Neural networks letter

Interaction of feedforward and feedback streams in visual cortex in a firing-rate model of columnar computations

Tobias Brosch, Heiko Neumann *

Institute for Neural Information Processing, University of Ulm, James-Franck-Ring, 89069 Ulm, Germany

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Visual sensory input stimuli are rapidly processed along bottom-up feedforward cortical streams. Beyond such driving streams neurons in higher areas provide information that is re-entered into the representations and responses at the earlier stages of processing. The precise mechanisms and underlying functionality of such associative feedforward/feedback interactions are not resolved. This work develops a neuronal circuit at a level mimicking cortical columns with response properties linked to single cell recordings. The proposed model constitutes a coarse-grained model with gradual firing-rate responses which accounts for physiological in vitro recordings from mammalian cortical cells. It is shown that the proposed population-based circuit with gradual firing-rate dynamics generates responses like those of detailed biophysically realistic multi-compartment spiking models. The results motivate using a coarse-grained mechanism for large-scale neural network modeling and simulations of visual cortical mechanisms. They further provide insights about how local recurrent loops change the gain of modulating feedback signals.

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1. Introduction

In visual cortex bottom-up streams convey sensory signals which are mirrored by top-down signals that re-enter earlier stages of processing to combine contextual or gist information with the sensory data (Bullier, 2006). These feedforward and recurrent signals are conveyed by different receptors in V1 neurons (Self, Kooijmans, Supèr, Lamme, & Roelfsema, 2012). The details of how these signal pathways fuse at the network level and even at the level of individual neurons is a topic of ongoing research investigations. Recent findings suggest that feedback signals arrive at sites distal from the soma while the sensory input is mainly integrated proximal to the soma (Larkum, 2013; Larkum, Senn, & Lüscher, 2004). The processing cascades along the dendritic tree of excitatory cells necessary to combine such converging input signals are regulated through small interconnected networks of excitatory and inhibitory cells (Palmer, Murayama, & Larkum, 2012). The modeling of such signal fusion, namely the combination of driving and modulating input signals, might focus on different levels of detail and complexity (Churchland, Koch, & Sejnowsky, 1990).

The goal of this paper is to provide a coarse-grained firing-rate model of single compartment units that fits data generated by biophysically realistic multi-compartment integrate-and-fire (IF) cells (as of Larkum et al., 2004). As a result, we suggest a computational logic of how visual feedforward and feedback streams combine and a neural network circuit that replicates physiological data. This functionality can be successfully described by a firing-rate model at the level of cortical columns.

2. Modeling the feedforward/feedback interaction in visual cortex

Visual perception is based on interactive processes in cortex, in which sensory inputs and contextual information are integrated (Bullier, 2006). The current state of the brain is characterized by the history and expectations given previous inputs and internal controls, such that a (visual) perceptor may lead to an activity trace in space–time (Larkum, 2013). Sensory (feedforward) input is associated with top-down (feedback) information at the cellular level when driving sensory input arriving at proximal dendrites near the soma is coincident with top-down inputs at distal dendrites (Cauller, 1995). Biophysically, the driving input opens a temporal window by generating back-propagating action potentials (bAP) to change dendritic conductance which, in turn, generates short activity bursts (Spruston, 2008).
2.1. Review of a biophysically realistic pyramidal cell model

Larkum et al. (2004) proposed a biophysically realistic 2-compartment layer 5 (L5) pyramidal cell model in which one compartment represents soma and proximal dendrites, S, and one compartment represents distal apical dendrite and tuft, D. The model dynamics are described by the change of membrane potentials $v_{S,D}$ of the interacting compartments

$$C_S \dot{v}_S = \frac{1}{R_S} (v_{rest,S} - v_S) + \frac{1}{R_T} (v_p - v_S) + \sum_{i \in T} g_{AHP} \cdot (E_K - v_S) \cdot \exp \left( -\frac{t - t_i}{\tau_K} \right) + I_{inj,S} \tag{1a}$$

