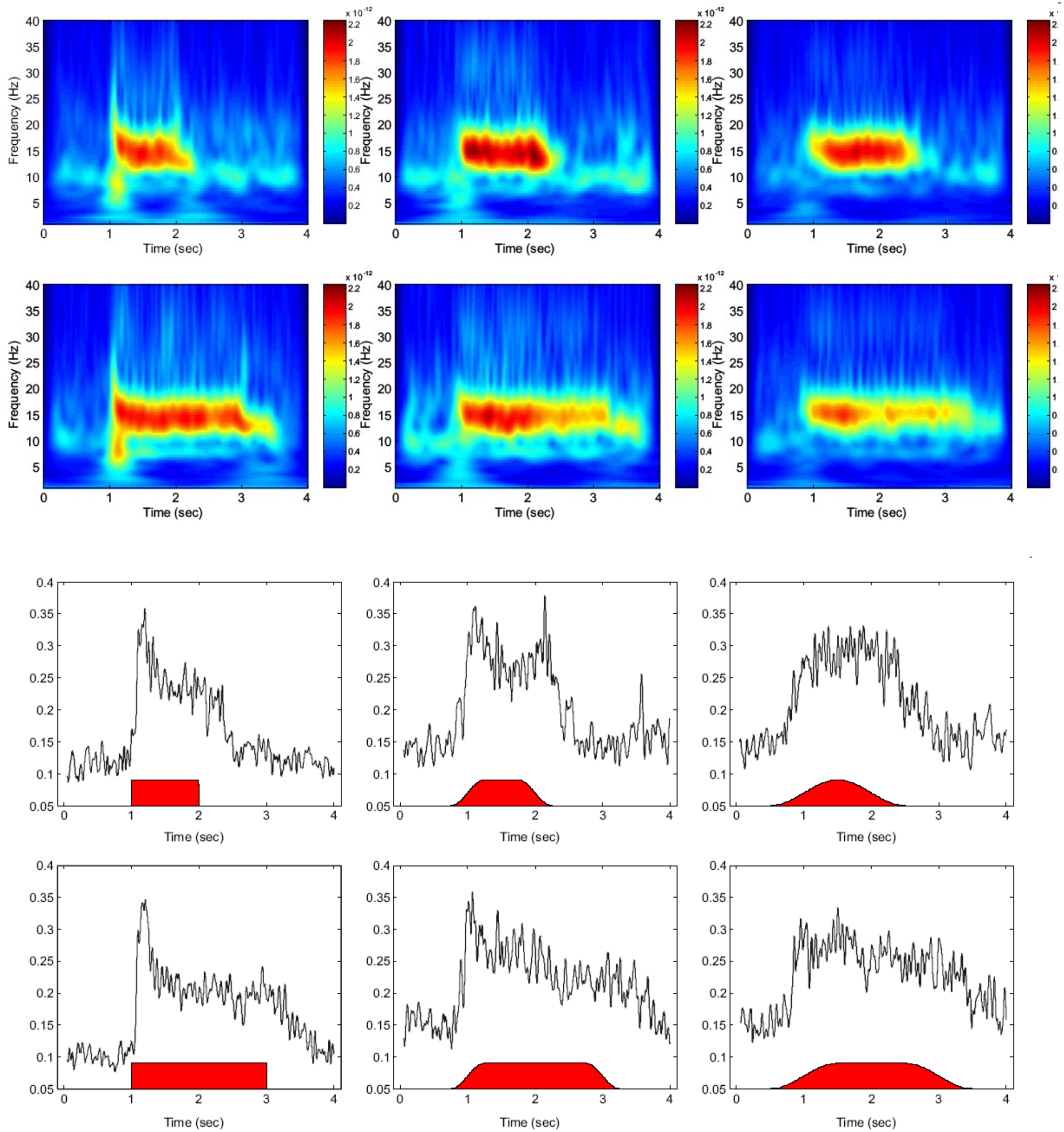


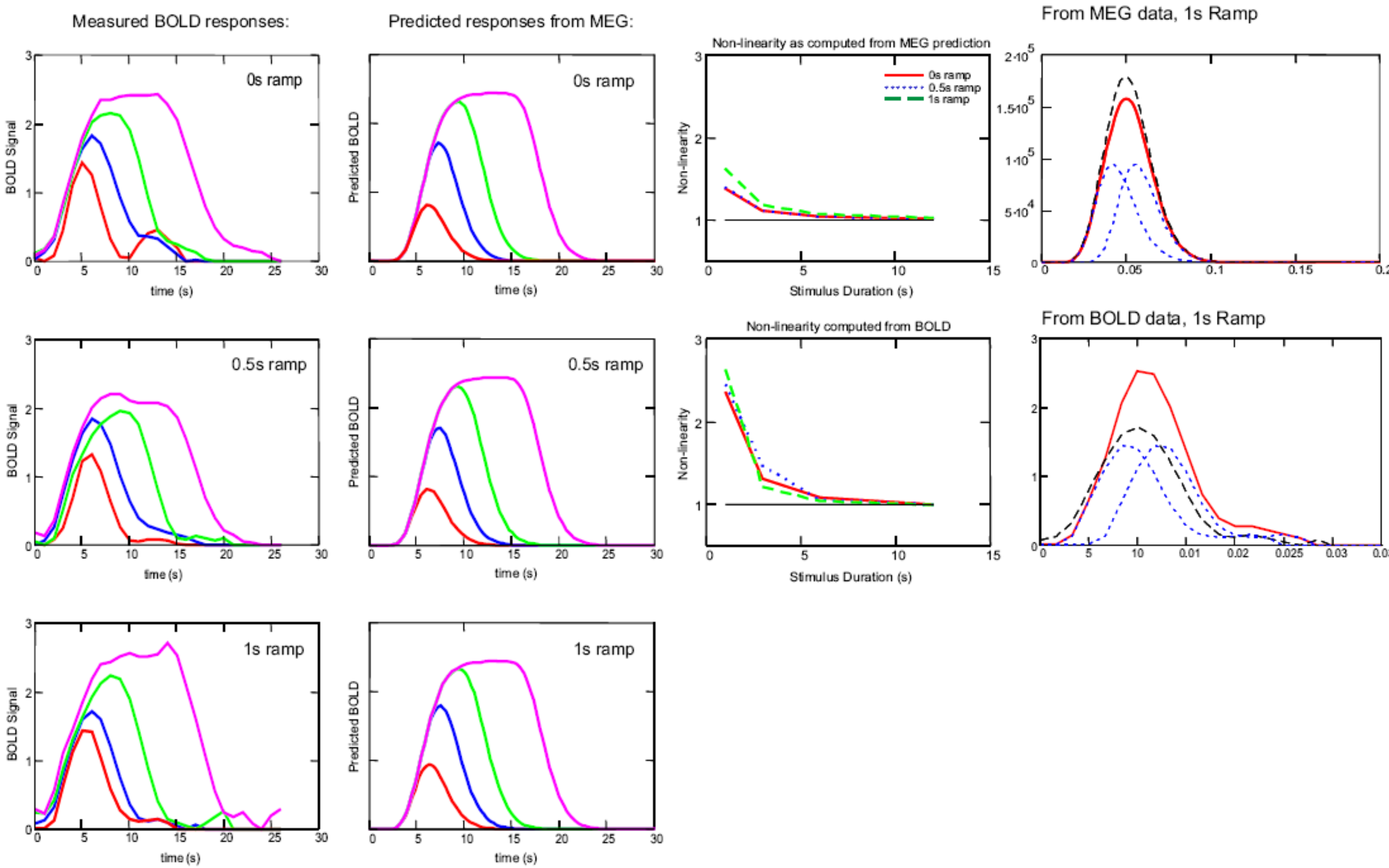





Abrupt
Stimulus
Ramped
Stimulus


1 sec
1.5 sec
1 sec
2 sec
3 sec
4 sec


Frequency (Hz)
Time (sec)
x 10^-12



Measured BOLD responses:
Predicted responses from MEG:
Non-linearity as computed from MEG prediction
From MEG data, 1s Ramp
0s ramp
0.5s ramp
1s ramp
BOLD Signal
Predicted BOLD
Non-linearity
