## Nanodiamond–Quantum Sensors Reveal Temperature Variation Associated to Hippocampal Neurons Firing

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Temperature is one of the most relevant parameters for the regulation of intracellular processes. Measuring localized subcellular temperature gradients is fundamental for a deeper understanding of cell function, such as the genesis of action potentials, and cell metabolism. Notwithstanding several proposed techniques, at the moment detection of temperature fluctuations at the subcellular level still represents an ongoing challenge. Here, for the first time, temperature variations (1 °C) associated with potentiation and inhibition of neuronal firing is detected, by exploiting a nanoscale thermometer based on optically detected magnetic resonance in nanodiamonds. The results demonstrate that nitrogen-vacancy centers in nanodiamonds provide a tool for assessing various levels of neuronal spiking activity, since they are suitable for monitoring different temperature variations, respectively, associated with the spontaneous firing of hippocampal neurons, the disinhibition of GABAergic transmission and the silencing of the network. Conjugated with the high sensitivity of this technique (in perspective sensitive to < 0.1 °C variations), nanodiamonds pave the way to a systematic study of the generation of localized temperature gradients under physiological and pathological conditions. Furthermore, they prompt further studies explaining in detail the physiological mechanism originating this effect.

## 1. Introduction

On the one side, temperature regulates the speed of ion channel opening,<sup>[1]</sup> the pattern activity of a firing neuron,<sup>[2]</sup> and the vesicular dynamics at the presynaptic terminal,<sup>[3]</sup> on the other side, intracellular temperature is affected by a variety of biochemical reactions occurring during cell activity. Pioneering findings dating back to the late 70s,<sup>[4,5]</sup> associated temperature increases to the impulse propagation in nonmyelinated fibers of the olfactory nerve and, more recently, a theoretical explanation about the heat production and absorption by neurons during nervous conduction has been formulated.<sup>[6]</sup> Intracellular temperature variations have been probed to detect the phases of cell-cycle division<sup>[7]</sup> and the mitochondrial activity.<sup>[8]</sup> In the brain, temperature fluctuations are likely associated with changes in neuronal functions such as the genesis of action potentials, secretion at the level of synaptic terminals, or transmembrane ion

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