$$C_D \dot{v}_D = \frac{1}{R_D} (v_{rest,D} - v_D) + \frac{1}{R_T} (v_S - v_D) + g_{Ca} \cdot m \cdot h \cdot (E_{Ca} - v_D) + I_{inj,D} \tag{1b}$$

with $C_{S,D}$ and $R_{S,D,T}$ denoting the respective membrane capacitances and resistances, $E_K, E_{Ca}$ specify the reversal potentials for the two compartments (K: sodium, Ca: calcium), $I_{inj,S,D}$ are the external input currents injected close to the soma and the distal dendrite, and $g_{AHP, Ca}$ denote membrane conductances of the respective compartmental subsystem. The set T denotes times at which spikes occurred. Conductances in the distal tufts compartment are regulated by a voltage-dependent mechanism, namely

$$r_m \dot{m} = -m + m_\infty (v_D),$$

$$m_\infty (v_D) = (1 + \exp (- (v_D - m_{0.5}) / s_m))^{-1}$$

$$r_h \dot{h} = -h + h_\infty (v_D),$$

$$h_\infty (v_D) = (1 + \exp (- (v_D - h_{0.5}) / s_h))^{-1} \tag{1b}$$

that leads to activity bursts through a backpropagating short-term voltage peak. This mechanism enables the coincidence detection between driving sensory and top-down inputs. The concentration of conductance changes is locally controlled by inhibitory microcircuits in cortical columns that influence the cellular compartments of excitatory cells (Larkum et al., 2004; Markram et al., 2004).

2.2. Development of a feedforward/feedback network-level circuit model

While the 2-compartment integrate-and-fire (IF) model described above captures realistic details of convergent bottom-up/top-down signal flows, the 4-D system model (Eq. 1a,b) is less suitable for large-scale neural network modeling and simulation. As an alternative we propose a simplified model with cell populations of cortical columns which covers the major computational properties of associating feedforward and feedback streams.

The following model is derived on the basis of evidences about circuit mechanisms involved at the cellular and sub-cellular level of interaction between small groups of cells in a cortical column. Pyramidal cells receive somatic, axonal and dendritic input signals. Proximal dendrites integrate excitatory input while the soma receives inhibitory input, like from Basket cells located in perisomatic regions (Markram et al., 2004; Spruston, 2008). Such inhibitory cells generally receive input from the same excitatory feedforward sources as the pyramidal cells that they inhibit (Callaway, 1998, 2004; Murayama et al., 2009). Accordingly, the chains $[p \to r]$ and $[p \to q \to r]$ (Fig. 1(a), left) form a feedforward self-inhibiting circuit for the driving input stream. We assume that the inhibition acts in a shunting, or divisive, fashion. We further assume that the inhibitory cell is tonically active to decrease the output cell sensitivity to input noise.

A pyramidal cell, or group of cells, can be brought to fire when enough synaptic feedforward input drives the cell to exceed a threshold $\theta$. Tonic inputs to the excitatory and inhibitory cells, r and q, respectively, decrease/increase the amount of excitation that is needed to reach the firing threshold. If the r cell in the circuit is activated then it becomes sensitive to available feedback signals that arrive at distal apical tuft dendrites (Larkum, 2013) to integrate the two separate signal streams (Bullier, 2006; Larkum, 2013; Larkum, Zhu, & Sakmann, 1999; Self et al., 2012; Spruston, 2008). In a nutshell, the circuit exhibits gating characteristics in which a dominant feedforward input enables feedback signals to modulate the driving signal (Callaway, 1998, 2004; Sherman & Guillery, 1998). At the cellular level the gating is realized by backpropagation-activated coupling (Larkum, 2013). Here, we
simplify the net interaction by a cascade of dis-inhibiting the self-inhibitory action for the driving input (Fig. 1(a)). Excitatory feedback netFB that arrives from higher stages of processing activates inhibitory interneurons (activity q), which, in turn, dis-inhibits the driving signal leading to a response facilitation at the output (Callaway, 1998; Palmer et al., 2012; Self et al., 2012). Recent evidence suggests that such specific local inhibitory-to-inhibitory cell connections build local microcircuit modules to implement in vivo disinhibitory mechanisms (Jiang, Wang, Lee, Stornetta, & Zhu, 2013; Pi et al., 2013). We assume that the [qD → q] interaction is divisive in nature. Furthermore, a weak recurrent excitatory chain [g(r) → qD] (Fig. 1(a), dashed arrow) is included so that the circuit output leads to an activation of the dis-inhibitory mechanism. Evidence suggests that such inhibitory mechanisms influence the more distal sites of pyramidal cells (Callaway, 1998, 2004; Spruston, 2008). Local inhibitory feedback circuits that involve Martinotti cells have been studied to investigate how they regulate the state of ensembles of pyramidal cells (e.g., Murayama et al., 2009, Palmer et al., 2012, Silberberg & Markram, 2007).

