Directed Structural Connectivity Inferred from Network Diffusion in Humans and Non-Human Primates

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OVERVIEW

Problem: Diffusion MRI (dMRI) tractography is used to estimate structural connectivity (SC) lacks directional information about white matter pathways.

Approach: Using the **H**igher **O**rder **Ne**twork **D**iffusion (HONeD) Model [1,2], we learn a diagonal matrix (**A**) that makes SC (**C**) directional. SC directionality is learned from fitting HONeD to the *symmetric* covariance in fMRI.

Impact: This framework offers a promising method to infer the directions of white matter pathways. Applications span cognitive neuroscience, developmental neuroscience, and neurodegenerative diseases.

METHODS

Human Dataset:
770 Healthy young adult subjects from the Human Connectome Project S1200 release. [3] with resting State (1-hour).
Parcellation: Schaefer 100 cortical parcels + 14 subcortical regions

Macaque Dataset:
9 Non-human primates' fMRI with macaque consensus SC and tracer data from CoCoMac. [4]

Processing: Subject's SC and fMRI were processed with micapipe. [5]

Math:

$$\tilde{C} = ACA^{-1}$$
$$\mathcal{L} = I - D_{\text{out}}^{-1}\tilde{C}$$
$$\langle \mathbf{x}(t)\mathbf{x}(t)^{\top} \rangle_t = e^{(-\beta\mathcal{L}+\xi\mathcal{L}^2)^{\top}} e^{(-\beta\mathcal{L}+\xi\mathcal{L}^2)}$$

Analyses:
1. We validated the HONeD-Asym model in simulation.
2. We determined model relationship to tracer directionality using fMRI from 9 non-human primates in the RM atlas.
3. We investigated regional degree asymmetry across 770 Human Connectome Project subjects.
4. We evaluated model replicability in 34 HCP test-retest subjects