time (s)
Stimulus Duration (s)
Non-linearity computed from BOLD
From BOLD data, 1s Ramp

An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds

Seiji Ogawa[†‡], Tso-Ming Lee[†], Ray Stepnoski[†], Wei Chen[§], Xiao-Hong Zhu[§], and Kamil Ugurbil[§]

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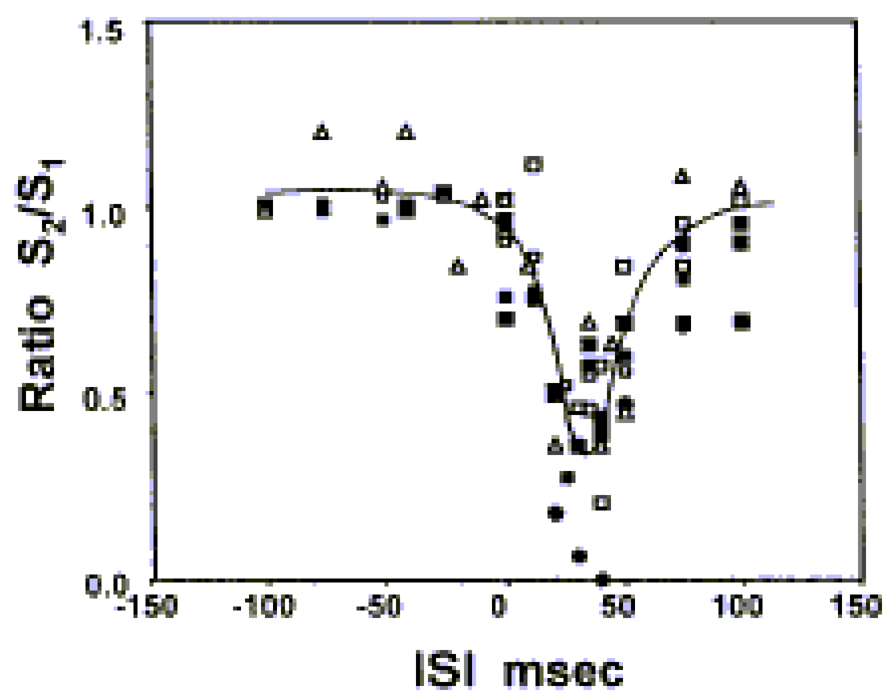
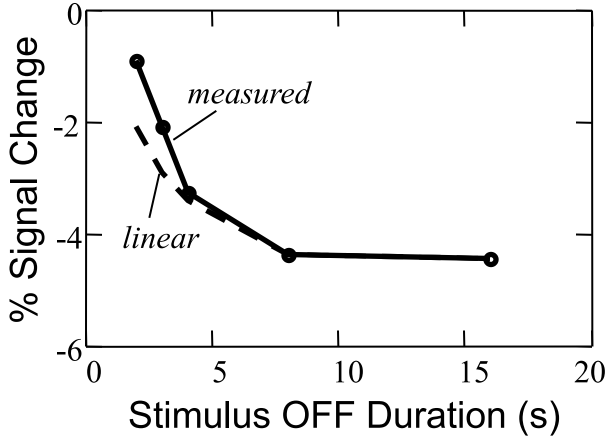