The circuit components suggested above can be formally defined by different elements each describing temporal state changes. The states are interpreted as cell membrane potentials (with activities r, q, and qD as in Fig. 1(a)). The components are mutually coupled via excitatory or inhibitory links and inputs to the circuit are provided by the driving feedforward activity p and the (modulating) feedback signal netFB. The equations contain several parameters, in which β denotes the output saturation level, αr,q,D Denote the passive decay rates, δ and γ denote constant weights for the respective shunting inhibition, ε controls the strength of the recurrent excitation from the output stage to the dis-inhibitory interneuron, and βr,q,D denote the membrane constants of the neurons. Signals li−q−r are constant tonic activations. The function g(·) denotes a firing rate function (assumed here as threshold-linear, e.g., $g_\theta(x) = \max(x - \theta, 0)$, with threshold $\theta$).

### 3. Properties of the circuit

#### 3.1. Analysis of steady-state and stability properties

We investigate two distinct model instances of the circuit defined in Eq. (2) with or without the internal recurrence [g(r) → qD]. First, when the recurrence is discarded ($\varepsilon = 0$), then the model can be analyzed in a straightforward manner. We calculate the steady-state output response $r_\infty$ by directly solving for the individual equilibrium states, i.e., $(r_\infty, q_\infty, qD_\infty) = (0, 0, 0)$,

$$r_\infty = \frac{(\beta \cdot p + li_{\text{ton}-r}) \cdot (\alpha_q + \gamma \cdot \text{netFB})}{(\alpha_p + p) \cdot (\alpha_q + \gamma \cdot \text{netFB}) + \delta \cdot (p + li_{\text{ton}-q})}. \quad (3)$$

Inspection of the numerator term shows that the net effect of the top-down signal yields a multiplicative enhancement of the driving input signal p (together with tonic li−q−r) by the feedback signal netFB. It captures the net effect as reported by Larkum (2013) that the driving feedforward input p acts as a gate (or switch) to make available feedback signals netFB become effective (compare Self et al., 2012). When the driving signal is missing (p = 0) no output activation can be generated by feedback signals (netFB > 0) alone (except for very strong netFB levels, as seen in physiological data as well; Larkum et al., 2004, their Fig. 1). If p > 0, the activity is enhanced by any feedback signal netFB > 0 leading to an effective increase of the output, i.e., $\Delta r \propto p \cdot \text{netFB}$ (for small to moderate inputs). If netFB = 0 the output yields r ∝ p (compare Bullier, 2006). The total activation is controlled by the normalization term in which the input signals determine the response saturation level. The influence of the tonic inhibition, li−q−q in the q-state (Eq. (2)), acts divisively on the r-state, indicating that an increased tonic self-inhibition down-modulates the responsiveness of the output cell r.

The second variant of the circuit that incorporates the internal recurrent loop [g(r) → qD] is investigated using $\varepsilon > 0$ in Eq. (2). Under the assumption that the dis-inhibitory mechanism (denoted by qD) quickly responds to any input, the network circuit can be simplified to a 2-D system by directly using the steady-state response of qD to yield (Fig. 1(b))

$$F(r, q) = r_\infty = -\alpha_r \cdot r + (\beta - r) \cdot (p - \delta) \cdot r \cdot q + li_{\text{ton}-r}$$

$$G(r, q) = \tau_q \cdot \dot{q} = -\alpha_q \cdot q + p - \gamma \cdot q \cdot (\text{netFB} + \varepsilon \cdot g(r)) + li_{\text{ton}-q}. \quad (4)$$

