Reconstructing Mechanistic Models of Cognition via Simultaneous MINDy Modeling for Resting-State and Task fMRI.

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Background: Big data initiatives have enabled dynamical models of neural activity[1] while also empowering the study of individual differences[2]. However, there remains a gap between dynamical models which have enabled mechanistic hypothesis-testing of circuit function and statistical models that dominate data driven studies of individual differences. **We aim to bridge this gap with MINDy modeling.**

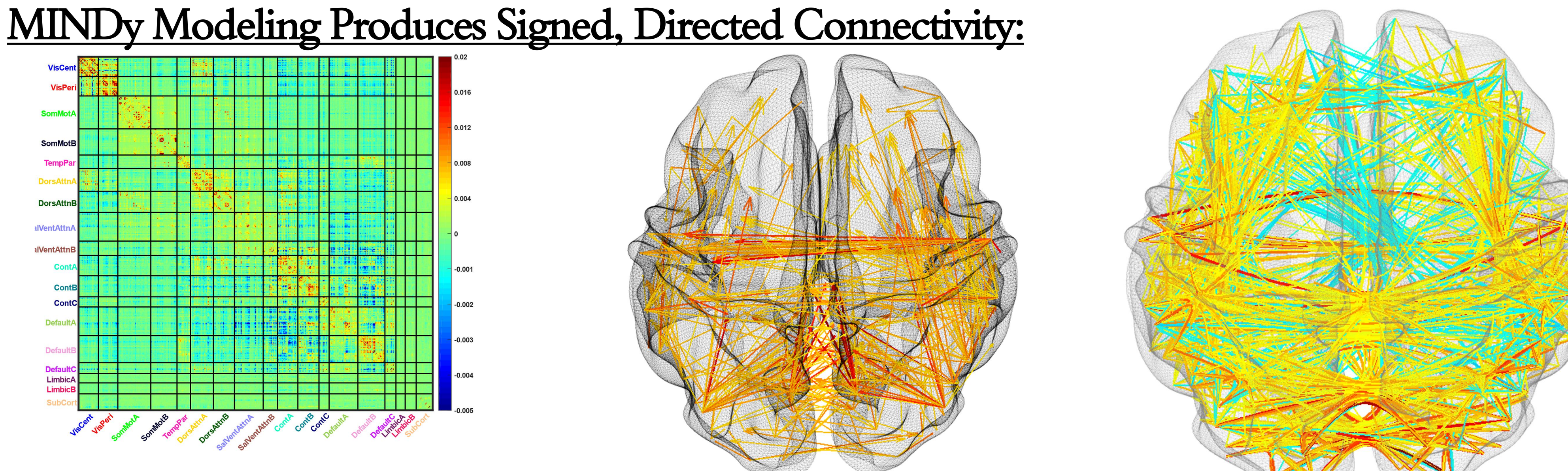
Mesoscopic Individualized NeuroDynamic (MINDy) modeling:

The entire brain is modeled as a network of **neural-mass** models[3] (1/region: "n" total) with 3 components each:

1. A weight matrix of connectivity: **W:** (nxn)
2. A transfer function transforms local neural activity into output signals: **Ψ**(X): (nx1)→(nx1)
3. A decay coefficient describes how quickly each neural mass returns to baseline activity: **D:** (nx1)

