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Single neuron dynamics and computation

Nicolas Brunel[1,*], Vincent Hakim[2] and Magnus JE Richardson[3]

At the single neuron level, information processing involves the transformation of input spike trains into an appropriate output spike train. Building upon the classical view of a neuron as a threshold device, models have been developed in recent years that take into account the diverse electrophysiological make-up of neurons and accurately describe their input-output relations. Here, we review these recent advances and survey the computational roles that they have uncovered for various electrophysiological properties, for dendritic arbor anatomy as well as for short-term synaptic plasticity.

Addresses
[1] Departments of Statistics and Neurobiology, University of Chicago, Chicago, USA
[2] Laboratoire de Physique Statistique, CNRS, University Pierre et Marie Curie, Ecole Normale Supérieure, Paris, France
[3] Warwick Systems Biology Centre, University of Warwick, Coventry, United Kingdom

Corresponding author: Brunel, Nicolas (nbrunel@uchicago.edu)

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Introduction

The computation performed by single neurons can be defined as a mapping from afferent spike trains to the output spike train which is communicated to their post-synaptic targets. This mapping is stochastic, because of various sources of noise that include channel and synaptic noise; and plastic, because of various sources of plasticity, both intrinsic and synaptic.

For many years, the dominant conceptual model for single neuron computation was the binary Mc-Culloch-Pitts neuron [45]. In this model, the input vector is multiplied by a weight vector, and then passed through a threshold (see Fig. 1a). Adjusting synaptic weights and thresholds lead to neurons being able to learn arbitrary linearly separable dichotomies of the space of inputs [63].

This model has been conceptually tremendously useful, but it ignores fundamental temporal and spatial properties of neurons: the complex dynamics generated by a panoply of voltage-gated ionic currents; and the fact that synaptic inputs are stochastic, history-dependent and spread over a large dendritic tree. In this paper, we will review recent advances in our understanding of how these properties affect computation in single neurons.

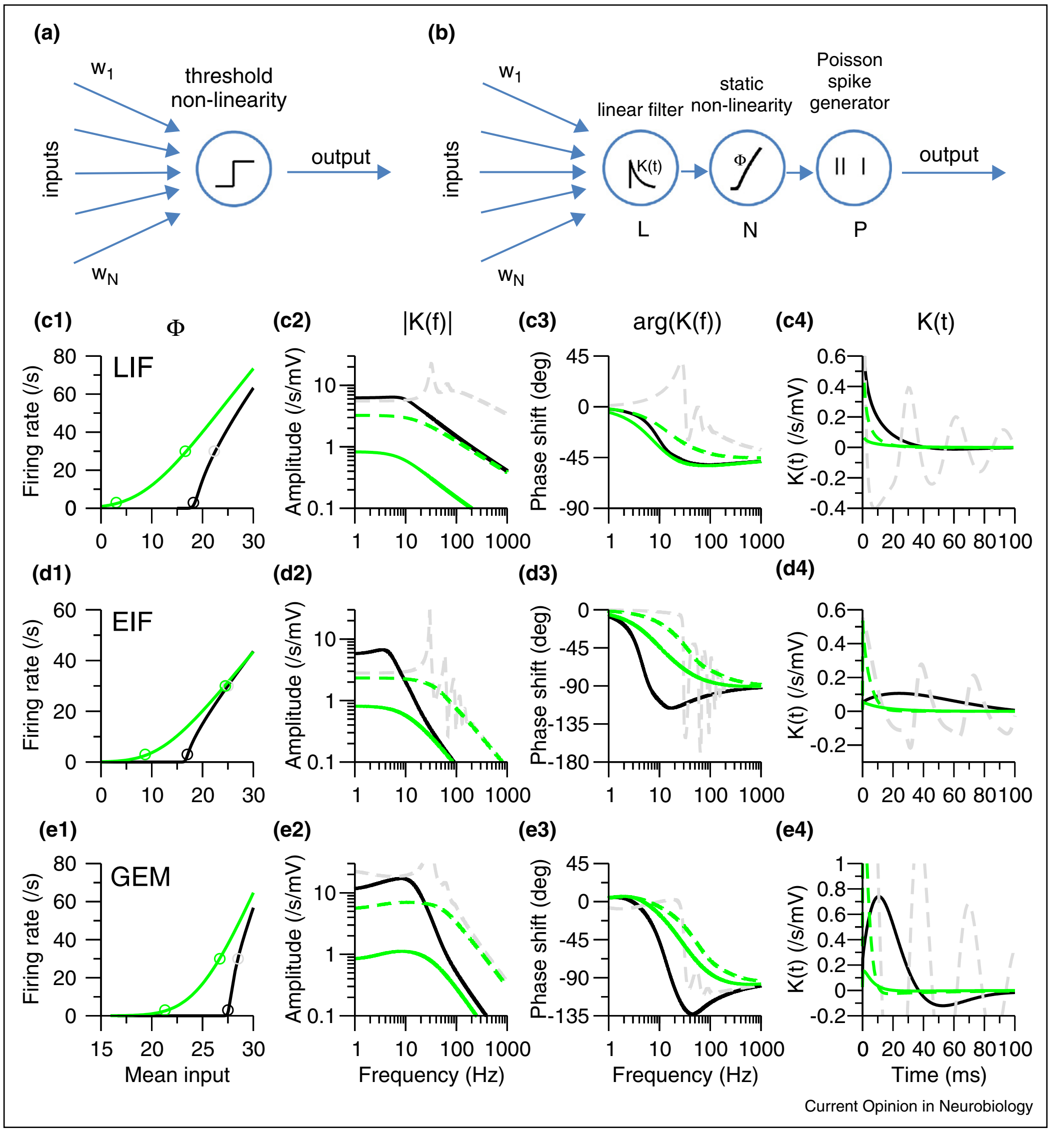
Computation and dynamics: LNP/GL models and their relationship to neuronal biophysics

