DBPS: Doob-Bridge Posterior Sampler with Balanced Endpoint-Population Control for Unpaired Neurodegenerative Pathology Transport

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Code

Balancing individual endpoint guidance with population guidance gives an exactly optimal stochastic controller and the best tau-PET transport in multi-cohort settings.

1 Problem: unpaired endpoint snapshots

- Cohorts give **cross-sectional snapshots** of healthy (CN) and impaired (MCI/AD) brains, not aligned trajectories.
- **Endpoint-conditioned** bridges (e.g. UniDB) anchor each subject to one target, but are sensitive to a noisy target y^*.
- **Population-level** Doob guidance uses the whole target distribution, but has no individual anchor.
- Neither extreme alone gives the best terminal-distribution fit.

2 Idea: mix desirabilities, not controllers

A convex mix of two optimal controllers is not, in general, optimal for any SOC problem. DBPS interpolates the **desirability functions** instead:

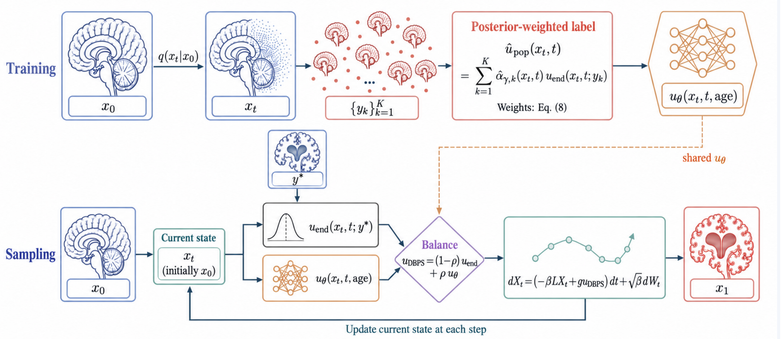
$$\Psi_\rho = \psi_{\gamma,y^*}^{1-\rho} H_\gamma^\rho \quad \Longrightarrow \quad u_\rho = \tfrac{\beta}{g}\nabla \log \Psi_\rho = (1-\rho)\, u_{\text{end}} + \rho\, u_{\text{pop}}.$$

Theorem 2.3. For every fixed $\rho \in [0,1]$, u_ρ is the **exact optimal feedback policy** of a linearly-solvable SOC problem with terminal cost $\Phi_\rho = -\eta \log \Psi_\rho(\cdot, T)$ and running cost

$$c_\rho = -\tfrac{1}{2}\rho(1-\rho)\left\|u_{\text{pop}} - u_{\text{end}}\right\|^2.$$

ρ	Recovered method	Guidance
0	UniDB	endpoint only
0, $\gamma \to \infty$	Doob h-transform	hard endpoint
1	Population Doob	population only
$(0,1)$	**New SOC family**	balanced

3 DBPS pipeline

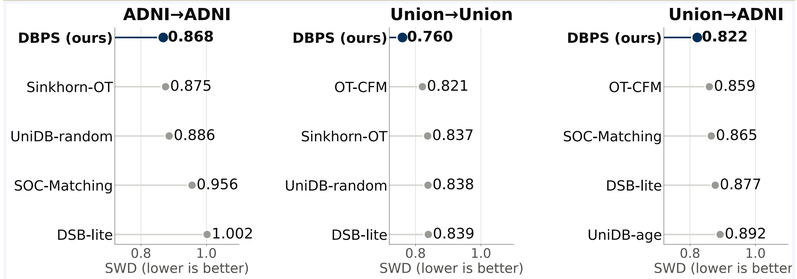


Train: distill the posterior-weighted label $\hat{u}_{\text{pop}}$ over K target candidates into u_θ. **Sample:** combine closed-form u_{end} with u_θ and integrate $dX_t = (-\beta L X_t + g\, u_{\text{DBPS}})\, dt + \sqrt{\beta}\, dW_t$, where L is a brain-connectome Laplacian.