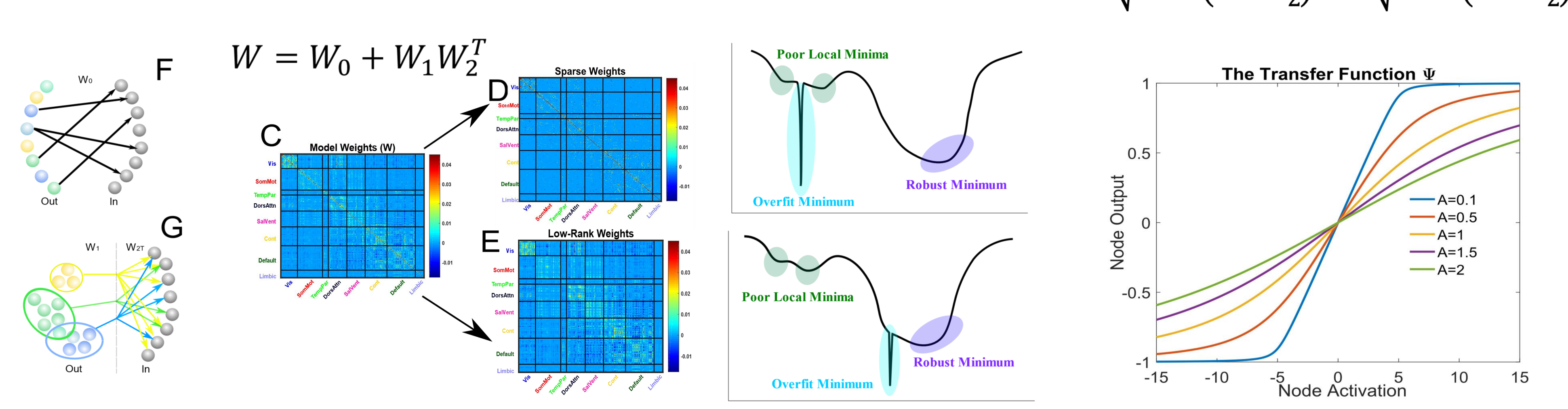
x(t): activation vector (all regions): $dx/dt = W\psi(x) - Dx$

MINDy Modeling Produces Signed, Directed Connectivity:



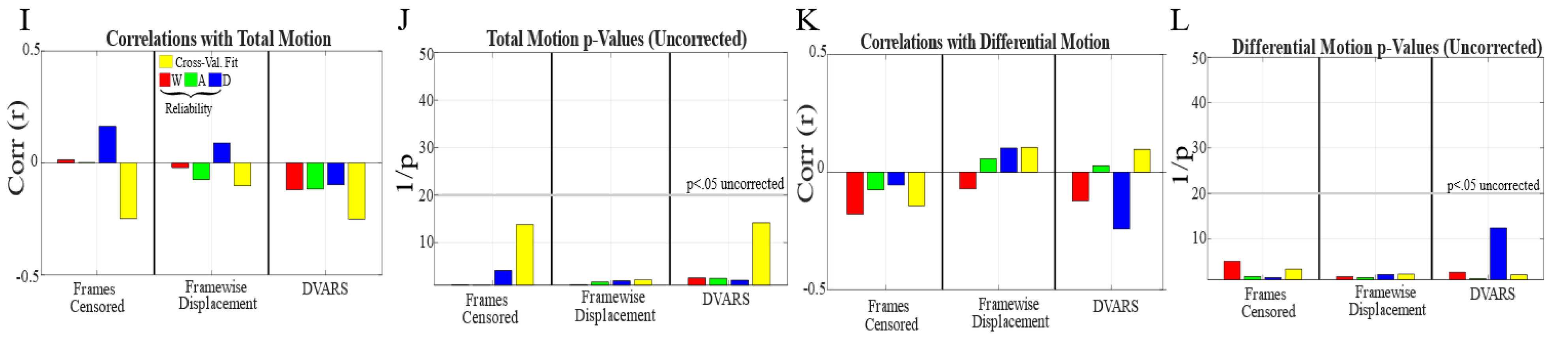
Fitting Individualized Models in High Dimensions:

1. Decompose the weight matrix into sparse (W_0) and low-rank/diffuse components ($W_1W_2^T$)
2. Stochastic gradient descent with adaptive momentum (NADAM)
3. Allow region specific curvature (A) in the transfer function: $\Psi(x)=\sqrt{A+\left(bx+\frac{1}{2}\right)^2}-\sqrt{A+\left(bx-\frac{1}{2}\right)^2}$



MINDy is Robust to Motion Artifact:

