What am I interested in?

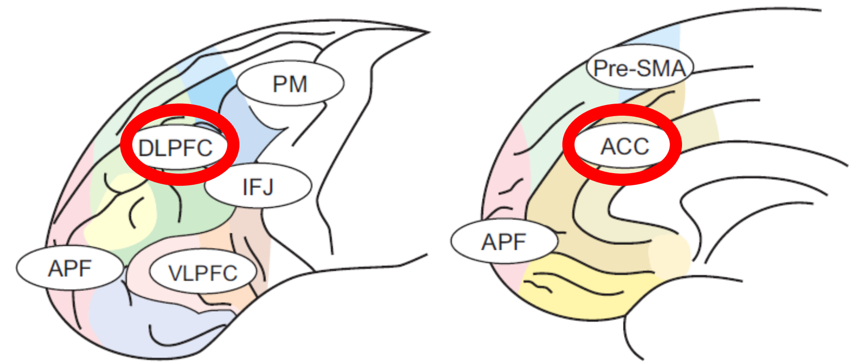
Cognitive Flexibility – How do we perform the appropriate action in different contexts?

Dynamics – How do we efficiently remap stimulus-response associations in different contexts without having to relearn everything or succumb to distractors?

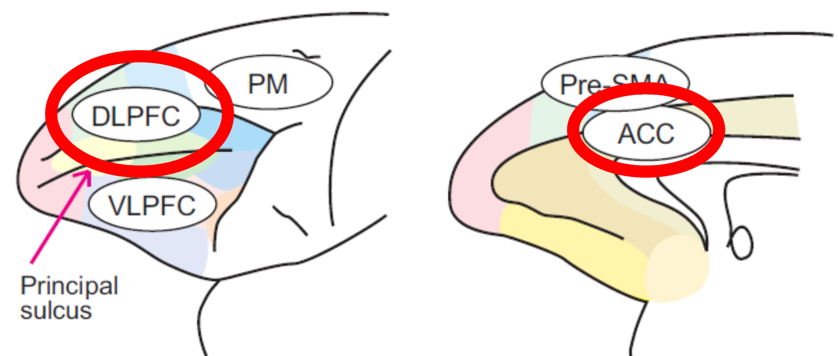
Spatial Scales – How does activity at different spatial scales relate (cellular, circuit, subdivisions)?

Prefrontal Cortex – How do different subdivisions of prefrontal cortex contribute to cognitive flexibility?

Human Frontal Cortex



Macaque Frontal Cortex

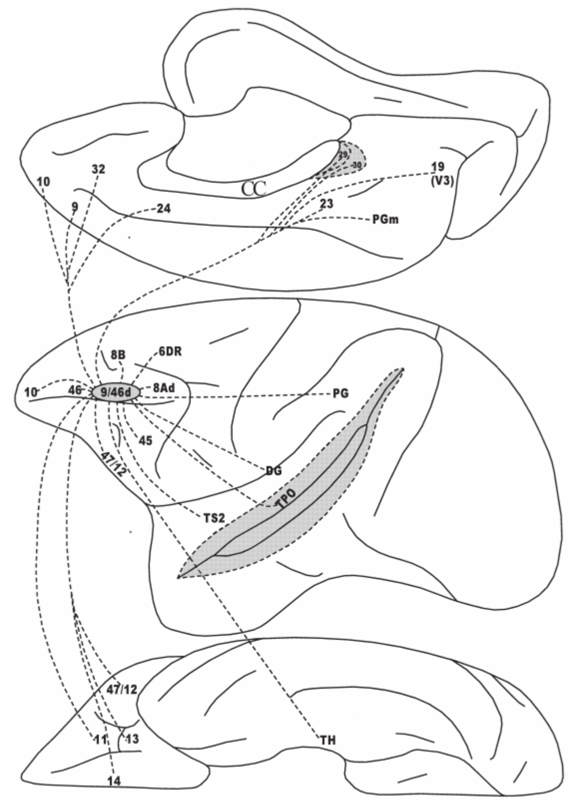


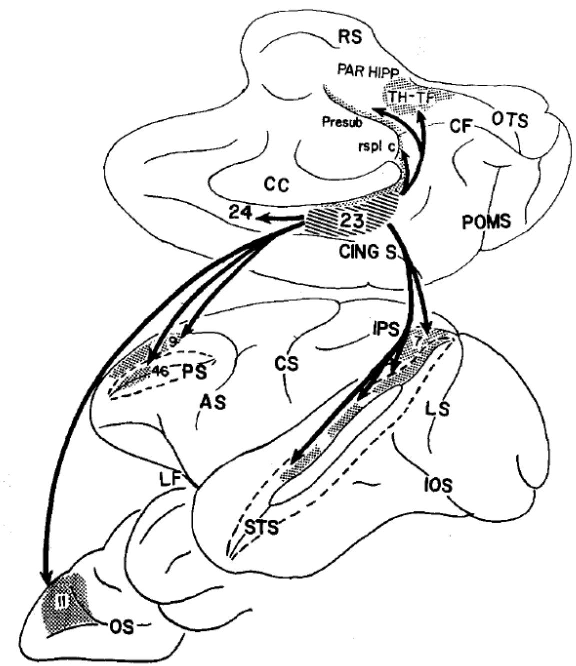
Lateral **Medial**

Challenges to Studying Prefrontal Cortex

Prefrontal neurons are known to integrate multiple parameters of a task (large receptive fields, lots of converging inputs, pyramidal cells have more spines)

Examining their effects individually might overestimate their importance



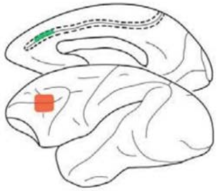


Challenges to Studying Prefrontal Cortex: Many Complex Theories, particularly ACC

Theory #1: Selection-For-Action – The ACC is responsible for selecting the relevant sensory information to make an action. It prevents competition between possible responses.

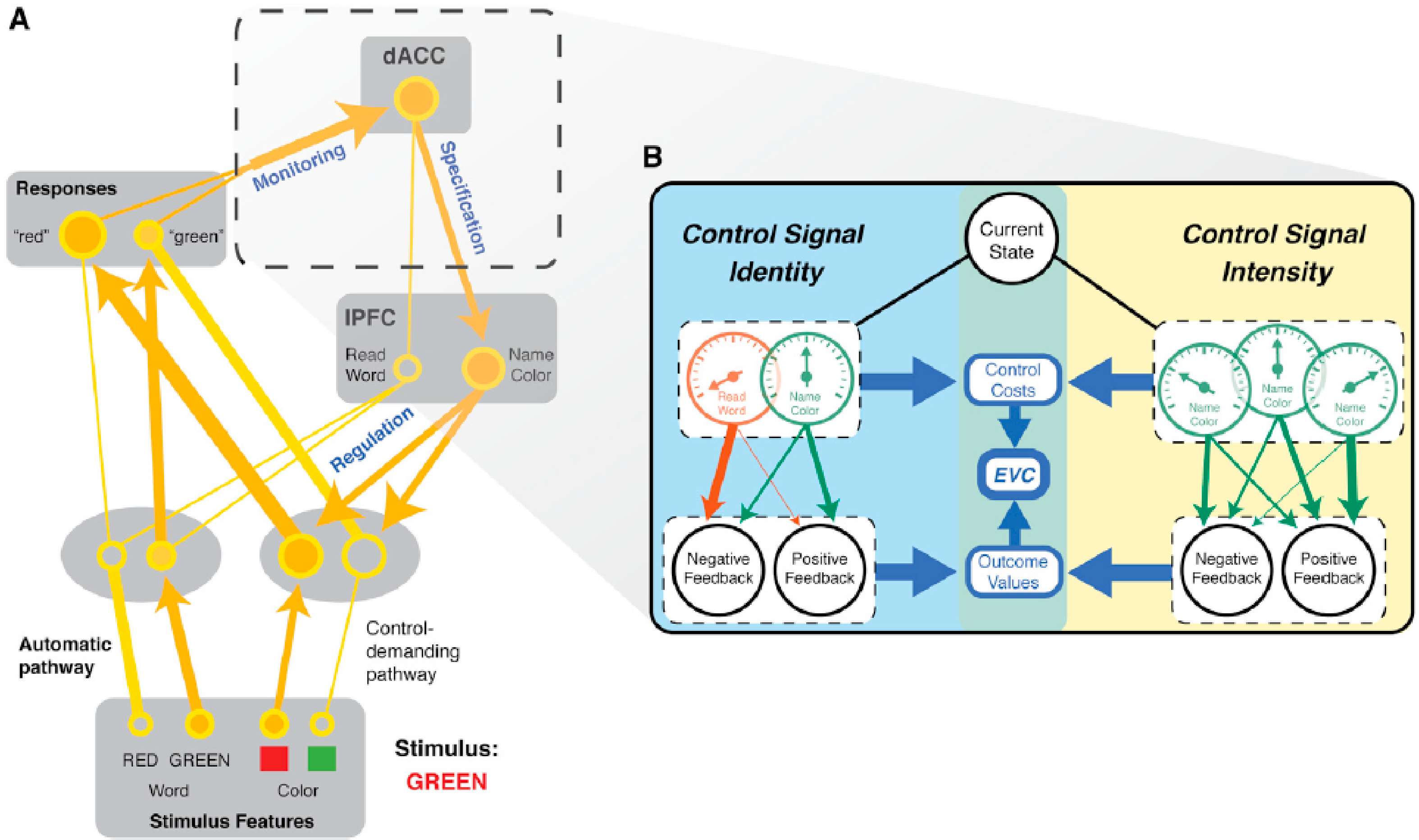
Theory #2: Error Detection, Error Likelihood – The ACC makes a comparison between the response in progress and the intended response (the correct response) or between the received reward and expected reward. Can also use that comparison to adjust or correct responses even as the response is ongoing.

Theory #3: Conflict Monitoring – The ACC detects incompatible representations (responses, stimuli, contexts, etc.) and signals lateral prefrontal areas to make attentional adjustments.