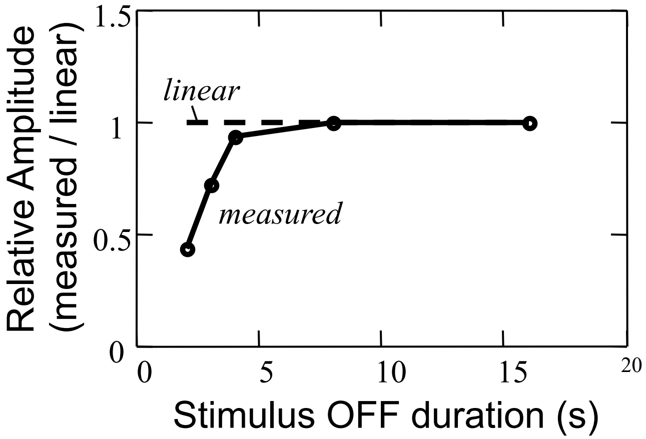
BOLD response amplitude and linearity

to different stimulus OFF periods

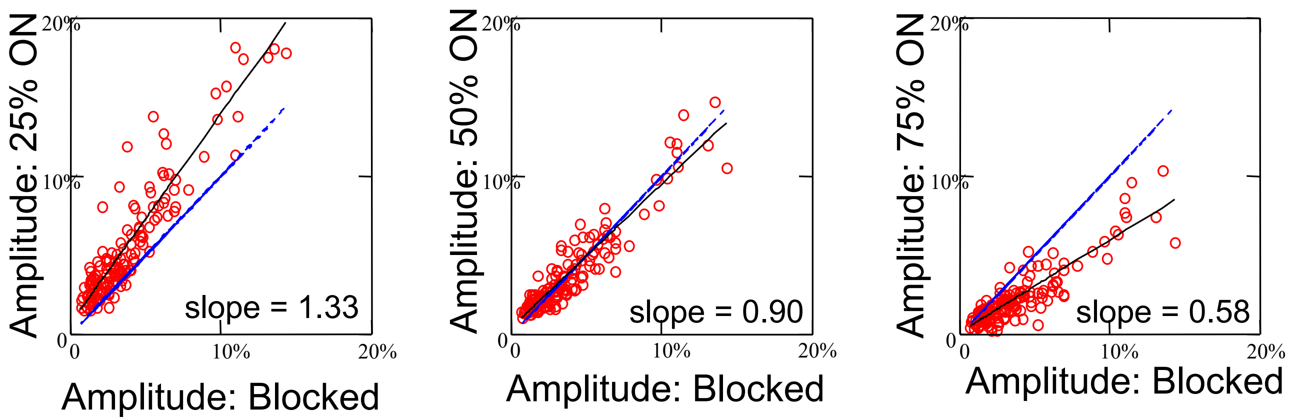
Amplitude



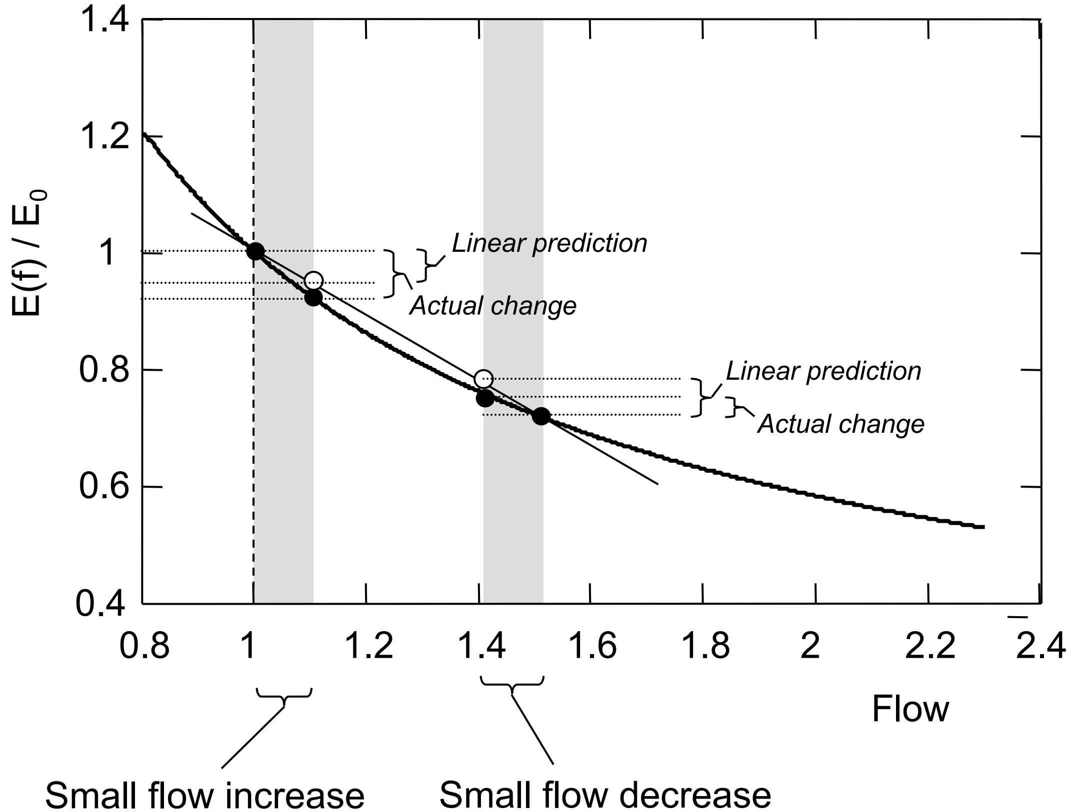
Linearity



BOLD response to different stimulus duty cycles

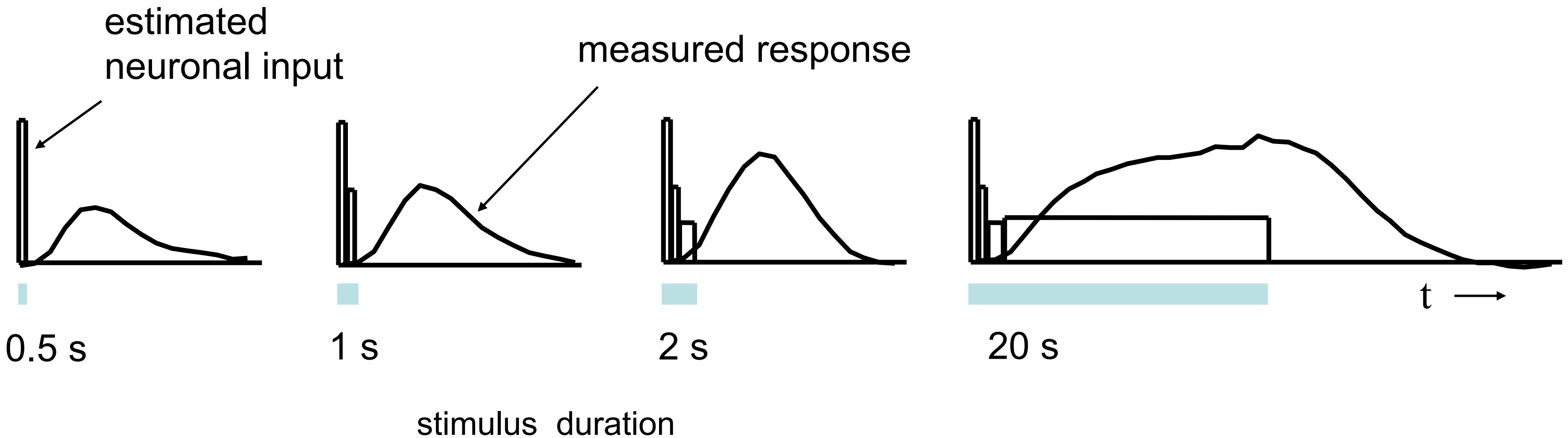


Nonlinearity of oxygen extraction, E(f)



