Cortical dynamics in anesthetized and behaving subjects

Amiram Grinvald

Rina Hildesheim

Yuval Toledo

Nitzan Mushketel

Tzion Eliahu

Chen Ben-Yaacov

Shlomith Kaplansky

Alexander Sterkin

Irena Bronshtein

David B. Omer

Shmuel Naaman

Li-Raz Rom

Tomer Fekete

Einav Oron

Our lab is focused on studies of mechanism underlying cortical functions, integrating classical neurophysiological techniques with Imaging based on Voltage Sensitive Dyes and intrinsic signals.

A. Anesthetized subjects: we study the dynamics of the transitions between different cortical representations. The responses of cortical neurons are significantly influenced by lateral interaction from other neurons in their local network. These interactions are considered to have a functional roll in cortical processing. Here we used optical imaging of voltage sensitive dye (VSDI) together with multi unit recordings in the primary visual cortex of the anesthetized cat to study the interaction between groups of neurons that are sensitive to different stimuli attribute. Multi parameter analysis indicates that the transition time (the time required for the cortex to change its state following by stimuli change) shows the most pronounce consistent variation with the conditioning stimuli attribute compared with the other parameters tested. Transition time become longer as the conditions stimuli attribute were characterized by slower drift velocities higher contrast and the optimal spatial frequencies. We confirm that this delay cannot be explained by a simple feed forward model but we have to consider interneuron interaction as an additional delay process. We also observed a columnar specificity of synaptic interactions, expressed as different temporal dynamics for each column during transition, indicating that different mechanisms are active in each column during the transition.

B. Awake Subjects: what happens in our brain when our eyes are closed? Recent findings from Voltage Sensitive Dye Imaging (VSDI) experiments done on anesthetized cats (Grinvald et al., 1991; Arieli et al., 1995; Arieli et al., 1996; Tsodyks et al., 1999; Kenet et al., 2003) indicated that activity in the visual cortex depends not only on the nature of a visual stimulus but also on the state of the cortex at the time of stimulation. Do those spontaneous cortical states have any functional significance, and what that might be? The natural next step is to investigate whether those states occur in the brains of animals that are awake. VSDI was recently implemented also on the awake monkey (Slovin et al., 2002; Seidemann et al., 2002) allowing monitoring of activity from the same patch of cortex for up to a year. We investigated the cortical activity in the primary visual cortex of a behaving monkey during both evoked and ongoing conditions. We combined simultaneous VSDI with electrophysiological recordings of local field potentials (LFP) and multi unit activities. In the evoked conditions, the monkey was trained to fixate for 10s while presented with a full field moving grating, whereas, during the ongoing condition, the monkey was required to sit quietly in a totally dark room. We found that the VSD signals in both

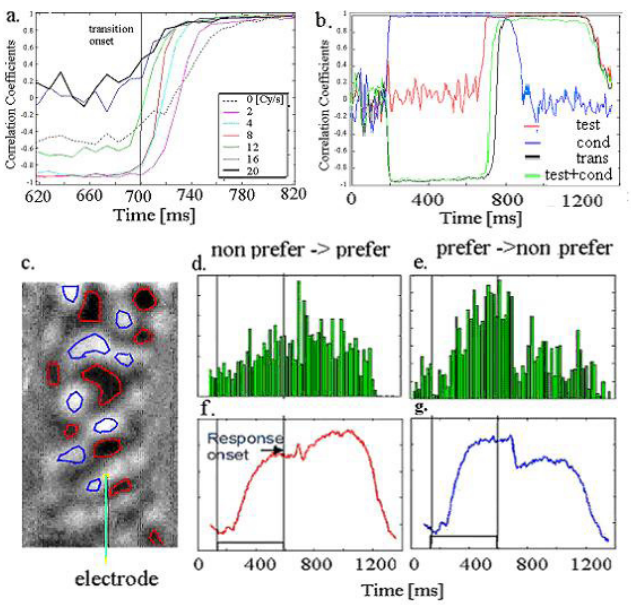

Fig. 1 *Anesthetized subjects.* ***a.*** *correlation coefficients time course during different transition.* ***b.*** *comparison between actual and feed forward model of transition.* ***c.*** *differential orientation map and the region of interest.* ***d,e.*** *multi unit recording and the corresponding VSD time courses (**f,g**) obtain simultaneously.*