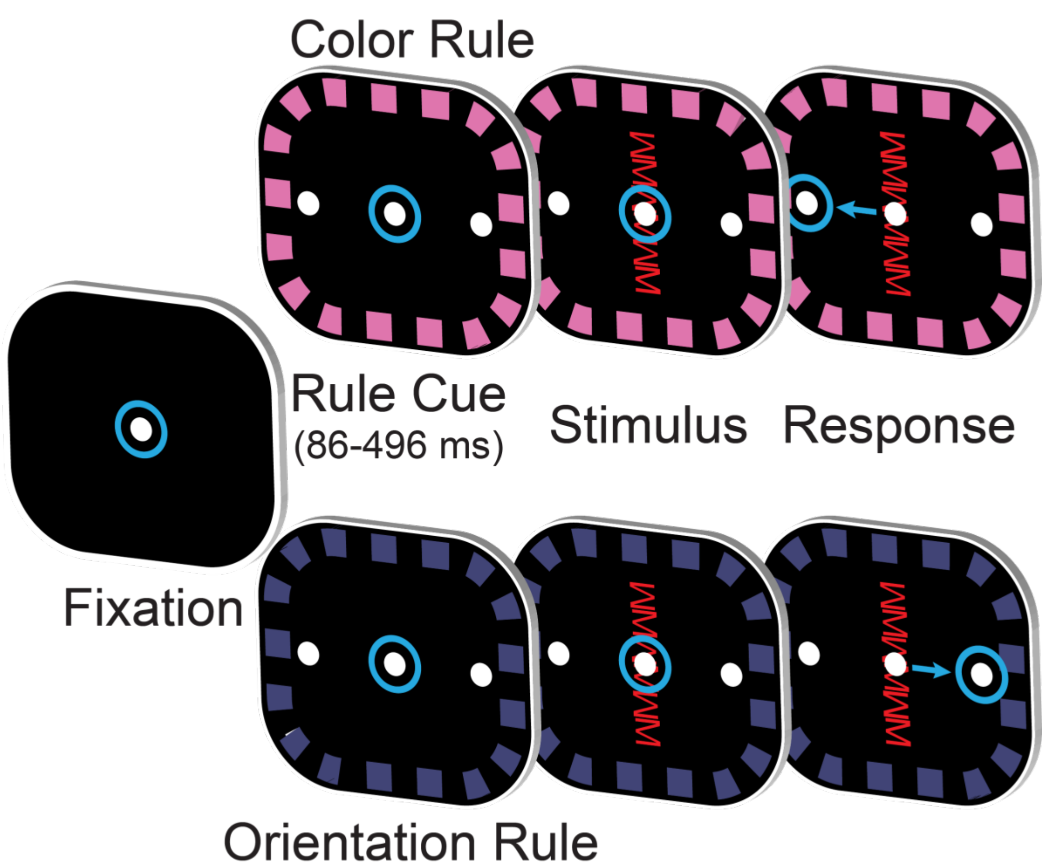


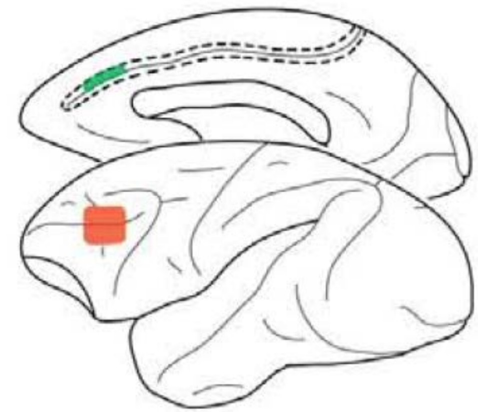
Theory #4: Reinforcement Learning – The ACC learns to associate responses with an expected outcome (positive or negative) and the amount of effort required to achieve that outcome (cost and frequency of response, action-reward ratios) – Pr(Outcome | Response).

Current Model of ACC and dlPFC



Cued Task Switching Paradigm





Factors that change the amount of attention needed

Switch History – Number of trials since the rule change

Error History – Number of trials since an error occurred

Congruency – Whether the correct saccade direction is the same for both rules

Preparation Time – Amount of time between rule cue and stimulus

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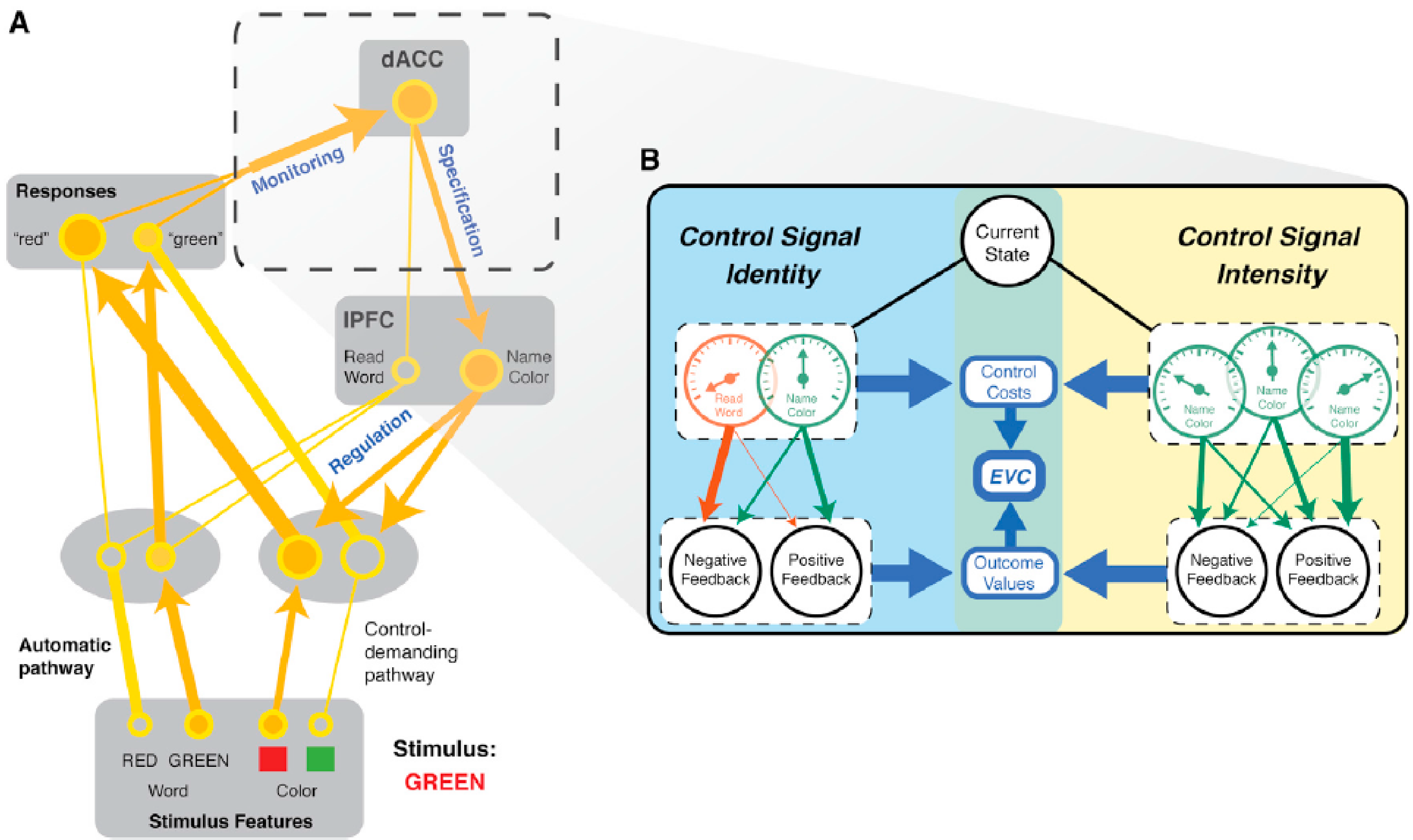
Predictions from the Current Model



Outline

Aim #1: To identify circuit-level coordination within and between ACC and dlPFC during task switching

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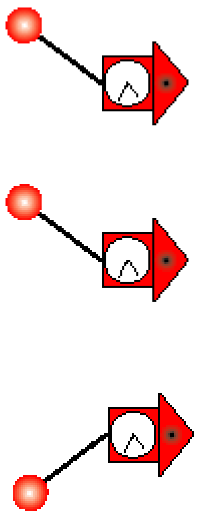
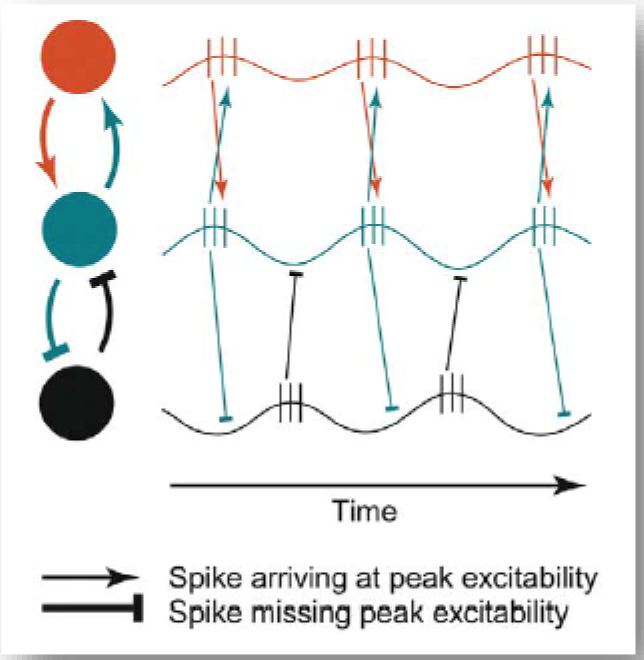
Hypothesis: Rule-dependent Communication through Coherence

Stable relationship between the phases of two oscillators

Short Conduction Delays





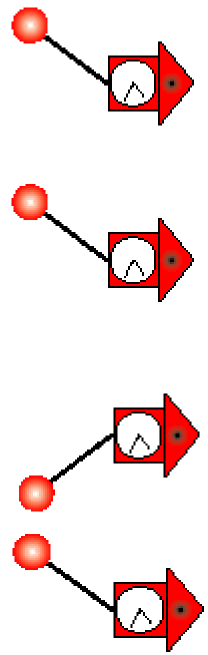
Fries, P. (2005). A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. Trends in Cognitive Sciences *9*, 474–480

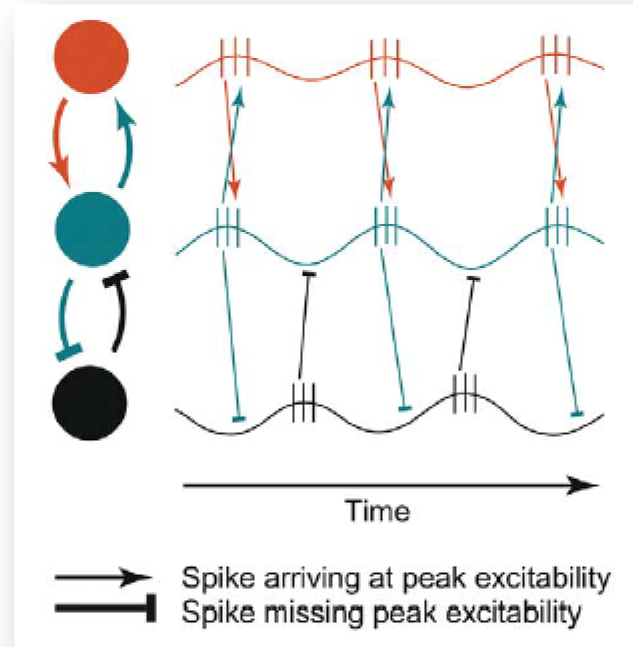
Hypothesis: Rule-dependent Communication through Coherence