REFERENCES

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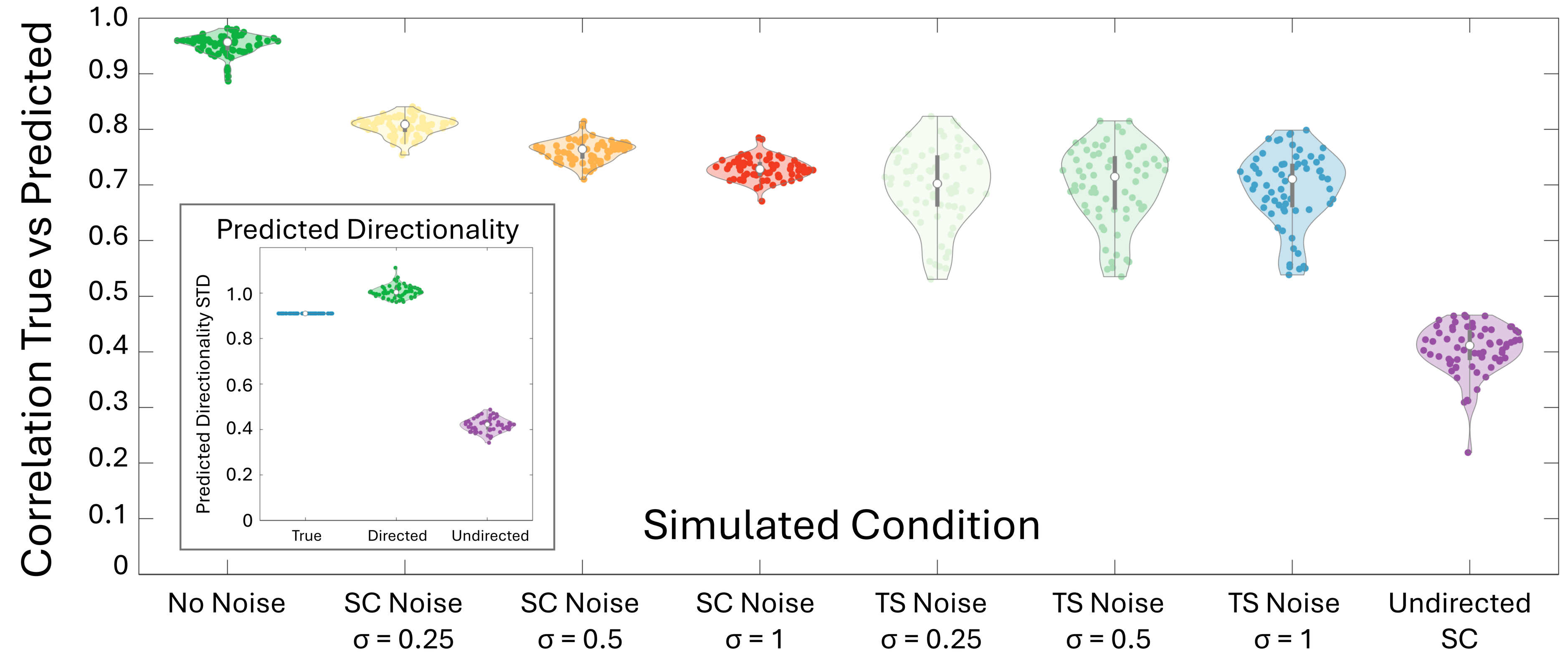
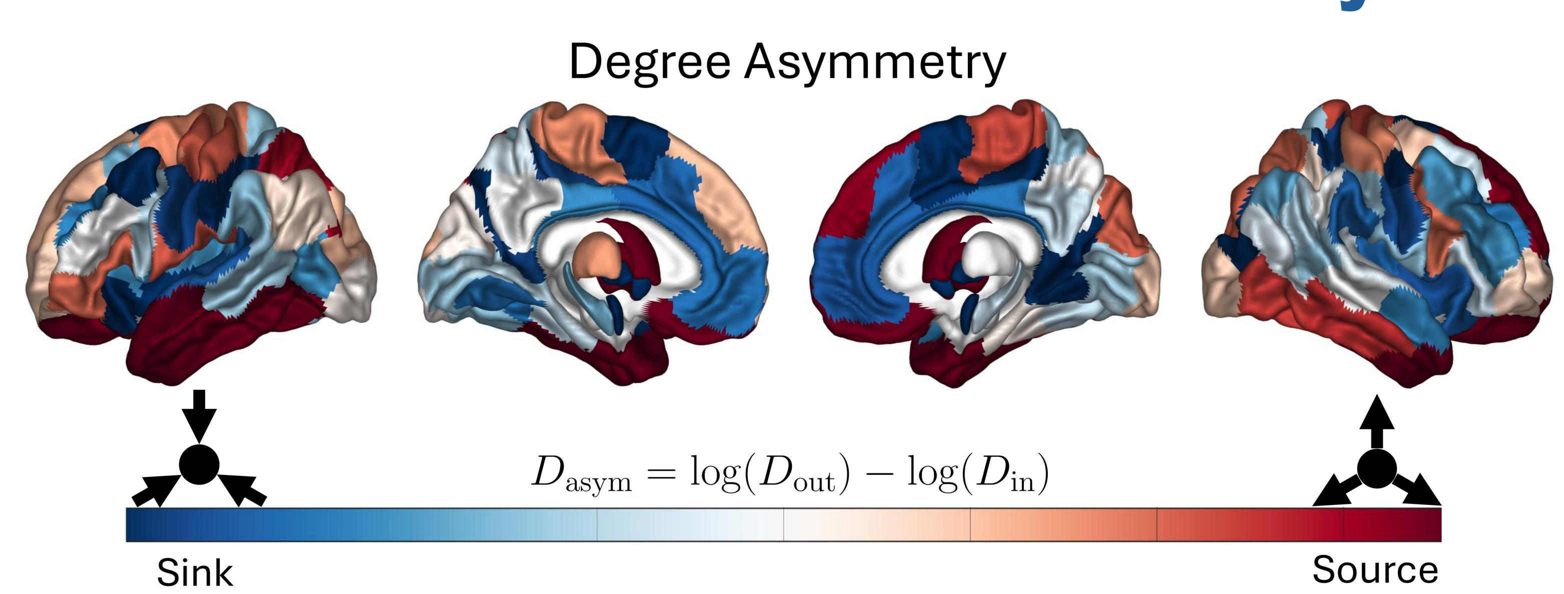
RESULTS