Estimate Neuronal Input from BOLD fMRI

Contrast-reversing Checkerboard



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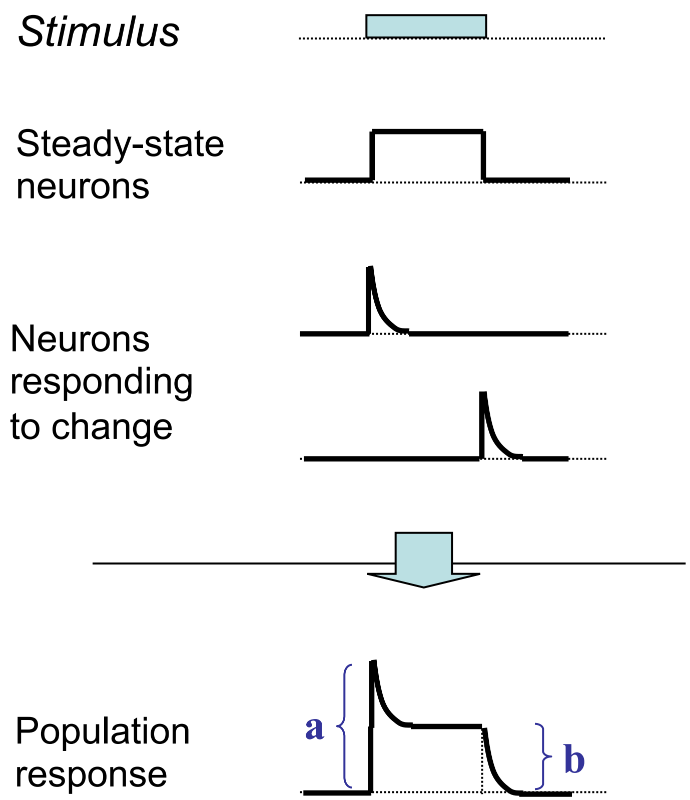
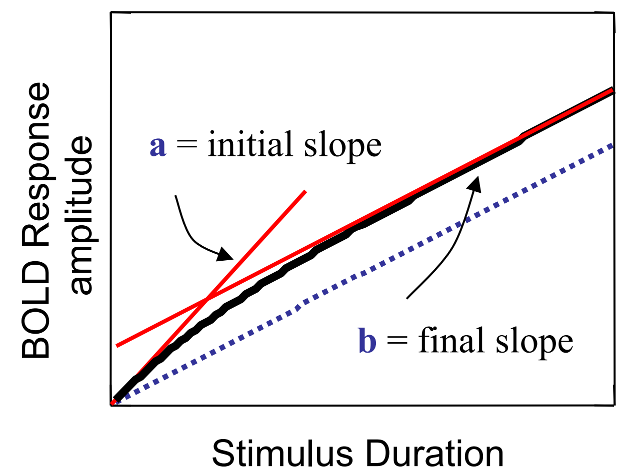
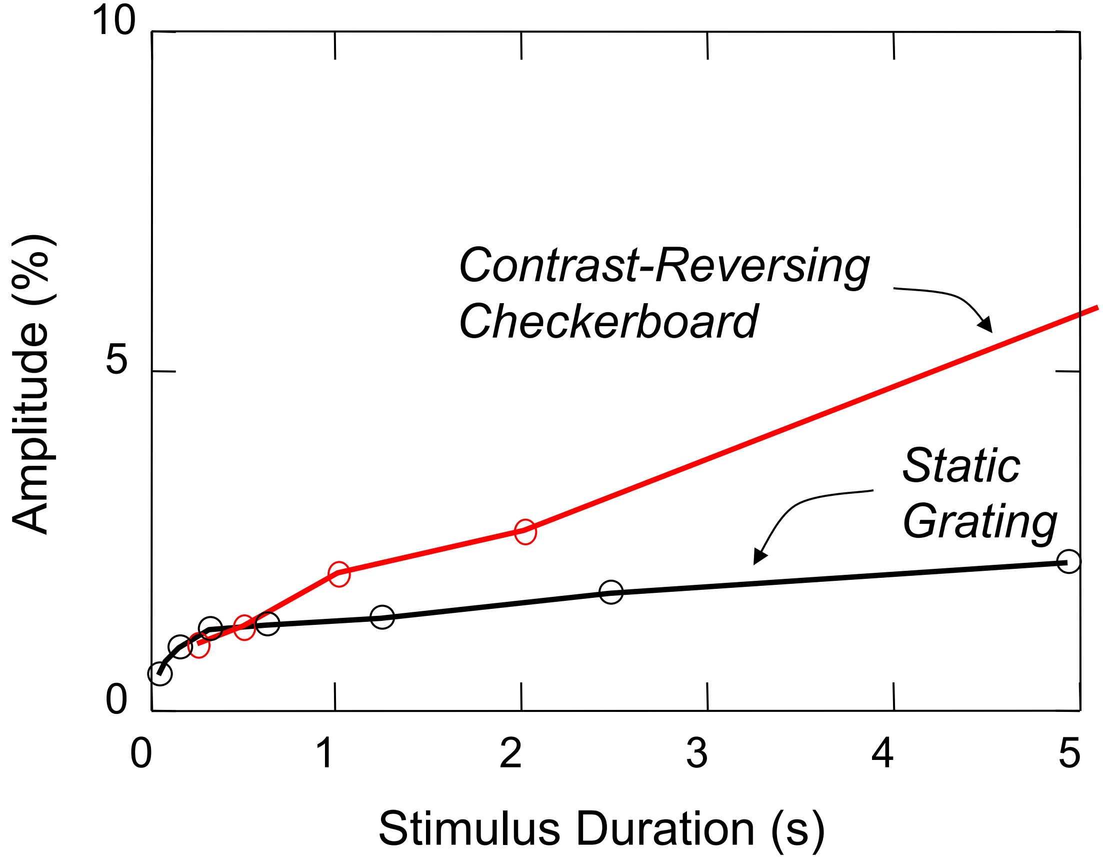
BOLD response to neuronal transients