Stable relationship between the phases of two oscillators

Short Conduction Delays

Not coherent





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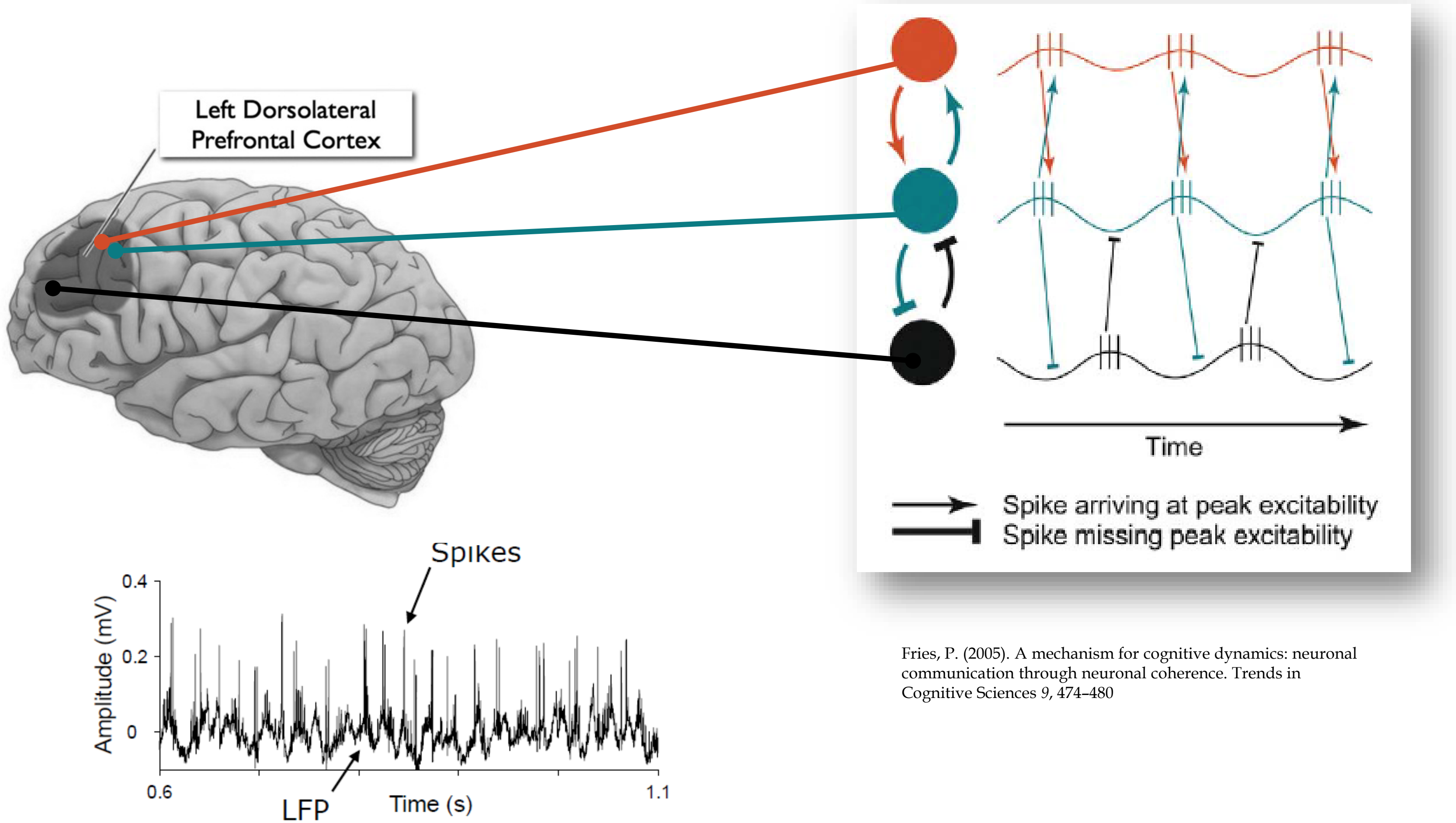

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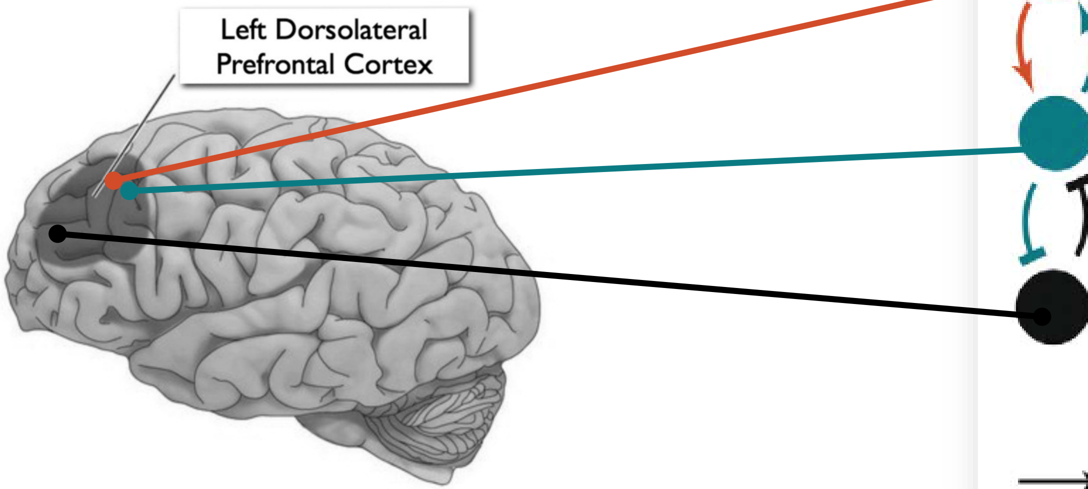

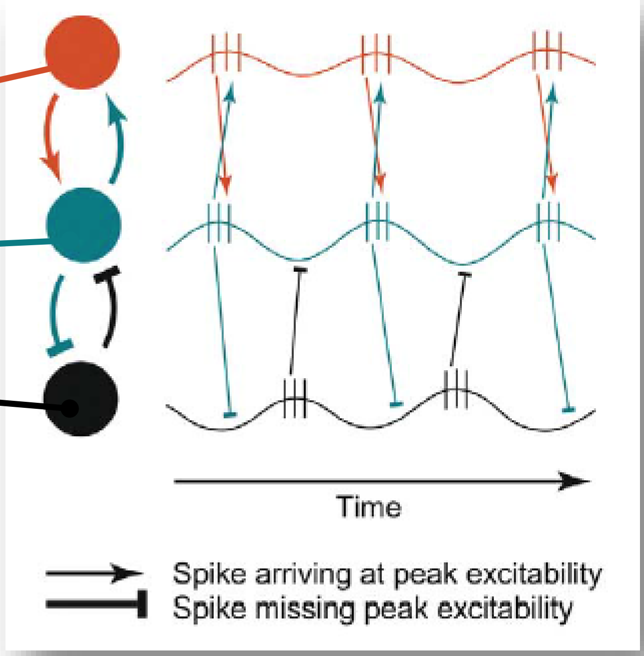

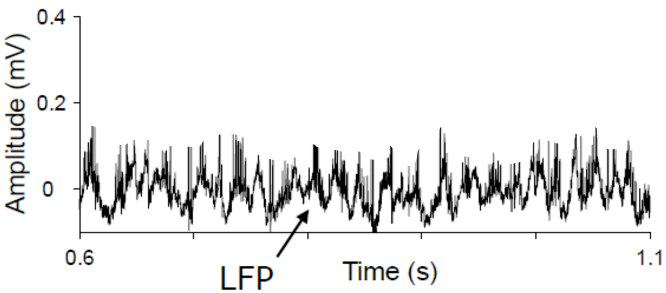

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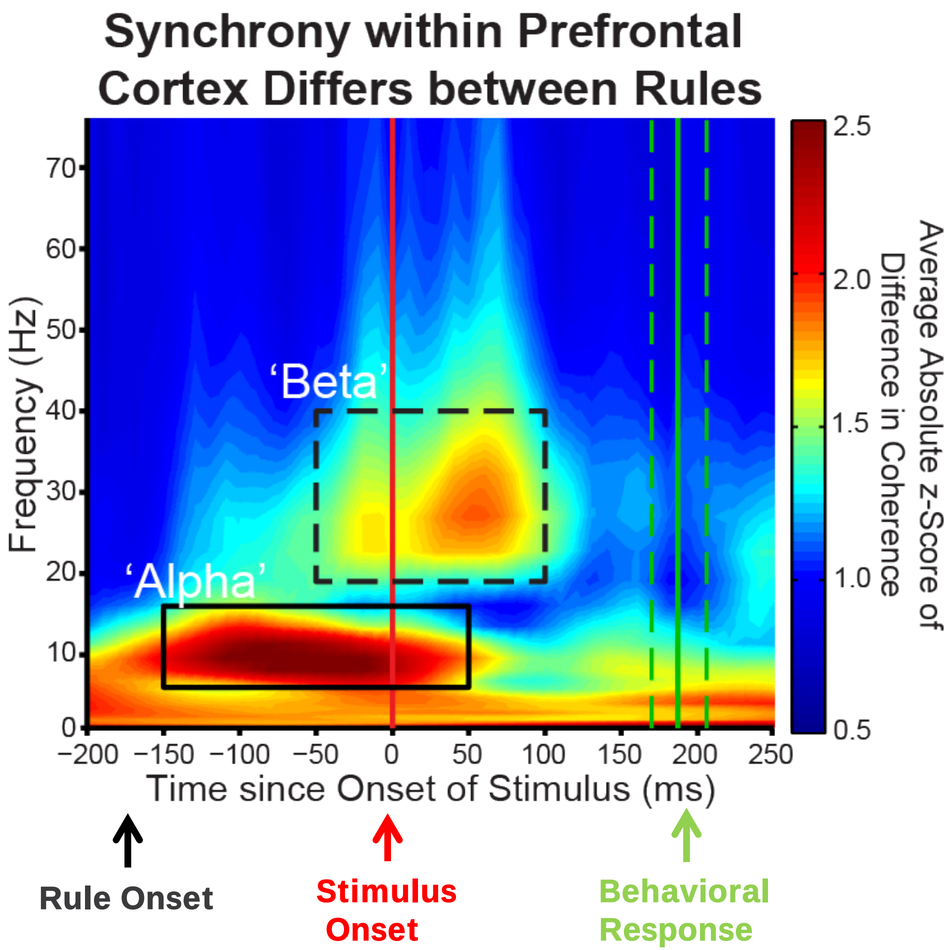
Rule-Selective dlPFC-dlPFC Coherence



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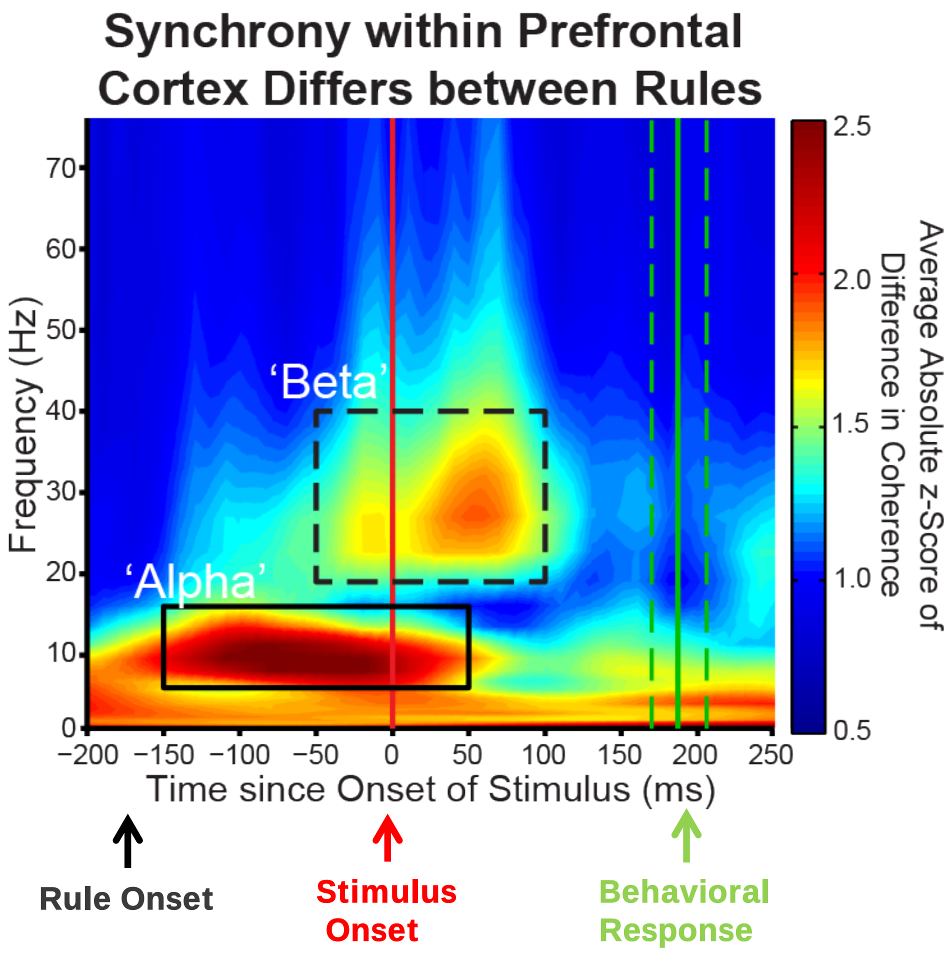