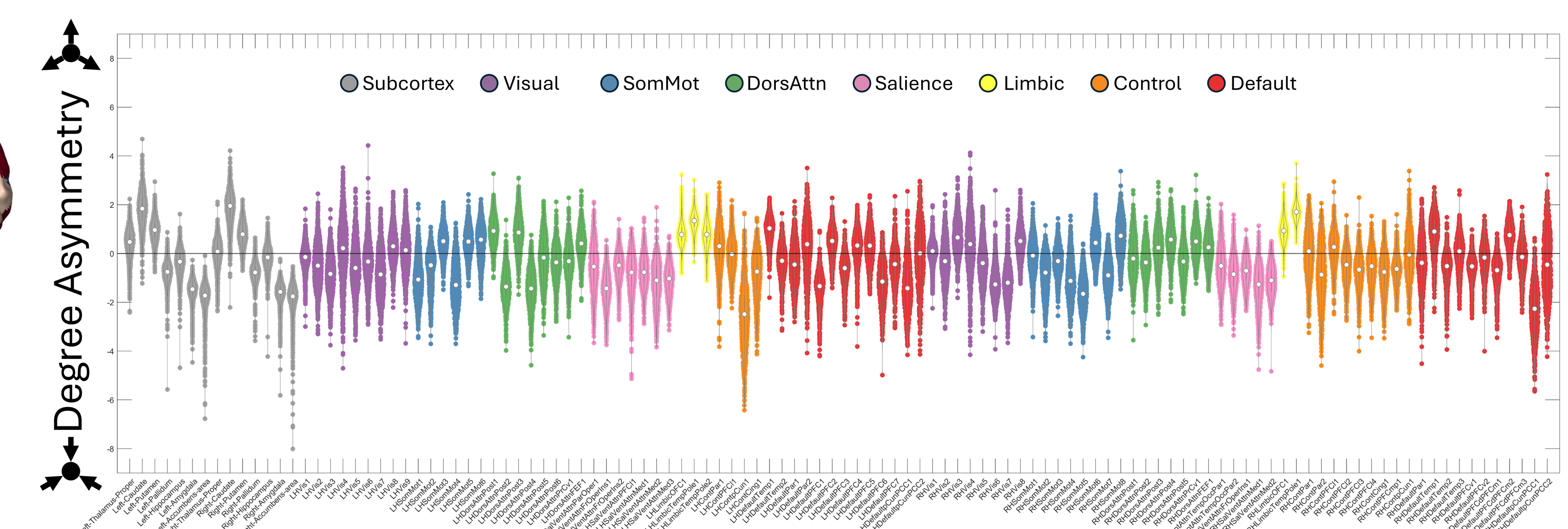
Simulation



- We simulated HONeD signals with a "ground-truth" directed SC, then fit our model to the simulated time series, varying SC noise and signal noise.
- Our model prediction significantly correlated with our ground-truth directionality (mean r=0.95), and it was moderately robust to noise.
- When the ground-truth was undirected, our model did not greatly hallucinate directionality (see inset).

