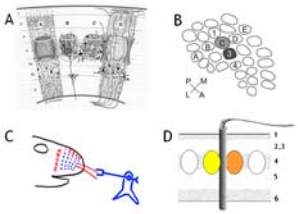
Physiologically constrained population modelling of cortical activity in rat barrel cortex measured with laminar electrodes

G.T. Einevoll[1], A. Devor[2], I. Ulbert[2,3], M. Kermit[1], E. Halgren[2], and A.M. Dale[2]

[1] Agricult. Univ. Norway; [2] NMR Ctr., MGH, Harvard Med. Sch., Charlestown, MA; [3] Hung. Acad. Sci., Budapest, Hungary

Laminar electrode recordings

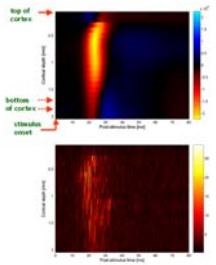
- Need for experiments probing cortex at level of cortical microcircuits [∼1 mm, ∼100000 neurons]
- Here: **Laminar electrode** recordings of response in barrel cortex in anesthetized rat following single-flick whisker stimulation
- Data interpretation in terms of **cortical populations**
- Present experimental setup: (i) 100 μm contact distance, (ii) saline on cortical surface, (iii) alphachlorolose as anesthetic



Cartoon of barrel cortex (A) and anatomical arrangement of barrels in layer 4 (B). Schematic illustration of experiment (C) and placement of laminar electrode (D).

Example single-trial data

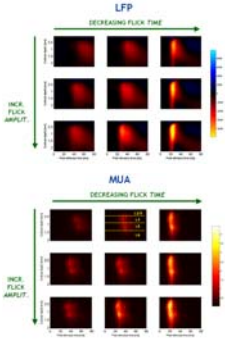
- **Local Field Potential (LFP):**
  - Low-pass filtered at 500 Hz
  - Thought to reflect ***dendritic response to synaptic input***
- **Multi-Unit Activity (MUA):**
  - High-pass filtered at 750 Hz
  - Rectified
  - Thought to be a measure of ***action-potential*** firing in populations



Example single-trial LFP data (top) and corresponding MUA data (bottom)

Trial-averaged data

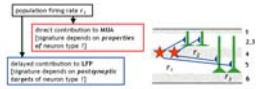
- Example data with 27 different stimuli; 40 repetitions of each



Trial-averaged LFP data, $\Phi_{LFP}(z_j, t_k)$, (top) and MUA data, $\Phi_{MUA}(z_j, t_k)$, (bottom) for 9 out of 27 stimulus conditions.Baseline is subtracted.

Joint LFP/MUA modelling

- Constraints in mathematical analysis:

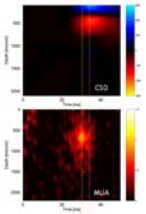


- Mathematical formulation:

$$\phi_{\mathrm{MUA}}(z_j, t_k) = \sum_i M_i(z_j)\, r_i(t_k)$$

$$\phi_{\mathrm{LFP}}(z_j, t_k) = \sum_i L_i(z_j)\, (h * r_i)(t_k)$$

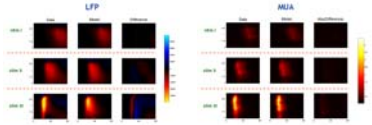
- Convolution kernel assumed to be be exponential: $h(t) \sim e^{-t/\tau}$
- Supported by particular weak-stimulus data example where only layer 4 population appears to fire action potentials. Then:
  $\phi_{\mathrm{MUA}}(z_j, t_k) \sim M(z_j) r(t_k)$,
  $\phi_{\mathrm{LFP}}(z_j, t_k) \sim L(z_j)\, (h * r)(t_k)$
  $\Rightarrow h(t)$ can be assessed directly
  - Exponential kernel gives excellent fit with $\tau \sim 10$ ms.



