An analysis of functional connectivity across time-scales

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Background

The interactions between neural signals can be estimated using signals recorded with a number of different techniques and, consequently, different temporal resolutions.

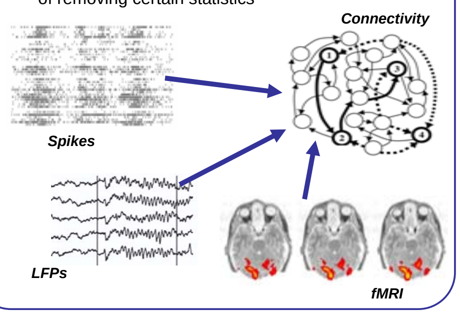
Questions

What does connectivity estimated using one technique tell us about other timescales?

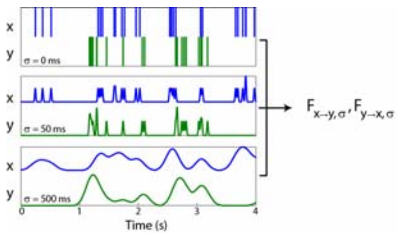
Can we combine estimates from different techniques?

Approach

1. Large-scale (>100) multi-electrode recordings
2. Low-pass filter the signals to mimic different techniques
3. Explore the relationship between connectivity estimates
4. Fit a model to spike data and simulate to see the effects of removing certain statistics



Filtering Analysis



After smoothing and down-sampling spike trains we…

1) Estimate pair-wise Granger Causality:

$$x(t) = \sum_{\tau=1}^{k} a_{1,\tau} x(t-\tau) + \epsilon_1(t)$$

$$x(t) = \sum_{\tau=1}^{k} a_{2,\tau} x(t-\tau) + \sum_{\tau=1}^{k} b_{2,\tau} y(t-\tau) + \epsilon_2(t)$$

$$F_{Y \to X} = \log\left(\frac{var(\epsilon_1)}{var(\epsilon_2)}\right)$$

2) Simulate spikes using a Generalized Linear Model:

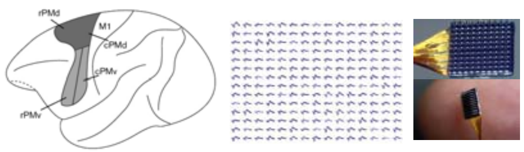
- Point-process likelihood function (Okatan 2005)
- Infer parameters using Maximum Likelihood Estimation

$$\lambda_i(t \mid \boldsymbol{\alpha}_i, \boldsymbol{H}_t) = \exp\left(\alpha_{i,0} + \sum_{c=1}^{C}\sum_{\tau=1}^{k} \alpha_{i,c,\tau} n_c(t-\tau)\right)$$

$$n_i(t) \sim Poisson(\lambda_i(t \mid \boldsymbol{\alpha}_i, \boldsymbol{H}_t)\Delta t)$$

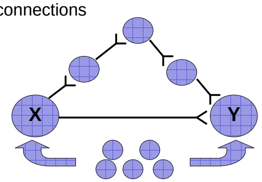
Data

- Multi-electrode arrays in PMd and M1 (Hatsopoulos et al. 2004)
- Dataset B: 183 neurons (108 in PMd, 75 in M1), ***Sleep (NREM)***
- Dataset R: 143 neurons (65 in PMd, 78 in M1), ***Reaching***