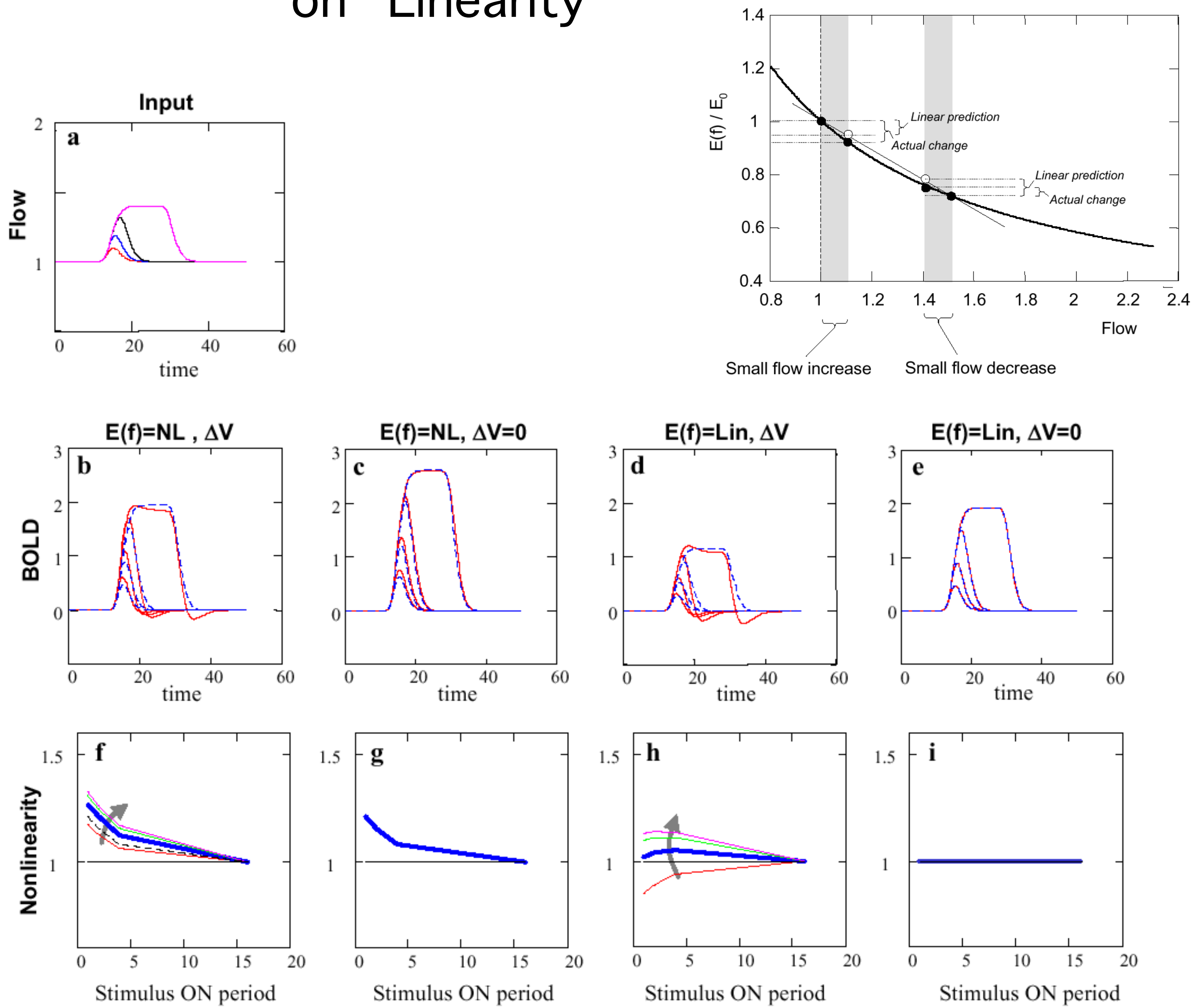
CR-Checkerboard vs. Static Grating



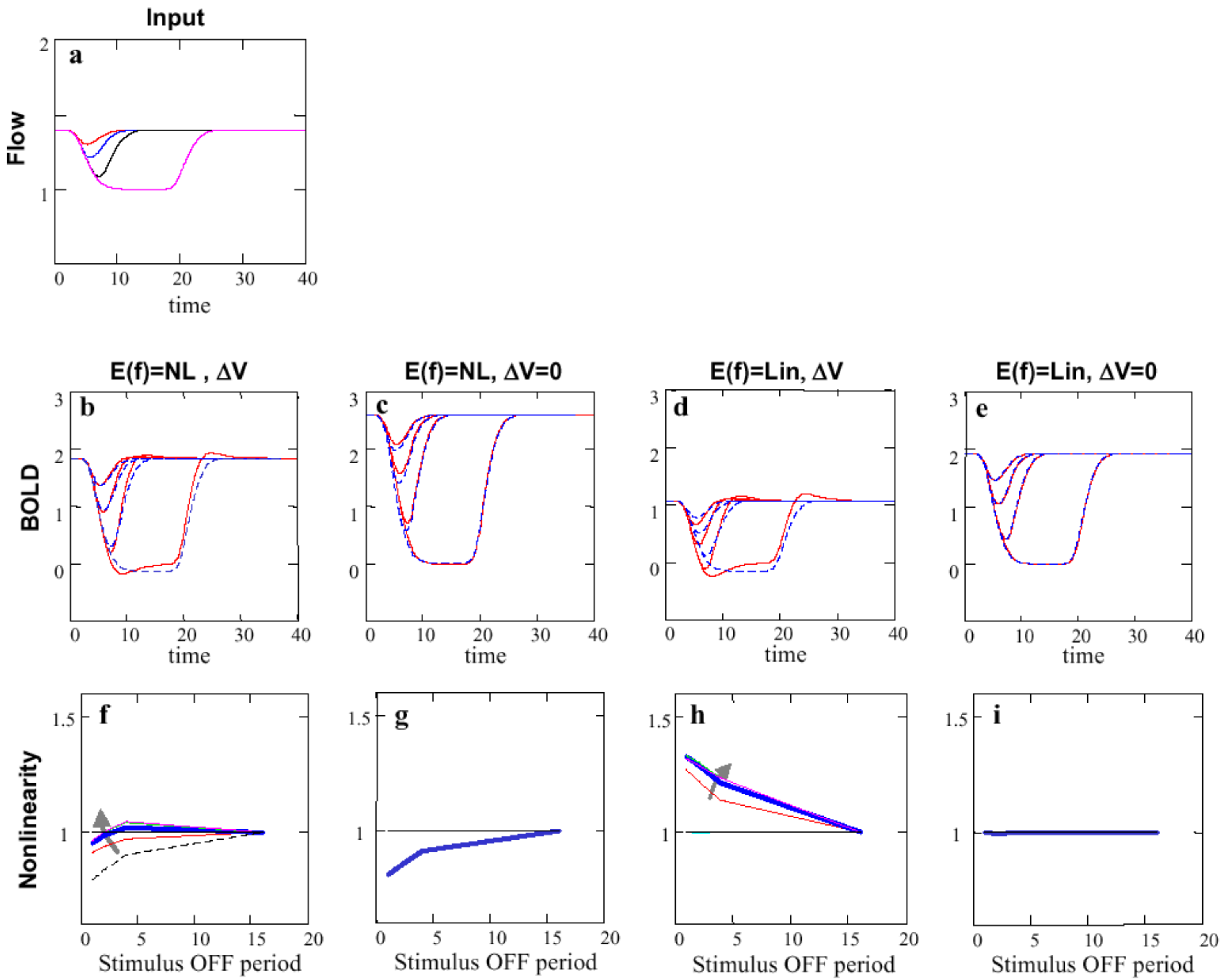
Balloon Model Parameters

Parameter	Description	Default Value	Range Evaluated
E_0	*Resting oxygen extraction fraction*	0.4	0.3 – 0.6
v_0	*Resting blood volume fraction*	0.03	0.03 – 0.18
f_0	*Resting relative blood flow*	0.01 s^{-1}	0.01 s – 0.16 s
Δf	*Fractional blood flow change*	0.4	–
α	*Steady-state flow-volume relationship*	0.4	0.25 – 1.0
τ_{MTT}	*Blood mean transit time (v_0/f_0)*	3 s	1.1 s – 18 s
τ_+	*Viscoelastic time constant (inflation)*	20 s	10 s – 40 s
τ_-	*Viscoelastic time constant (deflation)*	20 s	10 s – 40 s
a_1	*Weight for deoxyHb change*	3.7	2.8 – 5.6
a_2	*Weight for blood volume change*	1.1	0.7 – 1.9

