

Neural Substrates of Memory and Prospection

Loren Frank

Howard Hughes Medical Institute
Kavli Institute for Fundamental Neuroscience
Department of Physiology
University of California, San Francisco

Expected Properties of Memory-Related Activity

- Time-compressed.
- Contributes to representing future possibilities.
- Related to behavioral decisions.

Memory and Planning

- Memories allow past experience to inform future decisions.
- Prospection based on SWRs would be limited to behavioral states where SWRs are seen (immobility and slow movement).
- Question:
 - Are there other forms of non-local activity that could inform decision-making processes?



Kenny Kay

Hippocampal Theta Sequences

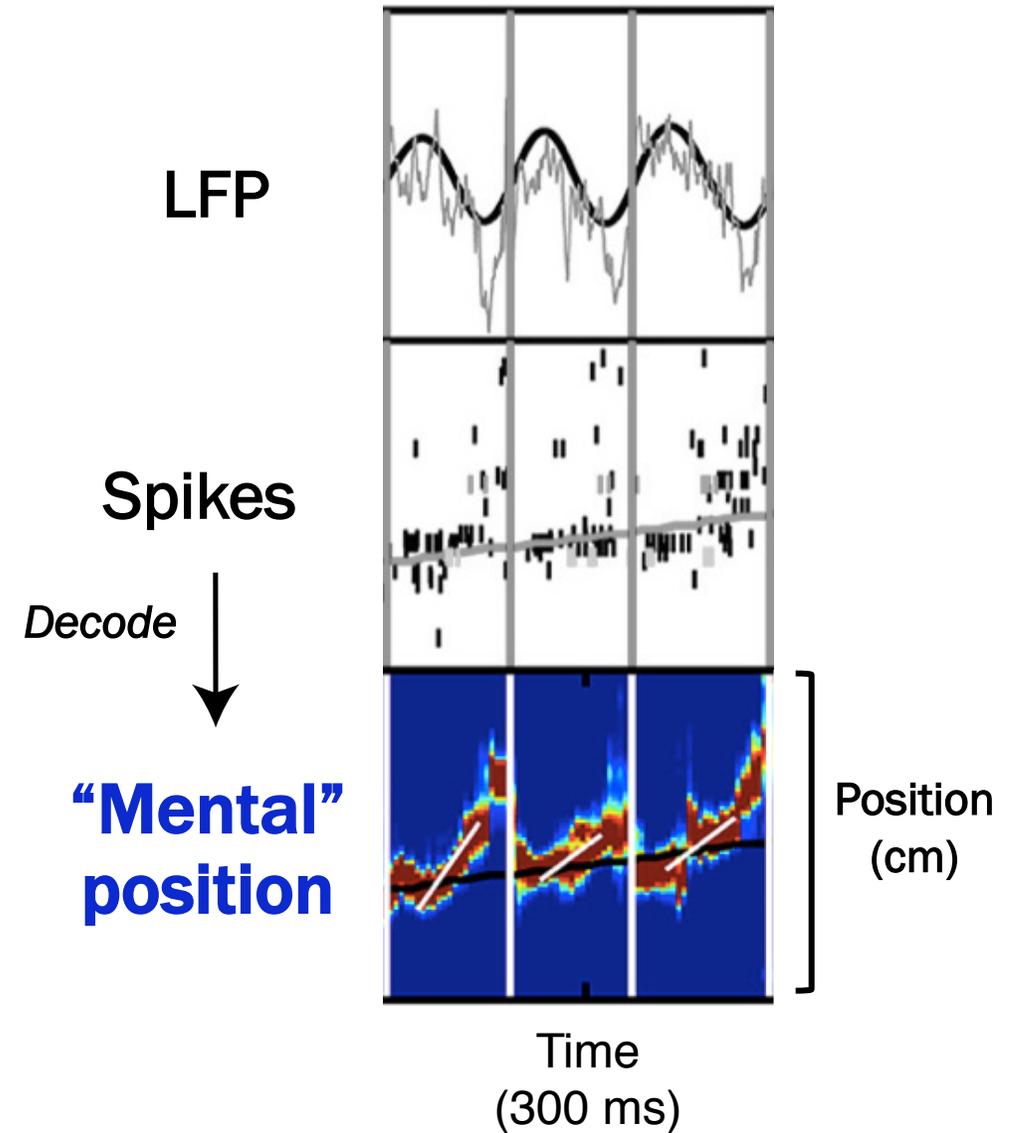
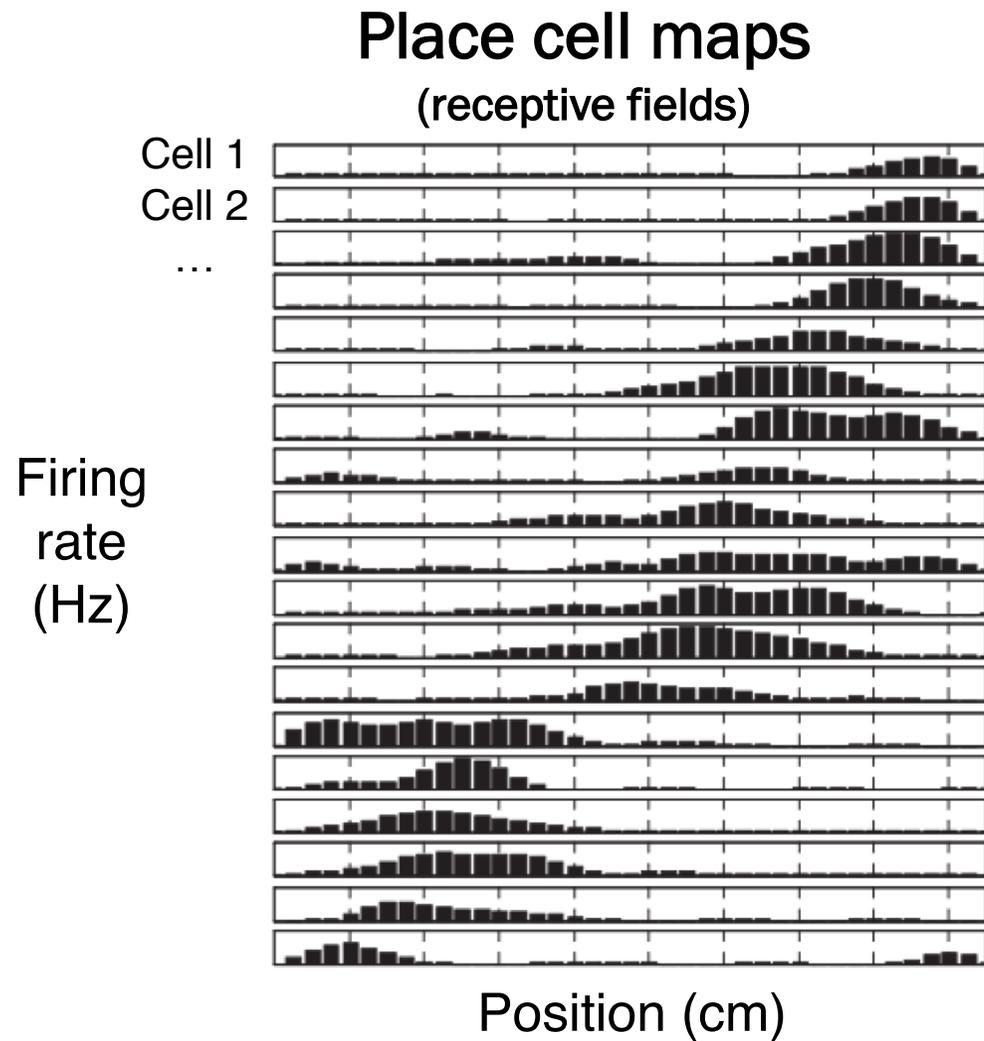


Figure from Feng & Foster (2015)

Hippocampal Theta Sequences

= Population firing sequences that encode sequences in space

Each sequence lasts ~100 ms.

