Synaptic input

Neurons in the brain receive thousands of synaptic inputs from other neurons. Synaptic integration is the term used to describe how neurons 'add up' these inputs before the generation of a nerve impulse, or action potential.

The transformation of synaptic input into action potential output is a fundamental single-cell computation resulting from the complex interaction of distinct cellular morphology and the unique expression profile of ion channels that define the cellular phenotype. Experimental studies aimed at uncovering the mechanisms of the transfer function have led to important insights, yet are limited in scope by technical feasibility, making biophysical simulations an attractive complementary approach to push the boundaries in our understanding of cellular computation.

Linaro et al. took a data-driven approach by utilizing high-resolution morphological reconstructions and patch-clamp electrophysiology data together with a multi-objective optimization algorithm to build two populations of biophysically detailed models of murine hippocampal CA3 pyramidal neurons based on the two principal cell types that comprise this region. They evaluated the performance of these models and find that the approach quantitatively matches the cell-type-specific firing phenotypes and recapitulates the intrinsic population-level variability in the data. Moreover, they confirmed that the conductance values found by the optimization algorithm are consistent with differentially expressed ion channel genes in single-cell transcriptomic data for the two cell types. They then used these models to investigate the cell type-specific biophysical properties involved in the generation of complex-spiking output driven by synaptic input through an information-theoretic treatment of their respective transfer functions. The simulations identify a host of cell type-specific biophysical mechanisms that define the morpho-functional phenotype to shape the cellular transfer function and place these findings in the context of a role for bursting in CA3 recurrent network synchronization dynamics [1].

1)

Linaro D, Levy MJ, Hunt DL. Cell type-specific mechanisms of information transfer in data-driven biophysical models of hippocampal CA3 principal neurons. PLoS Comput Biol. 2022 Apr 22;18(4):e1010071. doi: 10.1371/journal.pcbi.1010071. Epub ahead of print. PMID: 35452457.