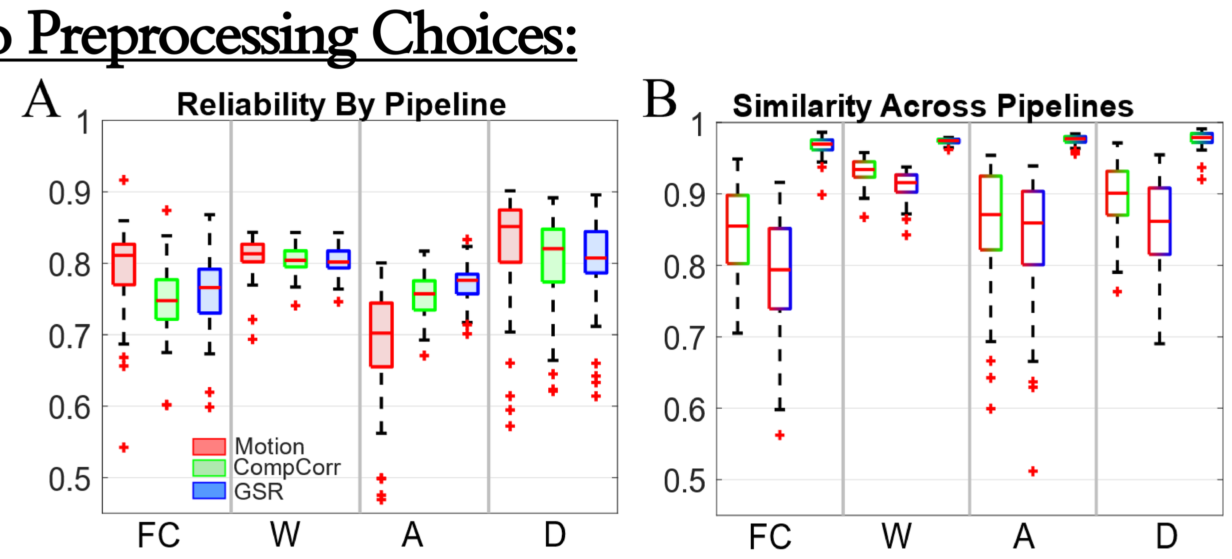
MINDy does not suffer under differences in motion (within a reasonable range) or differential motion between scans. This property holds for Frame-wise Displacement (FD), DVARS, and the proportion of censored frames (from FD, DVARS cutoff).



MINDy Parameters are Robust to Preprocessing Choices:

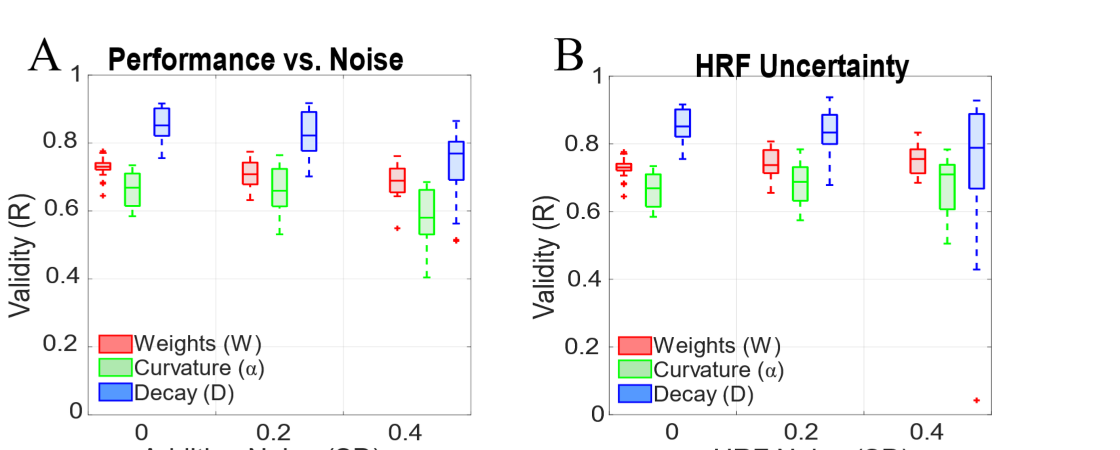
Considered 3 levels:

1. **Motion only[4]**: (scrubbing and censoring with DVARS and Frame Displacement)
2. **+CompCorr[5]**: White matter and CSF principle components regressed out.
3. **+Global Signal**: Mean signals for white matter, CSF and grey matter regressed out in addition to CompCorr



