Relating the diversity of interneuronal subtypes to their functional roles in development and sensory processing

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Introduction

Genetic Parvalbumin (PV+) and Somatostatin (Sst+) markers have been essential in disentangling GABAergic interactions in the cortex and linking circuits to function. Based on the current literature several broad properties can be assigned to PV+ neurons:

- Fast, strong responses, linearly integrating feedforward and recurrent input[1], weakly feature selective and also provide perisomatic inhibition[2].

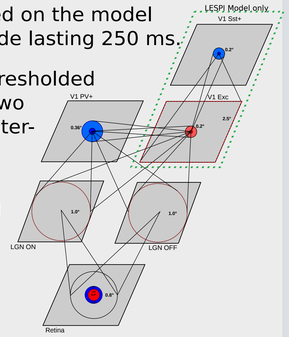
and Sst+ neurons:

- Slow, facilitating responses, recurrently driven, stronger feature selectivity and dendritic inhibition[3].

Here we present the first spatially calibrated model of cortical development, which incorporates the distinct properties of different neural populations. This allows us to make specific predictions about the computations performed by the different neural populations and will allow us to model the effect of different manipulations and modulatory inputs on the V1 circuit.

Model Structure

- Visual patterns are presented on the model retina for a simulated saccade lasting 250 ms.
- Activity is computed as a thresholded dot product propagated to two sheets with ON and OFF center-surround receptive.
- Contrast gain-control is mediated via divisive lateral inhibition in the LGN.
- The ON and OFF sheets project to V1 via initially random weight matrices.
- Feedforward activity in excitatory & inhibitory V1 sheets drive recurrent interactions until a steady state is reached.



LGN & V1: γ: projection strength, η: neural activity, w: weights, σ: threshold function, c constant
V1 : λ_{SM}: surround modulation, β: exponent, τ: hysteresis time constant

$$\text{Activity:} \quad \eta_j(t+\delta t) = \sigma\left(\left(\frac{\sum_p \gamma_p \sum_{i\in F_{jp}} \eta_i(t)\omega_{ij}}{c+\gamma_{gc}\sum_{i\in F_{jp}} \eta_i(t)\omega_{ij}}\right)\lambda_{SM}\right)^{\beta}$$

$$\text{Hysteresis:} \quad \eta_h(t+\delta t) = (\eta(t) + \tau[\eta(t+\delta t) - \eta(t)])$$

Self-organization is mediated by Hebbian learning, which adjusts connection weights after every saccade. The weights are constrained with divisive post-synaptic weight normalization per projection p with learning rate α_p.

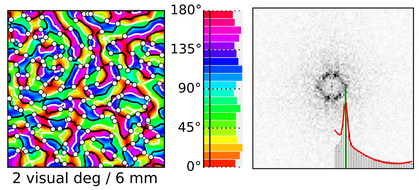
$$\text{Hebbian Learning:} \quad \omega_{ij}(t+\delta t) = \frac{\omega_{ij}(t)+\alpha_p\eta_j\eta_i}{\sum_{k\in F_{jp}} \omega_{kj}(t)+\alpha_p\eta_j\eta_k}$$

Inhibition and Development

A sensitivity analysis was used to determine how the linearity (β) and hysteresis time constant (τ) of the inhibitory population would affect the development of our model. In particular we investigate the effect of these parameters on orientation pinwheel density (ρ), which has been consistently confirmed to be near π across species[4]. Additionally the effect on map stability and selectivity of different populations was investigated.

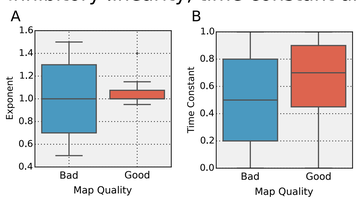
Additionally the analyses introduced as part of the GCAL single population model[5] will be replicated to confirm robustness and stability of the two population model.

Pinwheel and Hypercolumn Analysis



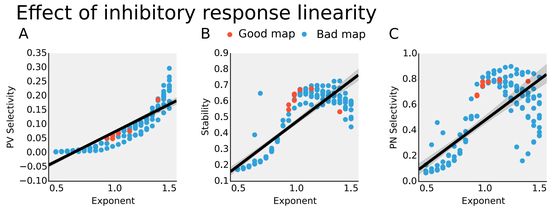
Hypercolumn distance is determined by fitting a function to the FFT power spectrum. Pinwheel density (ρ) is the number of pinwheels per hypercolumn.

Inhibitory linearity, time constant and map quality



Results were partitioned into good and bad maps based on a divergence from π pinwheel density (where a good map was defined as ρ=π±0.1). Both linearity of response and a fast time constant were associated with better map quality.

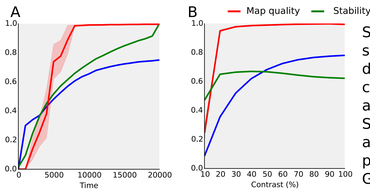
Effect of inhibitory response linearity



Effect of inhibitory response linearity on A) mean inhibitory selectivity, B) map stability and C) mean excitatory selectivity. Linear response was associated with low inhibitory selectivity, high stability and high excitatory selectivity.