The resulting non-linear system is a special case of the general competitive networks analyzed by Cohen and Grossberg (1983). In Suppl. 1 (see Appendix A), we demonstrate that all requirements are met such that for the system in Eq. (4) absolute stability is guaranteed by the existence of a Lyapunov function. In order to simplify the analytical results, we set li−q−r = 0 (Eq. (2)). The steady-state response of the system (F, G) is denoted by

$$r_\infty = \frac{1 - (\alpha_p + p) \cdot (\alpha_q + \gamma \cdot \text{netFB}) + (\gamma \varepsilon \beta \delta - \delta \cdot p - li_{\text{ton}-q})}{\varepsilon \cdot (\alpha_p + p)}$$

$$q_\infty = \frac{1 - (\alpha_p + p) \cdot (\alpha_q + \gamma \cdot \text{netFB}) - (\gamma \varepsilon \beta \delta - \delta \cdot p - li_{\text{ton}-q})}{\varepsilon \cdot (\alpha_p + p) \cdot (\alpha_q + \gamma \cdot \text{netFB})}. \quad (5)$$

The net output activation r is shown to be mainly determined by components of the form $p = (\alpha_p + \gamma \cdot \text{netFB})$ with the feedback signal gated by the feeding input as in Eq. (3). In addition, unlike Eq. (3), the net response contains linear difference terms of the feedforward and feedback signals which have low amplitude scaling from the circuit coefficients in Eq. (3). The feedback sensitivity is characterized by $d/d$ netFB $[r_\infty]$, which finally yields

$$\frac{d}{d\text{netFB}} r_\infty = \frac{4 \gamma \varepsilon \beta p \cdot (p + li_{\text{ton}-q}) \cdot (\alpha_q + \gamma \cdot \text{netFB})}{(\alpha_p + p) \cdot (\alpha_q + \gamma \cdot \text{netFB}) + (\gamma \varepsilon \beta \delta - \delta \cdot li_{\text{ton}-q})}\frac{r_\infty}{\varepsilon \cdot (\alpha_p + p) \cdot (\alpha_q + \gamma \cdot \text{netFB})}. \quad (6)$$

Eq. (6) shows that for large enough $\varepsilon$ and for netFB an increase in $\varepsilon$ decreases the feedback sensitivity of the circuit, in the limit, approaching lim$\varepsilon\to\infty d/d$ netFB $[r_\infty] = 0$. \footnote{The details of the results and their derivation are summarized as supplementary material (Suppl. 2, see Appendix A).}

#### 3.2. Network simulations and comparison with physiological recordings

Single cell recordings have generated current-to-rate-transfer functions with currents injected to different somato-dendritic compartments (Larkum et al., 2004). These data were fitted by the detailed 2-compartment model reviewed in Section 2 (Eq. (1)). We evaluated our circuit model by adjusting parameters for the model variant with different values of $\varepsilon$ to generate graded responses r as output firing rates. One of the model fits is displayed in Fig. 2. It can
be seen that the simplified network replicates the key functionality of integrating two input signals from the feedforward and the feedback path. This not only provides a functional interpretation of the backpropagating action potentials reported by Larkum et al. (2004) but also suggests an alternative way the brain can realize such gating. While driving input gates the circuit by defining a dominant path of integrated bottom-up sensory signals, available feedback activation from distal sites re-enters the computation by modulating the bottom-up sensory activation (Section 3.2). In extreme cases of high-level netFB signals the circuit could be excited even when \( p = 0 \) (like in physiology; Larkum et al. (2004)).

Furthermore, we investigated the influence the recurrent loop \( [g(r) \rightarrow q_D] \) on the overall output characteristics. The mathematical analysis of the steady-state circuit response has shown that the increase of the gain by correlated p and netFB input is still preserved. With the closed recurrence the amplitude of the output \( r \) is increased (due to reduced inhibition of the driving input signal). In addition, now the amplitude of the gain is reduced monotonically as a function of increasing value of \( \varepsilon \). Fig. 3 shows the results for \( \varepsilon \in \{0.0, 0.07, 0.14\} \).

