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Introduction

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This Special Issue, dedicated to DENDRITES, emerged as an initiative to compile the insights gained during the EMBO Workshop series on dendritic anatomy, molecules and function that takes place since 2016, biannually, on the island of Crete. The issue touches upon all complexity levels -from the molecular all the way to the behavioral-probed with different *in vitro*, *in vivo* and in computo techniques and ventures beyond neuroscience, into machine learning and neuromorphic engineering, placing dendrites at the center of numerous cross-disciplinary advances. We are thankful to all contributors, both speakers from the meeting and experts of the field, for making this Special Issue a wonderful journey about dendrites.

Dendrites are the primary recipients of synaptic input in neurons of the central nervous system. Over the past few decades and based on vast *in vitro* and theoretical modeling studies, concepts about the computational power of dendrites have radically changed. Once viewed as merely conveying electrical signals passively, dendrites of many neuron types are now known to serve as complex active structures that support local, nonlinear computations and plasticity (Magee, 2000; Spruston, 2008; Antic et al., 2010; Branco and Häusser, 2010; Major et al., 2013; Kastellakis et al., 2015; Stuart and Spruston, 2015; Stuart et al., 2016; Mel et al., 2017; Payeur et al., 2019). These features enable neurons with active dendrites to perform complex computations which were previously thought to be performed by networks of neurons (Poirazi et al., 2003; Jadi et al., 2014; Tzilivaki et al., 2019; Gidon et al., 2020; Poirazi and Papoutsi, 2020; Takahashi et al., 2020), thus greatly augmenting the computing power of single cells. In fact, according to a recent study, to capture the computational complexity of a single pyramidal neuron an 8-layer deep neural network was required (Beniaguev et al., 2021). This complex dendritic processing plays a central role in various brain functions, including sensory-motor perception and representation, spatial navigation, learning and memory.

In this Special Issue on Dendrites, a constellation of reviews, viewpoints and original studies highlight recent discoveries in dendritic research and place dendritic computation in a larger perspective, that of network function and behavior. Three main themes are being addressed:

The first theme examines the role of active dendritic processing for neuronal computations, within and beyond the family of excitatory pyramidal neurons. The wide diversity of dendritic spikes in cortical neurons is carefully examined and new insights regarding the role of these spikes in single neuron computations are derived (Larkum et al., 2022). Harkin et al. (2021) demonstrate that such diverse spiking phenomena can be exquisitely captured by cascade models, providing a unifying model for sub-cellular computations. Moreover, the modulation of NMDA spikes, their impact on plasticity induction and their role in expanding the range of dendritic computations is discussed in both experiments and computational models (Brandalise et al., 2021; Humphries et al., 2021). Plasticity, in turn, depends on how resources are distributed along the branched dendritic structures, described in pyramidal neurons by Harris et al. (2022). Going beyond the study of dendrites in excitatory neurons, a few studies highlight their nonlinear properties in interneurons. One review discusses the possible contribution of interneurons' nonlinear dendrites to neuronal arithmetic and memory formation (Tzilivaki et al., 2021) while another (Pancotti and Topolnik, 2021) elaborates on the modulatory effects of ACh on dendritic computations in the three main inhibitory interneuron subtypes (PV +, SST + and VIP +).

The second theme deals with dendritic processing and computation *in vivo* and its differences from *in vitro* studies. An important question that is addressed extensively in this special issue concerns the computational role dendrites may play *in vivo*, in the context of behaviorally-relevant paradigms. Technological advancements, and particularly the use of *in vivo* two-photon imaging to track synaptic, dendritic and neuronal activity in behaving head-fixed animals, have made it possible to directly examine the computations being implemented by dendrites during behavior. Discrepancies between *in vitro* and *in vivo*

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ionic conditions are highlighted along with their impact on dendritic excitability and plasticity induction (Gonzalez et al., 2022). Similar limitations are present when assessing synaptic input to dendrites in both excitatory and inhibitory neurons with whole-cell techniques (To et al., 2021) raising an important point about the adjustments needed for proper monitoring of dendritic processes *in vivo*. Moreover, a couple of reviews discuss the forms and mechanisms underlying the representation of information within dendritic compartments *in vivo* and pinpoint to the possible contributions of active dendritic computations to neuronal, circuit function and ultimately to behavior. These reviews discuss the difficulties in observing such local dendritic computations *in vivo* and the limitations imposed by existing technologies when localized dendritic activity is successfully recorded (Moore et al., 2021; Stuyt et al., 2021). The role of dendrites in the genesis and dynamics of local field potentials (LFP), which are often used as a readout in behaving animals, is highlighted by computational models (Sinha and Narayanan, 2021). Finally, the alternative computational power of cortical neurons with coordinated global spikes versus compartmentalized dendritic spiking is discussed (Francioni and Harnett, 2021).

In the third theme, the question of ‘‘why dendrites are important” is explored with various conceptual (Larkum, 2022) and theoretical approaches in both biological and artificial neural networks. Several studies focus on the contributions of active dendrites, in particular, dendritic spikes to complex functions implemented by biological networks, such as for example visual processing (Ramdas and Mel, 2021; Destexhe and Mehta, 2022; Jin et al., 2022). The bi-lateral relationships between artificial neurons in deep neural networks (DNN) and biological neurons with dendrites are highlighted. On one hand, DNNs can be used to infer the computations implemented by pyramidal neurons with elaborate active trees such as the layer-5 pyramidal neuron. On the other hand, introducing concepts from dendritic computations to the DNN architecture may augment the capabilities of artificial neurons (Acharya et al., 2021; Jones and Kording, 2021) and help solve some fundamental problems such as catastrophic forgetting. Finally, beyond digital processing, the ability to capture the advantages of dendritic computations in analog neuromorphic hardware and efforts towards this goal are presented by (Kaiser et al., 2021).

The challenges of the field in the coming years will be to merge the knowledge gained from *in vitro*, *in vivo*, theoretical and machine learning disciplines to gain a unified view as to how dendritic computation contributes to the sophistication of single neuron computations, network representation, learning and plasticity and ultimately to behavior. The progress made thus far and the numerous cross-disciplinary contributions that have already emerged indicate that a bright future lies ahead.

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