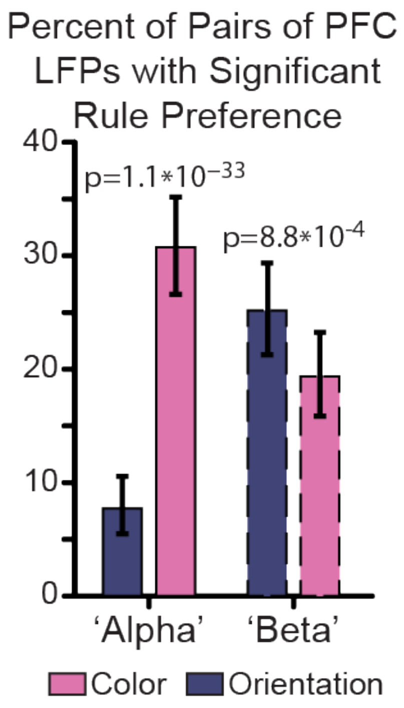

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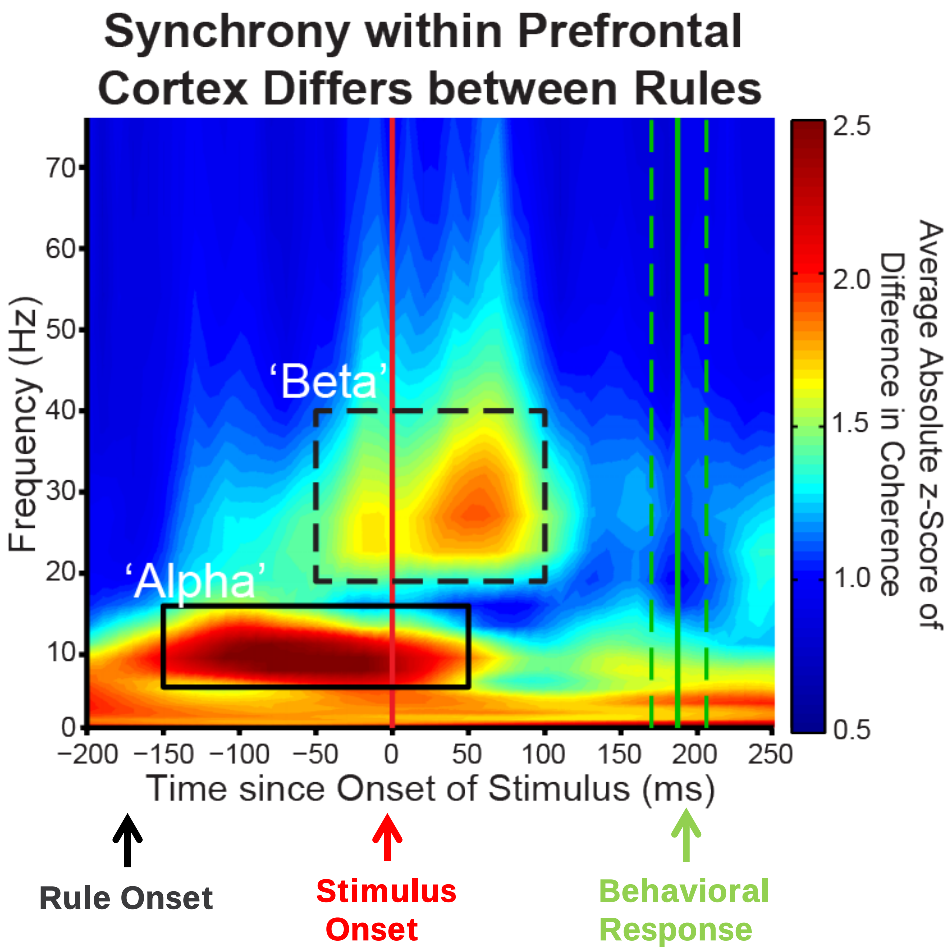
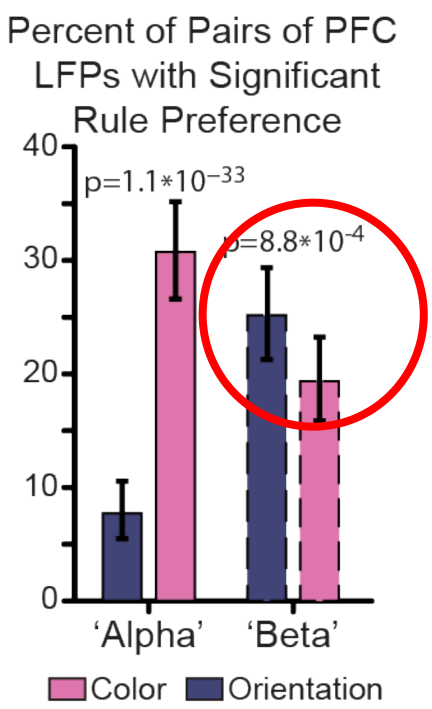
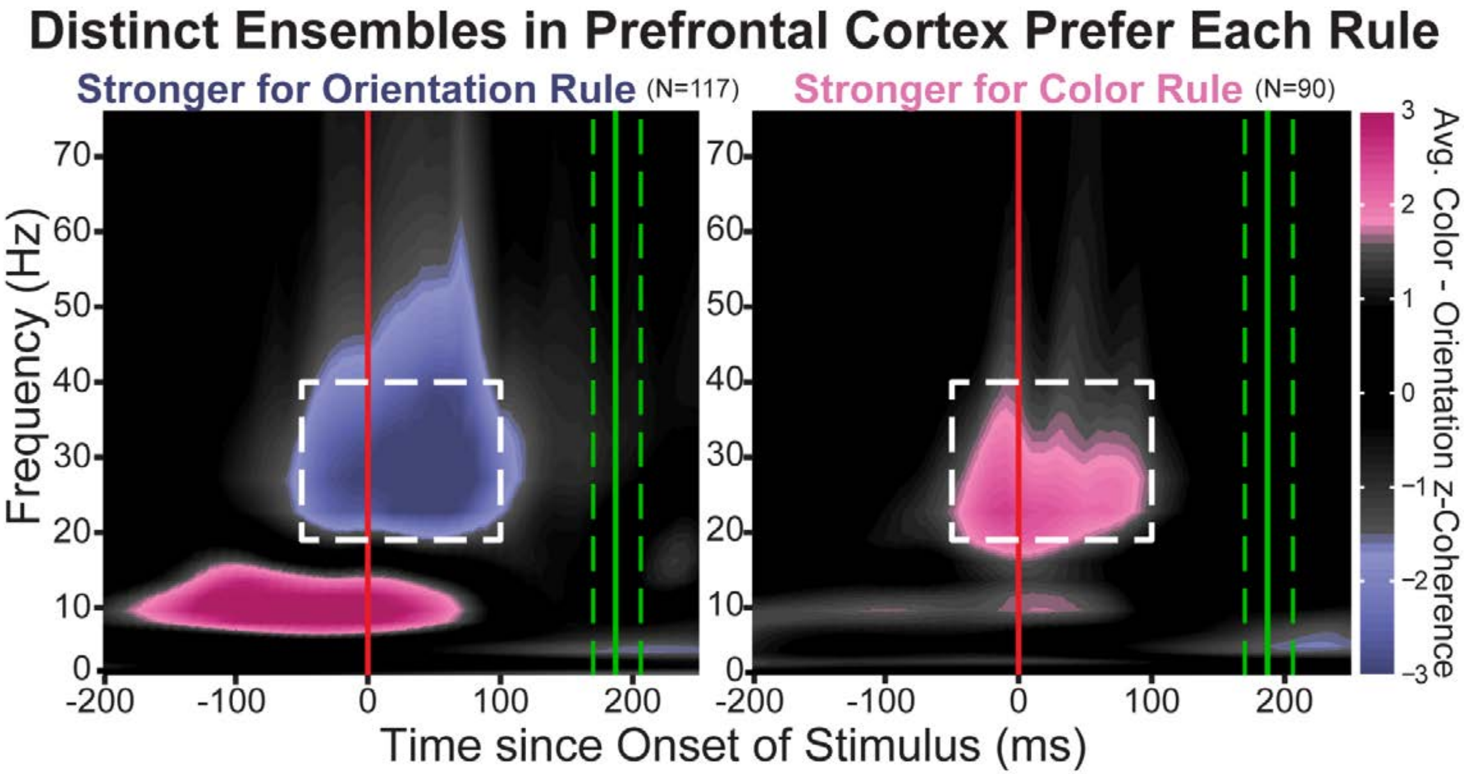
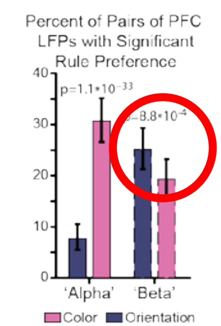




