PAPER OF THE MONTH 07/2025

TRR 295 ReTune

Using an ordinary differential equation model to separate rest and task signals in fMRI.

Kashyap A, Geenjaar E, Bey P, Dhindsa K, Glomb K, Plis S, Keilholz S, Ritter P.

Nat Commun. 2025; 16(1): 7128. doi: 10.1038/s41467-025-62491-6. PMID: 40753158.

Task-based functional magnetic resonance imaging (fMRI) has generated over 100,000 studies, yet characterizing task-induced activity against the large, non-stationary baseline cortical activity during rest remains fundamentally challenging. To untangle rest and task relationship, we used data driven methods to fit Ordinary Differential Equations to model how rest signal components persist during task activations. Our framework directly fits an ODE to measured fMRI data from the Human Connectome Project, by modeling each brain region's dynamics as the sum of network edge interactions minus hemodynamic decay rates. By training separate network ODEs on Rest, Gambling, Working Memory, Emotion, and Relational task datasets with identical hyperparameters, we tested whether stimulus-independent processes could be represented by linear combinations of Rest and Task ODE models, evaluating signal separation efficacy through five behavioral measures across fourteen subtasks.

Our key finding demonstrates that task-specific network ODEs are mathematical subsets of rest-specific ODEs across all tested cognitive domains, establishing the Active Cortex Model principle. This discovery reveals that the resting brain maintains a comprehensive repertoire of all possible cortical processes, with specific tasks merely elevating particular subsets rather than creating novel activity patterns. The optimal signal separation strategy—approximating background stimulus-independent activity as the difference between Rest and Task ODE models—yielded substantial behavioral prediction improvements. Specifically, we achieved a 9% increase in explanatory power (R^2) for reaction time predictions across 14 sub-tasks on a trial-by-trial basis, with enhanced predictions extending to missing trial rates and accuracy measures at the individual level. The framework also improved task trajectory classification and dynamic functional connectivity analysis, demonstrating that each task type exhibited distinct yet predictable network activity patterns that remained mathematically nested within the comprehensive rest network model.

This work provides the first mechanistic proof that cortical rest activity encompasses all task-related processes, fundamentally reshaping our understanding of brain organization. The unified ODE framework successfully links large-scale brain activity, structural connectivity, and behavioral variables within a single causal model—representing a critical step toward a complete „fMRI equation." Practically, this enables enhanced signal-to-noise ratios in neuroimaging studies by mathematically isolating task-specific signals from ongoing background activity. The approach offers immediate applications for both prospective study design and retrospective reanalysis of existing datasets, potentially improving statistical power across the vast repository of task-based fMRI studies. By revealing that task processes are subsets rather than additions to rest activity, this work resolves longstanding questions about rest-task relationships while providing quantitative tools for separating stimulus-driven from stimulus-independent neural processes.

Amrit Kashyap, PhD

Amrit Kashyap is a computational neuroscientist specializing in brain network modeling and multimodal physiological signal analysis in clinical contexts, particularly in Eilepsy, Stroke, and Parkinson's. Currently, he is completing his Postdoc at Charité Berlin in Ritter lab.

Prof. Petra Ritter

Petra Ritter heads the Brain Simulation Section at Charité Berlin and Berlin Ins¬titute of Health. Her research focus is on integrating multimodal health data in computational avatars of patients to discover complex mechanisms of healthy function and dysfunction.

RETUNE
CRC TRR 295 Berlin-Würzburg