Electrophysiological data in various sensory systems have been successfully fitted by linear-non-linear-Poisson (LNP) or generalized linear models (GLM) [65]. In the LNP model, the inputs are first convolved linearly with a temporal filter (also called a kernel - the L operation). This convolution is then passed through a static non-linearity (the N operation), yielding an instantaneous firing rate. Finally, an inhomogeneous Poisson process is generated from the instantaneous firing rate (the P operation). This model is sketched in Figure 1b. In a GLM, spikes emitted by the neuron are convolved by another filter, and added to the input to the static non-linearity, to account for post-spike effects such as firing rate adaptation.

Recently, a procedure for approximating arbitrary spiking neuron models to LNPs has been developed ([54•] — see [31] for an alternative strategy). The idea is that the static non-linearity corresponds to the average firing rate of the neuron, with a stationary input and background noise with a given statistics. The temporal filter corresponds to the linearized firing rate (or impulse) response - how the instantaneous firing rate responds to a small sharp pulse of input current. Both quantities can be computed analytically (either exactly or approximately) in several popular 1 or 2 variable simplified spiking neuron models: the leaky integrate-and-fire (LIF) model [22,59]; the exponential integrate-and-fire (EIF) and quadratic integrate-and-fire (QIF) models [23,60]; generalized two-variable integrate-and-fire (GIF) models [57]; and generalized exponential models (GEM) [58]. The interest in such simplified integrate-and-fire-type models has been boosted by two observations: (i) 2 variable IF models can reproduce a wide diversity of firing patterns of real neurons [33,51,71]; (ii) they accurately fit electrophyiological recordings of real neurons [56,5•,26,46].