4. Discussion and conclusion

4.1. Summary of key contributions

Re-entrant signals from higher-level stages of cortical processing tend to modulate cell responses driven by bottom-up driving input signals (Bullier, 2006; Grossberg, 1973). Such a modulation can be traced to the level of individual cells where a small network of interconnected neurons builds a cortical association unit of processing (Larkum et al., 1999, Larkum, 2013). The main contributions of this work are threefold. First, we propose a network model that captures the key functionality of combining feedforward and feedback signal streams demonstrating similar parametrically varying response properties as in a detailed multi-compartment integrate-and-fire model of pyramidal cells. The simplified functional description provides a neural network level model (Churchland et al., 1990) that fits detailed response characteristics of single cells. The pattern of match between the response characteristics were achieved already with a variant of the proposed circuit without the internal recurrent loop which makes the circuit model essentially linear in its response property. Adding a local recurrent loop in which the disinhibition is driven in part by the output firing-rate was motivated by neurophysiological findings (Palmer et al., 2012; see also Markram et al., 2004 for a discussion about strategic innervation schemes by local cell connections). The recurrence provided additional functional flexibility to adjust the impact of strong modulating feedback signals netFB. This makes the model valuable for large-scale network simulations in which additional small-scale detail is lumped into simplified components.

Second, the result derived from the analysis of the formal circuit equations demonstrates that the bottom-up and top-down signal fusion here operates such that the feedback sensory signals act as drivers while the feedback signals act as modulators (as observed in experimental findings; Bullier, 2006; Sherman & Guillery, 1998). The functional role of both signal streams is asymmetric: while non-zero feedforward streams drive the output of the circuit feedback signals re-enter by modulating, or enhancing, the driving signal. However, they cannot drive the target circuit alone. In the circuit the feedback signal's self-inhibition is dis-inhibited by the input delivered by feedback signals. This can be directly seen when \( i_{ton−r} \) in Eq. (3) is set to zero. For the general case when \( i_{ton−r} > 0 \) with \( \beta \cdot p \gg i_{ton−r} \) the output response is negligible when \( p = 0 \) (under these conditions only very strong feedback can excite the neuron above firing threshold, as reported in Larkum et al., 2004, their Fig. 1).

Third, an internal recurrent loop was incorporated in the proposed circuit which was motivated by evidence that somatic output recurrently excites proximal inhibitory cells which, in turn, synapse distal dendritic sites. Within the proposed circuit model we investigated such a loop in which the inhibitory cell is excited by the output cell (forming the \( [g(r) \rightarrow q_D] \) chain) which forms a loop of disinhibitory interaction \( [g(r) \rightarrow q_D \rightarrow q \rightarrow r] \) (Palmer et al., 2012). The relative strength of impact the output \( r \) has on \( q_D \) is parametrically controlled by the constant \( \varepsilon \). The analytical as well as computational investigations of the influence of the recurrent loop demonstrated that stronger weight of the recurrence weakens the influence of the reentrant modulatory feedback signal netFB.
4.2. Relation to previous models

While previous models of pyramidal cells considered the main feedforward drive of the input integration recent experimental evidence emphasized the importance of non-linear interaction. For instance, Poirazi, Brannon, and Mel (2003) have shown that the somatic integration can be represented in abstract terms by a 2-layer network that consists of spatially distributed dendritic sub-units, each providing a thresholded sensory input component, and a summation of these driving components passes a threshold non-linearity prior to generating a cell response. While the model does not consider effects that input at distal sites might have on the proximal integration, the authors already speculate about potential non-linearities in which distal sub-units might multiplicatively boost the proximally generated responses. Here, we propose how such non-linear modulatory effects might be implemented at a similar level of granularity replicating physiological data.

