J Physiol 592.16 (2014) p 3339

JPn The Journal of Physiology Neuroscience

PERSPECTIVES

How neuronal computations depend on network state: another piece in the puzzle

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Networks of neurons in the cerebral cortex operate in regime that are typically characterized by high levels of 'noise'. Contrary to many sources of noise in physical systems, the neuronal noise is generated for the most part internally, through the highly irregular nature of neuronal discharges, in awake animals in particular. It is still highly debated how neurons and populations of neurons make use of this internal noise and how important it is for neural computations.

In a very carefully carried out electrophysiological study, Altwegg-Boussac *et al.* (2014) identify an important piece in this puzzle by comparing, for the first time, the responsiveness of cortical neurons in different network states and for levels of noise (up to total suppression of activity) in the same neurons. By using intracellular recordings in rat barrel cortex *in vivo*, the authors examine the effect of suppressing network activity by systemic injection of high doses of anaesthetic. They compute the 'transfer function' of neurons in these different states, which is the first time this type of information has been available by comparing active network states with suppression of synaptic activity (it was previously shown by comparing Up and Down states; for example, see Shu *et al.* 2003). The main finding here is that the network activity does influence the transfer function of neurons quite drastically and changes their gain. This finding is not surprising and could be inferred from previous theoretical (Ho & Destexhe, 2000) and *in vitro* studies (Shu *et al.* 2003; see also further references and discussion in the Altwegg-Boussac *et al.* paper), but has not previously been demonstrated so clearly *in vivo*.

One surprise from these experiments, however, is that the apparent input resistance (R_{in}) is surprisingly similar following suppression of network activity. This finding contrasts with previous measurements in cats, where it was found that the R_{in} is greatly modified by suppressing network activity (Paré *et al.* 1998). The same discrepancy was also found when comparing the R_{in} between Up and Down states, which is vastly different in cats (Paré *et al.* 1998; Rudolph *et al.* 2007), but is similar in rats (Zou *et al.* 2005; Waters & Helmchen, 2006). These results were interpreted as being due to the presence of intrinsic currents in the subthreshold regime which may not be present in cats. It may also be that the apparent lack of impact of network activity on the R_{in} was found in primary sensory areas in rats, while it was found in cats in association (parietal) cortex, so it may represent a difference between brain areas rather than between species. Future experiments should shed light on this issue.

Furthermore, using light fentanyl anaesthesia, which induces low-amplitude, fast ('desynchronized') EEG activity similar to wakefulness, the authors found that cortical neurons display a depolarized membrane potential (around −65 mV), irregular firing and a low R_{in}. These findings are consistent with the 'high-conductance state' found in cats (reviewed by Destexhe *et al.* 2003). In such conditions, the transfer function was also different compared with the oscillatory (Up/Down) state typical of other anaesthetics. The high-conductance state confers more sensitivity in neurons, and this enhanced responsiveness is consistent with previous findings in cats (Destexhe *et al.* 2003).

Thus, the study by Altwegg-Boussac *et al.* (2014) provides very important data on how cortical neurons are affected by network activity. Together with previous studies, it shows that the responsiveness of cortical neurons must be considered with the appropriate 'context' and is completely dependent on network state. These findings have great consequences for computational models of network activity, which need to take into account the correct transfer function of neurons (a model with the wrong transfer function is very unlikely to make correct predictions). This study also highlights an interesting feedback between different neural scales, as the (global) network activity impacts on the (local) cellular properties, which in turn may influence the global scale. Understanding such interactions also constitutes a nice challenge for theoreticians.

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Additional information

Competing interests

None declared.

Funding

A.D was funded by CNRS and the European Community (BrainScales FP7-269921 and the Human Brain Project FP7-604102).

DOI: 10.1113/jphysiol.2014.277392