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# Computational roles of plastic probabilistic synapses

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The probabilistic nature of synaptic transmission has remained enigmatic. However, recent developments have started to shed light on why the brain may rely on probabilistic synapses. Here, we start out by reviewing experimental evidence on the specificity and plasticity of synaptic response statistics. Next, we overview different computational perspectives on the function of plastic probabilistic synapses for constrained, statistical and deep learning. We highlight that all of these views require some form of optimisation of probabilistic synapses, which has recently gained support from theoretical analysis of long-term synaptic plasticity experiments. Finally, we contrast these different computational views and propose avenues for future research. Overall, we argue that the time is ripe for a better understanding of the computational functions of probabilistic synapses.

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## Introduction

Animals have evolved in uncertain environments. For example, they have adapted to distinguish nutrition sources of different shapes, sizes, colours and tastes. Such perceptual uncertainty should be encoded by the brain to enable accurate decision making [1,2•,3]. This link between perception and decision is presumably achieved through communication between different brain areas, which ultimately relies on synaptic transmission [4,5]. Synaptic transmission is inherently stochastic: a presynaptic action potential may or may not trigger neurotransmitter release that in turn binds to postsynaptic receptors [6•]. For synaptic transmission to successfully trigger a behavioural decision synaptic response statistics should be tuned during learning [4,7,5]. However, it has remained unclear exactly which aspects of probabilistic synapses should be modified during learning.

There is wide evidence of plasticity occurring at the key components that underlie synaptic transmission statistics. For example, not only does plasticity change the properties and number of postsynaptic receptors, but also the intricate presynaptic machinery responsible for stochastic neurotransmitter release [8,7]. Because synaptic plasticity is believed to underlie learning [4,5], this body of experimental work suggests that the brain shapes probabilistic synapses as animals adapt to the environment. This has important theoretical implications [9•,10,11••,12••], but most computational models of learning and synaptic plasticity have considered only changes in the mean synaptic weight (e.g. [13–15]). Below we review recent experimental and theoretical developments on the plasticity and computation roles of probabilistic synapses.

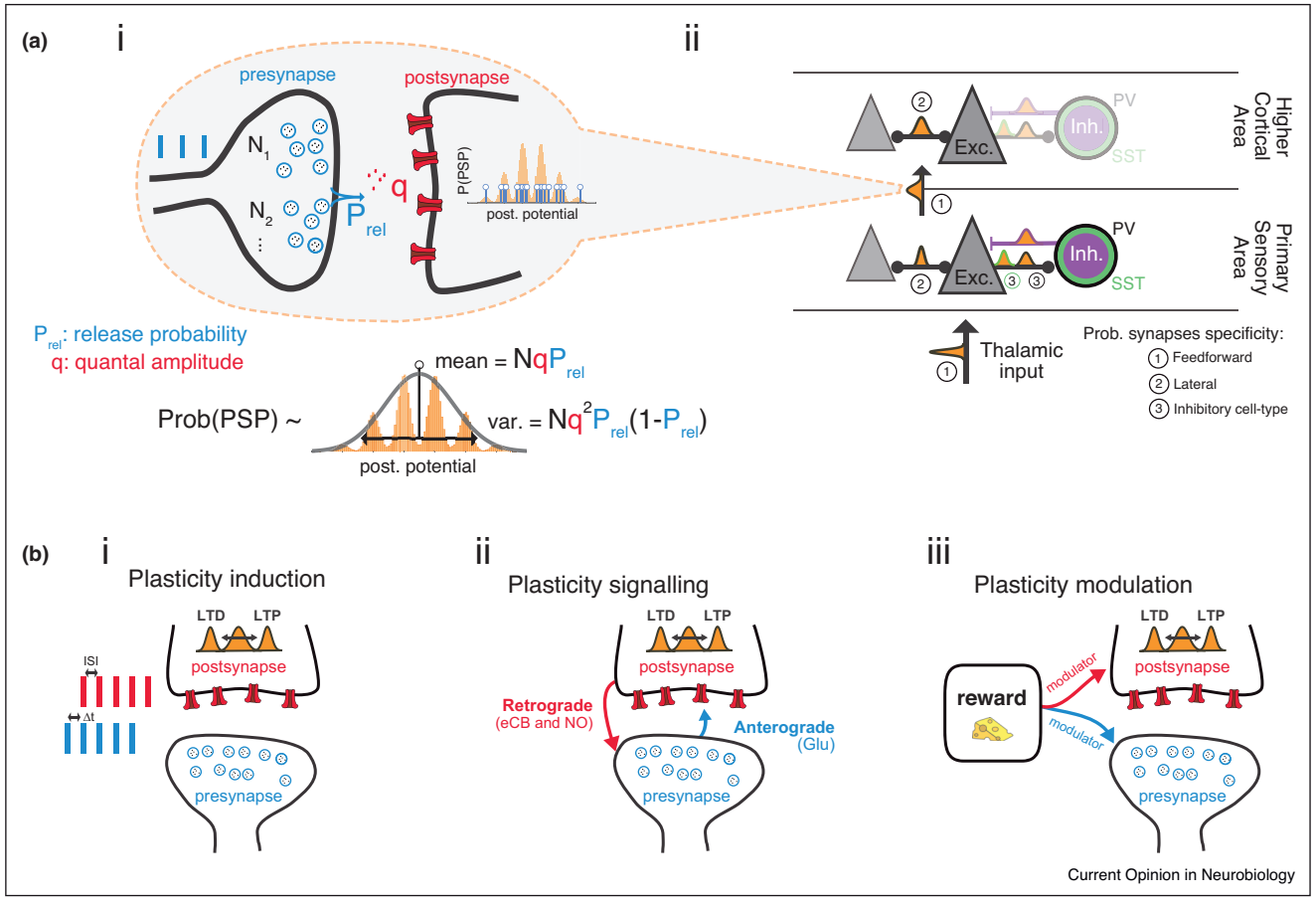
## Specificity of synaptic transmission statistics

