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Fundamental Mechanisms Underlying Higher Brain Functions; Seeing The Brain In Action

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Objectives: Our long term goal has been to contribute to the discovery of principles underlying cortical processing, visual perception and higher brain functions.

Background: A precondition to deciphering the "neural code" is to determine the functional architecture of cortex. Clearly one must first understand what is the basic function(s) actually performed by a given neuronal group(s) before one can hope to understand the strategy they employ. Next, one should define how these groups of neurons are organized in space. Subsequently, spatio-temporal patterns of electrical activity should be monitored and only then can the code in these tangled communication networks be deciphered. Long-standing questions related to perception and higher cognitive functions can be finally resolved by direct visualization of the architecture and function of mammalian cortex in unprecedented detail (e.g. Fig. 1) . This advance has been accomplished with the aid of two optical imaging techniques one based on voltage sensitive dyes and one on intrinsic signals (1). Utilizing these techniques one can "directly see" how the brain functions. Our explorations are combined with traditional neuroanatomical and neurophysiological techniques and are guided by computational theories and modeling. The combination of real time optical imaging and single unit recording have facilitated the direct visualization of neuronal assemblies. Recently, a number of imaging techniques such as PET, EEG, MEG f-MRI and optical imaging have made feasible many experiments which were considered neuroscientists' "fantasy" only a decade ago. Among these imaging techniques, optical imaging are the only imaging techniques offering the temporal and spatial resolutions (3) required to study the functional organization and the dynamics of cortical columns and neuronal assemblies.

Recent findings: Recent progress in studies of cortical dynamics utilizing real time optical imaging based on voltage sensitive dyes including the combination of, single and multi- unit recordings, LFP, intracellular recordings and microstimulation. To image the flow of neuronal activity from one cortical site to the next, in real time, we have used optical imaging based on newly designed voltage sensitive dyes and a Fuji 28x128 fast camera, which we modified. A factor of 20-40 fold improvement in the signal to noise ratio was obtained with the new dye during in vivo imaging experiments (2). This improvement facilitated the exploration of cortical dynamics without signal averaging in the millisecond time domain. We confirmed that the voltage sensitive dye signal indeed reflects membrane potential changes in populations of neurons (8). We found that the degree of cortical synchronization as reflected from the relationship between the membrane potential changes in individual neurons and the population activity was large (4). We showed that the dynamics of coherent activity in neuronal assemblies could be visualized and found that the instantaneous cortical activity is the sum of a reproducible stimulus response component and the on-going network dynamics. In addition we showed that the firing of single cortical neurons is not a random process but occurs when the on-going pattern of million of neurons is similar to the functional architecture map which correspond to the tuning properties of that neuron. Furthermore, we showed that spontaneously occurring cortical states, in the absence of any visual input often correspond to the orientation domain and are dynamically switching (9). We have also investigated the dynamics of shape processing by exploring the development of orientation selectivity in the millisecond time domain (5). The cortical correlates of a visual illusion were revealed in another study (10). Chronic optical

imaging, combined with electrical recordings and microstimulation, over a long period of times of more than a year, was successfully accomplished thus allowing also the study of similar questions in the behaving macaque monkey (6,7).

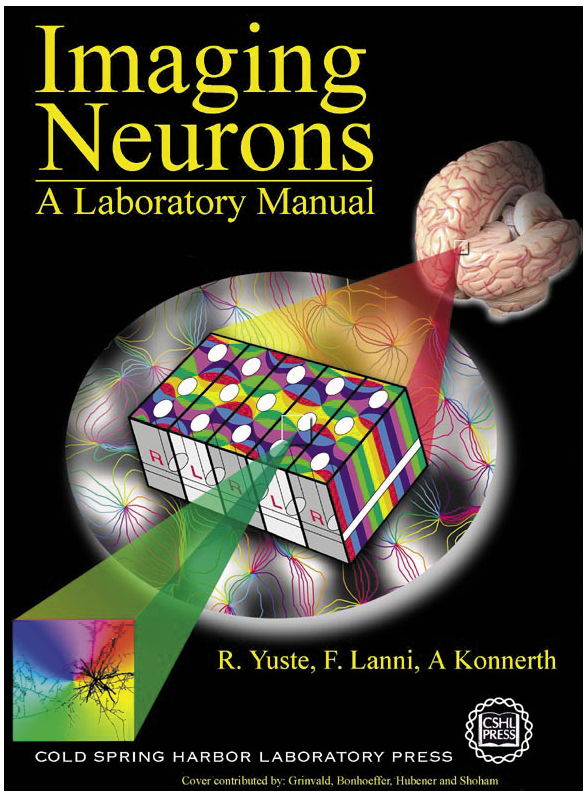

Fig. 1 *Mapping of the geometrical relationships between various processing modules underlying visual perception in primary visual cortices of monkeys (the cube) and cats (the ellipse) by Intrinsic optical imaging. (The "ice cube" model was first put forward by Hubel and Wiesel and Livingstone, and then revised based on optical imaging findings;). Intrinsic optical imaging can be combined with anatomical methods such as biocytin labeling of single neurons thus lucidating the relationship between neuronal structure and function (bottom left square). To explore cortical dynamics, intrinsic optical imaging can be combined also with optical imaging based on voltage sensitive dyes electrophysiological recording and microstimulation. Figure courtesy of Amiram Grinvald and Tobias Bonhoeffer ("Imaging Neurons" book cover , CSHL Press 1999).*

Selected Publications

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