Based on these results, the linear and fast responses of PV+ neurons make them ideally suited to drive map development.

Developmental timecourses and contrast sensitivity

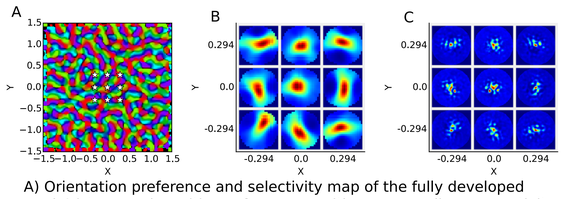


Stability, map quality and selectivity A) over development and B) across contrasts replicating GCAL analysis[5]. Demonstrates SEPI model exhibits robust and stable development on par with single population GCAL model.

Long-range Interactions

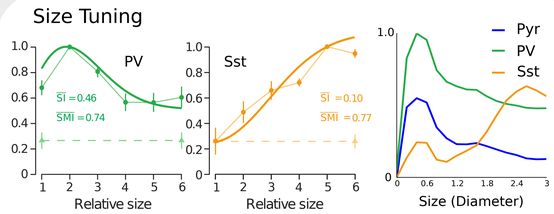
In this section we will explore how a long-range disynaptic excitatory circuit driving Sst+ neurons can give rise to their orientation and size tuning properties and allows them to mediate a switch from long-range facilitation to suppression.

Developed connectivity



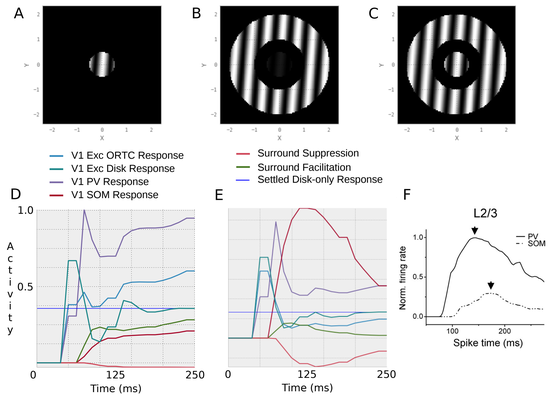
A) Orientation preference and selectivity map of the fully developed model (stars mark positions of neurons, with corresponding connectivity profiles shown in B and C. B) Afferent connection weights. C) Lateral connection weights.

Size Tuning



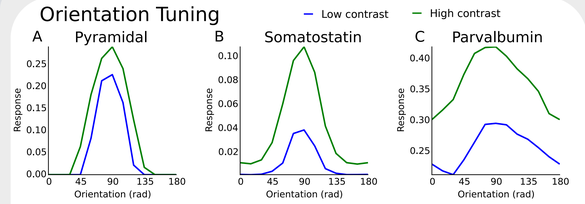
Divergent size tuning profiles of PV and Sst neurons. A, B) Reproduced from Adesnik et al. (2012)[3], C) Model size tuning curves. Exponential activation function induces Sst neurons only to respond strongly under strong local stimulation or for large stimuli.

Time Course of Surround Modulation



A, B, C) Orientation contrast stimuli, disk only, low contrast disk and high contrast annulus and high contrast disk with annulus respectively. D, E) Detailed time courses demonstrating how long-range interactions can give rise to both facilitation and suppression depending on local contrast. Low local contrast gives rise to facilitation from the surround, while high local contrast induces strong Sst+ activity, which cancels out surround facilitation and results in net suppression. F) PSTHs of PV+ and Sst+ activity in mouse V1, reproduced from Ma et al. (2011)[2].

Orientation Tuning



Orientation Tuning curves of a model A) pyramidal, B) Sst and C) PV neuron in the same retinotopic location all displaying contrast invariance. PV neurons have significantly broader tuning due to their persistently higher activity and linear response function.

Discussion

Based on the known properties of PV+ and Sst+ neurons our model makes multiple predictions.

PV+ neurons:

- Linear integration, strong inputs and low threshold sufficient to explain broad tuning.
- Essential for robust and stable orientation map development, due to their ability to locally decorrelate activity.

Sst+ neurons:

- Facilitating responses and weaker inputs sufficient to explain their sharp tuning.
- Mediate switch from facilitation to suppression dependent on local contrast, visual context and attentional state.

Conclusion

In this model we demonstrated how the distinct firing properties of different neural populations can give rise to their functional tuning through development. The model also reconciles the assumed Mexican hat connectivity of developmental models with the anatomical reality of short-range inhibitory and long-range excitatory interactions.

In future the model will allow us to perform cell type specific manipulations to test different hypothesis about state dependent modulation and the role of different neural subtypes in the neural circuit. Finally it will allow us to investigate how co-occurence statistics embedded in lateral connections can dynamically modulate the response of neurons depending on visual context and attentional state.

References

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