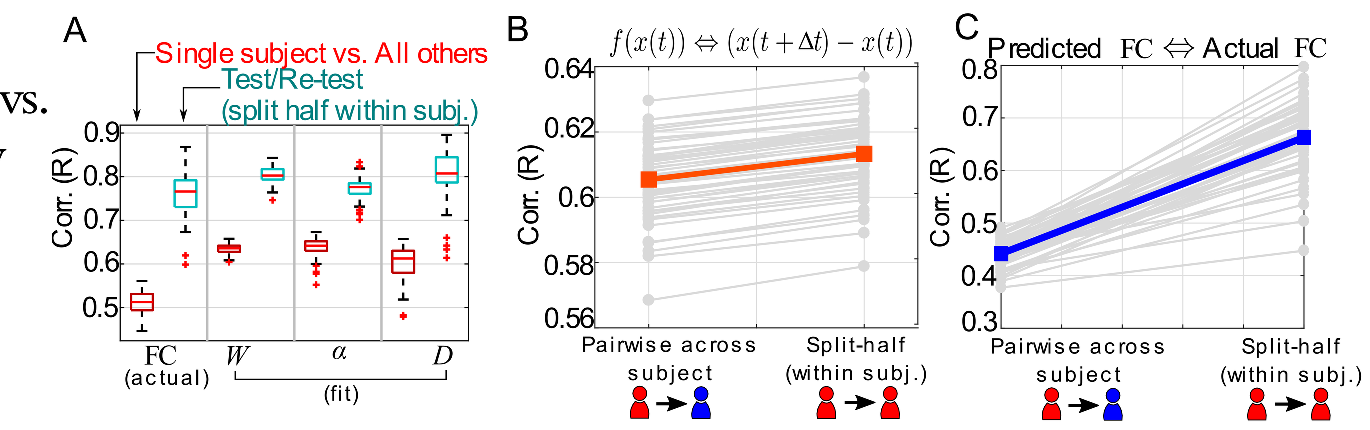
MINDy Retrieves Ground-Truth Connectivity and Decay Under Realistic HRF Uncertainty and Noise:

- Simulated MINDy with parameters randomly selected from individuals
- Retrieved parameters while varying measurement noise and variability in HRF

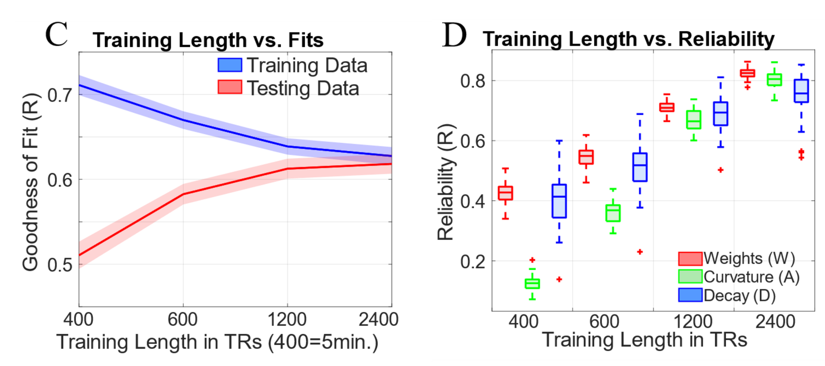


MINDy Models & Parameters Differentiate Individuals

- "Fingerprinting" analysis compared within-subject vs. between subject similarity
- Parameter similarity and cross-validated model fits uniquely identify individuals