The static non-linearities and temporal filters of such models are summarized in Figure 1c-e. In IF-type models, the static non-linearity is a monotonically increasing, sigmoid-shaped, function of the inputs (Fig. 1c1-e1) - note however that non-monotonic f-I curves can be observed in a specific class of model neurons [40] as well as in specific types of real neurons [30]. In the sub-threshold range,

Figure 1



Computational properties of single-compartment neurons. a. The classic McCulloch-Pitts neuron performs a weighted sum of its synaptic inputs (each input i is multiplied by a synaptic weight w_i), and then a thresholding operation. b. The LNP neuron replaces the threshold by the LNP cascade: (L) convolution with a temporal filter $K(t)$, (N) application of a static non-linearity Φ, (P) generation of a Poisson process, with an instantaneous firing rate given by $\Phi(K\cdot$ input). c-d. Static non-linearities and temporal filters of selected simplified spiking neuron models. c: Leaky integrate-and-fire neuron (LIF). d: Exponential integrate-and-fire neuron (EIF). e: Generalized exponential model (GEM). In this series of panels, the first column shows the static non-linearity, for two different levels of noise (black, 1mV; green, 10mV). Circles indicate the points at which the temporal filters are computed in the other columns. The second and third columns show the amplitude and phase of the temporal filter in the Fourier domain (color indicates level of noise as in first column; full lines, firing rate of 3Hz; dashed line, firing rate of 30Hz). The fourth column shows the temporal filter (or impulse response) for the same parameters as in the 2nd and 3rd columns.

where firing is induced by fluctuations around the mean inputs, the gain of the transfer function strongly depends on the amplitude of the noise. The temporal filter also strongly depends on the noise (Fig. 1c2-e4). For strong noise, neurons fire in a highly irregular fashion. In this regime, one-variable IF-type models behave as low-pass filters, with a cut-off frequency that depends on membrane time constant, background firing rate, and spike generation dynamics (Fig. 1c2, c3, d2, d3). Two-variable models in which the second variable represents the dynamics of ionic currents providing negative feedback on the membrane potential (IH, IKs, etc) behave as band-pass filters, in a frequency range determined by the time scales of these intrinsic currents (Fig. 1e2, e3). For low noise, neurons are close to oscillators, and consequently temporal filters develop strong resonances at integer multiples of their firing frequency (Fig. 1c2-e3). The experimentally measured temporal filters of cortical neurons [35,7,70•] are roughly in agreement with this picture, but have an unexpectedly high cut-off frequency, consistent with very sharp action potential generation in cortical neurons [52].

Neurons can therefore perform different types of computations, depending on the expression of ionic channels and the levels of background noise. The operation they perform can vary from leaky integration (in the absence of strong negative feedback) to differentiation (with strong negative feedback, e.g. firing rate adaptation) or even fractional differentiation in the presence of multiple time scales of adaptation [41]. Close to perfect integration can be realized by positive feedback due to calcium-activated non selective ICAN currents, explaining persistent activity seen in entorhinal cortex [20,24]. An inverted integration (hyperpolarization-activated graded persistent activity) can be induced by adding a calcium modulation of H currents [73]. Single neuron bistability can occur thanks to the non-linear voltage dependence of NMDA channels [38], and/or Kir channels [64].

Before concluding this brief tour of the potential computational properties of single-compartment neurons, it is worth emphasizing that both linear filter and static transfer functions can be modified, by changing the expression of specific channels (intrinsic plasticity, see e.g. [18]) and/or the amplitude of noise, through non-specific inputs (leading to 'gain modulation', see e.g. [16,32]). In particular, they could be modified so that the neuron optimizes the information that it conveys about its inputs [69,11,46].

Impact of dendritic non-linearities on computation

Dendritic trees are highly complex structures allowing for computations that are richer than mere linear summation [39,9,67,42]. Qualitatively, four different types of behavior can arise at the level of local dendritic branches, shown schematically in Figure 2:

