

Beyond the DSM: Engineering Mechanistic Models of Psychiatric Disease

October 28

Tuesday, 12:30 pm

Billings Building—Rosedale Room

SPEAKER:



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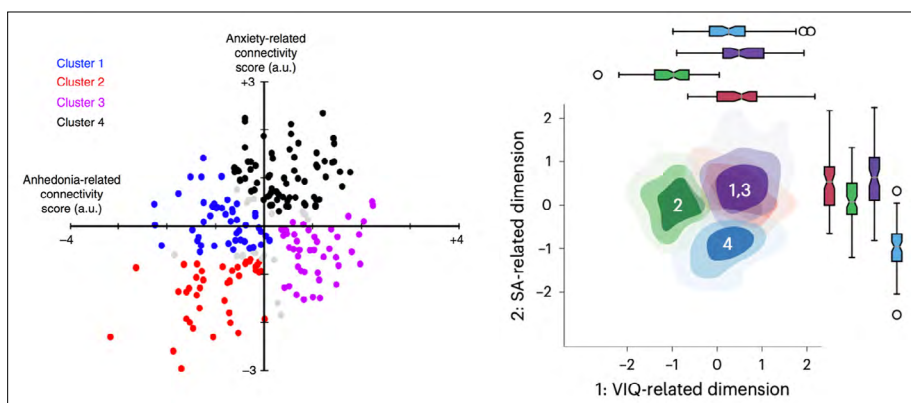
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Abstract

Psychiatry is among medicine's last pre-mechanistic frontiers. While oncologists select treatments based on tumor genetics, and cardiologists using physiology, psychiatrists still rely on symptom checklists and trial-and-error. The result is predictable: many patients fail first-line treatments, and broad diagnostic categories like "autism" and "depression" often create as much stigma as they do solutions. A central barrier to progress has been heterogeneity: patients with the same diagnosis can differ profoundly in biology, symptoms, and treatment response.

Our work has shown that reproducible biological subtypes of depression (e.g., Drysdale et al. Nat Med 23, 264–264, 2017) and autism (1) are robust and can predict clinical outcomes. To build on this, we are developing new AI frameworks that move beyond complex, opaque multistep pipelines. These models learn representations where clusters and dimensions can coexist (2) and employ adaptive architectures that route data differently for each patient (3). By flexibly handling heterogeneity, these methods make it possible to exploit large-scale clinical datasets while preserving interpretability.

Together, these advances illustrate how computational and AI based approaches, coupled with new benchmarks and data representations, are transforming psychiatry into a modern quantitative, mechanistic science capable of revealing biology, predicting treatment response, and ultimately enabling more personalized, stigma-reducing, and effective care.



Publications

1. Buch, A. M. et al. Molecular and network-level mechanisms explaining individual differences in autism spectrum disorder. Nat. Neurosci. 1–14 (2023).
2. Buch, A. M., Liston, C. & Grosenick, L. Simple and Scalable Algorithms for Cluster-Aware Precision Medicine. Proc Mach Learn Res (AISTATS) 238, 136–144 (2024).
3. M. Ajirak, O. Bein, E. R. Bowen, D. Kanellopoulos, A. Falk, F. M. Gunning, N. Solomonov, L. Grosenick, Learning to route: Per-sample adaptive routing for multimodal multitask prediction. Accepted at Advances in Neural Information Processing Systems (NeurIPS) 38 (2025). preprint: <https://arxiv.org/abs/2509.12227>.

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