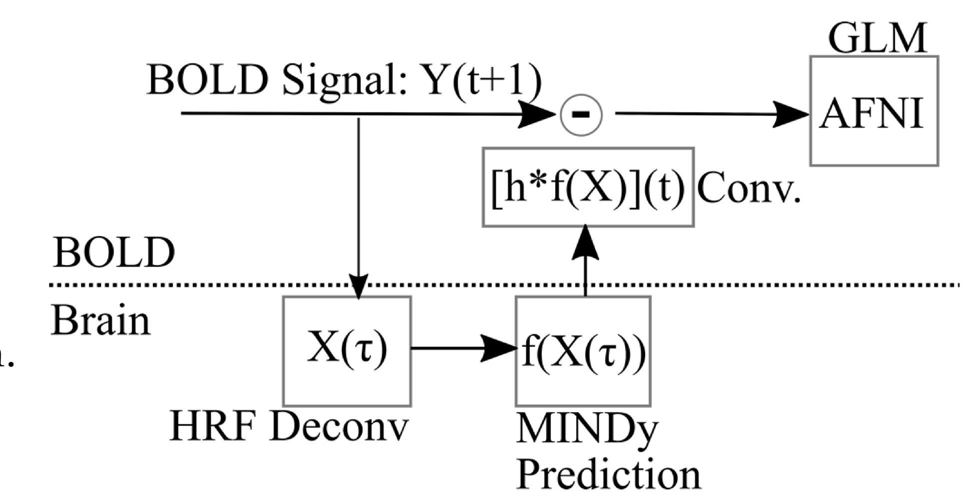
MINDy Only Requires 15 Minutes of Scan Time



- Divided full data into variable length segments
- Compared cross-validated model fits and parameter reliabilities
- Performance was strong at 15 minutes., but more data improves reliability.

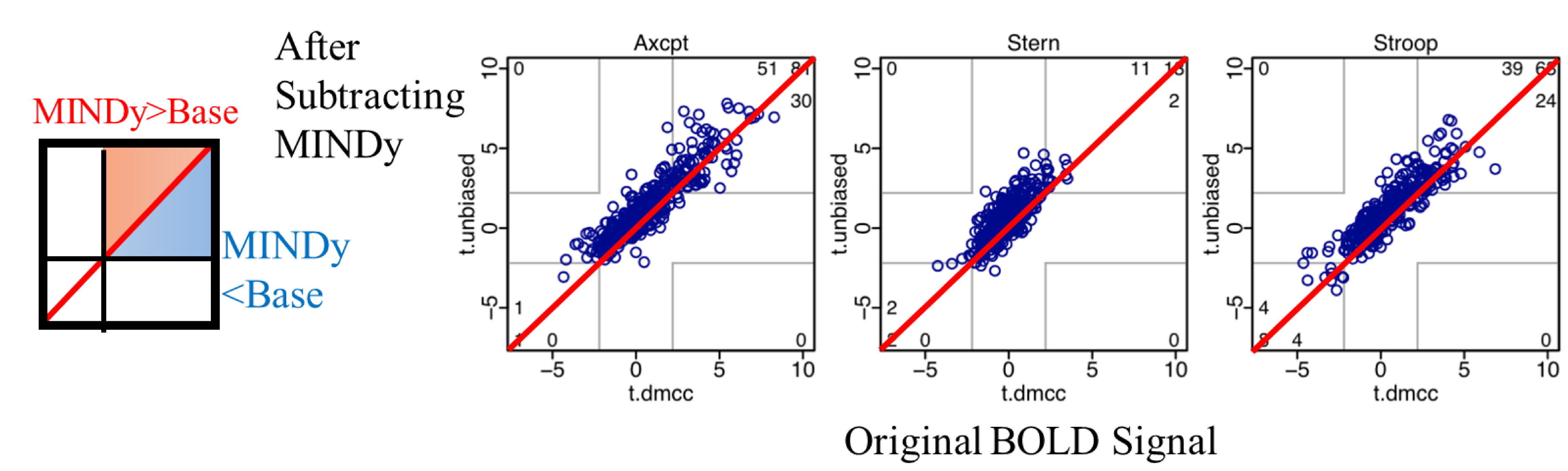
Isolating Task Effects with MINDy

- Activity during task consists of direct task-modulation and the flow of this activity through brain networks.
- By filtering-out the resting-state model predictions, we better isolate task-modulation.



