Coding in primate cortex during memory, real-time detection and manipulation of neuronal assemblies

Introduction and Scientific Aims
Memory is one of the most fundamental features of information processing and brain function. Except for very reductionistic concepts like modifications of synaptic transmission at the cellular level or sustained activity of neurons, we have little knowledge about how memory is organized at the network level. However, there are hypotheses for how cortical areas may interact by using oscillatory signals [1] which need to be tested empirically. Distributed neuronal activity patterns including field potential oscillations [2], millisecond precise synchrony [3], and rate covariation [4] carry stimulus information (Fig.1). In order to prove that the brain under study actually uses this information, activity patterns need to be manipulated, reversibly and in real time.

Fig.1 Left: Local field potentials in prefrontal cortex of memory performing monkeys are both correlated to behavioral performance (green) and visual stimuli (red). During several epochs in the time course of the task, frequencies match or express harmonic relationships, suggesting cross-frequency interactions between cortical processes related to attention and information coding [2]. Right: Frequency of joint spike events (excess synchrony (3ms) after rate correction (15ms)) based on multi-unit recordings in PFC shows stimulus dependence in higher order patterns across sites [3].

On search for neuronal coding mechanisms beyond firing rate changes, we dare to understand coding well enough that we can change the memory trace by patterned electrical manipulation of distributed neuronal population activity such that the animal will change its behavior. If this approach will proof to be successful, we intend to determine the most active regions (ROI) in PFC by fMRI and want to test their contribution to behavioral performance by reversible cryo-inactivation. Later we intend to implant microelectrode grids into individual ROIs. With this kind of interface, we will try to “read and write” stimulus specific information from and to prefrontal memory circuits and study behavioral effects.

Brain signals which reflect information processing are highly state-dependent. As we would like to determine the neural context of more local neuronal processes, we studied mesoscopic (LFP) and macroscopic (EEG) potentials also in behaving primates. A classical problem of combining and comparing neuronal and mass signals is to choose the appropriate features of
the mass signals which encompass frequency/power, phase relations or stimulus locked components like ERPs, which not always consist of additive signal components as we tested directly [5]. In a recent study we determined time resolved mutual information based on the power in different frequency bands of primate EEG [6].

Methods
We developed a new spike sorting method [7] which can successfully separate temporally superimposed spike wave forms from tetrodes (Fig.2 left). We have implemented a real-time spike sorting system based on Bayesian Optimal Template Matching (BOTM) which has been validated with ground truth using intracellular signals [6] and which will drive a multisite micro-stimulation system that can be triggered either by behavioral events and/or real time sorted spiking activity. We will use EEG concurrent with tetrode and microarray recordings in order to distinguish state-dependent aspects from local information processing. We have recently started the development of MR compatible cooling probes and are currently setting up to start imaging experiments for testing reversible cryo-inactivation in monkey cortex.

Initial results and conclusions
Field potentials [1] as well as distributed synchronous spike events [2] in prefrontal cortex are correlated with, both, behavioral performance (correct/error) and memory content (stimulus information). Sorting of synchronous spikes (Fig.2 left) recorded at the same tetrode was tested with simultaneous intra- and extracellular recordings in vitro [8]. Real time spike sorting (<20 ms) is working for multiple tetrodes (Fig.2 right) and can be used for identifying synchronous patterns during the experiment and drive spatiotemporally patterned microstimulation.

Fig.2 Left: Validation of sorting synchronous spikes: distribution of time differences (delta \(\tau\)) of near simultaneous spikes (blue). Synchronous spikes are correctly classified in more than 95% of cases (red performance curve) with respect to the intracellular signals. Right: Latencies of real-time spike sorting in an earlier implementation [8].

References