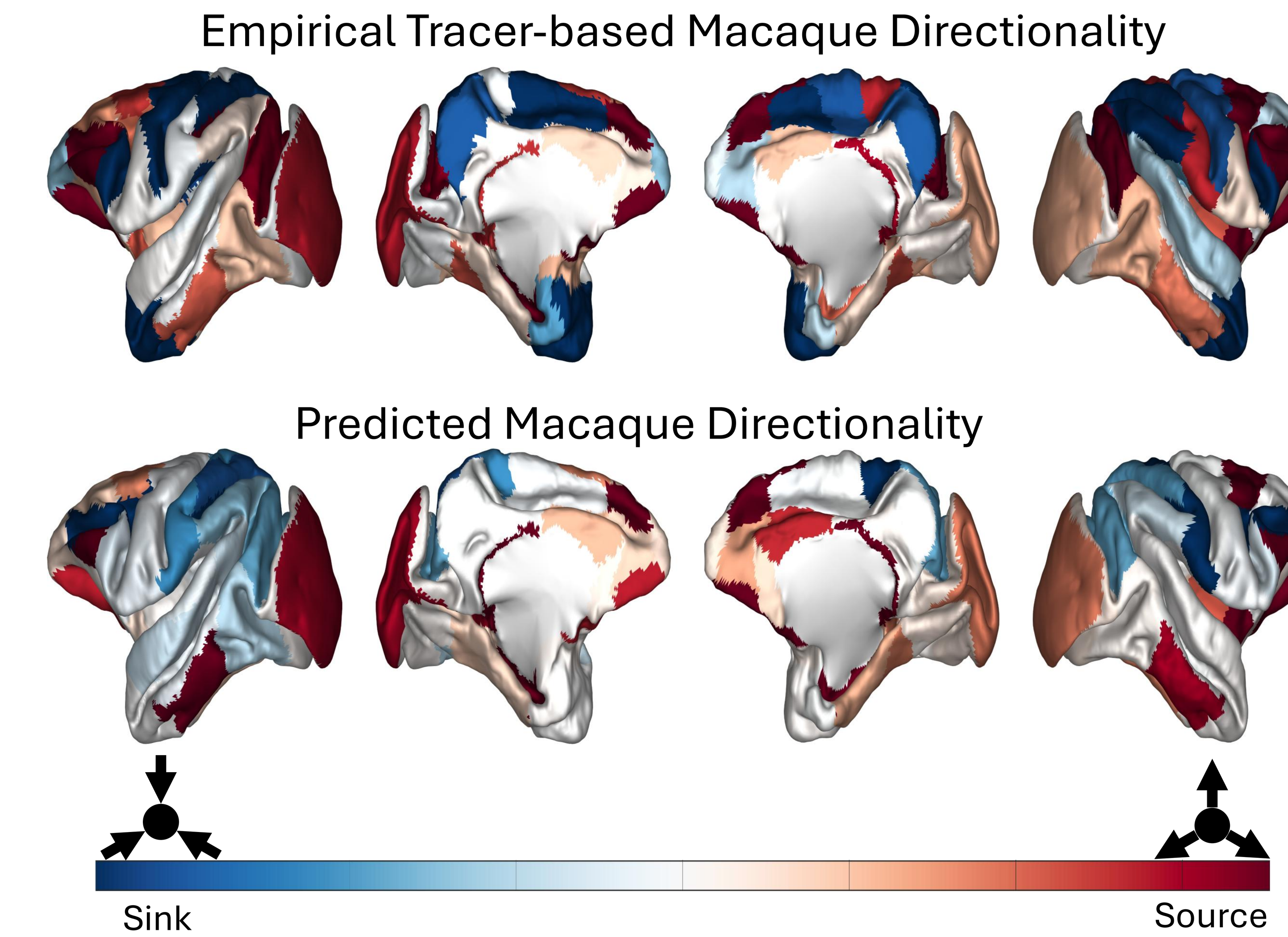
Predicted Human Directional Connectivity





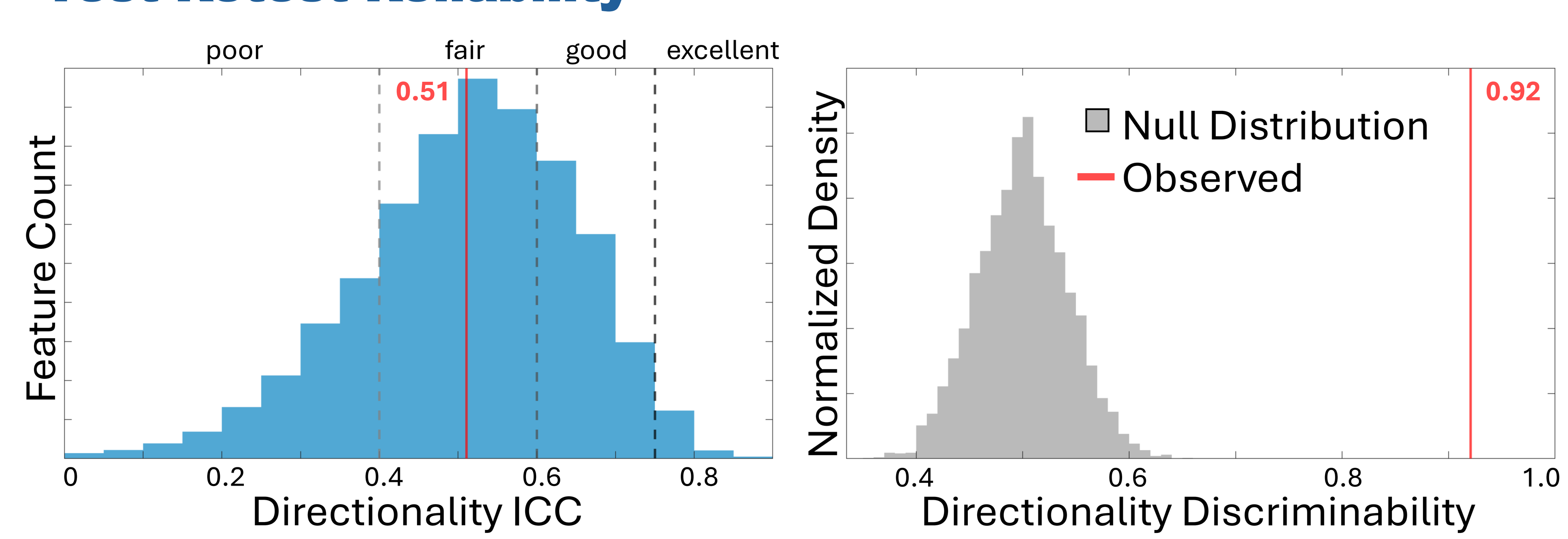
- Limbic and reward regions are the strongest sources
- Medial prefrontal, insula, and sensory-motor areas are sinks

