

# Practical Course on Molecular Dynamics and Trajectory Analysis

## Episode 7: Models and spectra with deeptime

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## 1 Episode 7: Models and spectra with Deeptime

- Transfer operators
- Spectrum and modes
- Bases and projections
- tICA and VAMP
- Advanced models
- Validation and scores
- Pipeline with Deeptime
- Summary

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

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

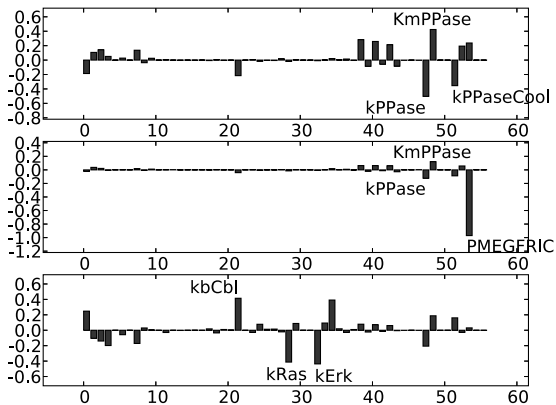
# Koopman vs Perron-Frobenius

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

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

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

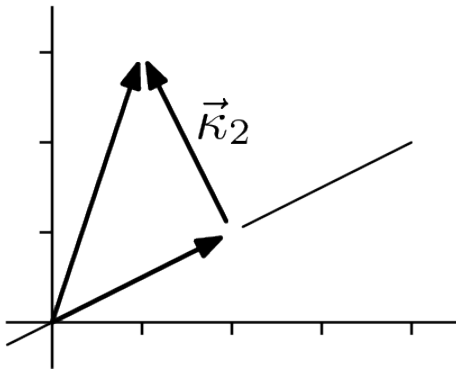
# Modos espectrales



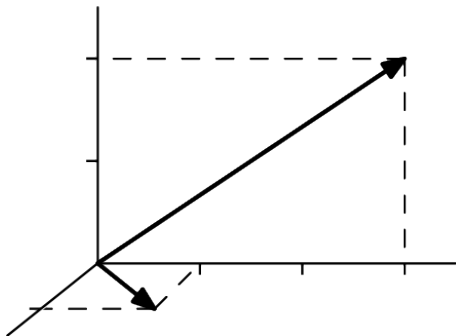
$$f(x) = \sum_i c_i \phi_i(x).$$

- 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.

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

- Maximizes long-term correlation.

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

- Evaluates spectral quality to select features.

# 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.

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

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

- 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](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.