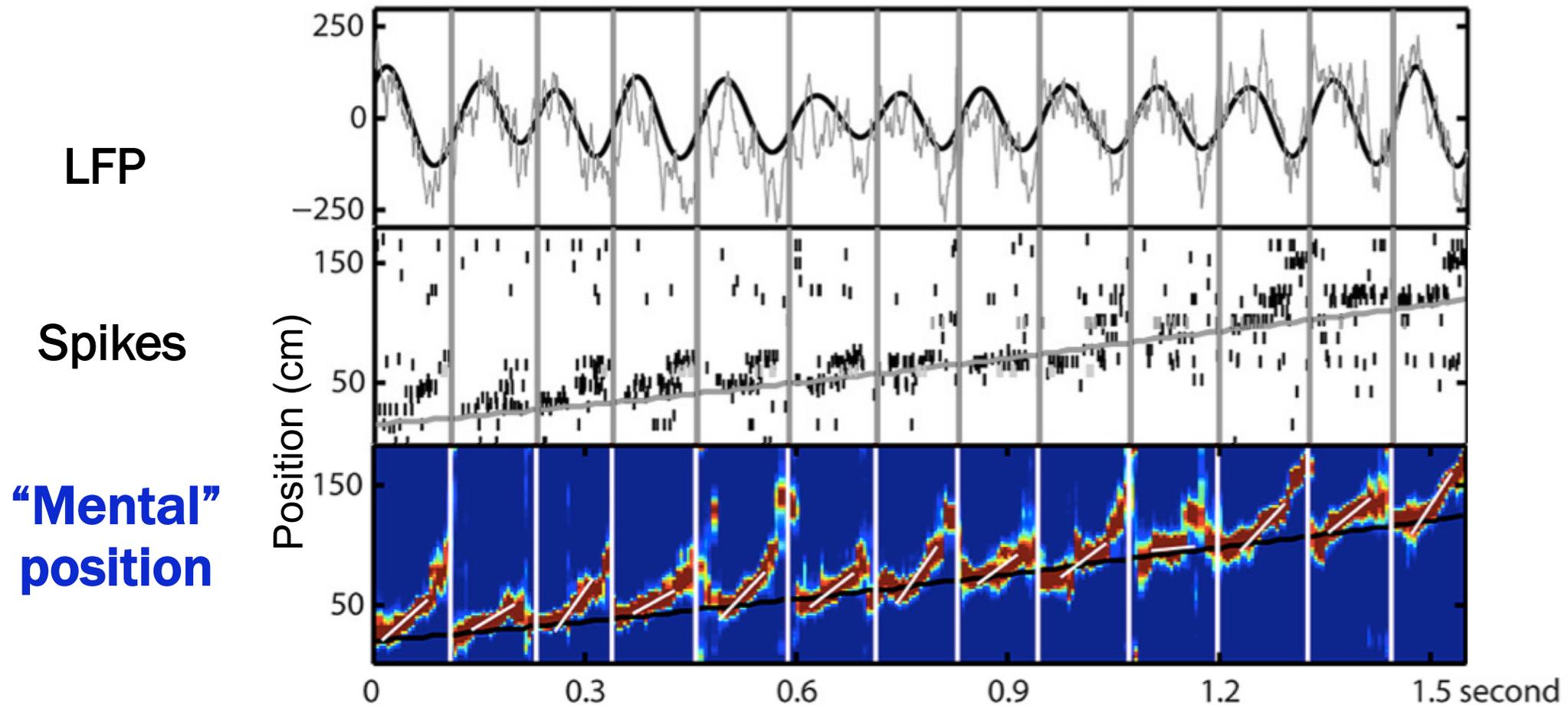


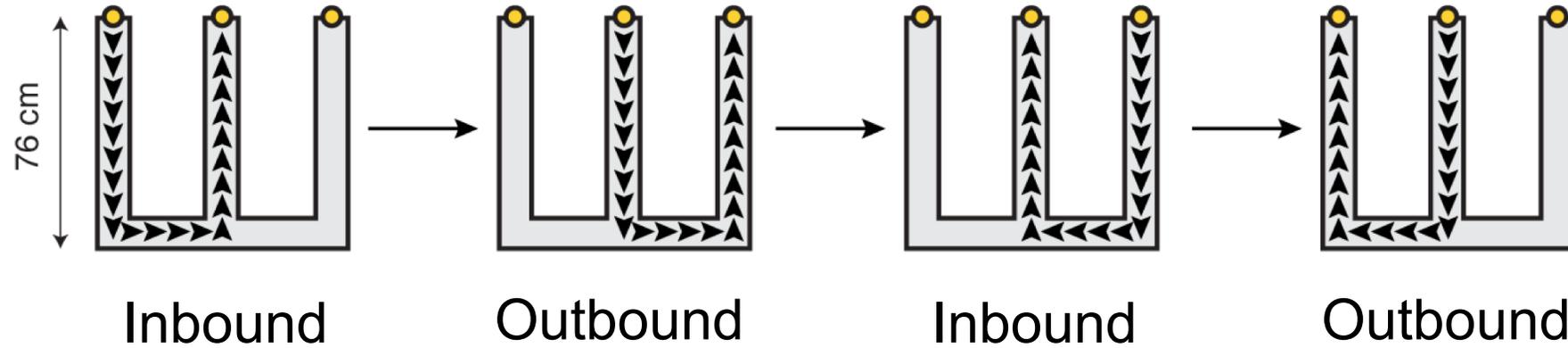
Figure from Feng & Foster (2015)

Spiking During Hippocampal Theta Sequences

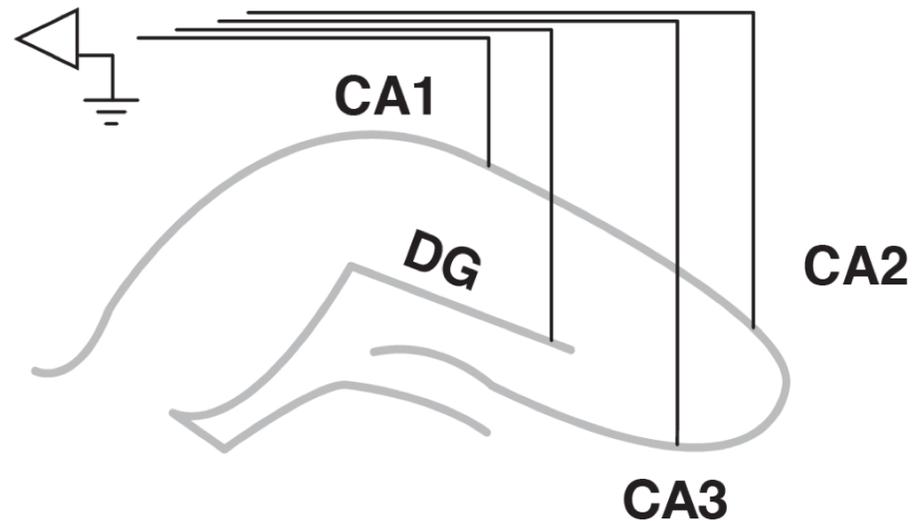
Time-compressed.

Capable of representing future possibilities?

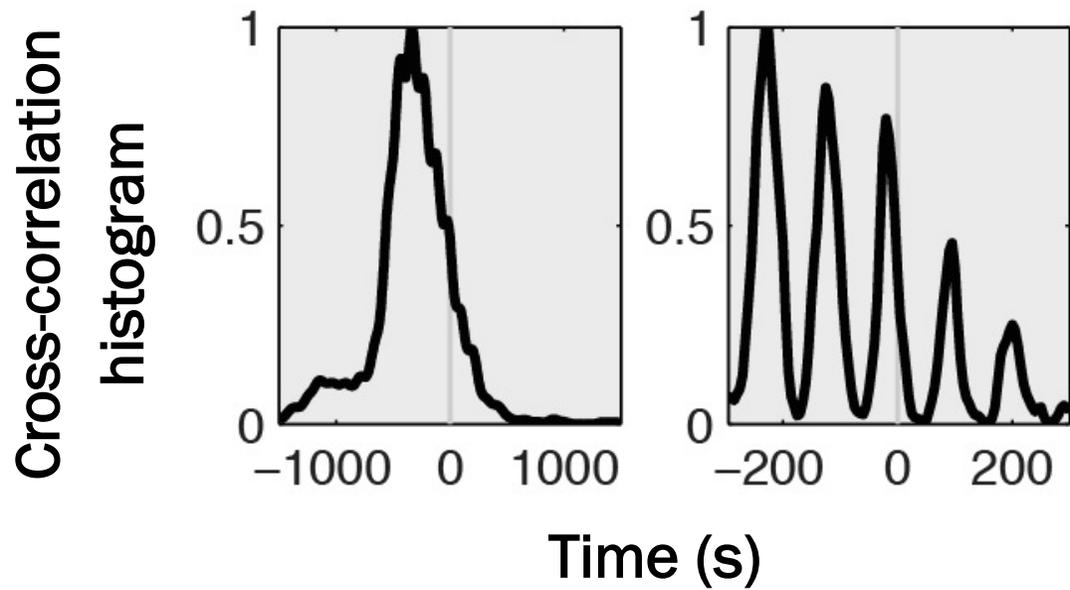
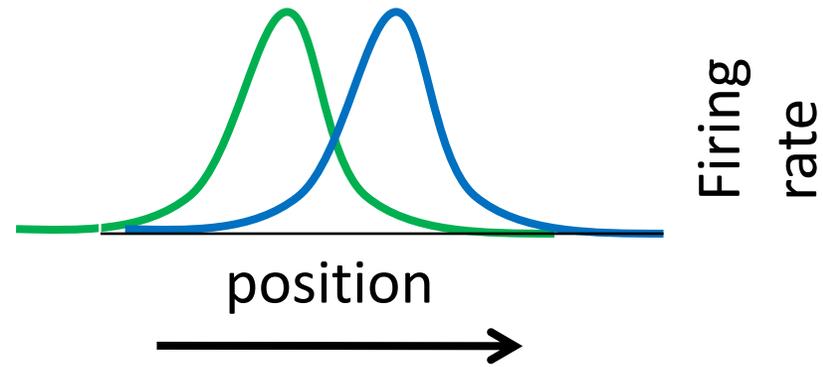
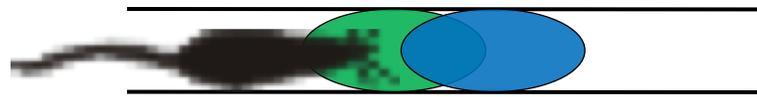
Continuous Alternation Task and Regional Targeting