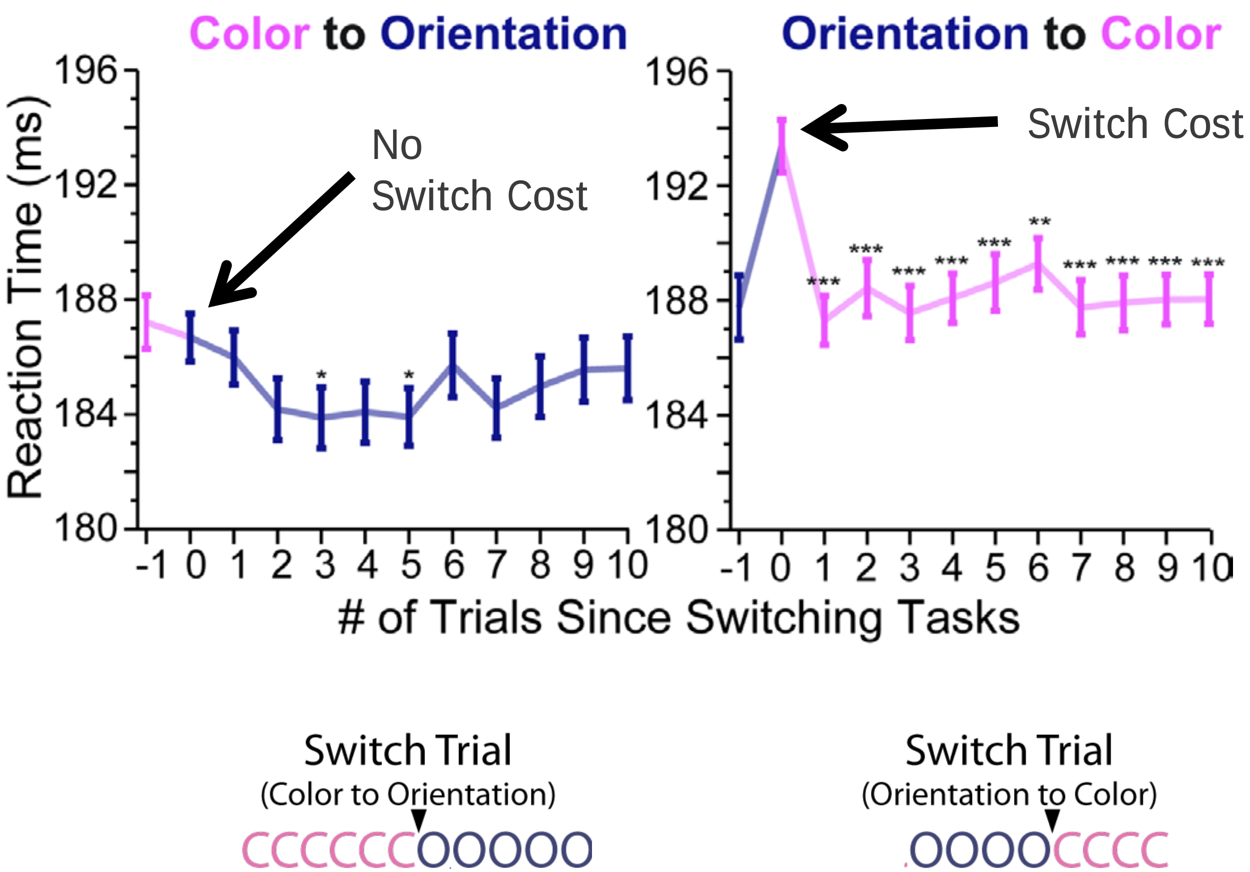
Rule-Selective Beta Networks



Orientation-preferring electrodes in the beta band also show increased **alpha** synchrony.

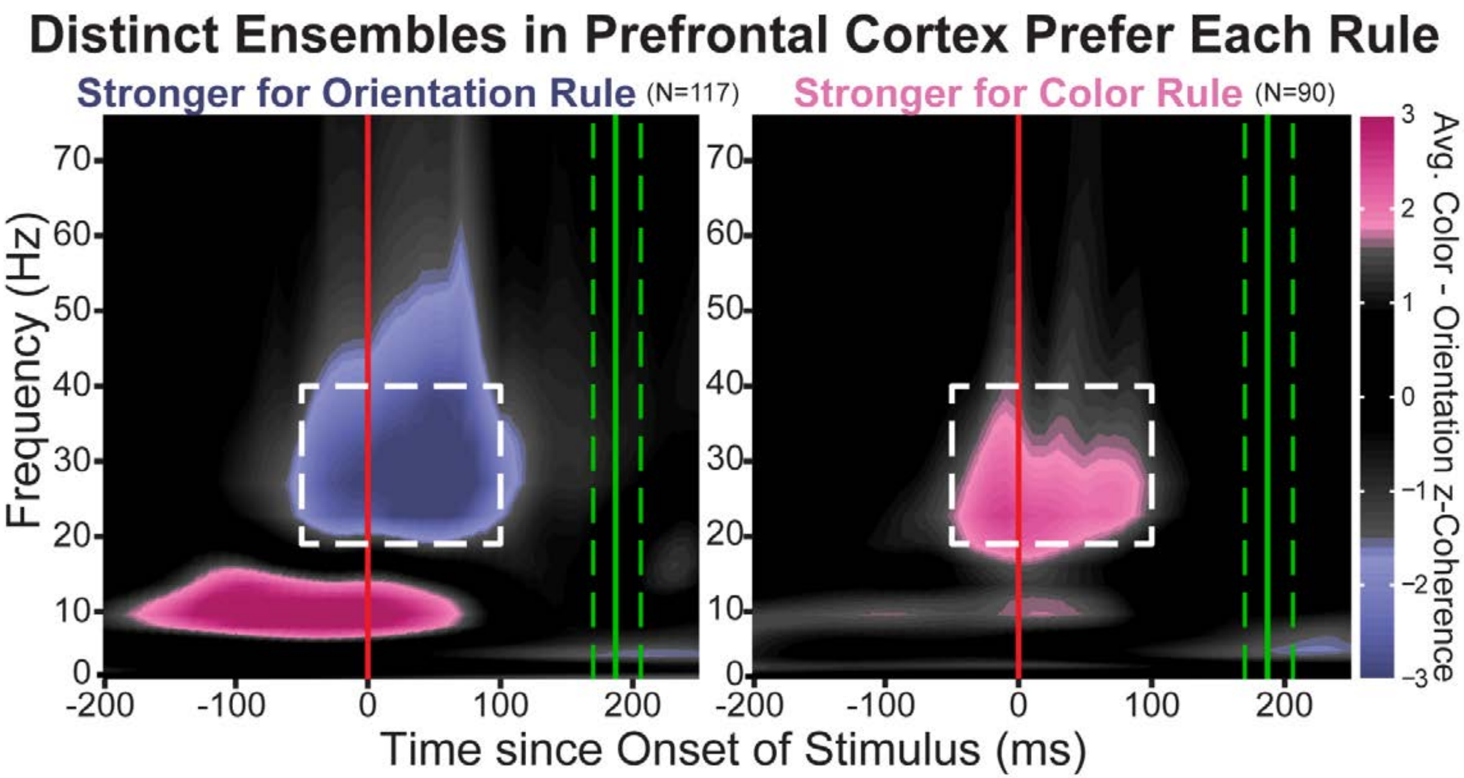


Orientation is the more dominant, default behavior



Harder to switch away from orientation

Rule-Selective Beta Networks



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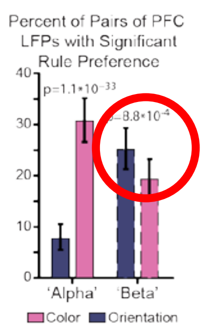
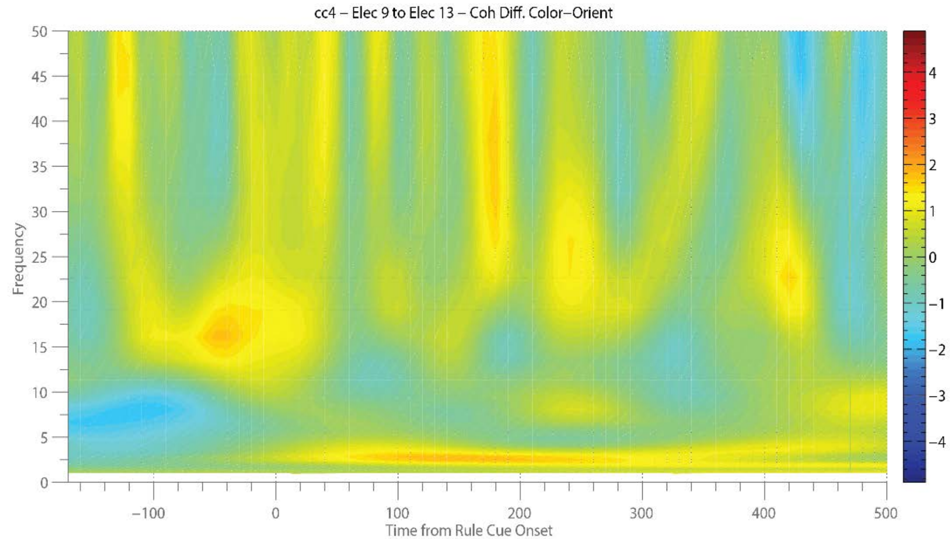
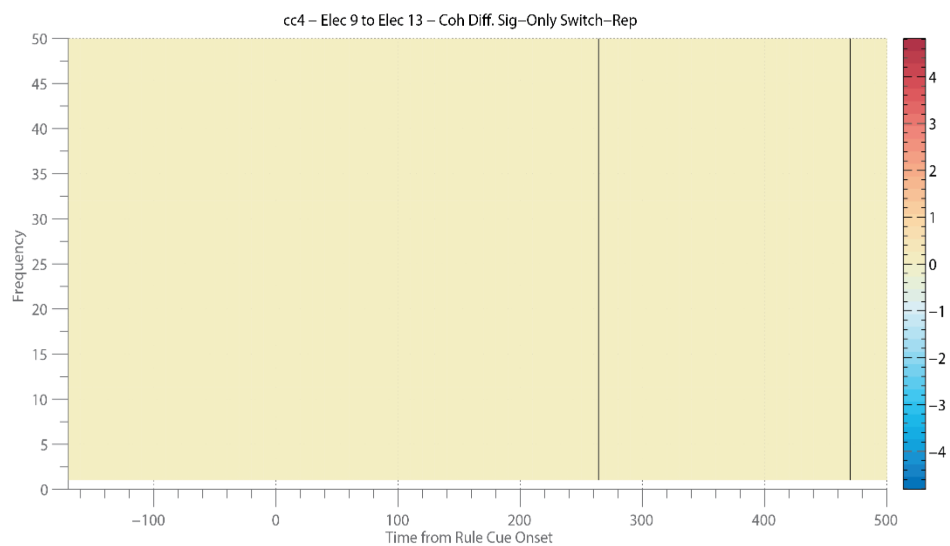
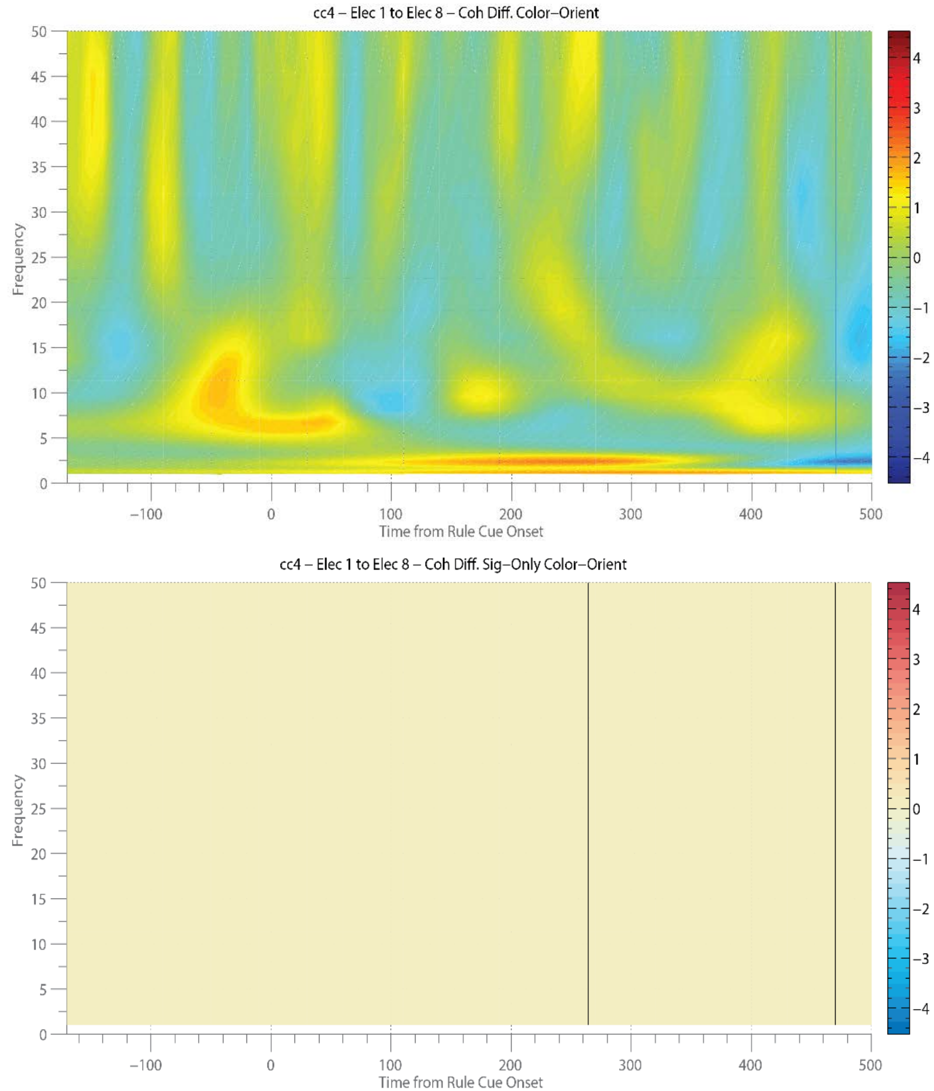