Comparison to Tracer-based Directionality



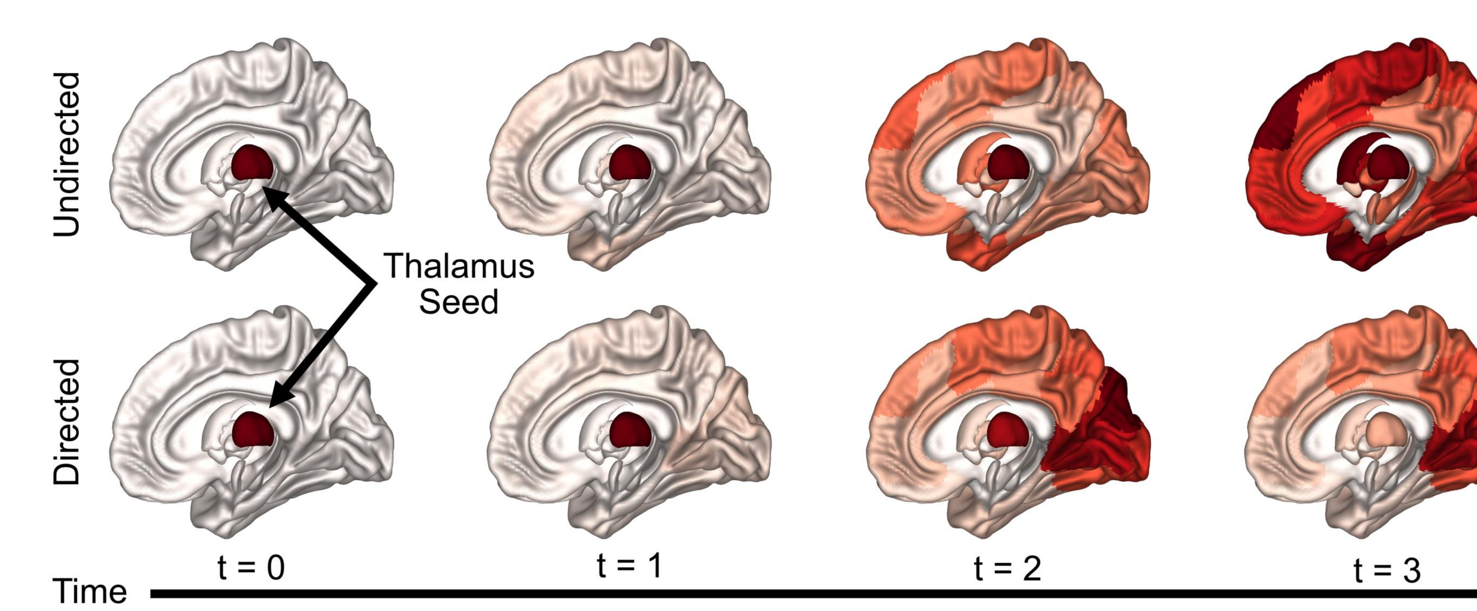
- We estimated the skew degree of the prediction and empirical directionality from tracer data, finding a significant correlation with skew degree (Spearman Rho=0.42, p_spin<0.01)

Test-Retest Reliability



- Directionality parameters showed fair to good Intraclass Correlation Coefficients (ICCs), suggesting that directional estimates are stable.
- Directionality was highly discriminative of individual subjects, indicating that they capture subject-specific features.

Directionality Changes Signal Spread



- We demonstrate how signal spreads with network diffusion when seeding the right thalamus in an undirected (top) and directed (bottom) network.
- Without directionality, thalamus signal goes everywhere, but with directionality, thalamus signal moves toward visual areas.