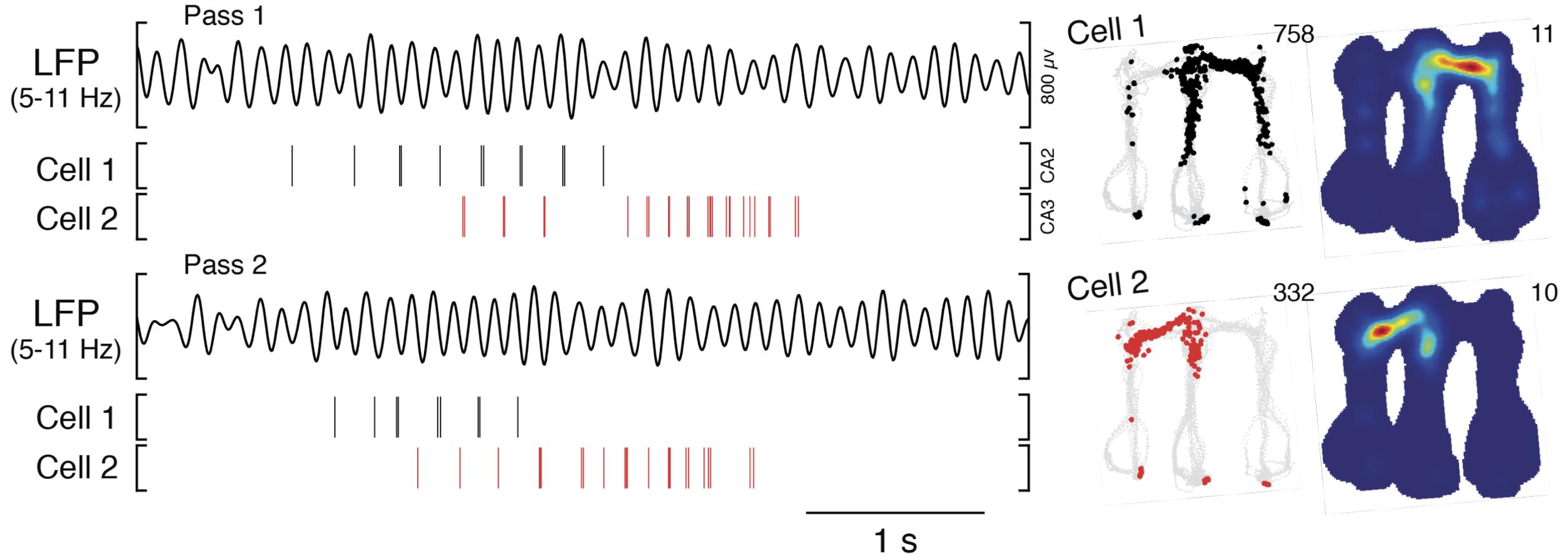
Outbound trials require memory of previous outbound choice



Expected Co-firing Patterns



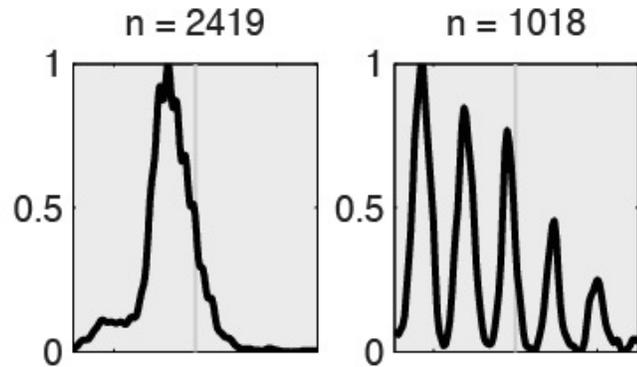
Observed Co-firing Patterns (in a subset of pairs)



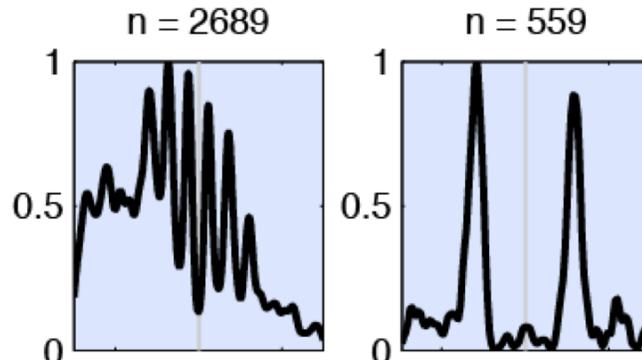
Example 1

Normal, Anti-synchronous and Synchronous Pairs

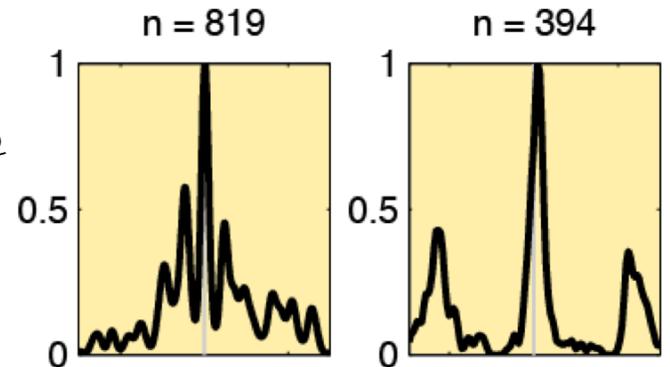
Ex. 1



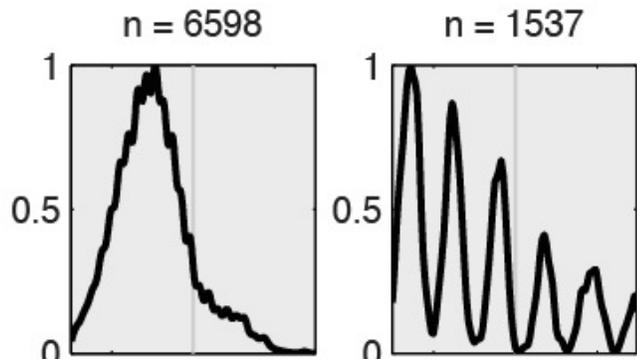
Ex. 3



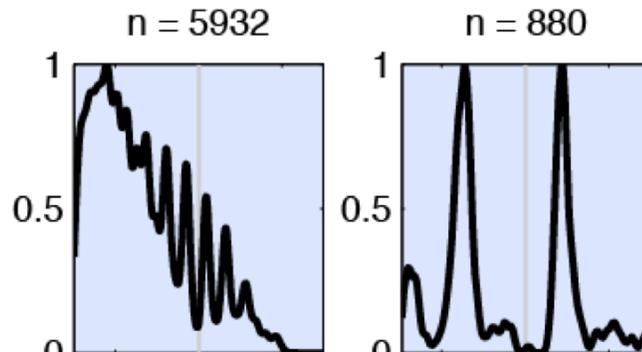
Ex. 5



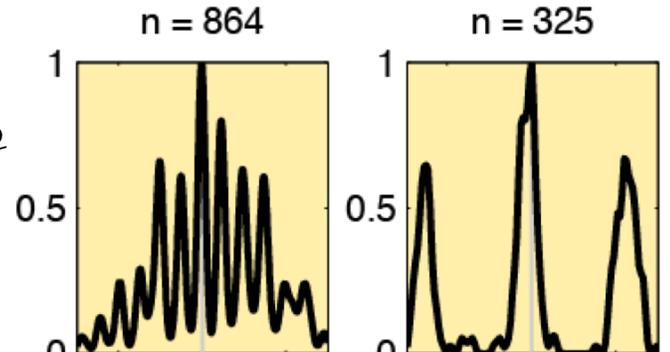
Ex. 2



Ex. 4



Ex. 6



~66%

~8%

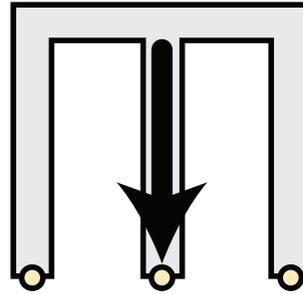
~16%

~9400 pairs total

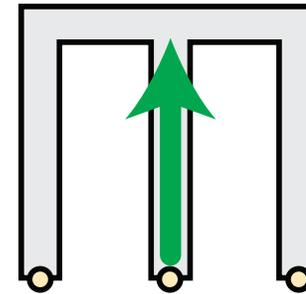
Prevalence in Single Units – Theta Skip Index