No rule selective coherence, ACC-ACC





No rule selective coherence, ACC-dlPFC



Potential reasons for no observed ACC-ACC, ACC-dlPFC coherence

- ACC is not involved in cued task switching
  - ACC connections with visual areas are weak
  - ACC lesions do not impair task switching
  - Unclear if context is important in ACC
- ACC does not communicate with dlPFC via oscillations
  - Broadband signal
  - Transient signal

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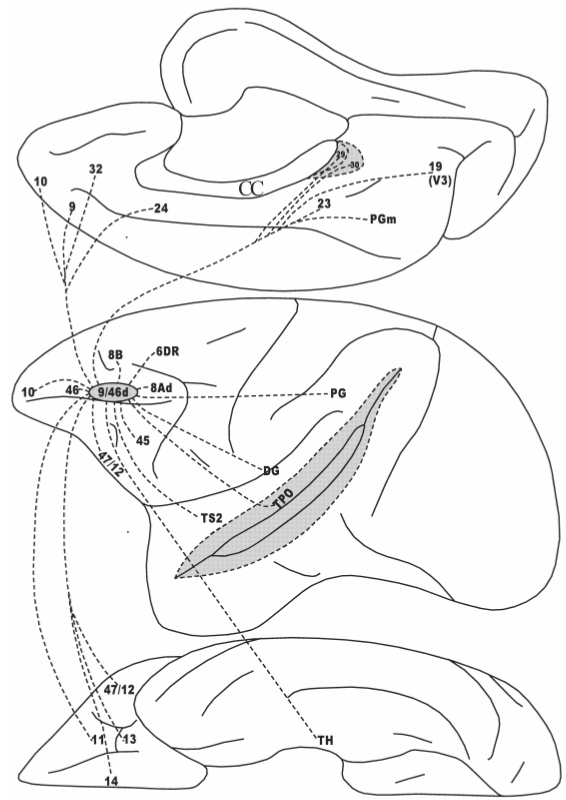
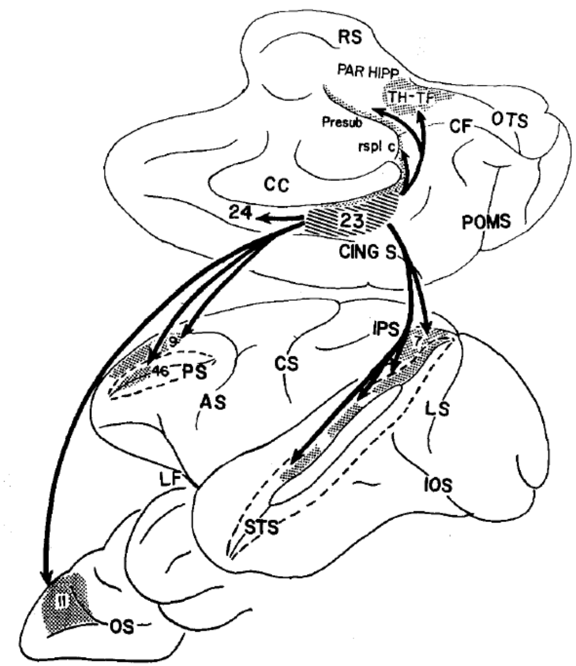
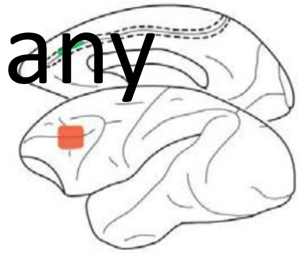




Challenges to Studying ACC: Many Theories…



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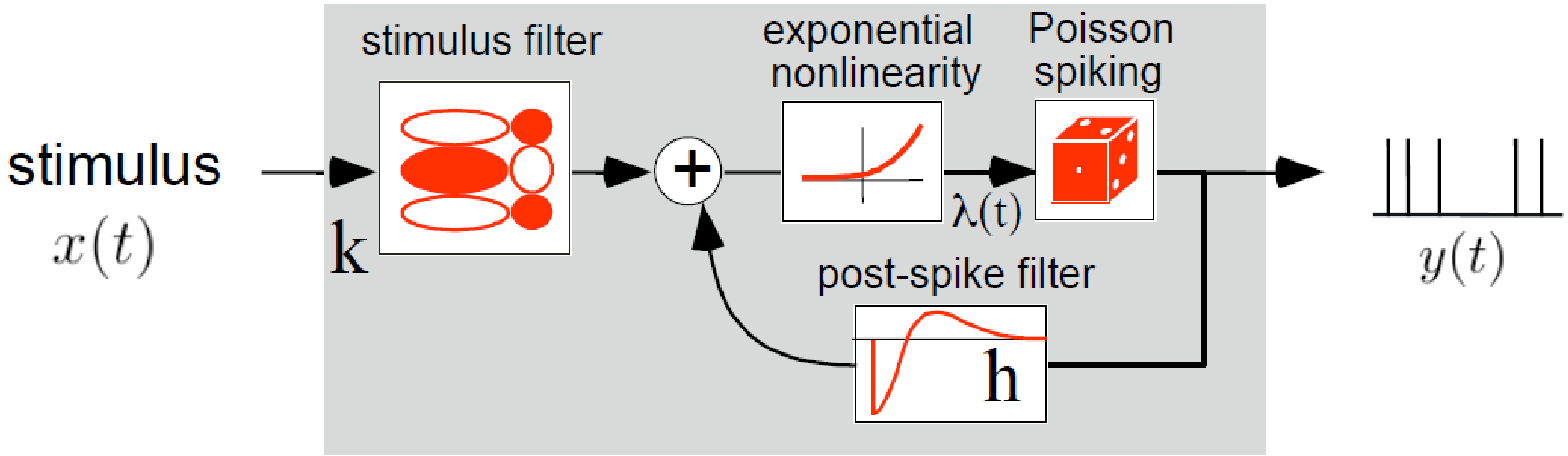
Methods: High-dimensional Regression Models

- Can account for many task factors simultaneously
- Can use regularization to control overfitting
- Flexible, efficient framework

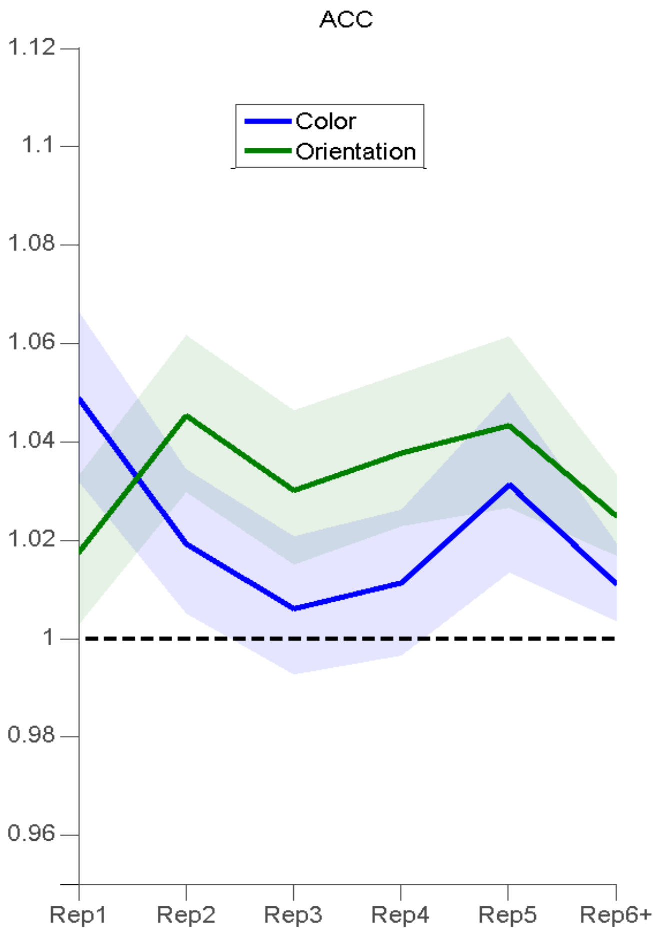


Model #1: Influence of factors on individual neurons

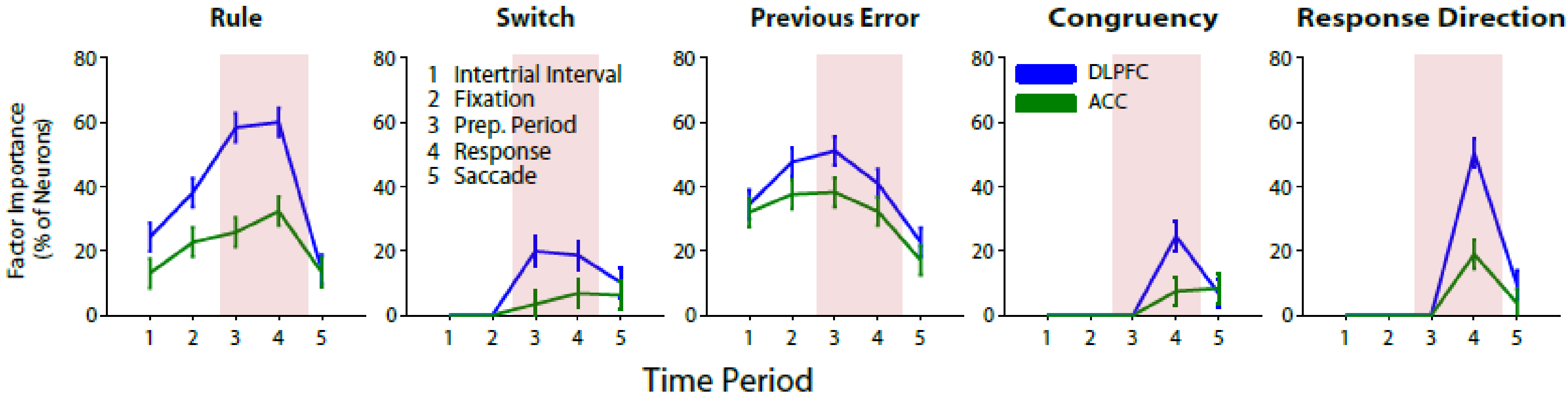
$$
\begin{aligned}
&\log \mu(t) \\
&= Rule\ * Switch\ History + Rule * Error\ History \\
&+ Rule\ * Congruency + Rule\ * Preparation\ Time \\
&+ Response\ Direction + Spike\ History
\end{aligned}
$$

Previous Error - Prep Period
ACC
PFC
Color
Orientation
1.12
1.1
1.08
1.06
1.04
1.02
1
0.98
0.96
Error1
Error2
Error3
Error4
Error5
Error6+

Switch - Prep Period

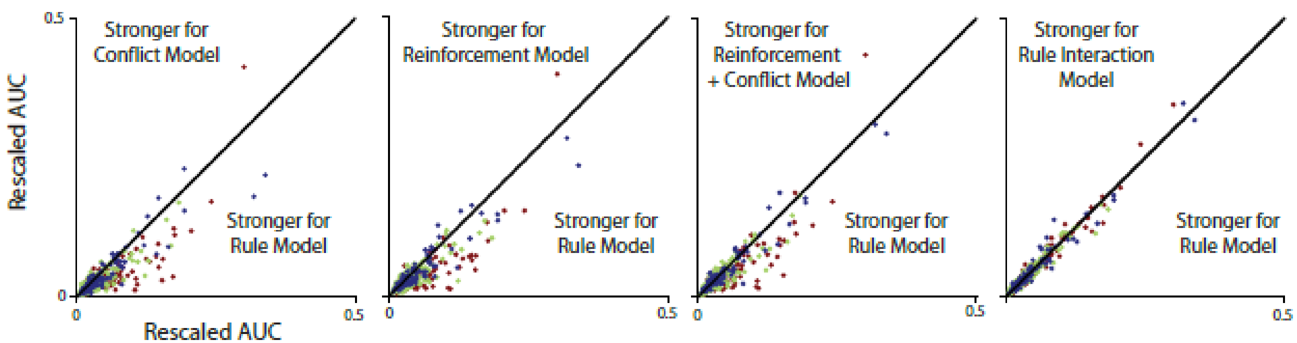


Which factors best predict ACC and DLPFC activity?