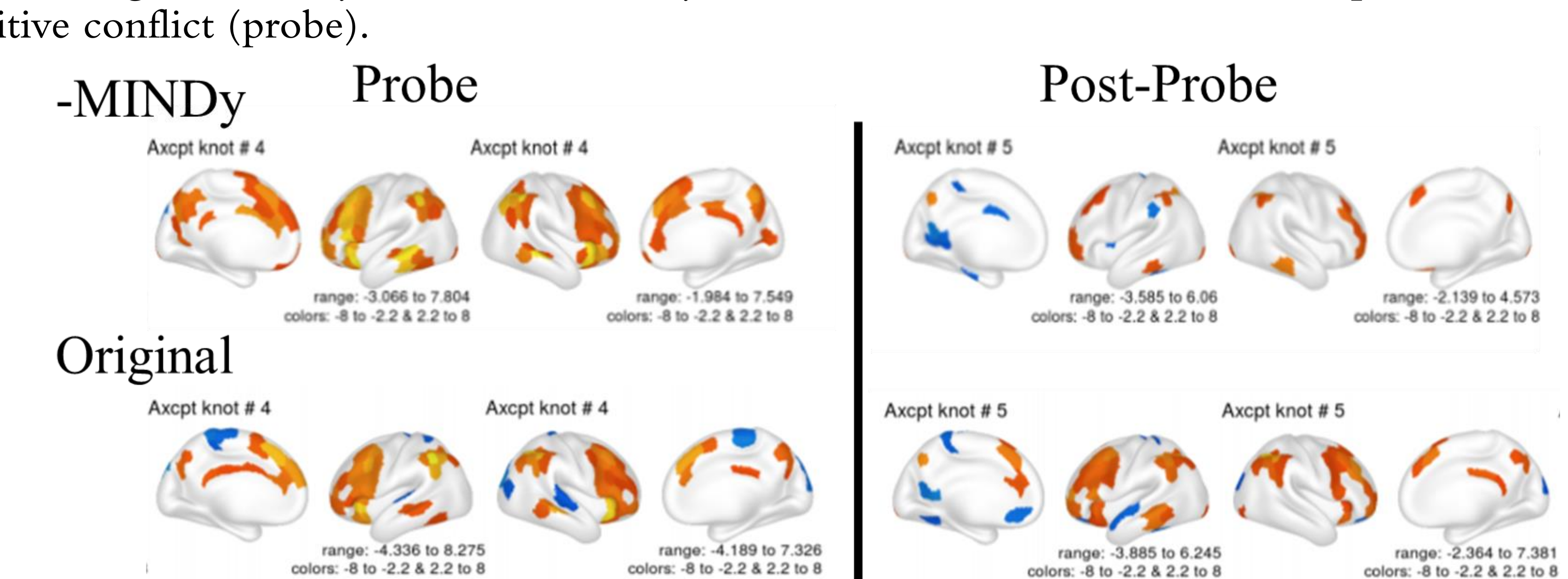
Isolating Cognitive Conflict Signatures

- High vs. low conflict conditions in three tasks:
1. AX-CPT, 2. Sternberg, 3. Stroop
- Same AFNI GLM applied to either the original BOLD time-series or after subtracting MINDy (resting-state) predictions.
- Compared group-level t-Tests across parcels



Removing Intrinsic Dynamics Improves Temporal Precision

- Compared GLM estimates for the effect of cognitive conflict during and after the probe period.
- After filtering intrinsic dynamics (via MINDy), task effects are centered about the period of cognitive conflict (probe).



Applications: We have validated a powerful new tool for directly fitting high-dimensional dynamic networks to individual subject's data and envision the following applications:

1. An improved **measure of effective connectivity**
2. Nonlinear **analysis of human brain dynamics**
3. A more general method to **isolate task-related brain signals**: unlike Dynamic Causal Modeling[6], we generate large models using only resting state, so we need not constrain task dynamics. Subtracting model predictions leaves a full time-series of task-induced changes.

References: **1.** Van Essen et al. (2013), *N.Image.* **2.** Sanz Leon et al. (2013), *Front. Neuroinform.* **3.** Wilson & Cowan (1972), *Biophys. J.* **4.** Siegel et al. (2013), *HBM.* **5.** Salimi-Khorshidi (2013) *N.Image.* **6.** Friston (2003), *N.Image.*

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