$CSD(z,t) \sim -\partial^2 \phi_{LFP}(z,t)/\partial z^2$ *(top) and* $\phi_{MUA}(z,t)$ *(bottom) for weak stimulus example*

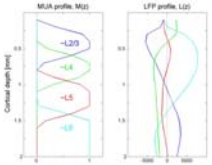
Model fit

- Assumption: 4 cortical populations
- Fitted model accounts for ∼90% of LFP and ∼95% of MUA data variance



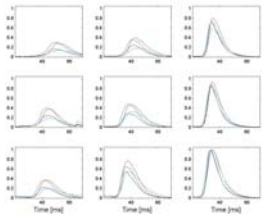
Model predictions

- Fitted time constant: $\tau = 10$ ms



Fitted spatial profiles $M_i(z)$ (left) and $L_i(z)$ (right), i=1,2,3,4

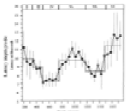
- Spatial MUA profiles $M_i(z)$ suggest that fitted cortical populations correspond to 1:**L2/3**, 2:**L4**, 3:**L5**, 4:**L6**



Fitted synaptic drive $h * r_i(t)$ from four cortical populations. Data normalized to maximum response.

- Predicted temporal order of population firing activity:
  L4 → L2/3 → L5 → L6

- Both observations compatible with literature (cf. *Thompson & Bannister, Cerebral Cortex* **13**, *5–14 (2003)*; *Armstrong-James et al., J. Neurophys.* **68**, *1345–58 (1992)*)

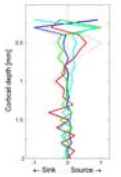


Average latencies to principal whisker stimulation (from Armstrong-James et al., 1992)

Interpretation of LFP profiles

METHOD I: Estimate of postsynaptic CSD

- Characteristic *current-source density (CSD)* following firing activity in each population found by
  - Cylindrical Current-Source Density (CCSD) method (cf. *Pettersen & Einevoll, SFN meeting, 2004*)
  - Standard Current-Source Density method (SCSD)
    $[\, CSD(z_j) \sim -(\phi(z_{j+1} - 2\phi(z_j) + \phi(z_{j-1}))/\Delta^2 \,]$

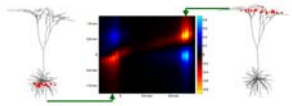


- Observations:
  - L2/3 ⇒ sink-source pair in top layers
  - L4 ⇒ source in top layers; wider sink in granular and infragranular layers
  - L5 ⇒ sinks and sources in all layers; sink in infragranular layer

Predicted CSD profiles following firing in cortical populations i, $i = 1, 2, 3, 4$. Solid lines: CCSD for 0.8 mm diameter. Dashed lines: SCSD.

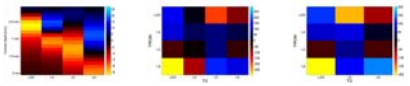
METHOD II: Estimate of synaptic connection pattern

- Step 1: Calculation of LFP-signatures for synaptic drive of cylindrical populations of reconstructed L2/3, L4, and L5 cells [using NEURON + Maxwell's equations]

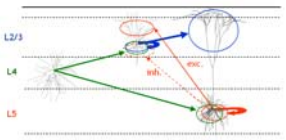


Example LFP signatures at axis of cylindrical population (diameter 1 mm) of layer 5 cell (cells used in Mainen & Sejnowsky, Nature 382, 363–6 (1996).

- Step 2: Fit LFP data to templates (here 1. principal component) to determine (i) population diameter (∼ 1 mm), (ii) electrical properties at cortical surface
- Step 3: Project predicted $L_i(z)$ to fitted population LFP templates to obtain synaptic *connection matrix*



Fitted LFP templates (left) and predicted synaptic connection matrices including all populations (middle) and excluding LFP contributions from L4 (right)



Tentatively suggested synaptic connections