Analysis of spontaneous activity patterns in the developing retina: extracting and analyzing dynamical networks

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Aim

Our interest is to unravel dynamics and characteristics of small scale neural networks; more specifically, we aim to develop tools to characterize and quantify these properties. We use recordings of spontaneous activity in the retina to refine our analysis tools. Traditionally, retinal data processing focuses on burst analysis of extracted spikes; however, these methods do not necessarily detect subtle network communication differences. Burst analysis combined with network and wave analysis can reveal more about the underlying dynamics.

Methods and Analysis

We collected MEA recordings of mouse retina from various investigators covering a range of developmental ages and genetic backgrounds. Data (over the entire developmental period, Post-Natal Day 3 (P3 to P44) was collected from Wildtype (WT) animals in Evelyne Sernagor's laboratory. Data (P7 to P42) was collected from WT mice in Rachel Wong's laboratory, and data was collected from WT and β2 gene knockout animals in both Marla Feller's and Leo Chalupa's laboratories (P2 to P11). The analyzed datasets were extracted spike times.

We quantified data using:

Burst Measures: Fano Factor (Fano), Entropy (Ent), Firing Rate (FR) and Inter-Spike Interval (ISI);

Wave Measures: Wave Duration (WD) and Inter-Wave Interval (IWI);

Network Measures: Degree, Jaccard Coefficient (Jaccard), Transitivity and Betweenness.

Burst analysis is most adequate for characterizing changes in firing rates. Combining burst analysis measures with extracted network information and wave properties allows one to generalize the activity type, to see how 'burstiness' can translate to the global network activity, or to quantify wave structures across changes in firing frequency.

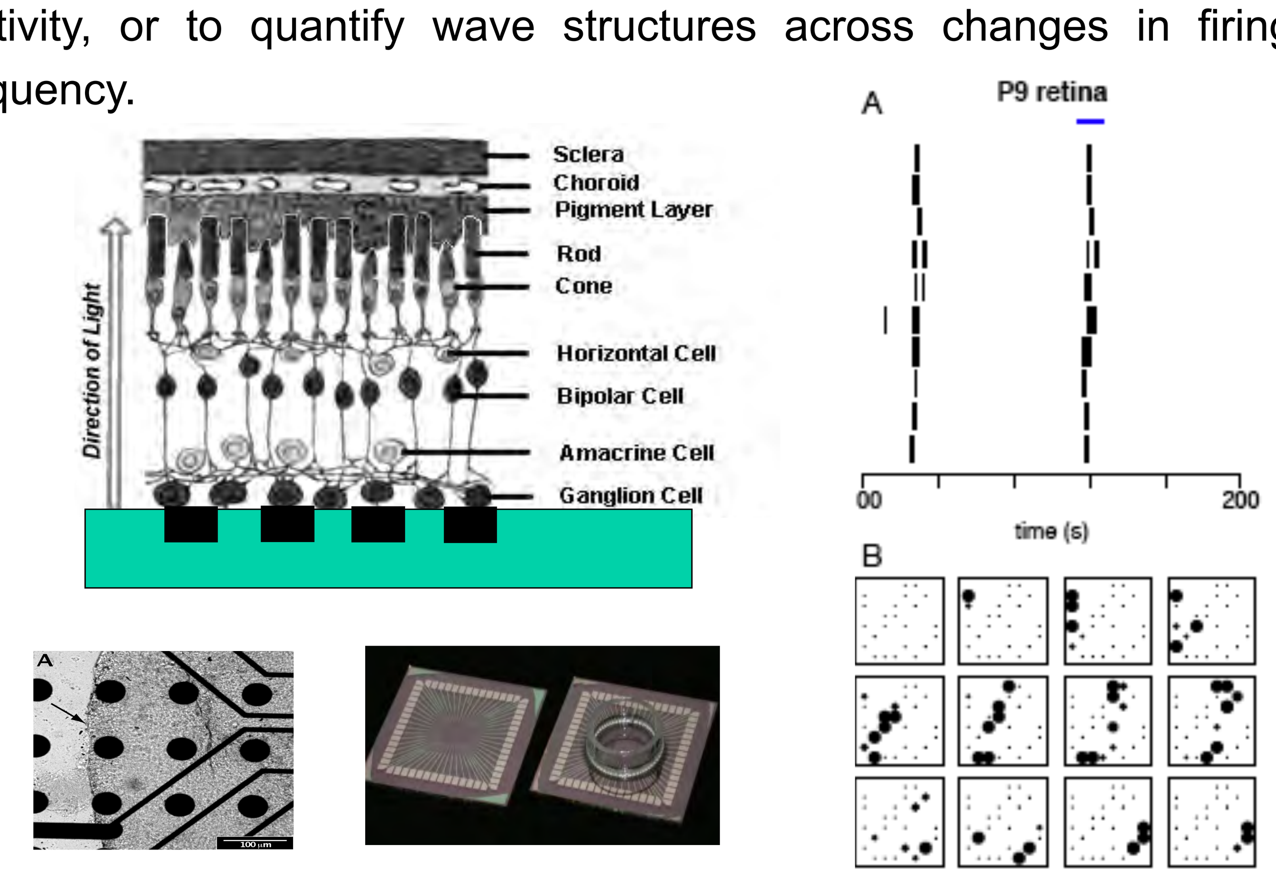

Figure 1: Diagram of retina on MEA. Most of the data is acquired from a 8 x 8 (without the 4 corners) grid of electrodes (30 μm across, 200 μm apart), acquired at 25 kHz. Local field potentials as well as individual spike times are typically recorded. We extract spike times and record activity bursts/waves across the array.