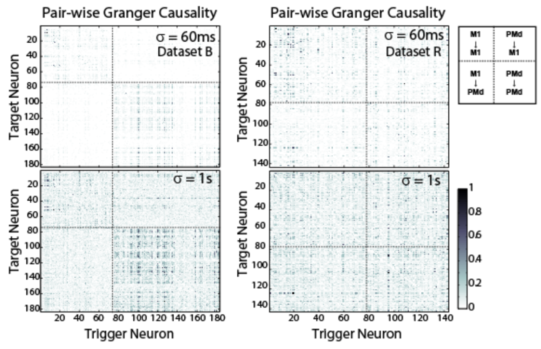


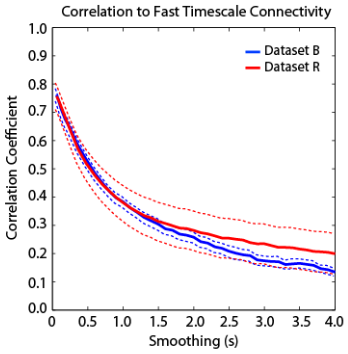
Functional connectivity methods estimate the influence of one neuron (or neural signal) on another, this includes…

Direct (monosynaptic) connections
Indirect (polysynaptic) connections
Correlated input



Results: The predictive value of slow-timescale connectivity



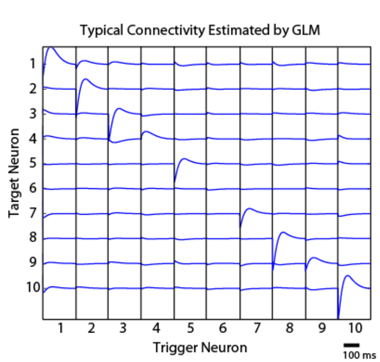


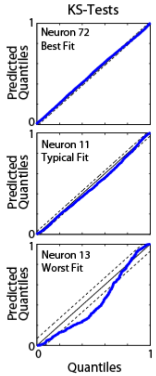
- Slow timescale connectivity is well correlated with fast timescale connectivity down to ~0.5 Hz
- The rate at which this correlation decays is conserved across animals and tasks (sleep and reaching)
- The patterns of connectivity are quite different and are likely to be task dependent

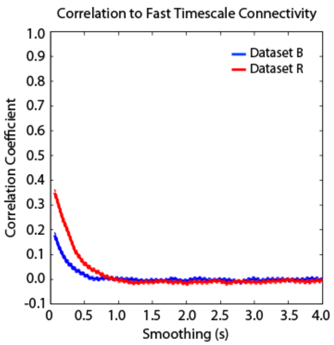
Error bars denote SEM across 10-min segments of data (N=5)

Results: Simulations removing slow-timescale connectivity

- To test the hypothesis that fast (synaptic-like) interactions cause slow timescale correlations we simulate only fast timescales
- By fitting the model to data we can preserve certain statistics (firing rates, inter-spike intervals, pair-wise correlations)



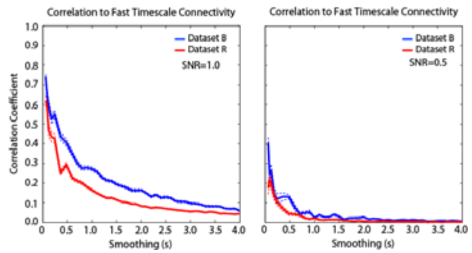




Error bars denote SEM across simulations (N=100)

Results: Robustness to noise

Adding uncorrelated Gaussian noise to the original spikes…



Conclusions

Slow timescale connectivity is predictive of fast timescale connectivity down to ~0.5 Hz

The correlations across timescales are robust to relatively high levels of additive noise (down to SNR<1)

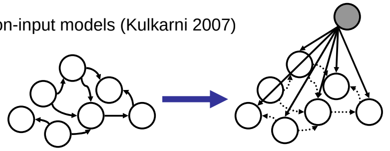
This suggests that functional connectivity estimated from multiple techniques can be combined for better estimates of interactions between *individual* neurons

Simulation results suggest that slow timescale connectivity cannot be explained by fast interactions alone

Interactions on multiple timescales and/or common-input may drive slow timescale connectivity observed in LFPs and fMRI

Future Directions

- Common-input models (Kulkarni 2007)



- How task-dependent is functional connectivity?
- Does this correlation across timescales exist for all connectivity estimation methods - DCM, conditional GC?
- What is the relationship between these results, with individual neurons, and a analyses of population signals?

References

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