Department of Neurobiology

972 8 934 3832

972 8 934 3833

Amiram.Grinvald@weizmann.ac.il

www.weizmann.ac.il/brain/grinvald

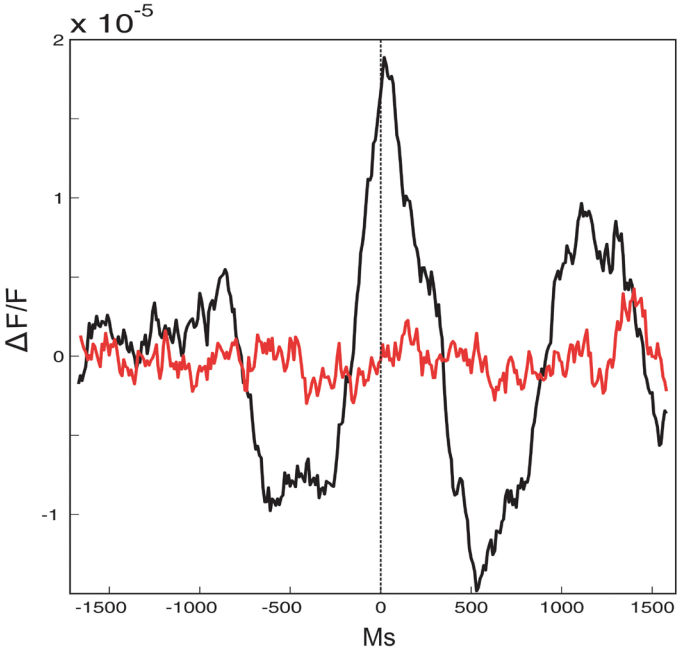

Fig 2 *Black trace represents Spike-Triggered averaging of VDSI signal averaged around the electrode tip, from epochs of spontaneous ongoing activity (no visual input). The red trace serves as a control. It is also Spike-Triggered averaging of the same VSDI epochs, but this time triggered on randomly generated spikes.*

conditions were often highly similar to the LFP, just like in the anesthetized cat. The similarity between the VSD signals and LFP was highest within the α (9-14 Hz) frequency band although the ratio between amplitude of ongoing and evoked activity was much smaller (~1/6) than what was found in the anesthetized cats. However, extensive spike triggered averaging (STA) of the VSD signals revealed coherent spontaneous activity in the awake primate also. These results suggest that ongoing activity plays an important functional role in the awake primate rather than being an epi-phenomenon of anesthetized preparations.

Selected publications

Nelson, DA. S. Krupsky, A. Pollack, E. Aloni, M. Belkin, I. Vanzetta, R. Mordechai, and A. Grinvald (2005) Noninvasive Multi-parameter Functional Optical Imaging of the Eye Ophthalmic Surgery, Lasers and Imaging, 36(1):57-66.

Shmuel, A., M. Korman, , M. Harel, R. Malach and A. Grinvald. (2005). Relationship of feedback connections from area V2 to orientation domains in area V1 of the primate. J. Neurosci. 25: 2117-2131.

Vanzetta I. and A. Grinvald (2005). Direct Visualization of Sensory-Evoked Hemodynamic Responses in the Various Cortical Microvascular Compartments. J. Neurosci. 25:2233-2244.

Grinvald A (2005) Imaging input and output dynamics of neocortical networks in vivo: Exciting times ahead. Proc. Natl. Acad. Sci., USA, 102:14125–14126.

Acknowledgements

The Norman and Helen Asher Chair for Brain Research Supported by grants from the Israel Science Foundation, The National Institute of Health, and the Heineman Foundation, The Goldsmith Foundation, the EU, and the Grodetsky Center.