Practical Course on Molecular Dynamics and Trajectory Analysis

Episode 7: Models and spectra with deeptime

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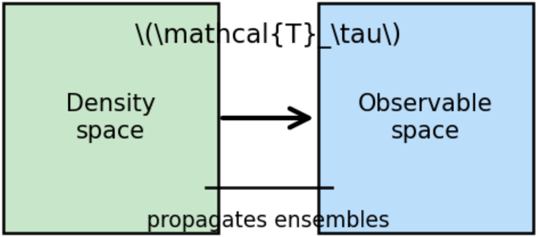
Definition

$$(\mathcal{T}_\tau f)(x) = \mathbb{E}[f(X_{t+\tau}) \mid X_t = x].$$

- Extends MSM to the continuous space of observables.
- PyEMMA and Deeptime share the dataset generated by `simulateAmber.py`.

Transfer-operator diagram



Visual summary of the operators linking observed coordinates to future distributions.

Koopman vs Perron-Frobenius

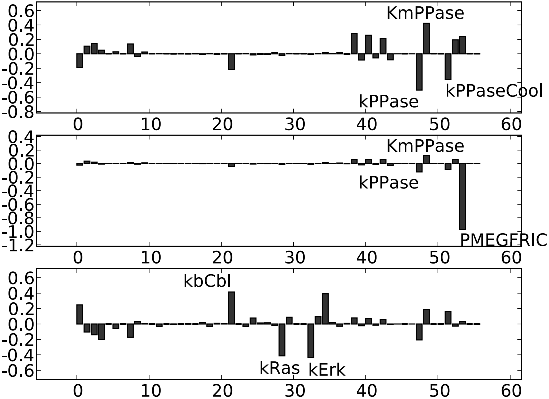
- Koopman acts on observables (functions).
- Perron-Frobenius acts on densities.
- They enable building the ‘TransferOperator‘ in Deeptime.

Spectral problem

$$\mathcal{T}_\tau \psi_i = \lambda_i \psi_i .$$

- The eigenvalues λ_i define implied times $t_i = -\tau / \ln \lambda_i$.
- $\lambda_1 = 1$ for equilibrium and values close to 1 signal slow processes.

Modos espectrales

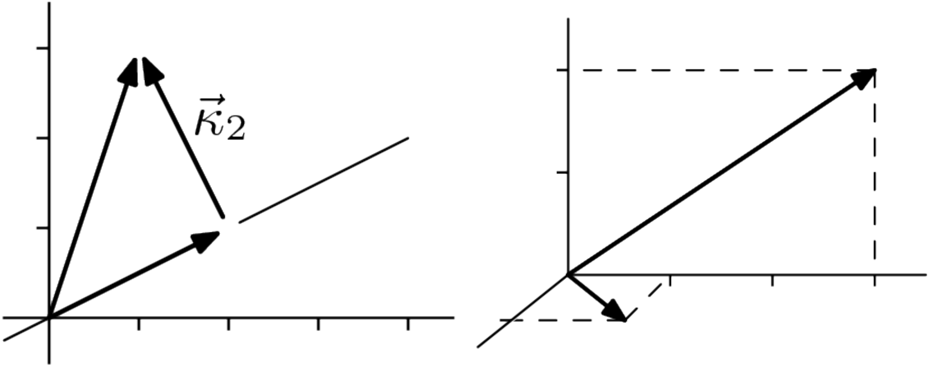


Basis expansion

$$f(x) = \sum_i c_i \phi_i(x).$$

- Deeptime allows linear/nonlinear bases: kernels and networks.

Bases y proyecciones



Source: reference pending. [2]

Error and regularization

- Poor bases introduce spectral bias.
- Regularize with L_2 and cross-validation.

tICA in Deeptime

$$C_\tau \mathbf{w} = \lambda C_0 \mathbf{w}.$$

- Maximizes long-term correlation.

VAMP score

$$\mathcal{R}_2 = \sum_i \sigma_i^2 .$$

- Evaluates spectral quality to select features.

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Koopman approximation

- Expand observables in linear/nonlinear bases.
- Obtain reduced, more interpretable representations.

Kernel and neural models

- Kernels capture nonlinearities; networks demand strict validation.
- Regularize with dropout or L_2 to prevent overfitting.

Validation and robustness

- Splitting into time blocks prevents information leakage.
- Compare spectral scores across ensembles.
- $T(n\tau) \approx T(\tau)^n$ tests temporal consistency.
- Vary τ and clustering to detect sensitivity.

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Basic workflow

- Features $\rightarrow$ tICA/VAMP $\rightarrow$ spectral model.
- Use `simulatePdb.py` to generate trajectories and 'OpenMMTools' to prepare 'REST'.

Visualization

- 2D projections with FES and comparison with MSM.

Episode summary

- Deeptime extends MSM with spectral operators and cross-validation.
- Combine features, VAMP, and scores to select robust models.

References I

[1] OpenMM Cookbook. *Eigenvectors espectrales en Replica Exchange Solute Tempering*. CC BY-SA 4.0. URL: https://openmm.github.io/openmm-cookbook/latest/notebooks/tutorials/Running_a_REST_simulation.html (visited on 01/12/2026).

[2] Autor desconocido. *Reference pending*. Fuente no localizada. n.d.

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