Unifying observables through latent dynamics: shared trajectories of brain, body, and behavior

Ryan V. Raut[1,2,*], Zachary P. Rosenthal[3], Xiaodan Wang[4], Adam Q. Bauer[4], Steven L. Brunton[2], Bingni W. Brunton[2], and J. Nathan Kutz[2]

[1]Allen Institute, Seattle, WA, USA
[2]University of Washington, Seattle, WA, USA
[3]University of Pennsylvania, Philadelphia, PA, USA
[4]Washington University in St. Louis, St. Louis, MO, USA
[*]Correspondence to: ryan.raut@alleninstitute.org

A fundamental challenge in neuroscience is the general lack of governing laws relating macroscopic variables. With recent strides in the ability to obtain high-dimensional, multimodal recordings from awake animals, there is growing need for physiologically principled, low-dimensional descriptions of the effective dynamics. To this end, we have hypothesized the existence of an intrinsic, arousal-related dynamical process whose regulation of organism-wide physiology underpins fluctuations observed across diverse neural, physiological and behavioral measurements [1]. We support this hypothesis by introducing a computational framework that ultimately allows us to construct high-fidelity nonlinear mappings between such measurements (e.g., pupillometry and neural calcium imaging) from a latent, low-rank representation of their dynamics.

Specifically, to test our hypothesis, we introduce a data-driven approach to parsimoniously link observables that evolve according to a common but unknown dynamical mechanism. Our approach exploits Takens' embedding theorem from dynamical systems theory, which permits the (topology-preserving) reconstruction of a full-state attractor manifold from a single observable and its time history. Takens' theorem enables a strong prediction – and thus, a challenging test – of our framework: in theory, a single arousal-related observable (e.g., pupil size) should suffice to reconstruct high-dimensional observables, to the extent that a dynamical mechanism is shared. We test this prediction by performing simultaneous pupillometry and widefield calcium imaging in awake mice. The latter reports the large-scale spatial structure of cortical activity, which we hypothesize to be tightly regulated in accordance with arousal dynamics [1]. We train neural networks to approximate the hypothesized mapping from delay-embedded pupil time series (i.e., a scalar measurement) to (high-dimensional) widefield measurements, where delay embedding is achieved via dimensionality reduction of the associated Hankel matrix [2].

Following this procedure, we are able to reconstruct a surprising extent of cortex-wide spatiotemporal dynamics in awake mice from simultaneously measured pupil diameter (i.e., $74 \pm 8\%$ of variance < 0.2 Hz in held-out data, vs. $13 \pm 10\%$ without delay embedding (mean $\pm$ std, n=7 mice)). We achieve similar success using a scalar index of behavioral arousal (whisker movement), and in predicting widefield measurements of brain metabolism or hemodynamics, suggesting the ability of our procedure to elucidate low-dimensional generative factors that underlie physiologically diverse, high-dimensional measurements. Taken together, our framework and findings elucidate an arousal-related dynamical mechanism that is both richer and substantially further-reaching than presently recognized. Our data-driven approach may be easily generalized to other settings in which a unified dynamical mechanism is hypothesized to underlie high-dimensional and potentially nonlinearly-related observables.