The figure above shows the percentage of neurons for which inclusion of that factor enhanced prediction of spikes. **Rule, previous error**, and **response direction** are the most important factors for predicting the firing rate in ACC and DLPFC. **Switch** and **congruency** are less predictive of firing rate, but a number of DLPFC neurons show that accounting for **switch** improves prediction.

Are Rules Important for ACC?



Conflict Model
Switch + Congruency + Previous Error

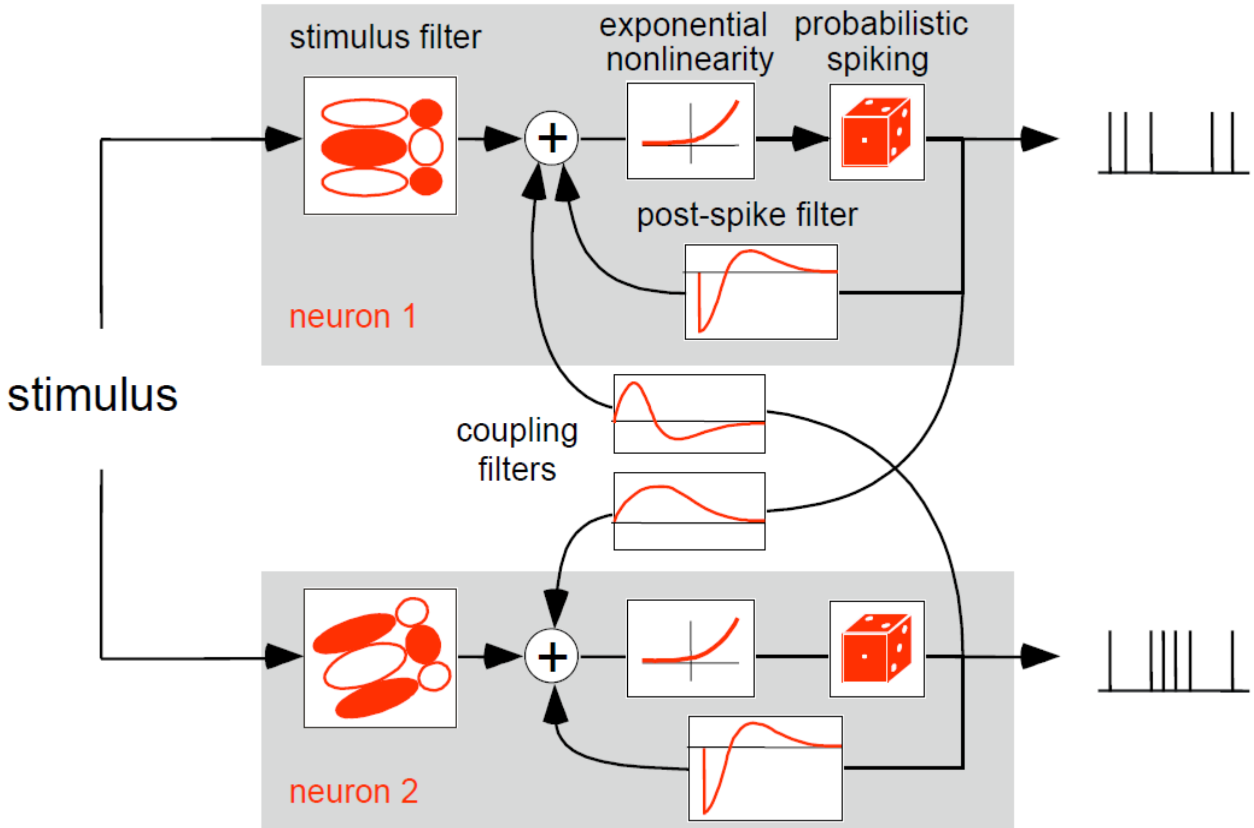
Reinforcement Model
Previous Error * Response Direction

Rule Model
Rule + Conflict + Reinforcement

Rule Interaction Model
Rule * Switch + Rule * Congruency + Rule * Previous Error + Previous Error * Response Direction

Including **rule** as a factor improved prediction of spikes for ACC neurons, even when accounting for conflict and reinforcement factors. We also tested for possible dependence between rule and conflict factors (rule interaction model), but there was no clear preference between the rule model and the rule interaction model.

Model #2: Relationship of individual neurons to circuit level activity



Model #2: Relationship of individual neurons to circuit level activity

$$\log \mu(t) = Rule * Attention\ Factor * Population_{Same\ area} + Rule * Attention\ Factor * Population_{Other\ Area + Spike\ History}$$

Work to be done

- Need to better understand the interpretation of coefficients for model #1
- Need to fit and analyze model #2

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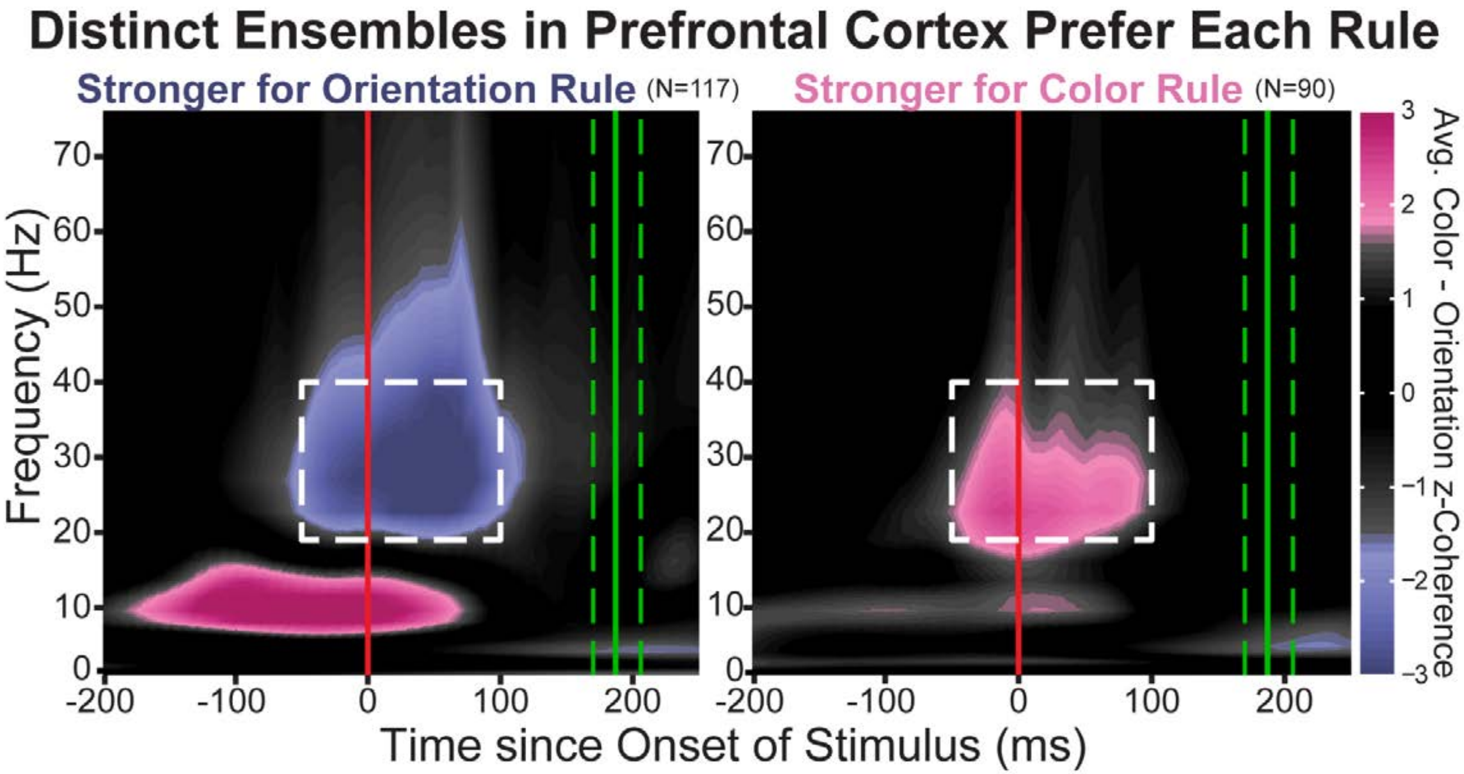
Rule-Selective Beta Networks