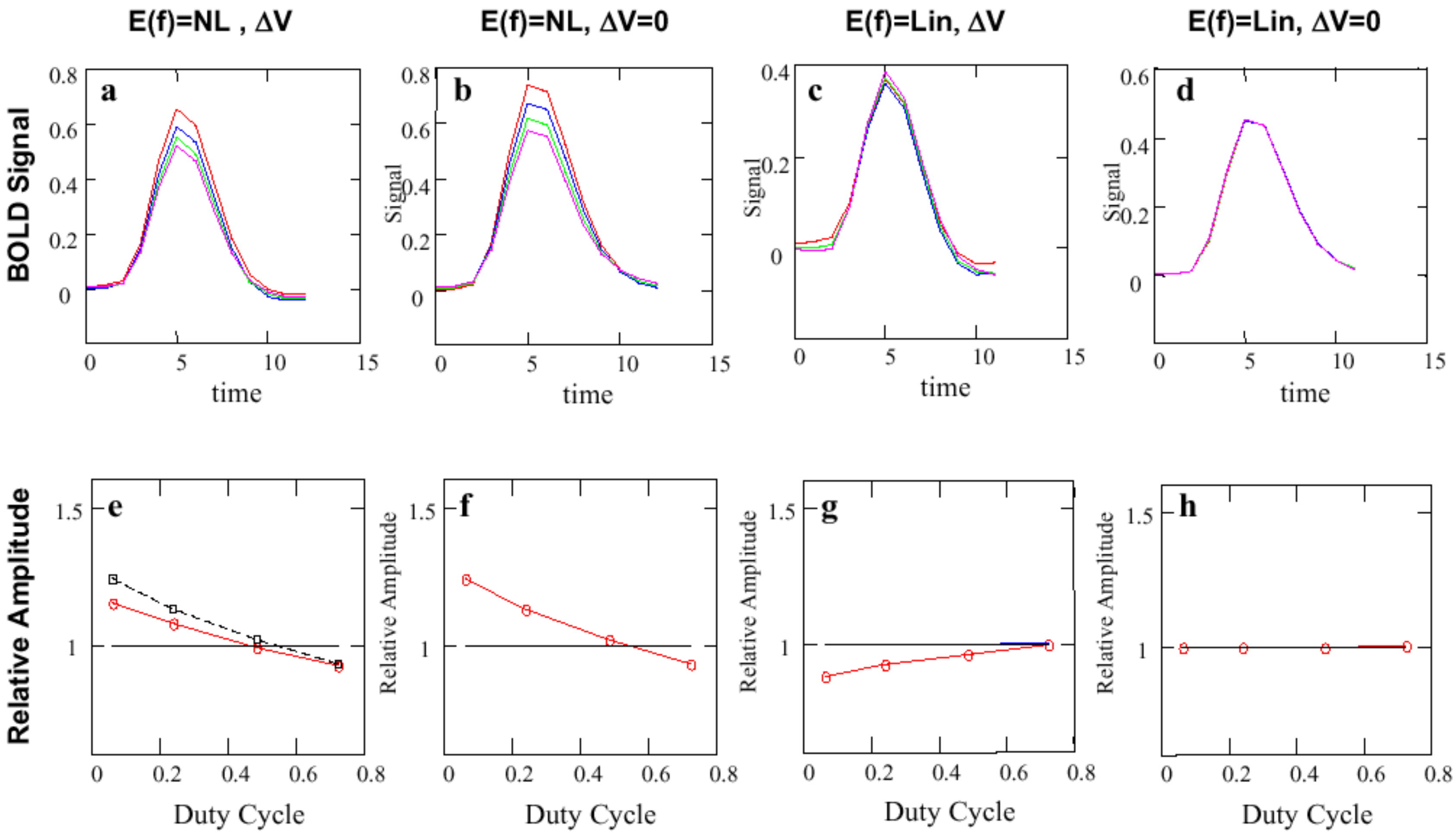
“on” Linearity



“off” linearity

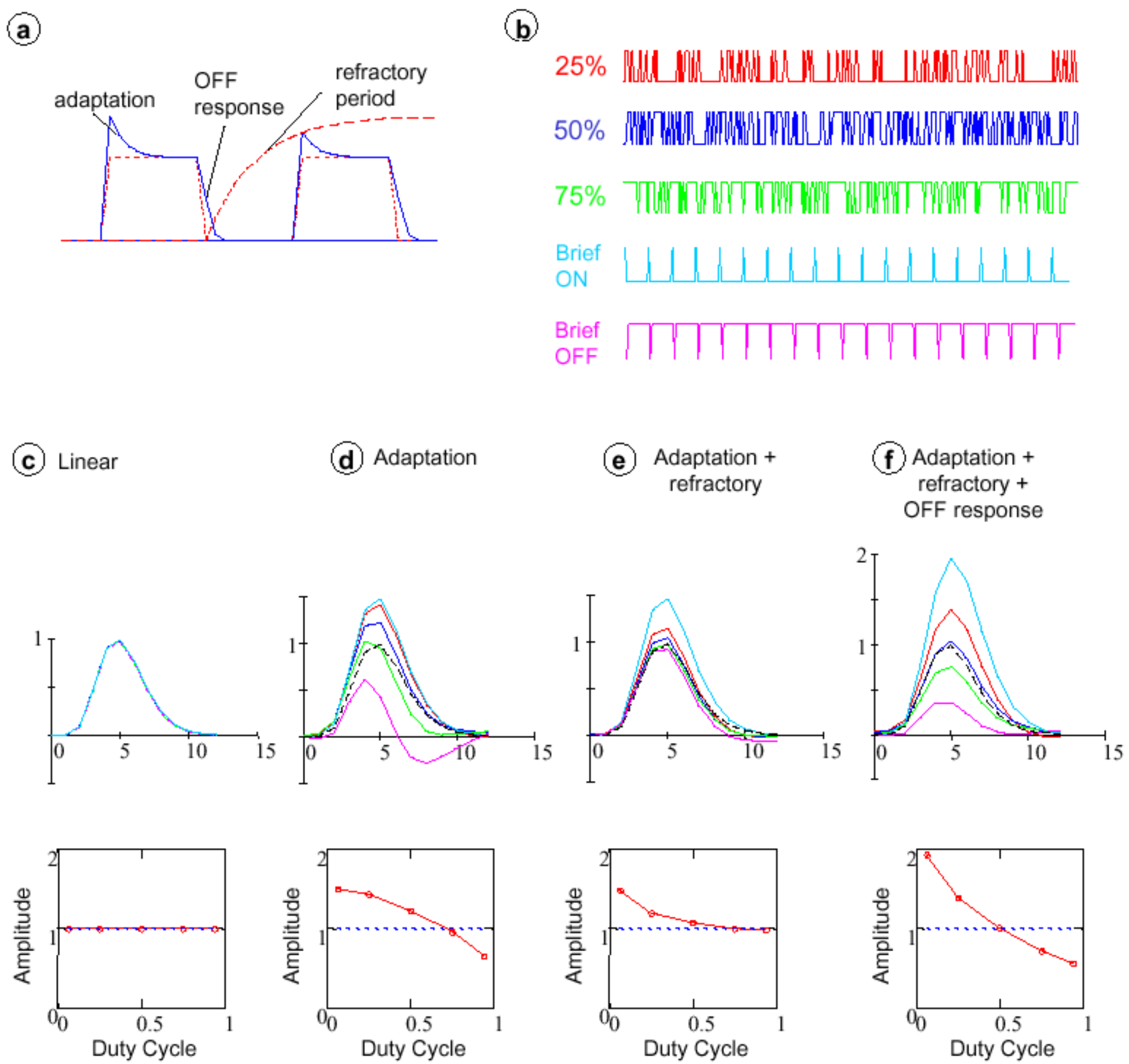


Duty Cycle