(i) Sub-linear summation due to passive cable properties of thin dendrites has been observed in cerebellar stellate cells [3•], which could allow these cells to be selective to sparse, rather than focused, presynaptic activity;
(ii) Linear summation of inputs has been observed both in hippocampal pyramidal neurons [14] and cerebellar Purkinje cells [13]. An approximately linear summation could be due to a compensation between passive cable properties and active conductances in dendrites [14];
(iii) Supra-linear, monostable behavior could arise due to active conductances in dendrites, triggered by NMDA receptors, calcium channels or sodium channels leading to dendritic spikes [36•,42,68•]. Thanks to these active conductances, neurons become more similar to multi-layer perceptrons: each dendritic branch functions as a first dendritic non-linearity (due to NMDA channels); their outputs are then summed and fed to the soma (see Figure 2b). Another non-linear unit could be realized by the apical tuft [36•]. Non-linear interactions between apical and basal regions of the dendritic tree of cortical pyramidal cells could serve as a mechanism for cortical associations [36•].
(iv) Bistable behavior of dendritic compartments can be realized by various positive feedback mechanisms. L-type calcium channels in a dendritic compartment of a motoneuron model have been shown to lead to bistability [6]. NMDA currents can also lead to bistability, as shown in single compartment models. Multiple bistable dendritic compartments can lead to robust multistable behavior in single neurons [27].

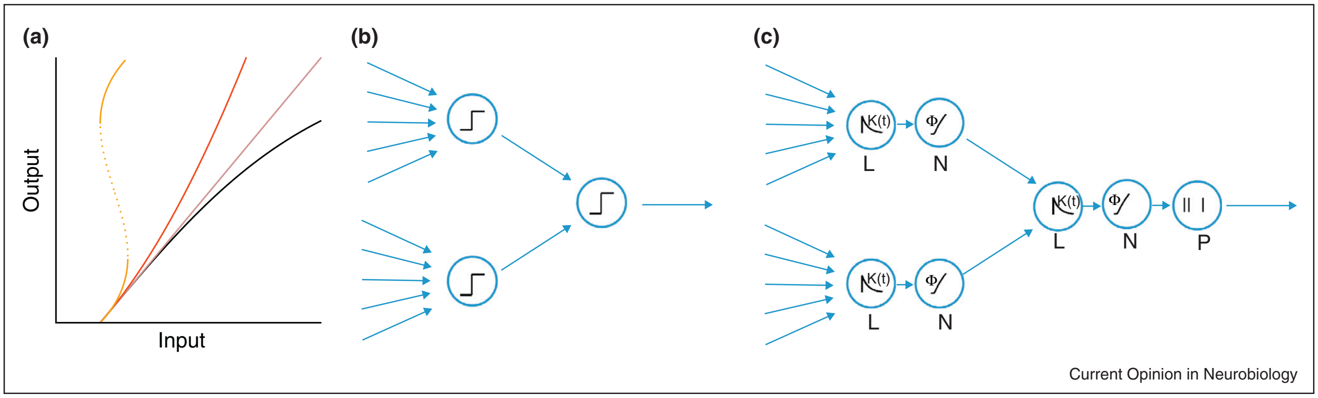
Current theoretical descriptions of spatially extended neurons are similar to the Mc-Culloch Pitts neuron, with added 'hidden units' (corresponding to each functional dendritic non-linear compartment - see several variants in Figure 2b). Single neurons therefore become similar to multi-layer perceptrons. These descriptions however typically ignore the temporal dimension, which suggests an extension of the conceptual framework to consider spatially extended neurons as trees of LN units, followed by a spike generation process at the soma or axonal initial segment (a 'LNLNP' model, see Figure 2c).

From the computational point of view, it is worth mentioning that spatially extended neurons with both sub-linear [15•] and supra-linear [55] dendrites can compute linearly non-separable functions, unlike the simple perceptron. Dendrites can therefore greatly enhance the computational power of neurons. Many types of computations relying on the spatial structure of dendrites have been described, such as discrimination of input sequences [8•], generation of direction selectivity [75], and detection of looming stimuli [21]. We also note that there have been significant recent advances in mathematical methods to reduce spatially extended neurons to reduced models that preserve the spatial specificity of inputs [28].