4 Setup

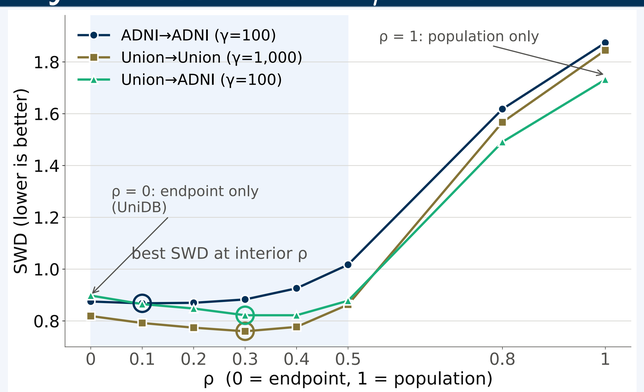
- **Data:** tau PET, 84 brain regions; ADNI and NACC.
- **Settings:** ADNI→ADNI (single cohort), Union→Union (multi-cohort), Union→ADNI (held-out ADNI, no retraining).
- **Baselines:** 10 methods from diffusion bridges, flow / OT / SOC matching, and non-learning references.
- **Metric:** sliced Wasserstein distance (SWD) over 250 / 80 / 200 sampling repeats; also FD and MMD.

5 Main results: best SWD in every setting



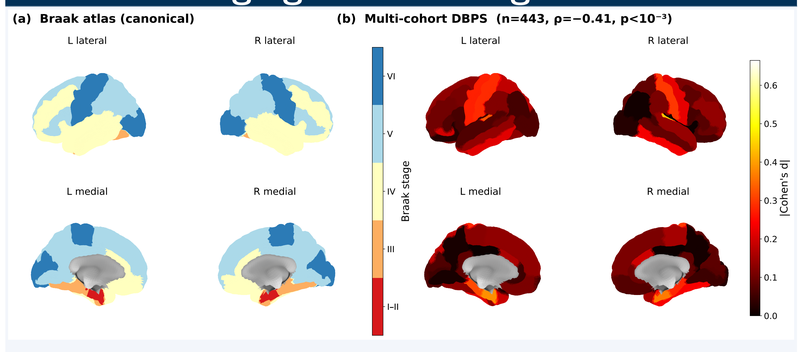
- **Union→Union:** SWD **0.760** vs. 0.821 (−7.4%); paired t-tests vs. every baseline $p < 0.01$.
- **Union→ADNI:** SWD **0.822** vs. 0.859 (−4.3%); all $p < 0.001$.
- **ADNI→ADNI:** best mean on all metrics (SWD 0.868 vs. 0.875), but not significant vs. the two closest baselines.

6 Why balance: interior ρ wins



- $\rho = 1$ (population only): SWD $\approx$ 1.7–1.9, about 2× worse.
- $\rho = 0$ (endpoint only): 0.8% / 7.2% / 8.5% higher SWD than DBPS.
- DBPS also uses **5–16% less control energy** than UniDB.

7 Braak staging without stage labels



- Age-sensitive control strength $|d_k|$ is negatively correlated with Braak stage: **Spearman** $\rho = -0.41$, $p < 10^{-3}$ over 72 regions.
- Strongest effects in early regions: entorhinal, parahippocampal, fusiform cortex.
- The model never sees Braak labels; it uses only tau, age, and a connectome prior.

8 The brain graph matters for biology

- ADNI-only model: rewiring or permuting the connectome leaves SWD almost unchanged (≈ 0.87),
- but **removes the Braak alignment** (all 10 randomized graphs non-significant).
- Model endpoint shifts match the empirical ADMCI-vs-CN regional ranks: Spearman $\rho = 0.95$ (ADNI), 0.99 (Union).

Takeaways

1. Geometric desirability interpolation turns controller blending into an **exact SOC problem**.
2. DBPS gives the **best SWD and FD** in all three settings, with significant gains in multi-cohort transport.
3. Learned controls **recover Braak-stage organization** without stage supervision.

Limitations. Paths between endpoints are model-imposed and not validated against individual longitudinal trajectories; regional tau is standardized within cohort but not harmonized across tracers.

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*Data used in preparation of this poster were obtained from the ADNI database (adni.loni.usc.edu). **Paper:** openreview.net/forum?id=GLIYSpGCJP **Code:** github.com/pathology-dynamics/NeurIPS2026_DBPS