The probabilistic nature of synaptic transmission has been described as a binomial process [16,6•,7], which is parametrised by the (i) number of synaptic release sites $N$, (ii) presynaptic release probability $P_{rel}$ and (iii) quantal amplitude $q$ — proportional to the number of postsynaptic receptors [7] (Figure 1a-i). Together these three parameters define the statistics of synaptic responses, with mean given by $NqP_{\mathrm{rel}}$ and variance by $Nq^2P_{\mathrm{rel}}(1-P_{\mathrm{rel}})$ (Figure 1a-i).

The exact mean and variance of synaptic transmission depends on where the synapse is located. In cortical circuits the statistics (e.g. means and variances) of synaptic responses exhibit a high degree of variability that

[7] This is a simplified view of the complicated release machinery. For example, the quantal amplitude $q$ also depends on the amount of neurotransmitter per (presynaptic) vesicle and on the sensitisation of postsynaptic receptors.

**Figure 1**




Specificity and plasticity of probabilistic synapses. **(a)** Throughout the brain virtually every synapse is probabilistic. (i) When a presynaptic spike (blue vertical line on the left) occurs a presynaptic vesicle (blue circles) *may* release neurotransmitters (red dots) that bind to postsynaptic receptors (red) which elicits a postsynaptic potential (PSP; PSPs of different amplitudes are represented by the small vertical blue lines). The key parameters that determine the statistics of probabilistic synaptic responses are the number of presynaptic release sites ($N$, groups of vesicles in blue), release probability ($P_{rel}$, blue arrows) and quantal amplitude which is proportional to the number of postsynaptic receptors, $q$, red). This process is typically modelled as a binomial probability distribution (orange histogram, with $N = 5$, $P_{rel} = 0.5$ and $q = 1$ for illustration), which in the limit of large $N$ can be approximated as a Gaussian distribution (black line) with mean=$NqP_{rel}$ and variance=$Nq^2P_{rel}(1 - P_{rel})$. (ii) Simplified representation of cortical circuits, with both excitatory (black) and inhibitory (purple) synapses and neuron types. Each synaptic connection is stochastic (represented as a Gaussian distribution). Two different inhibitory cell-types are represented: somatostatin (SST, dashed green circle) and parvalbumin (PV, black circle); here these two separate inhibitory cell-types are represented as overlapping circles for simplicity. Note that different connections exhibit statistics of different means and variances (see main text for more details). **(b)** Long-term plasticity of probabilistic synapses. (i) Different induction protocols have been shown to trigger changes in the probability of postsynaptic responses. Schematic on the left represents presynaptic and postsynaptic spikes in a spike-timing-dependent plasticity protocol, which depending on the timing between presynaptic and postsynaptic spikes ($\Delta t$) as well as the inter-spike interval (ISI) may lead to long-term potentiation (LTP) or depression (LTD). This in turn changes not only the mean synaptic response, but also its variance. (ii) Modifications to probabilistic synapses during plasticity are known to rely on specific retrograde (e.g. endocannabinoids (eCB) and nitric oxide (NO)) and anterograde signals (glutamate (Glu)). (iii) Behavioural outcomes (e.g. reward) may rely on neuromodulation (e.g. Dopamine) to regulate plasticity at probabilistic synapses.

depends on cell-type [17], connection-type [17–19], layer [17,20], brain area [21], age [22], and even species [23]. For example, excitatory synapses from thalamic projections onto layer-4 granule cells are more reliable [24] than synapses between layer-5 pyramidal cells [19]. Remarkably, connections from pyramidal cells onto lateral inhibitory cells can also be dramatically different: synapses onto somatostatin-positive interneurons cells communicate with a low basal release probability, whereas synapses onto parvalbumin-positive interneurons are stronger with higher release probability [18,19] (Figure 1a-ii). Such high specificity of probabilistic synapses suggests that they are modified during learning.

## Plasticity of probabilistic synapses

Accumulating evidence suggests that synaptic plasticity underlies learning in the brain [4,5]. Synaptic plasticity not only modifies the mean synaptic response, but also its