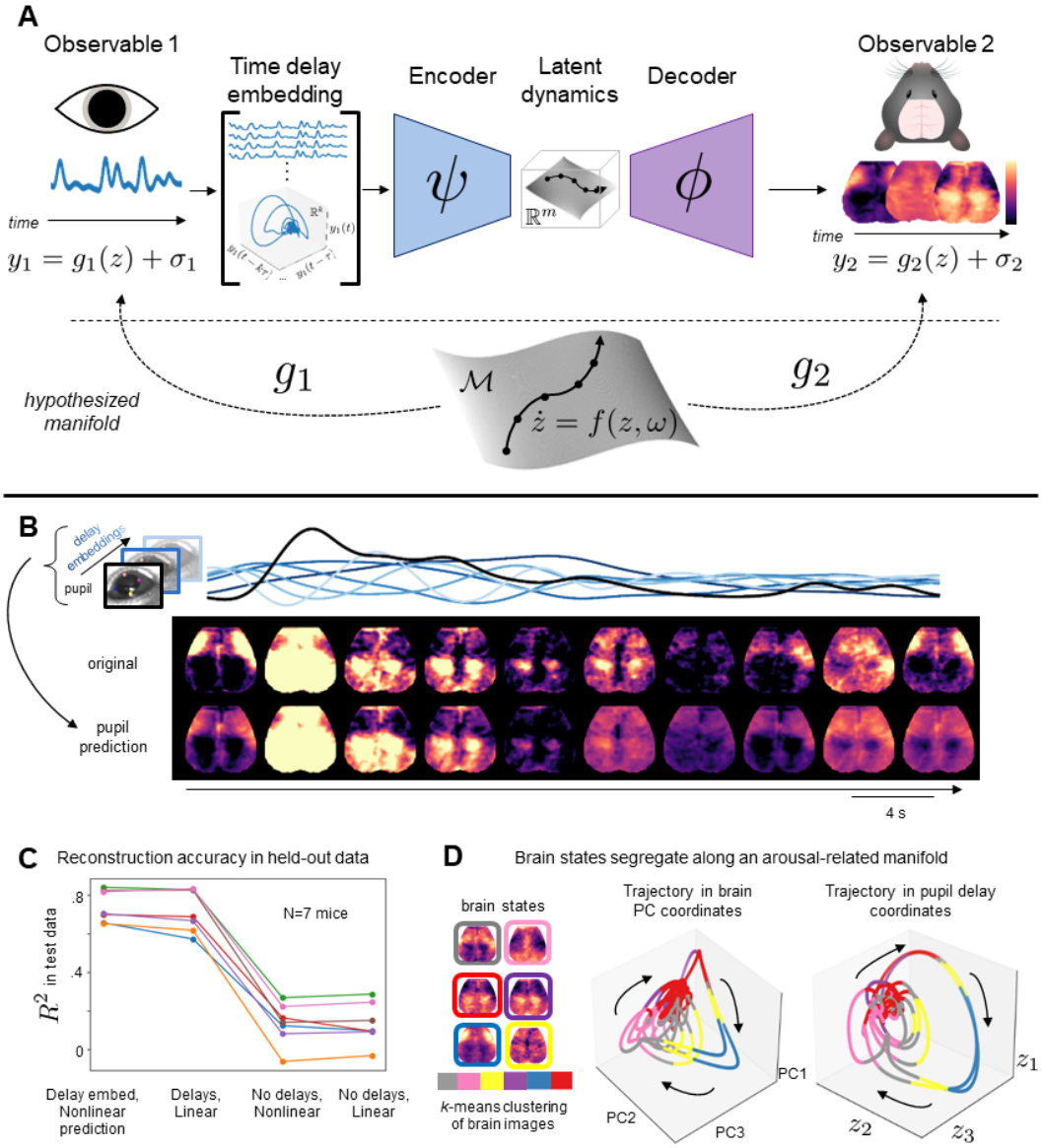

Fig. 1 (A) We consider fluctuations in diverse observables as partially reflecting a common, latent "arousal" state z and its stochastic evolution $f(z, \omega)$ occurring on a low-dimensional manifold $\mathcal{M}$. Formally, we represent these relations via the observation functions $g_n(z)$, each with observation-specific noise σ_n. We test the specific hypothesis that pupil size and large-scale brain activity are both tightly regulated by a common arousal-related dynamical process (cf. [1]). If true, Takens' embedding theorem implies the possibility of relating these observables via a composition of functions that map between these observables and a reconstructed latent space (i.e., ψ and ϕ). **(B)** Example epoch contrasting original and pupil-reconstructed widefield images (held-out data from one mouse). **(C)** Variance explained in held-out widefield data for each of N=7 mice. The approach described in (A) ("Delay embed, Nonlinear prediction") consistently predicts $60-85\%$ of the observed variance < 0.2 Hz. Control analyses (see "Analysis Methods") demonstrate that delay embedding is crucial to our model's success, while estimation of ψ with a nonlinear map (via a neural network) only marginally improves performance over a multivariate linear regression model that incorporates delay embedding. **(D)** Example state trajectories visualized in coordinates defined by the first three widefield (brain) PCs (left) or the three leading PCs of the delay-embedded pupil time series. Trajectories are color-coded by cluster identity as determined by k-means clustering (k=6) applied to the widefield image frames. (i.e., clusters defined without reference to temporal information or pupil size).

References

1. Raut, R. V. *et al.* Global waves synchronize the brain's functional systems with fluctuating arousal. *Science Advances* **7,** eabf2709. ISSN: 2375-2548. `https://www.science.org/doi/10.1126/sciadv.abf2709` (2022) (July 23, 2021).

2. Brunton, S. L., Brunton, B. W., Proctor, J. L., Kaiser, E. & Kutz, J. N. Chaos as an intermittently forced linear system. *Nature Communications* **8,** 19. ISSN: 2041-1723. `http://www.nature.com/articles/s41467-017-00030-8` (2022) (Dec. 2017).