COMPUTATIONAL ASSAYS OF MINIATURE INHIBITORY POSTSYNAPTIC CURRENTS (minis, mIPSCs) IN THALAMOCORTICAL NEURONS SHOW VARIABILITY IS DOMINATED BY INTRASYNAPTIC MECHANISMS

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In brain slice preparations of thalamocortical neurons with TTX, APV, CNQX, DNQX, and cesium present, spontaneous miniature inhibitory postsynaptic current (GABA mIPSCs) amplitudes are widely varying (5-80pA), with a skewed distribution. In computational models of reconstructed thalamocortical neurons, with the same currents blocked but without intra-synaptic variables, mIPSC amplitudes are narrowly varying (10-15pA) and have an opposite skew. The contrast suggests that much of the observed variability arises from intra-synaptic factors including cleft morphology, vesicle content, and receptor number/subtypes. Controls for morphology, pharmacology, and experimental parameters support this finding and extended it to awake, behaving animals. Considering several of the unique attributes of the thalamus, such as the dual role of inhibition during cognition and during sleep, we conclude that this system is well suited for molecular genetic studies of synaptic variability and synaptic plasticity.

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