All passed vs. imminent comparisons
 $P < 0.01$

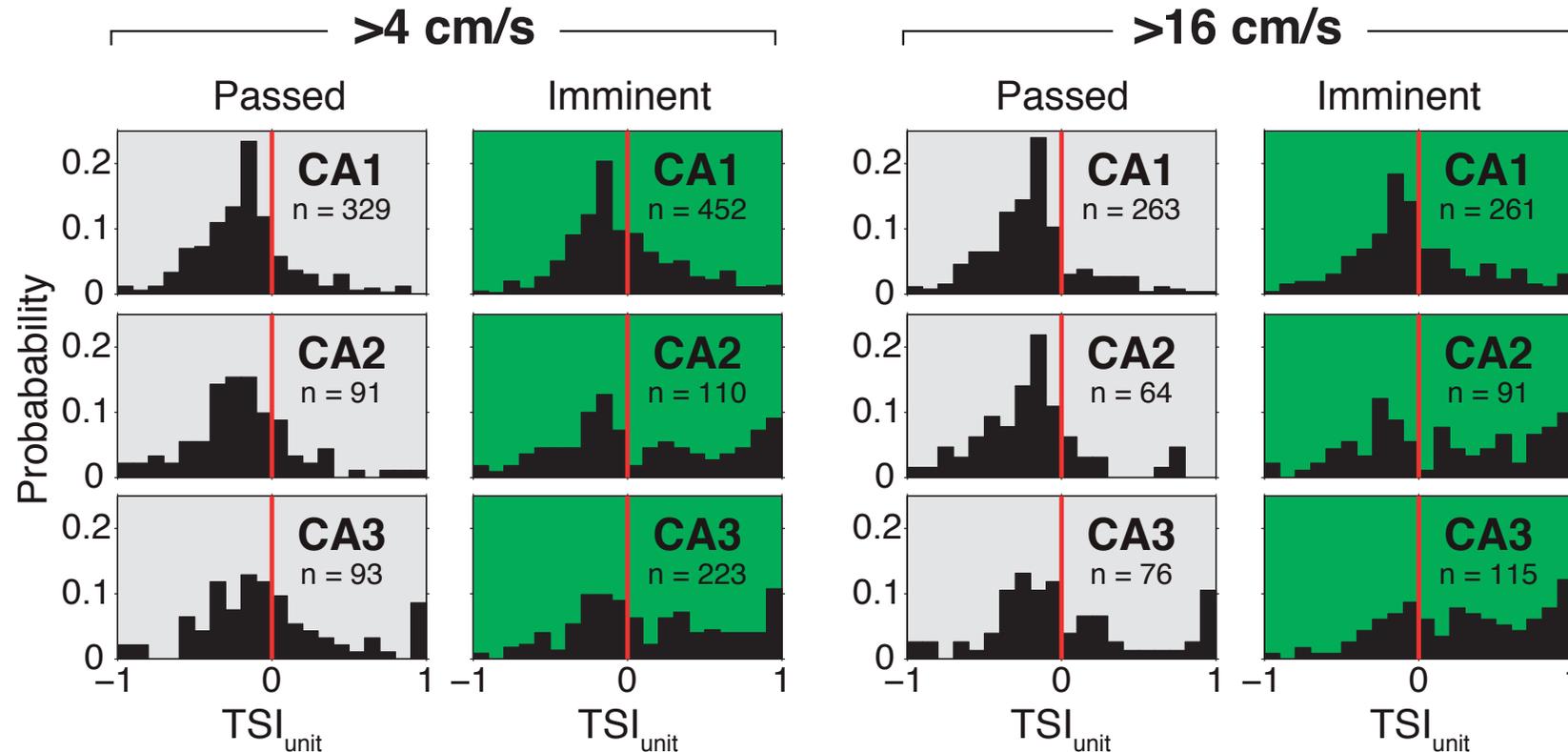
Choice
passed



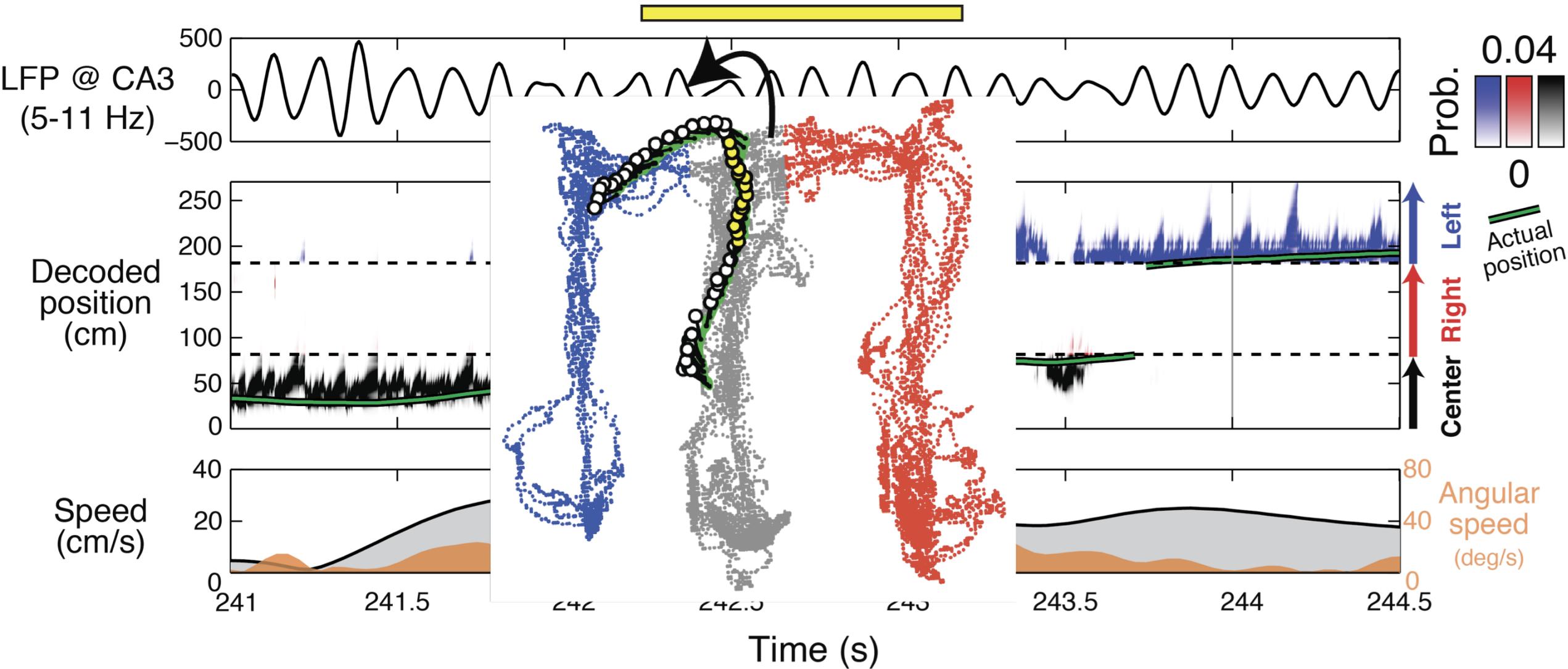
Choice
imminent



Adapted from:
Deshmukh et. al. (2010)
Brandon et. al. (2013)