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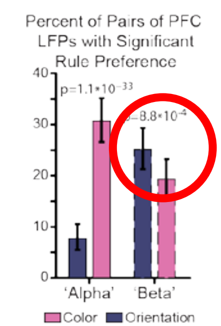
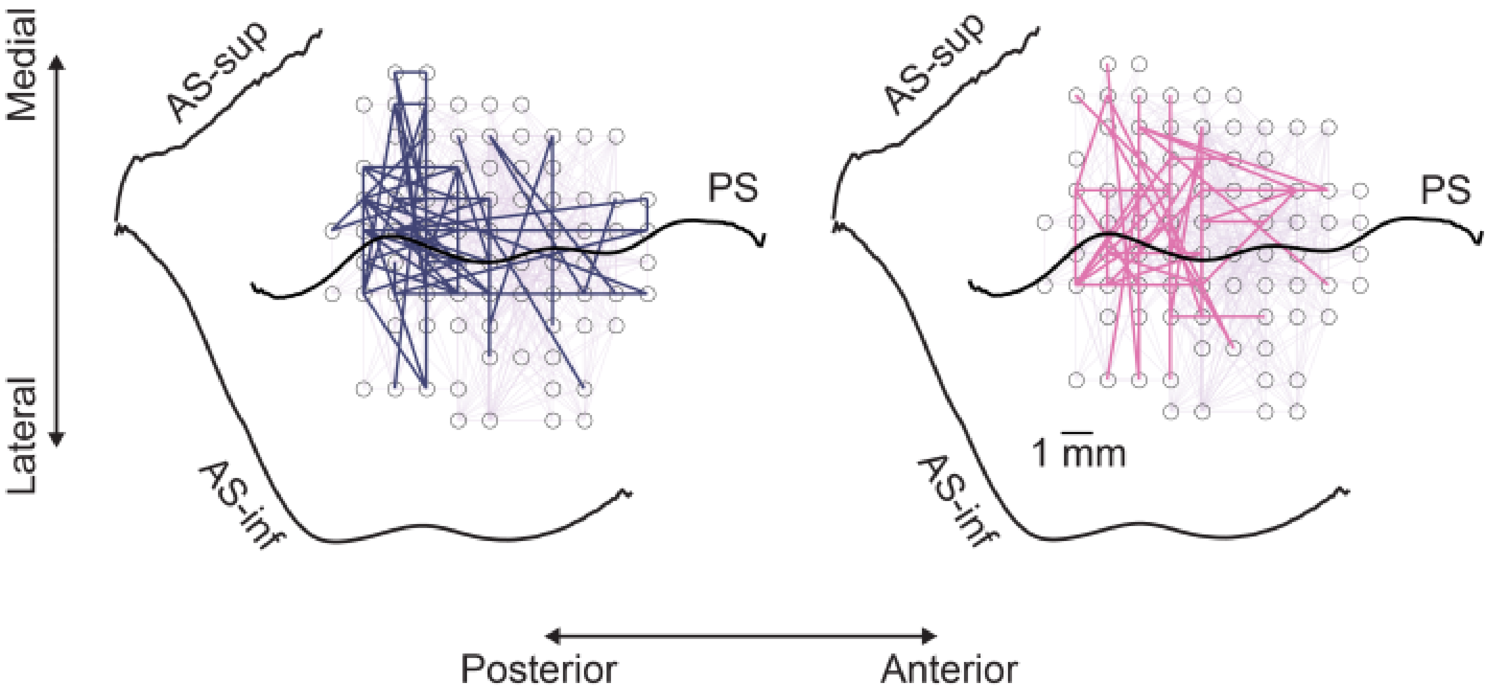


Spatial Organization of Rule-dependent Coherence

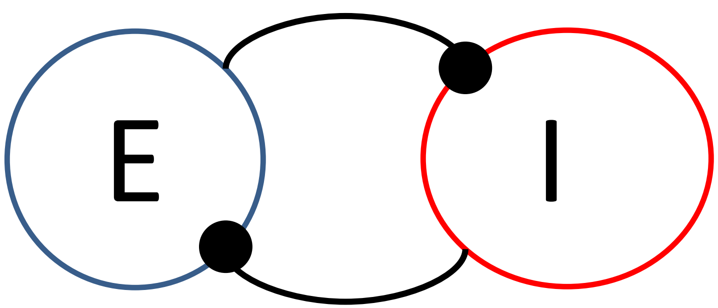
Network that is more synchronous for **Orientation Rule** (N=115)

Network that is more synchronous for **Color Rule** (N=76)



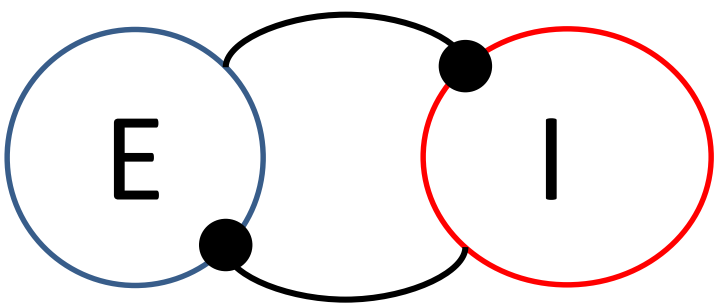
Alpha Generation

- Alpha rhythms can be generated by layer V pyramidal neurons
- Hyperpolarization-activated currents have a time course similar to alpha and they promote rebound spiking between an inhibitory-excitatory pair (Jones et al. 2000)

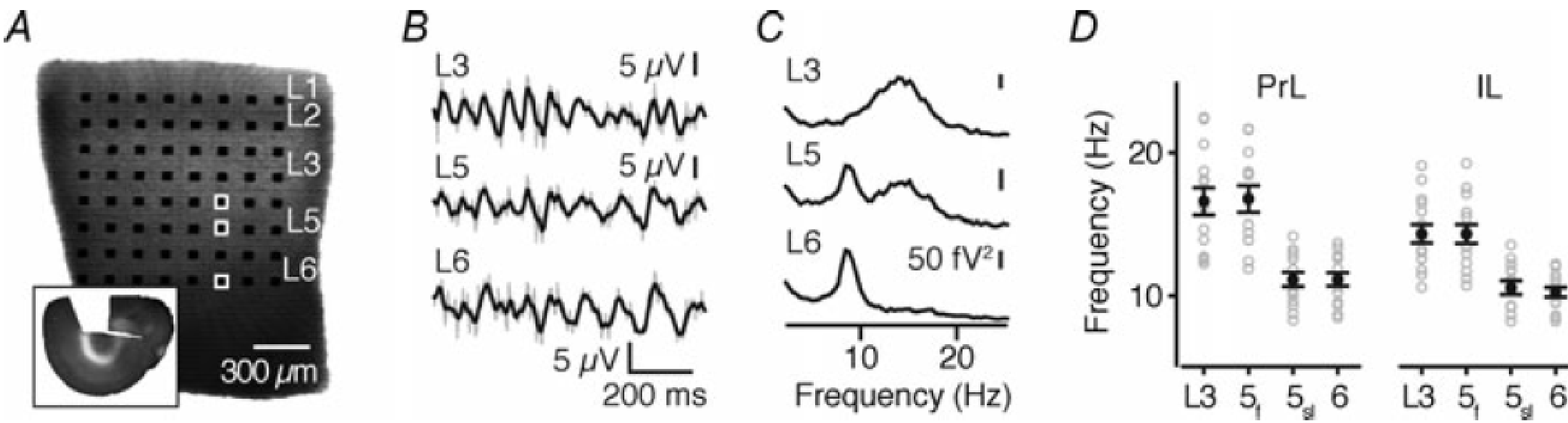


Beta Generation

- Generated within cortex
- Paced by muscarinic type potassium currents in Intrinsic Bursting cells (Roopun et al. 2006)



Van Aerde et al. 2009



Work to be done

- Defining the connectivity of the network
- Figuring out how to generate the right coherence patterns
- Explaining how coherence can select among heterogeneously selective neurons
  – Can generate heterogeneity by adding a pool of randomly weighted neurons (Rigotti et al.)
  – Or use the data
- Incorporating experimental observations
  – Observed firing rate ranges
  – Observed coherences/changes in coherence

Timeline: Estimated Time of Completion

Aim #1: ~2 weeks

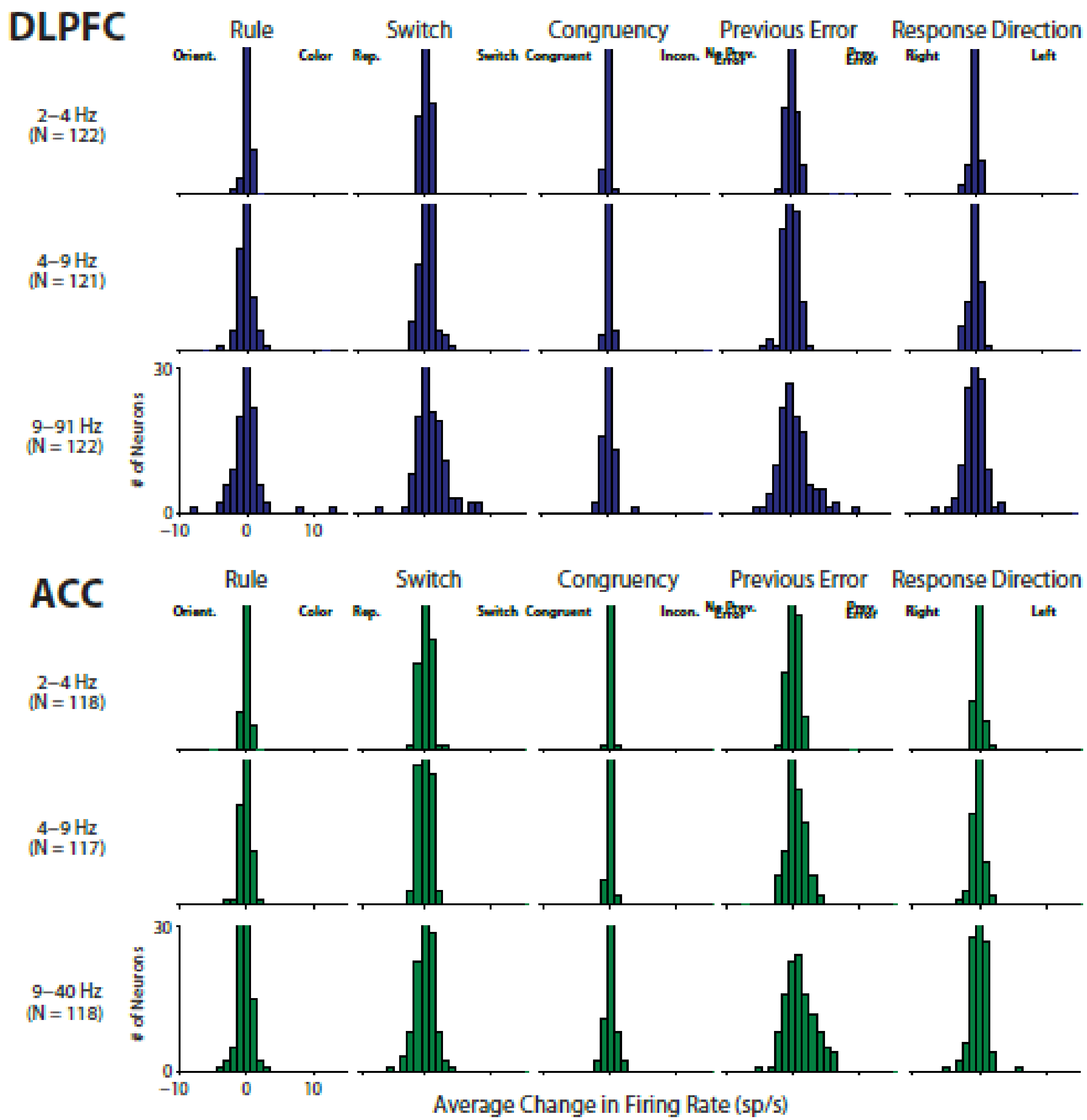
Aim #2: ~2 months

Aim #3: ~8 months

Goal Graduation Date: April 2015

Potential Issues

- Scope and Focus of Aim #2,3
- Distinguishing Aim #2 from the Johnston et al. 2007 Paper (Cued versus Uncued Task switching)
- The Jason Sherfey Issue (Aim #3)
- End of CELEST funding


DLPFC
Rule
Switch
Congruency
Previous Error
Response Direction
Orient.
Color
Rep.
Switch
Congruent
Incon.
No Prev. Error
Prev. Error
Right
Left
2–4 Hz (N = 122)
4–9 Hz (N = 121)
9–91 Hz (N = 122)
# of Neurons
30
0
−10
0
10
ACC
Rule
Switch
Congruency
Previous Error
Response Direction
Orient.
Color
Rep.
Switch
Congruent
Incon.
No Prev. Error
Prev. Error
Right
Left
2–4 Hz (N = 118)
4–9 Hz (N = 117)
9–40 Hz (N = 118)
# of Neurons
30
0
−10
0
10
Average Change in Firing Rate (sp/s)