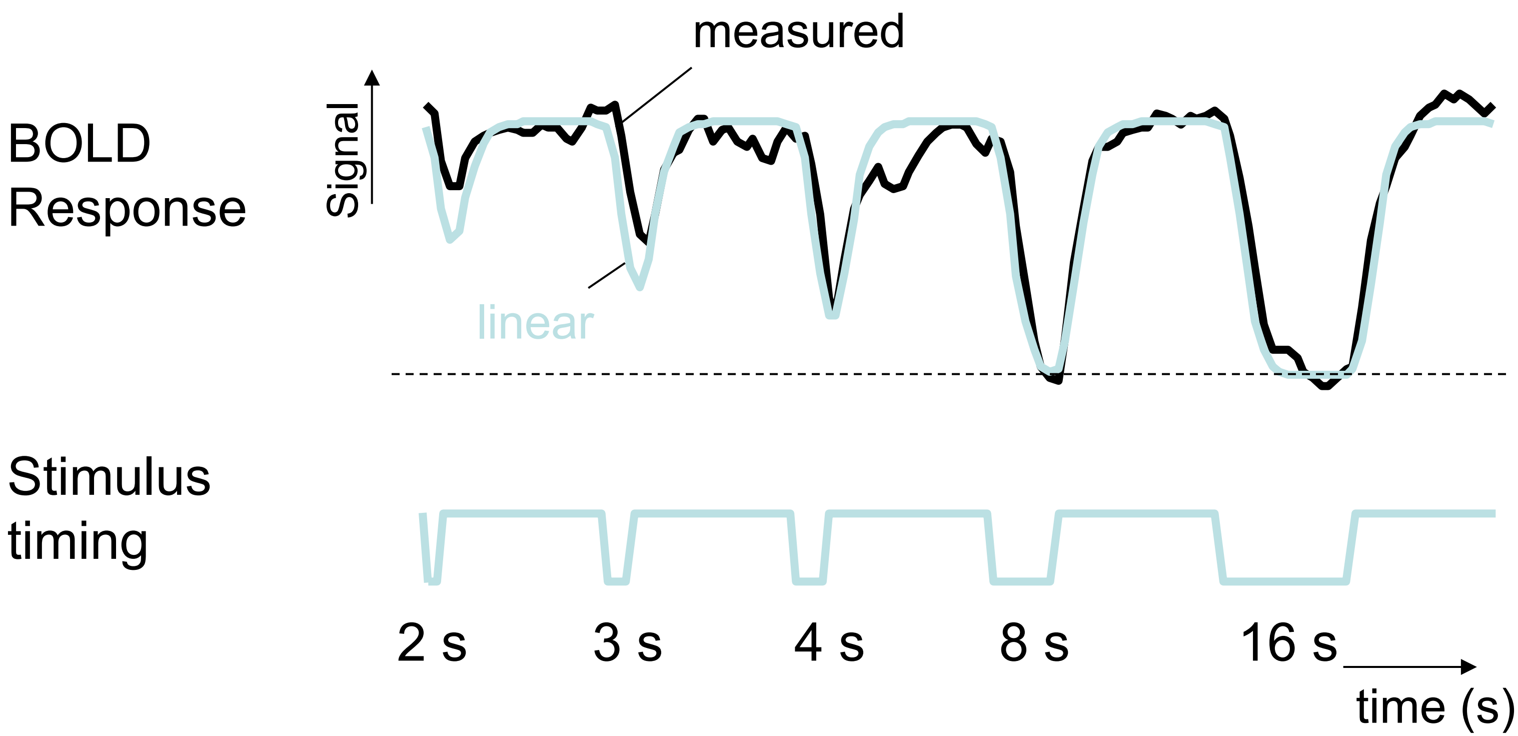
E(f)=NL , ΔV
E(f)=NL, ΔV=0
E(f)=Lin, ΔV
E(f)=Lin, ΔV=0
BOLD Signal
Signal
time
Relative Amplitude
Duty Cycle
a
b
c
d
e
f
g
h