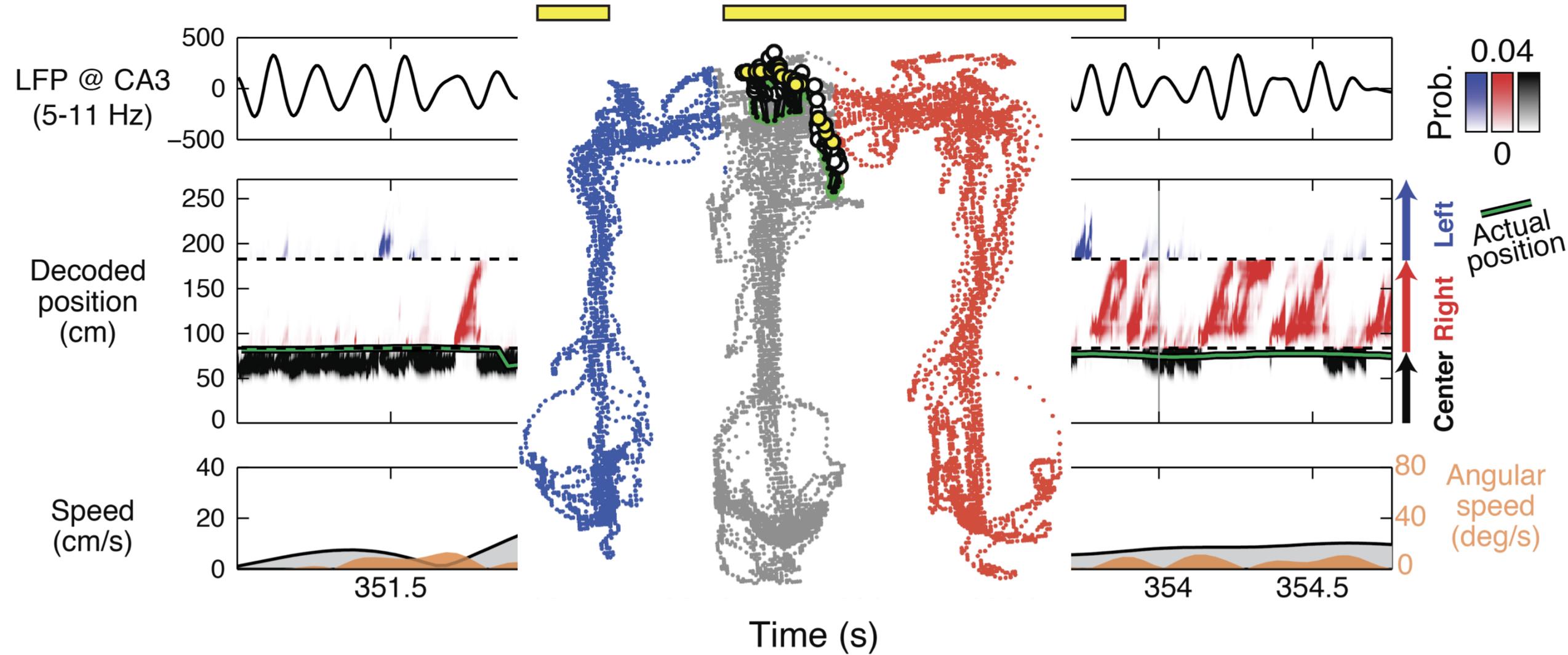


Alternating Representations of Future Possibilities



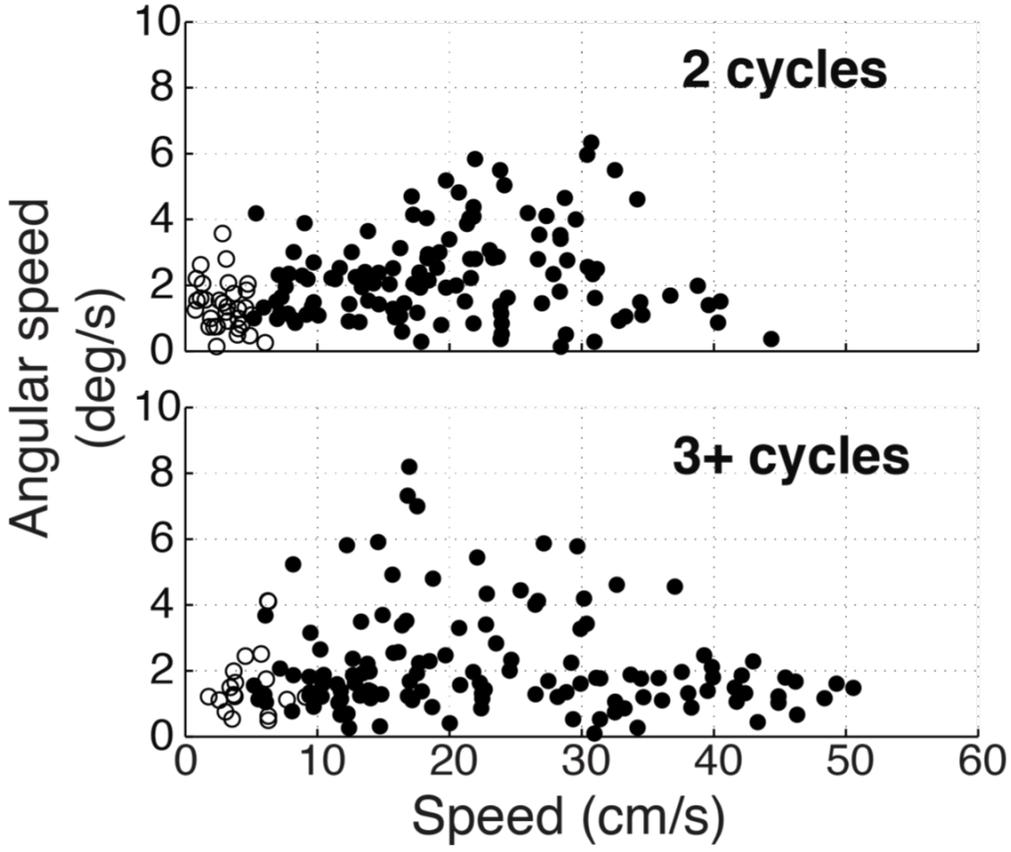
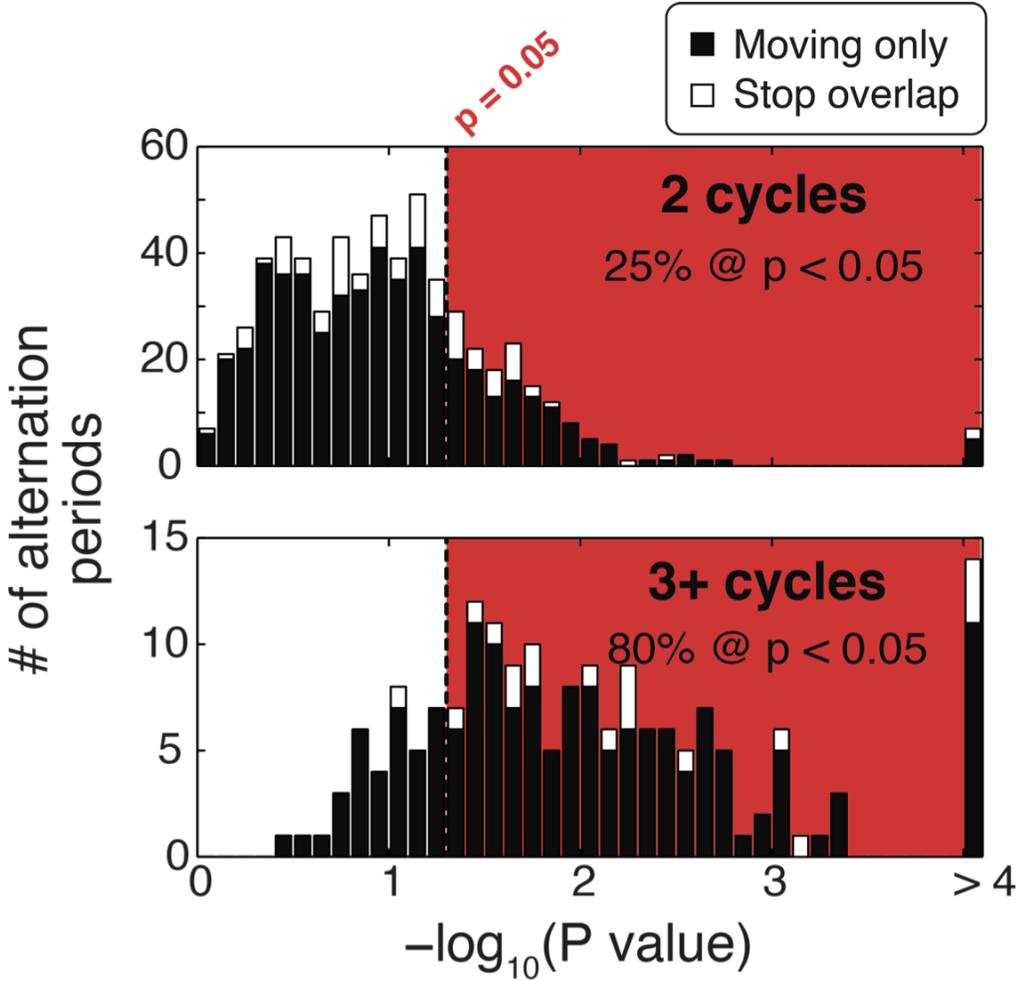
Clusterless decoding method:
Deng et. al. *Neural Computation* (2015)
See also Jezek et. al. *Nature* (2011)

Alternating Representations of Future Possibilities



Clusterless decoding method:
Deng et. al. *Neural Computation* (2015)

Alternating Representations - Quantification

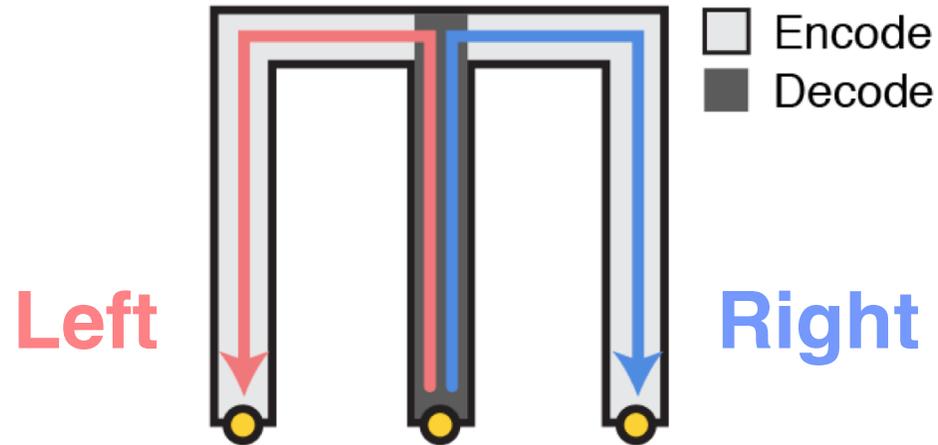


Spiking During Theta Sequences

- Time-compressed.
- Capable of representing future possibilities
- Related to behavioral decisions?