Various modeling investigations have suggested that top-down feedback signals are used to modulate the bottom up driving input. Examples are pyramidal cell spike synchronization (Eckhorn, Reitboeck, Arndt, & Dicke, 1990), brightness perception (Gove, Grossberg, & Mingolla, 1995), boundary detection and grouping (Grossberg, Mingolla, & Ross, 1997; Neumann & Sepp, 1999; Thierscher & Neumann, 2003), motion integration (Bayerl & Neumann, 2004; Berzhanskaya, Grossberg, & Mingolla, 2007), figure-ground segregation (Barnes & Mingolla, 2013), and feature attention (Reynolds & Heeger, 2009). The core FF–FB interaction term in all these models reads

\[ r \propto \text{net}^{FF \cdot \text{FB}} \cdot (1 + \lambda \cdot \text{net}^{FB}) \]  

(7)

where \( \text{net}^{FF/FB} \) denote activations in the bottom-up feedforward driven pathway and the top-down feedback pathway, respectively, and \( \lambda \) is a constant amplification factor. The right-hand side of Eq. (7) can be observed in the numerator of Eq. (3) by defining \( p \equiv \text{net}^{FF}, \gamma \equiv \lambda, \) and for \( u_{q} = 1 \) while assuming \( k_{\text{on-r}} = 0. \) This concludes that above-mentioned models that were defined on a rather ad-hoc basis are now justified by generic circuit mechanisms that occur at the level of cortical columns, like in V1.4

A normalizing factor \( N(p, \text{net}^{FB}) \) that occurs as the net effect in Eq. (3) guarantees that the output activation \( r \) stays within bounds. Such mechanisms can be intrinsic to the current location (as in Rust, Mante, Simoncelli, & Movshon, 2006 or generated by a mechanism of divisive pool normalization Carandini & Heeger, 2012, Carandini, Heeger, & Movshon, 1999, Grossberg, 1973). The normalization enforces an energy conservation property such that previously enhanced activation, in turn, tends to suppress other activation in the pool (biased competition; Desimone & Duncan, 1995).

4.3. Perspective

Recent investigations have demonstrated that different receptor types convey feedforward and feedback signals in V1 (Selt et al., 2012). In a similar direction, we suggest that the proposed model makes some testable predictions concerning the network architecture on the columnar level. For example, the dynamics of our model of cortical columns suggest a computational role for the local circuits with inhibitory-to-inhibitory cell connections which can implement the same gating mechanism as reported by (Larkum et al., 2004). Also, the self-inhibition from cells near the soma assume a specific functional role in which the self-inhibition can be disinhibited by feedback. Specific physiological and pharmacological methods might be used to target these microcircuit mechanisms. Selective blocking might eliminate the enhancement effects by feedback but paradoxically enhancing the effect of driving feedforward signals alone without any feedback.

The suggested circuit also explains why the effectiveness of the modulating feedback signals \( \text{net}^{FB} \) might vary its strength for different cells. A systematic increase of the strength of the recurrence \( [g(r) \rightarrow q_{0}] \) leads to a reduced modulation gain feedback signals have on the driving feedforward signals. It has been reported that some cortical cells show enhancement, e.g. by top-down attention effects, while others do not (labeled as A- and N-sites; Roelfsema, 2006). We hypothesize that excitatory cortical cells of both types can be described by the proposed generic circuit model. A single parameter variation with settings in different parameter regimes might lead to such distinctive response properties and categorically different characteristics.

To sum up, the suggested neural network circuit provides evidence that modulating feedback is gated by bottom-up driving input signals in a multiplicative fashion. The numerous computational models discussed above now receive a computational justification that relates the core functionality to detailed experimental data of single and groups of cortical pyramidal cell responses. The results suggest that the gating mechanism in Eq. (7) captures the core functionality of linking bottom-up driving input and reentrant feedback streams. In concert with activity normalization this defines an organization principle in neural computation and as a canonical association mechanism for complex neural interactions in visual cortex (Carandini & Heeger, 2012).

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Appendix A. Supplementary data

Supplementary material related to this article can be found online at http://dx.doi.org/10.1016/j.neunet.2014.02.005.

References


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4 Here, the mechanism denotes the net effect a driving bottom-up stream that self-inhibits its output activation has when it is disinhibited by coexisting feedback signals.