Synaptic computation and filtering

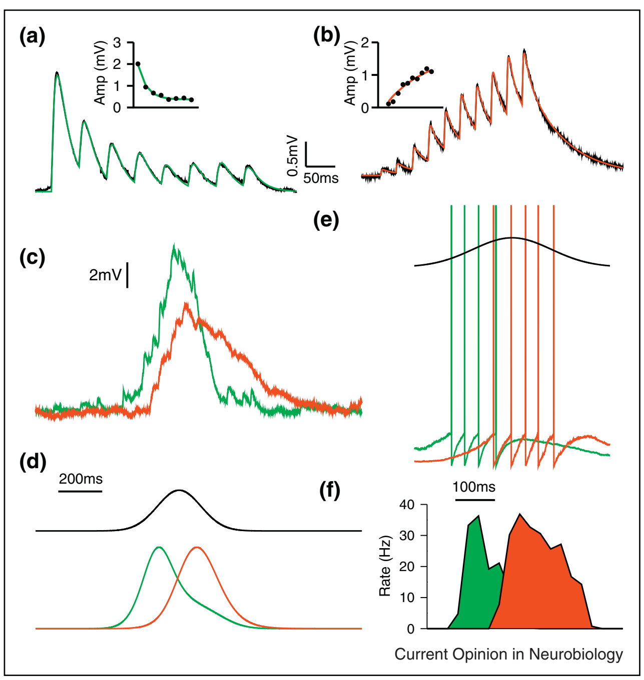
The dynamics of synaptic transmission lead to a form of pre-post cell-class specific short-term plasticity that shapes amplitudes of successive post-synaptic potentials (PSPs). This history dependence of the synaptic response (Fig. 3) can be characterised as exhibiting either: *depression* in which the successive synaptic amplitudes decrease due to depletion of presynaptic resources such as neurotransmitter vesicles that take a finite time - of the order of 100s of milliseconds - to replace; or *facilitation* in which

Figure 2



Computations by spatially extended neurons. a: Dendritic input/output transformations: sublinear (black), linear (brown), supralinear (red), bistable (orange). b: Dendritic static multi-layer perceptron model. Each dendritic branch is modelled as a threshold non-linear device. c: Dynamic multi-layer model (tree of LNPs, or LNLNP model).

Figure 3



Filtering of afferents by synaptic dynamics. (a) Neocortical layer-5 pyramidal-cell depressing response to a presynaptic pyramidal cell (PC) spike train and (b) Martinotti-interneuron (MI) facilitating response to a presynaptic PC spike train. Experimental data (black; Silberberg et al, 2004) are compared with a model (green and red) of synaptic dynamics (Tsodyks et al, 1997). Insets show amplitudes of successive EPSPs. (c) Simultaneous intracellular voltage recordings (Silberberg et al, 2004) of a PC and MI during a population burst in the PC population. Both cells have been hyperpolarised to prevent postsynaptic firing and so reveal the waveforms of the filtered synaptic drive. Note that the different short-term plasticity results in a signficant delay between the peak responses. (d) This subthreshold response can be captured by models of the synaptic dynamics (Richardson et al, 2005) and predict that, in the presence of a threshold, the MI population will fire with a relative delay to the PC poplation (e-f).

the amplitudes increase over a period of 10s of milliseconds due to accumulation of the calcium required to trigger vesicle release in the presynaptic terminal [1]. Though connections are typically classified as depressing or facilitating, they may exhibit a mixture of both depending on the frequency content of the presynaptic action-potential train.

These dynamics have been sucessfully modelled by an extension of the [19] binomial model, featuring n contacts, synaptic efficacy q, probability of release p to include time constants of recovery from depression τ_D and facilitation τ_F[72,2] allowing for the parameterization of a broad range of dynamics [10] between different pairs of cell classes. A number of elaborations of the basic model have been proposed to capture further experimental features such as activity-dependent restock rates [25], refractoriness of presynaptic release sites [53], and vesicle pool dynamics [44]; see [29] for a recent review of extended models.