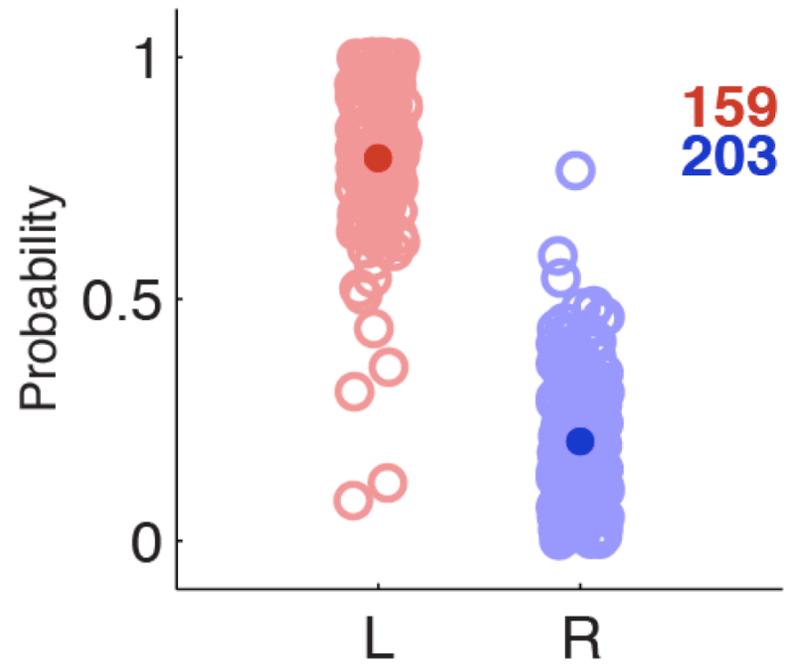
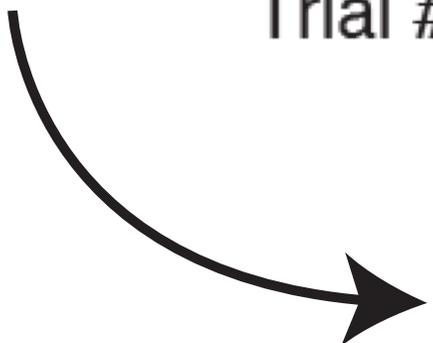
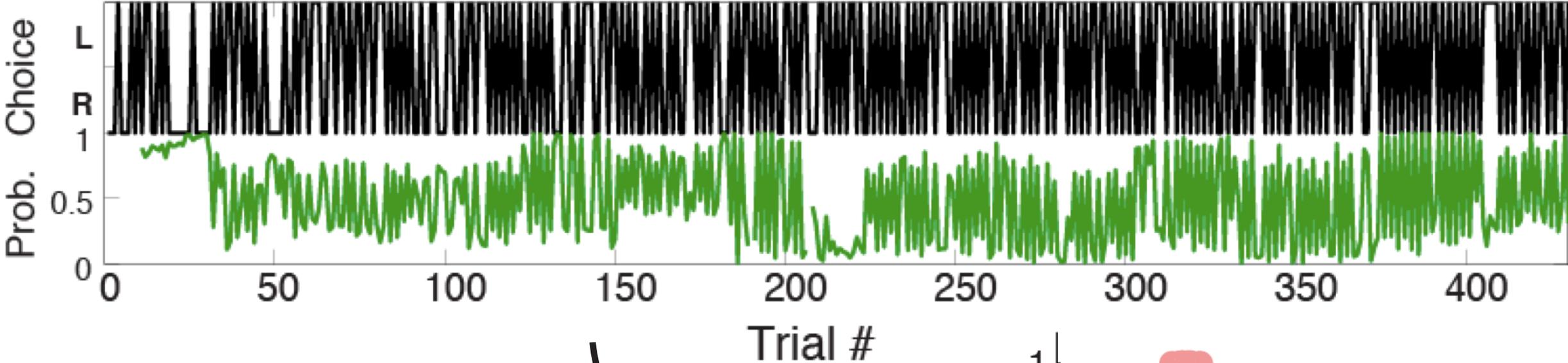
Relating Theta-timescale Activity to Behavior

Bayesian decoding of prospective (L vs. R) representation from place cells



Decode each theta cycle over entire time
in middle arm (>2 s).

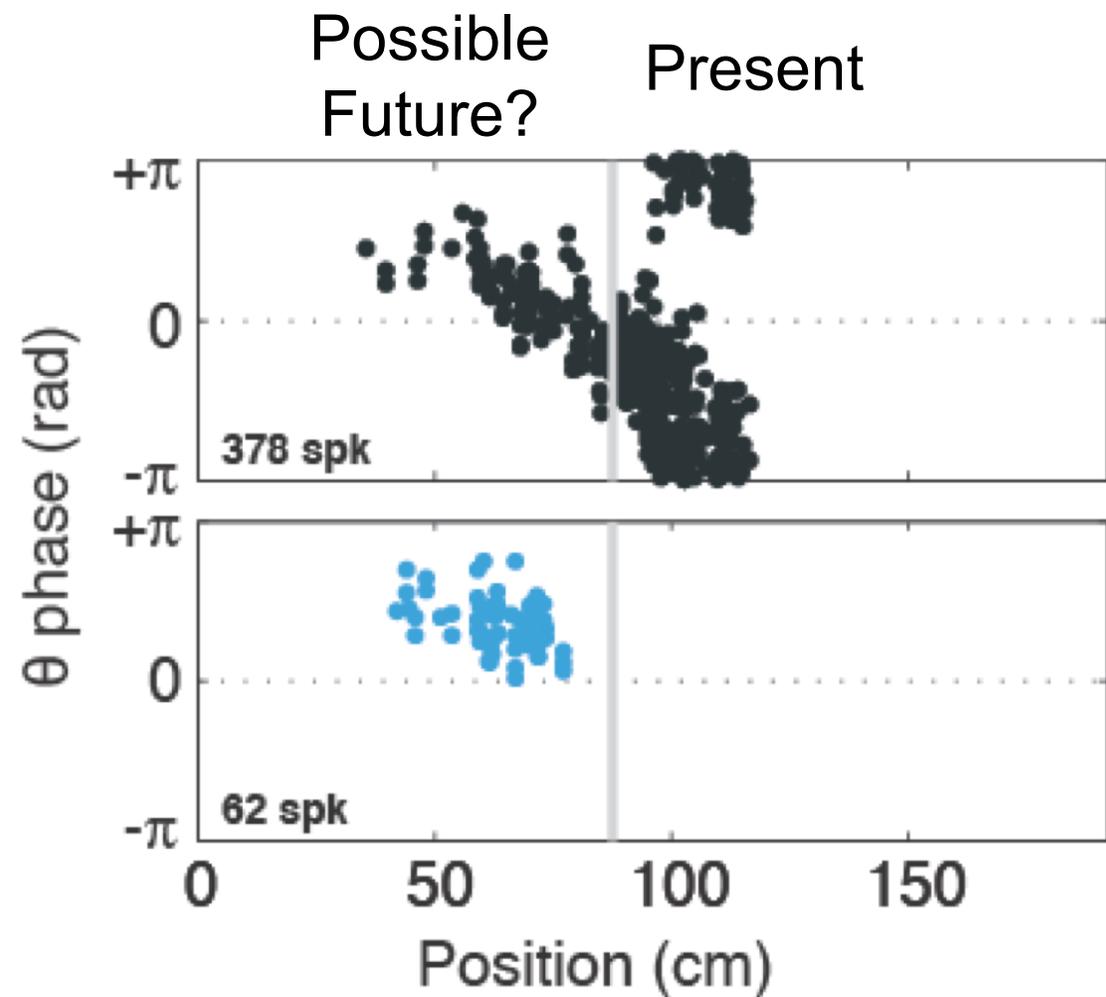
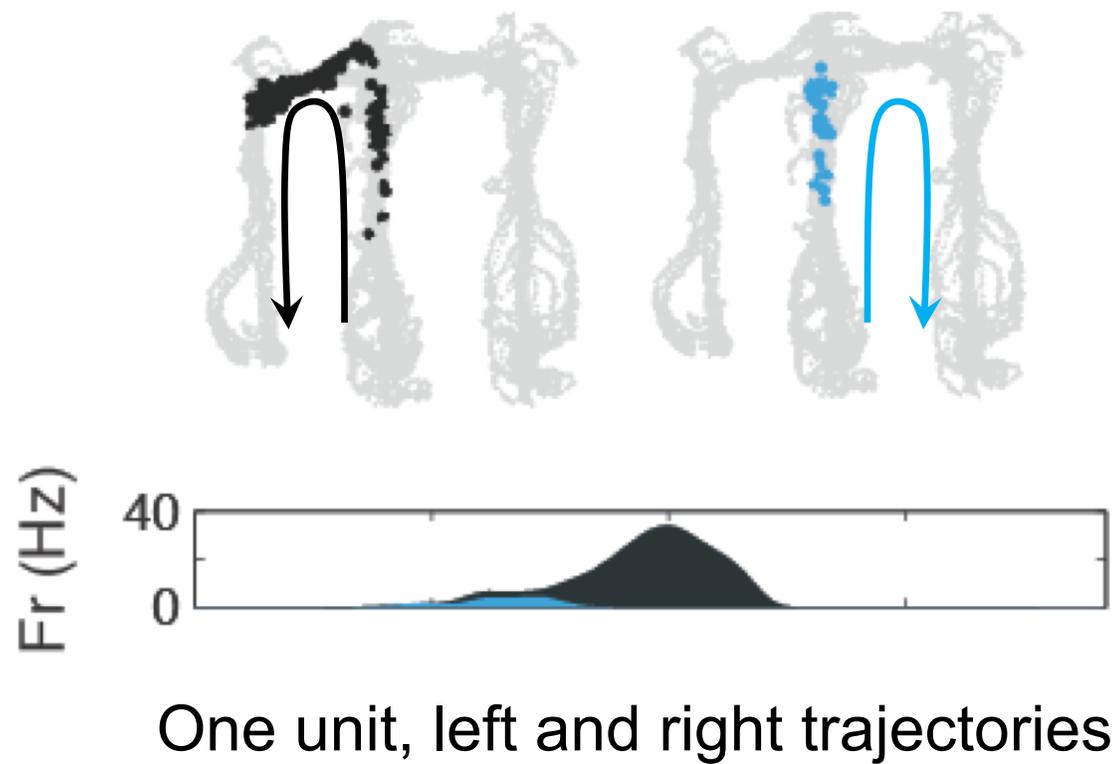
Theta-timescale Activity Predicts Upcoming Choices