WT Analysis comparison across labs

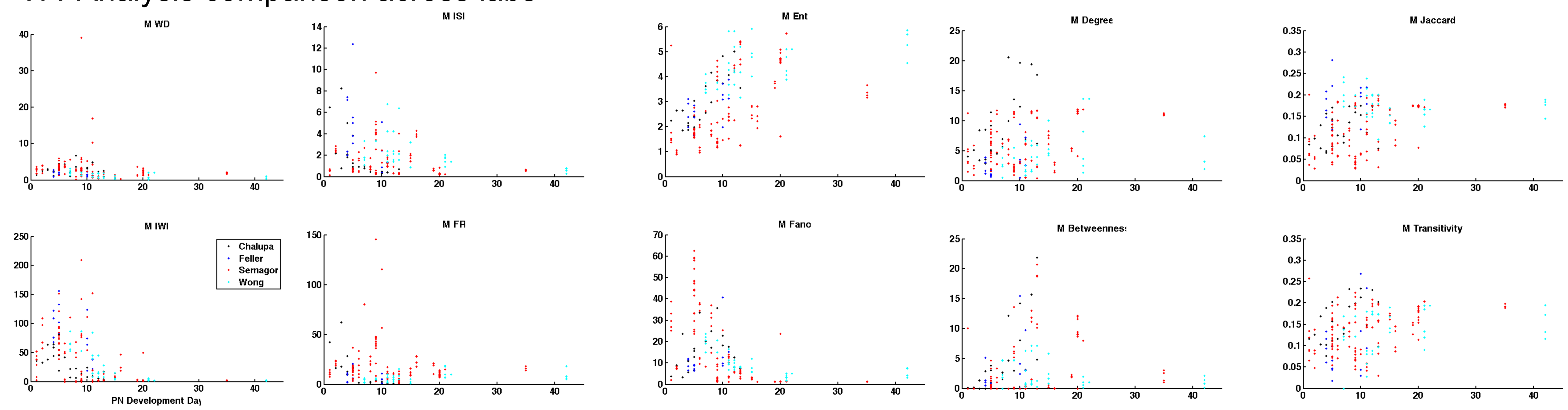

***Figure 2:** Mean Wave, Burst and Network Characteristics for Wild-Type (WT) data from the Chalupa, Feller, Sernagor, and Wong labs.*

Analysis of all the WT data across labs reveals that the data is fairly consistent. This means we can then compare the same gene knockout animals from different labs, as well as different gene knockout animals from different labs. Entropy and some of the network and wave measures seem to be particularly dynamic over the developmental period (for all labs) indicating that these measures reflect the dynamic developmental characteristics.

Beta 2 comparison across labs

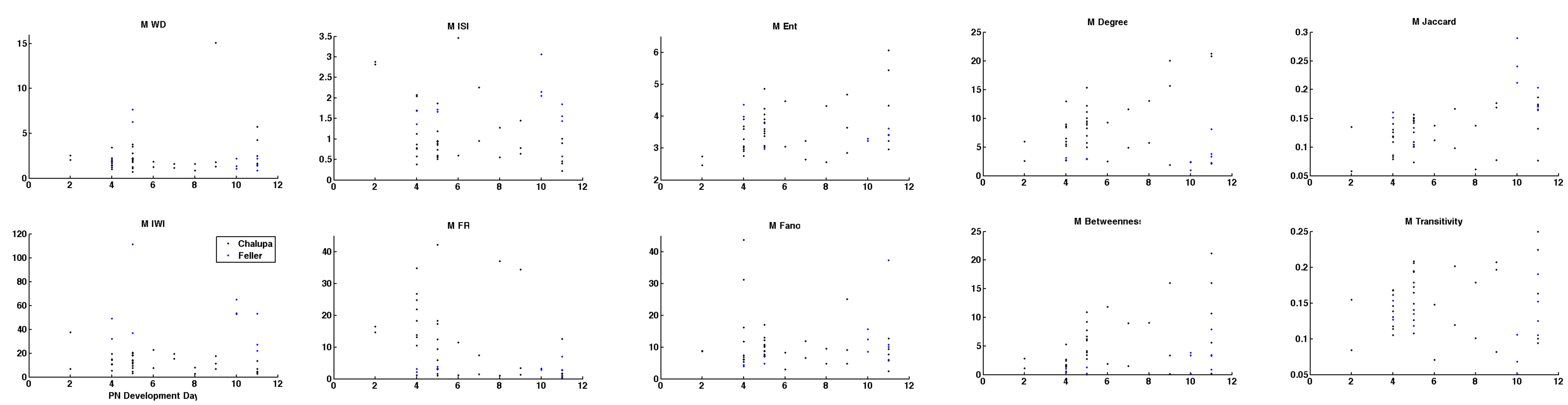

***Figure 3:** Burst, Network, and Wave Characteristics for Beta 2 data from the Chalupa and Feller labs.*

Analysis of β2 (receptor subunit knockout) data from different labs is fairly consistent, which is surprising given the conflicting reports of waves/no waves over the developmental period. Seems to be what one lab is calling a wave, another lab is not (but our definition picks up waves in datasets from both labs).

Conclusions

This type of meta-analysis is not always straightforward, but it can reveal new tools or new uses for old tools in seeing differences in developmental day and genetic phenotype for retinal arrays. This can be generalized to just about any array-acquired data. Additionally, all data and developed tools will be made available on the CARMEN website shortly(http:///www.carmen.org.uk).

Acknowledgements

This study is part of the CARMEN Consortium Work Package 6 investigating small neural networks dynamics EPSRC (EP/E002331/1). We thank the CARMEN Consortium for their support. We additionally thank Leo Chalupa, Marla Feller, and Rachel Wong for providing data.