Neuronal effects to explain duty cycle effects



Different stimulus "OFF" periods

R.M. Birn, et al. Proc. ISMRM, 2001.

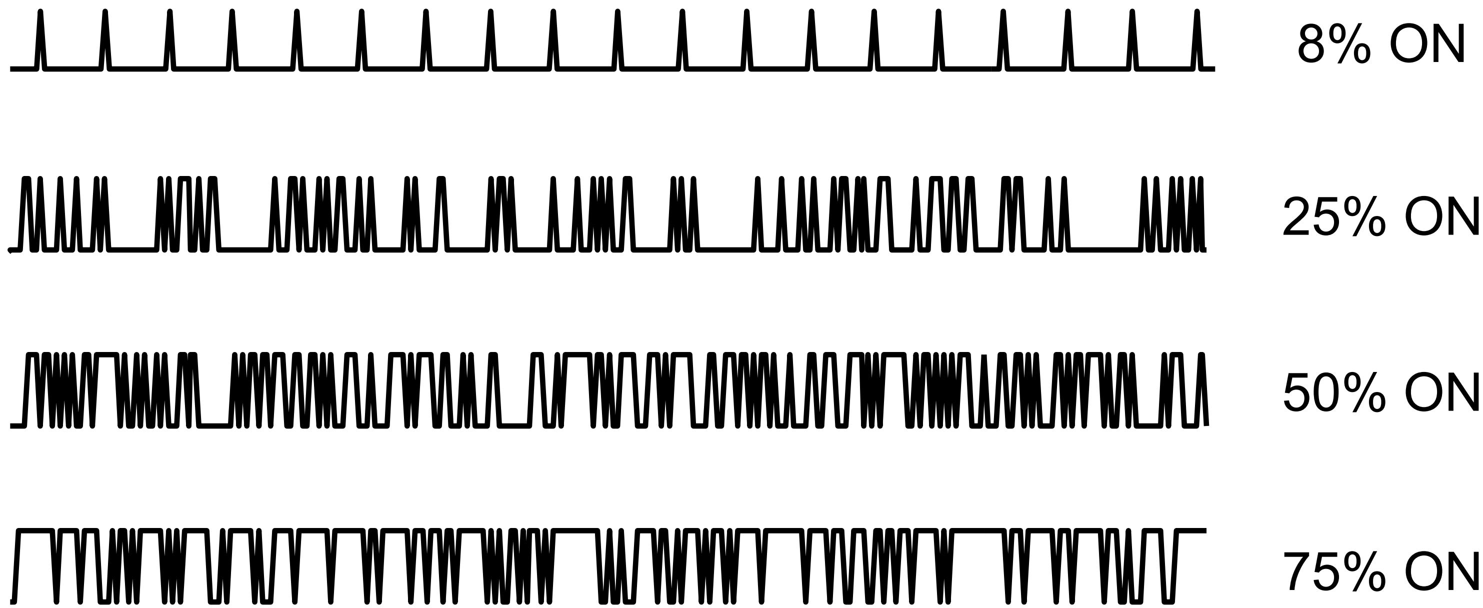


Brief stimulus OFF periods produce smaller decreases than expected

Varying “ON” and “OFF” periods

R.M. Birn, et al. Proc. OHBM 2001.

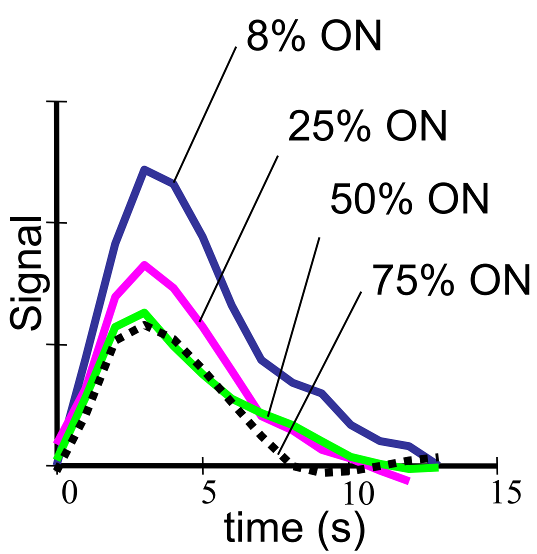
- *Rapid event-related design with varying ISI*



Varying "ON" and "OFF" periods

R.M. Birn, et al. Proc. OHBM 2001.

Estimated Impulse Response



Predicted Responses to 20 s stimulation