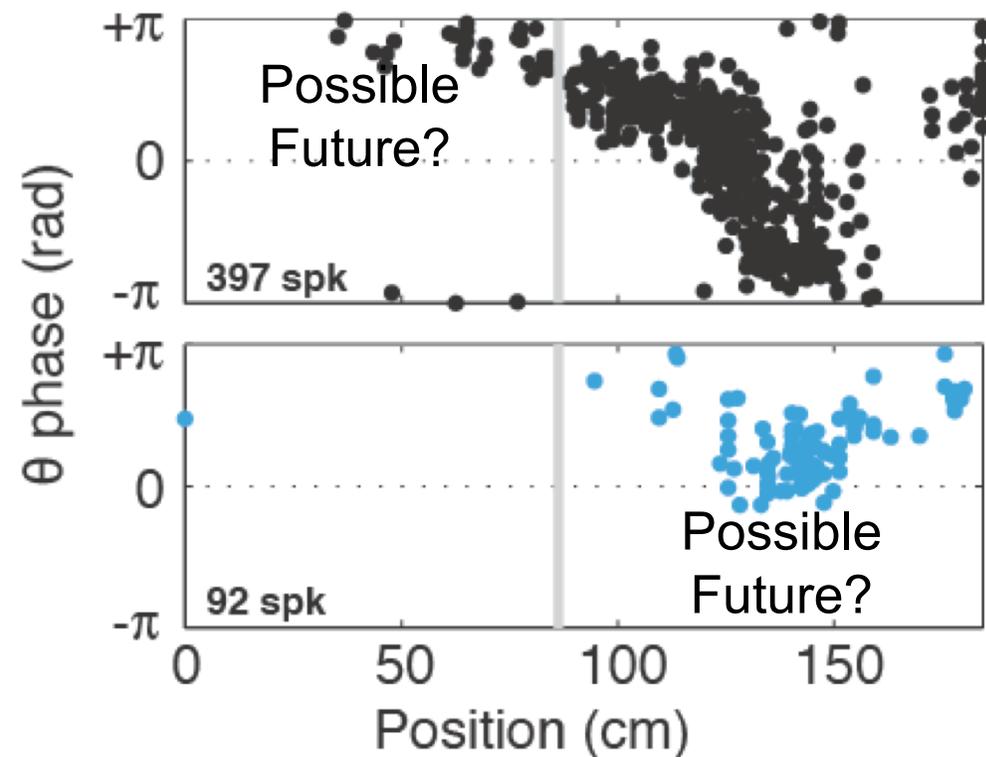
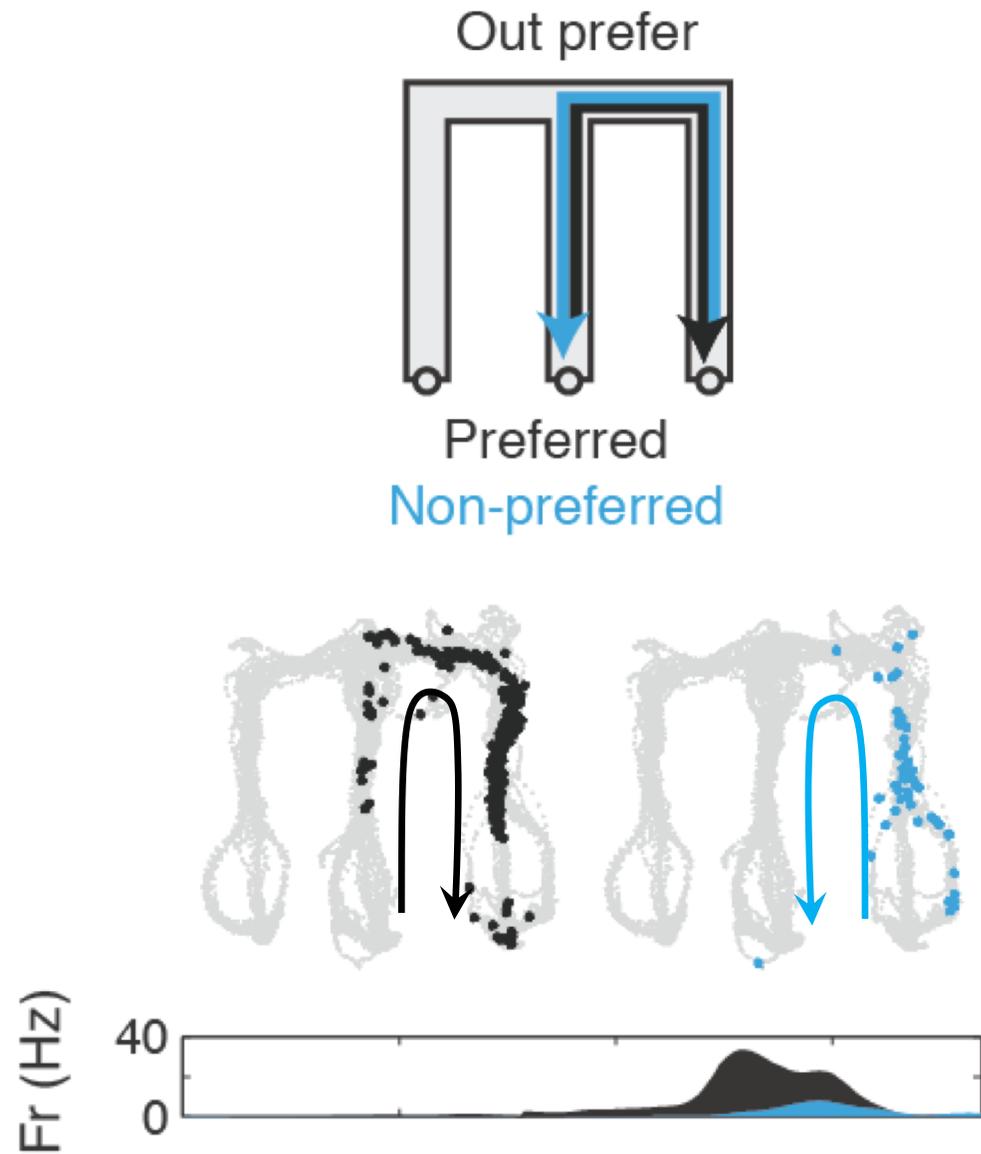
Spiking During Theta Sequences

- ☑ Time-compressed.
- ☑ Capable of representing future possibilities.
- ☑ Related to behavioral decisions.

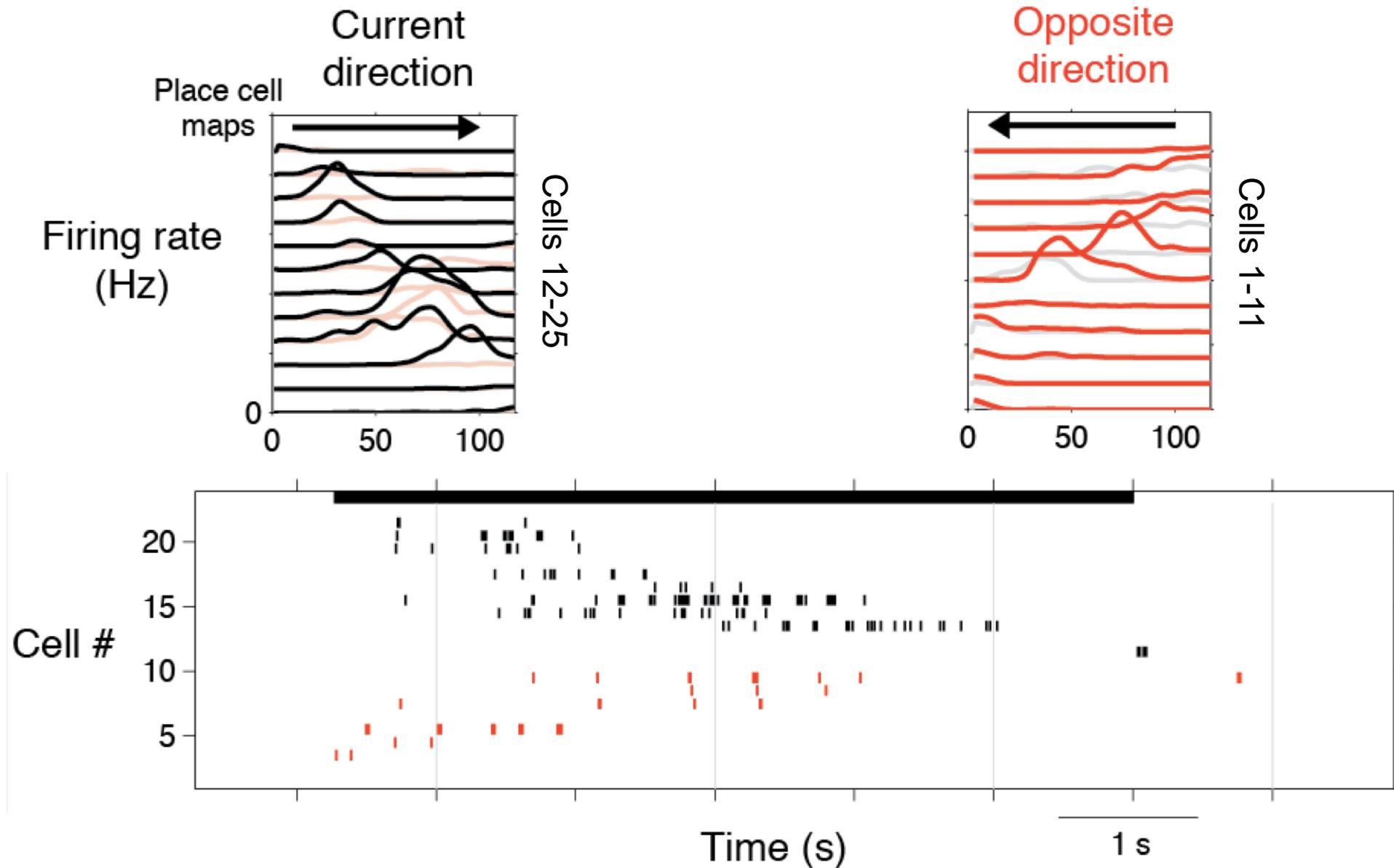
Current vs. Future Representations and Theta Phase