Because synaptic dynamics are specific to pre and post-synaptic cell pairs it allows differential signalling via the same axon [43] as a presynaptic cell can make depressing and facilitating synaptic contacts onto different postsynaptic classes. Response to synchronous bursts of activity in the neocortical layer-5 pyramidal-cell network can produce peaks of activity that are separated by 100s of milliseconds in their postysnaptic targets [66,61] due to the decreasing or increasing response of depressing or facilitating synapses, respectively.

Synaptic filtering has been assigned many computational roles. Depression provides gain-control; during a steady, high presynaptic rate r the fraction of vesicles available for release is depleted and the charge delivered scales as $1/r$ and so the mean synaptic current, which is charge times rate, loses its dependency on the presynaptic rate. This saturation [72,2] has the effect of equalising responsiveness to afferent drive over a range of rates. The synapses nevertheless respond strongly to transient changes: a rate change Δ_r will result in a transient synaptic current of strength Δ_r/r. Synaptic depression therefore acts as a differentiator, responding to temporal changes in afferent drive and has been linked [2] to Weber's psychophysical law relating stimulus discrimination to the inverse of its intensity. The combined negative and positive feedback from depression and facilitation can also lead to a resonant effect, with the postsynaptic neuron responding preferentially to presynaptic bursts [34]. Later analyses have focussed on the effects of fluctuations at synapses. The stochasticity of the neurotransmitter-release process can recover the post-synaptic sensitivity to high-rate afferents [17] if the mean synaptic current saturates below the spike threshold. Both depression and facilitation have also been shown to provide a broadband filtering (frequency independence) of modulated Poissonian afferent drive, when the post-synaptic rate is high [37•]. Together with a recent study [62], these analyses have highlighted the significant role that short-term plasticity has in shaping the transfer of information through neuronal populations.

As the present survey shows, recent years have witnessed many advances in our understanding of the computational properties of single neurons. The analysis of neuron dynamics in a single compartment description has reached a rather mature stage. It provides a satisfactory account of different electrophysiological properties and of their contribution to the information processing of single neurons in the CNS *in vivo* when numerous and strongly fluctuating inputs are received in each integration time window. This is also the case for short-term synaptic plasticity with the qualification that it remains to be seen how the recent advances, mainly gained by the study of the singularly large Calyx of Held, apply to diverse synapses in the CNS. Very promising results have also been recently obtained on the potential contributions of dendrite dynamics and architecture to various computational tasks. These come mostly from experiments performed *in vitro*. The intense synaptic bombardment that is present *in vivo* could drastically change the picture, since it could potentially linearize the dynamics of perturbations around this background activity [4]. Recent *in vivo* studies have however demonstrated the presence and functional relevance of dendritic spikes *in vivo*[74•,68•]. A potentially promising direction would be to extend the analytical methods that have been used successfully to analyze the stochastic dynamics of point spiking neurons to spatially extended ones. This would certainly be helped by the development of simplified multi-compartment models that capture the essence of dendritic computations, perhaps along the lines that we have suggested above.

Another promising avenue for future research is to understand better the consequences of the rich computational properties of neurons and synapses at the network level. Theoretical studies have shown how steady states of network activity are determined by the neuronal transfer functions, as well as the statistics of synaptic strengths between the different populations connecting the network, while the dynamics is to a large extent determined by the neuronal and synaptic temporal filters. In particular, one expects the speed of the response of a network to be limited by the cutoff frequency of neuronal temporal filters, [70•]. Neuronal and synaptic properties also determine the nature of synchronized oscillations that can appear at the network level [12]. Short term synaptic plasticity also gives rise to oscillatory behavior at the population level [47] and can also be used to maintain information in short-term memory [50]. Finally, dendritic non-linearities have been shown recently to allow stable propagation of synchronous activity in random networks [49] or generate high-frequency network oscillations [48].

These theoretical developments, allied to the use of powerful experimental techniques, such as optogenetics and release of caged compounds, lead one to expect significant advances in the coming years in the understanding of the contribution of neuron-specific properties and anatomy to network dynamics and information processing.

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