SIF 2020 Ruzzier Lecture: SPACE AND TIME IN THE BRAIN

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In memory of Natale Belluardo

Neural networks in the hippocampus and entorhinal cortex provide dynamic maps of our position in space. These networks contain specialized position-coding cell types, including grid cells, which we discovered in the medial entorhinal cortex of rats in 2005. Grid cells are active only when animals are at certain locations, locations that tile environments in a periodic hexagonal pattern. During the years since 2005 we have shown that the same region contains a further variety of specialized cell types, including also cells that monitor speed, vicinity to local borders, and vector relationships to salient landmarks. However, while the existence of individual cells with strong feature correlates is a striking property of this space-coding brain network, I will propose that the functions of entorhinal cortex, like any cortex, can be understood only by a population-analytic approach to neural coding. I will show how hundreds to thousands of entorhinal grid cells collectively form low-dimensional representations that persist across behavioural tasks and activity states, independently of specific sensory inputs, which points to network architecture as a determinant of the grid pattern. I will also show that entorhinal neural networks are organized in time. During stereotyped running, entorhinal population activity follows fixed trajectories through the low-dimensional manifold, identifying such sequences as putative elements for encoding of experience in the entorhinal-hippocampal network. Deficiencies in these mechanisms may be at the core of neurological diseases characterized by early entorhinal cell death, spatial disorientation and memory dysfunction, such as Alzheimer´s disease.