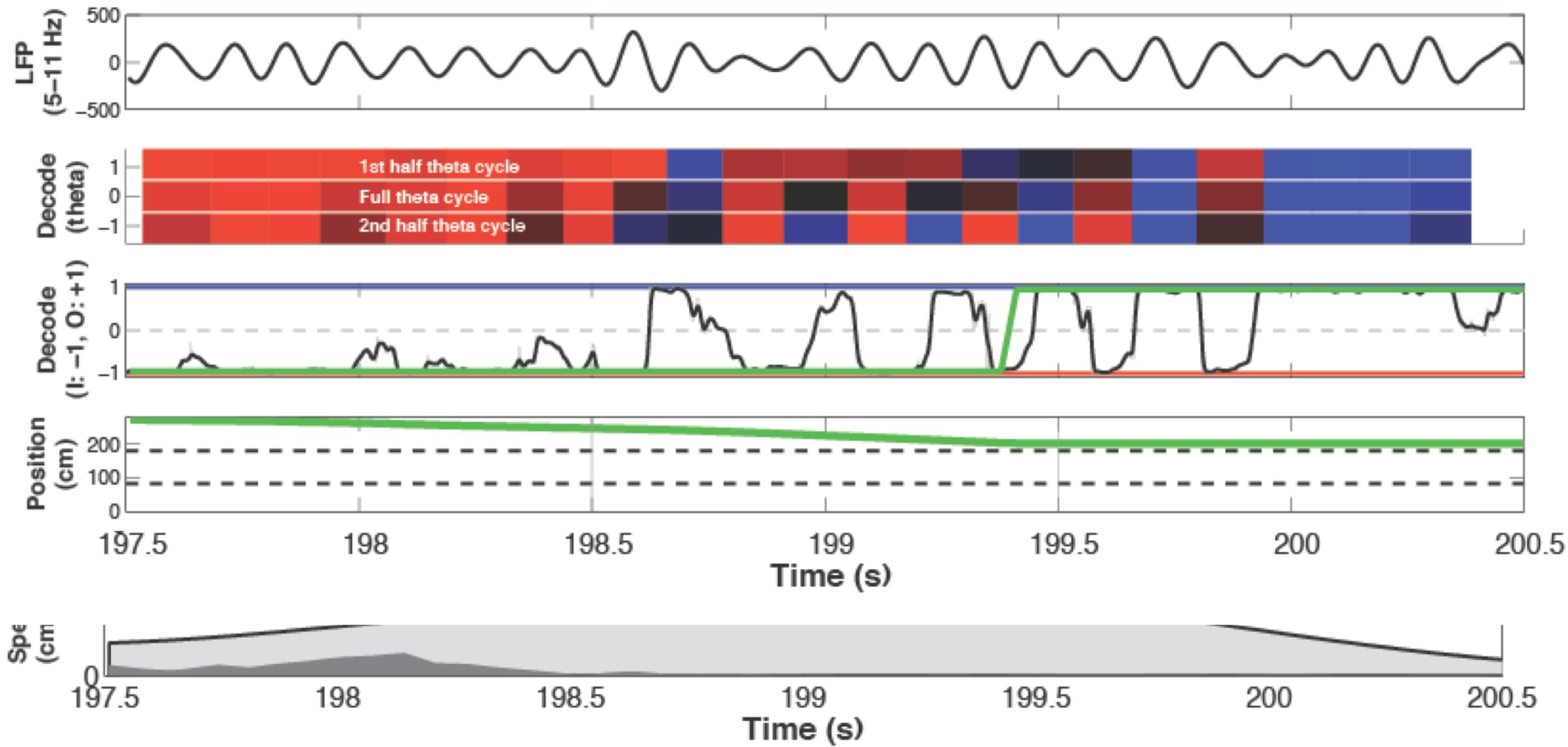
Preferred vs. Non-preferred Directional Representations



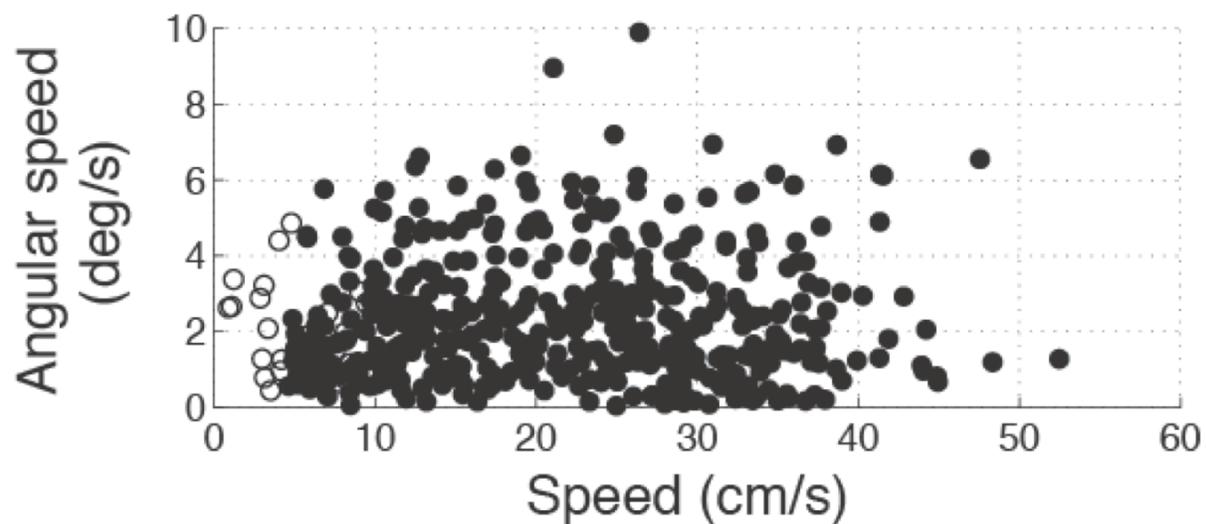
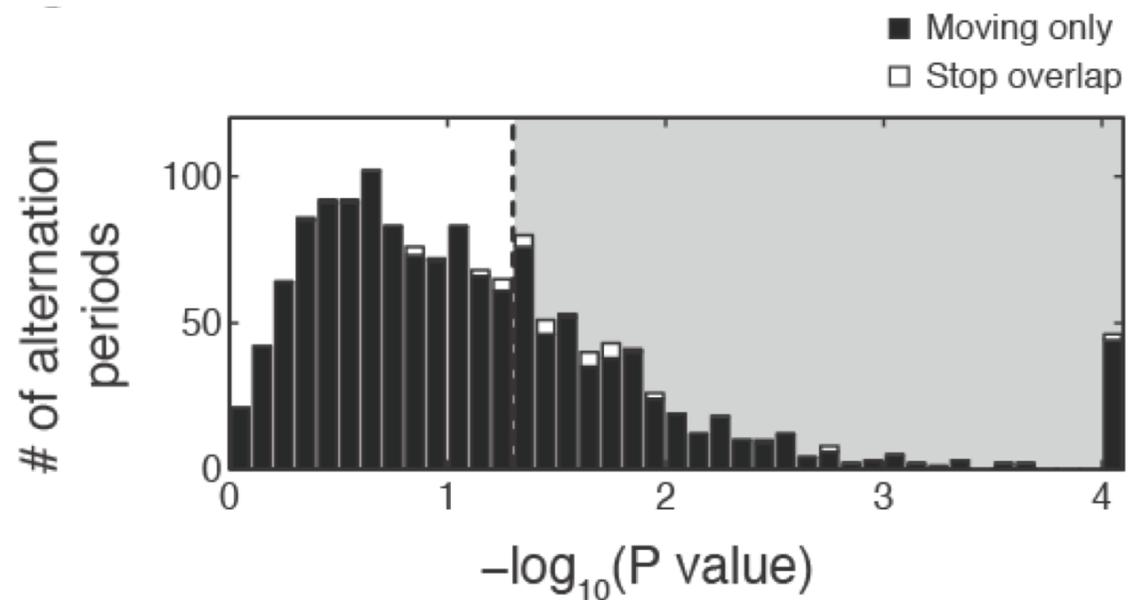
Ensemble Organization of Directional Representations



Theta-paced Alternation of Directional Representations



Ensemble Organization of Directional Representations



Conclusions

- We find frequent alternation between representations of future possibilities across theta cycles.
- This alternation is not limited to Vicarious Trial and Error (VTE) behaviors.
- Alternation occurs for both divergent paths and opposite directions of travel.
- Theta-paced alternation could inform upcoming decisions and/or reflect previous decisions.

Lab members and collaborators

Lab Members

Jason Chung

Tom Davidson

Anna Gillespie

Hannah Joo

David Kastner

Kenny Kay

Daniel Liu

Demetris Roumis

Marielena Sosa

Jai Yu

Former Lab Members

Kevin Fan (UCSF/UCB)

Shantanu Jadhav (Brandeis)

Mattias Karlsson (SpikeGadgets)

Gideon Rothschild (U. Michigan)

Collaborators

Uri Eden (BU)

Jeremy Magland (Flatiron)

Alex Barnett (Flatiron)

Leslie Greengard (Flatiron)

Magnus Karlsson (SpikeGadgets)

Supin Chen (LLNL / Neuralink)

Razi Haque (LLNL)

Vanessa Tolosa (LLNL / Neuralink)

Angela Tooker (LLNL)

Kris Bouchard (LBNL)

Peter Denes (LBNL)

Funding: HHMI, Simons Foundation, NIH, UCOP