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Bayesian analysis of the kinetics of quantal transmitter secretion at the neuromuscular junction

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Abstract The timing of transmitter release from nerve endings is considered nowadays as one of the factors determining the plasticity and efficacy of synaptic transmission. In the neuromuscular junction, the moments of release of individual acetylcholine quanta are related to the synaptic delays of uniquantal endplate currents recorded under conditions of lowered extracellular calcium. Using Bayesian modelling, we performed a statistical analysis of synaptic delays in mouse neuromuscular junction with different patterns of rhythmic nerve stimulation and when the entry of calcium ions into the nerve terminal was modified. We have obtained a statistical model of the release timing which is represented as the summation of two independent statistical distributions. The first of these is the exponentially modified Gaussian distribution. The mixture of normal and exponential components in this distribution can be interpreted as a two-stage mechanism of early and late periods of phasic synchronous secretion. The parameters of this distribution depend on both the stimulation frequency of the motor nerve and the calcium ions' entry conditions. The second distribution was modelled as quasi-uniform, with parameters independent of nerve stimulation frequency and calcium entry. Two different probability density functions for the distribution of synaptic delays suggest at least two independent processes controlling the time course of secretion, one of them potentially involving two stages. The relative contribution of these processes to the total number of mediator quanta released depends differently on the motor nerve stimulation pattern and on calcium ion entry into nerve endings.

Keywords Neuromuscular junction · Quantal release of neurotransmitter · Kinetics of quantal secretion · Statistical model, Bayesian method

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Abbreviations

TCS	Time course of secretion
EPC	Endplate current
EMG	Exponentially modified Gaussian
$[Ca^{2+}]_{out}$	Extracellular calcium concentration
$[Mg^{2+}]_{out}$	Extracellular magnesium concentration
4-AP	4-aminopyridine
QU	Quasi-uniform process

1 Introduction

The neuromuscular junction, a specialized area of contact between the axon terminal of a motor neuron and a muscle fibre, has been the subject of a wide range of neurophysiological studies. The mechanisms underlying neurosecretion are common to those of the fast chemical synapses of the central nervous system (Tarr et al. 2013). Under normal physiological conditions, the arrival of the action potential at the nerve ending triggers the secretion of up to several tens of quanta of