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Session P121 - Structural Plasticity: Neurons, Glial, Microcircuits, and Networks

P121.05 - Synergistic interactions among intrinsic, synaptic, and structural heterogeneities drive synaptic plasticity profiles in dentate gyrus granule cells

 November 11, 2021, 8:45 AM - 9:45 AM

 Virtual Only

Grant Support

DBT/Wellcome Trust India Alliance [Senior Fellowship No. IA/S/16/2/502727]

Grant Support

Department of Biotechnology through the DBT-IISc partnership program

Grant Support

Revati and Satya Nadham Atluri Chair Professorship

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Disclosures

S. Shridhar: None. **P. Mishra:** None. **R. Narayanan:** None.

Abstract

Granule cells (GC) in the dentate gyrus exhibit pronounced heterogeneities in their intrinsic properties and synaptic connectivity, with these heterogeneities further amplified by the expression of adult neurogenesis. The impact of such heterogeneities on synaptic plasticity rules has not been quantitatively analyzed. Here, we assessed the ramifications of the expression of intrinsic, synaptic, and structural heterogeneities on synaptic plasticity profiles induced through two protocols: the BCM-like 900-pulses protocol and the theta-burst stimulation (TBS) protocol. First, we addressed the impact intrinsic heterogeneities had on plasticity profiles obtained with both induction protocols, with a fixed baseline synaptic strength across models. We found that heterogeneities in intrinsic properties resulted in heterogeneities in the modification threshold of the BCM-like protocol and the amount of plasticity induced by TBS. However, pair-wise correlations between these plasticity measurements and any of the intrinsic measurements or parameters were weak ($|r| < 0.4$). Next, we examined the relationship between excitability properties and synaptic strength and showed that similar plasticity profiles could be obtained across all models with different synaptic strengths, thereby demonstrating plasticity degeneracy whereby the impact of heterogeneities in intrinsic properties could be counterbalanced by heterogeneities in synaptic strength. However, we did not find strong pair-wise correlations between synaptic strength and any intrinsic measurement or parameter governing the model. We then explored the role of neurogenesis-induced structural heterogeneity, by progressively altering the diameter of the model neurons, mimicking maturation-induced increase in GC surface area. When synaptic strengths were fixed, we found a progressive rightward shift in the plasticity profile with an increase in diameter. Importantly, in immature neurons with extremely small diameters, the plasticity profile manifested no long-term depression for a large range of baseline synaptic strength values. Finally, when the plasticity profiles were tuned to be similar by altering synaptic strengths, we found the emergence of plasticity degeneracy involving intrinsic, structural, and synaptic parameters. Together, our analyses provide a biophysical framework for understanding the role of various heterogeneities and the synergistic interactions among them in engram cell formation, in effectuating the maturation-induced switch in synaptic plasticity regimes, and in the emergence of plasticity degeneracy.

*SS & PM contributed equally to this study.