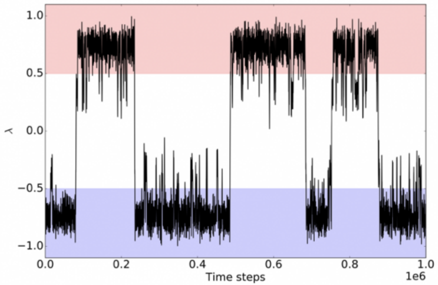
Learning “slow” manifolds from dynamical data

F. Noé[1]

Deep Learning Classes, FU Berlin 2018

Objective: find "collective coordinates" in which events are rare



Collective coordinate: Linear projection $u = \mathbf{x}_t^\top \mathbf{w}$ or nonlinear function $u = f(\mathbf{x}_t)$.

Nomenclature

- Time series $\{\mathbf{x}(1), \ldots, \mathbf{x}(T)\}$. Time-lagged data subsets:

$$\mathbf{X} = \begin{bmatrix} x_1(t=1) & \cdots & x_D(t=1) \\ \vdots & & \vdots \\ x_1(t=T-\tau) & \cdots & x_D(t=T-\tau) \end{bmatrix}$$

$$\mathbf{Y} = \begin{bmatrix} x_1(t=\tau) & \cdots & x_D(t=\tau) \\ \vdots & & \vdots \\ x_1(t=T) & \cdots & x_D(t=T) \end{bmatrix}$$

- Assume that the data is mean-free:

$$\sum_{t=1}^{T-\tau} \mathbf{x}(t) = \mathbf{0} \qquad \sum_{t=1}^{T-\tau} \mathbf{y}(t) = \mathbf{0}$$

Otherwise remove the mean in $\mathbf{X}$ and $\mathbf{Y}$ *separately*

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Whitening

- Compute covariance matrix and perform PCA:

$$\mathbf{C} = \mathbf{X}^\top \mathbf{X} \qquad \mathbf{CU} = \mathbf{U\Sigma}^2$$

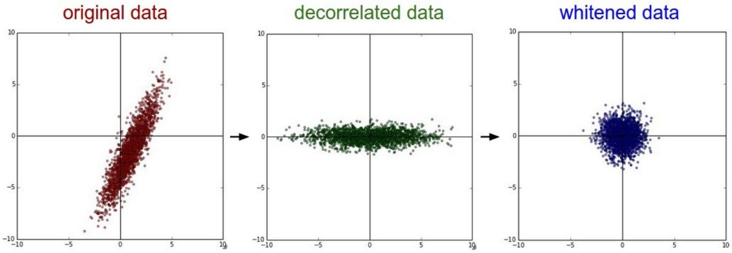
- Decorrelate data:

$$\mathbf{X}' = \mathbf{XU}$$

- Whiten data:

$$\tilde{\mathbf{X}} = \mathbf{XU\Sigma}^{-1} = \mathbf{XC}^{-\frac{1}{2}}$$

which uses: $\mathbf{C}^{-1} = \mathbf{U\Sigma}^{-1}\mathbf{\Sigma}^{-1}\mathbf{U}^\top = \mathbf{C}^{-\frac{1}{2}}\mathbf{C}^{-\frac{1}{2}}$



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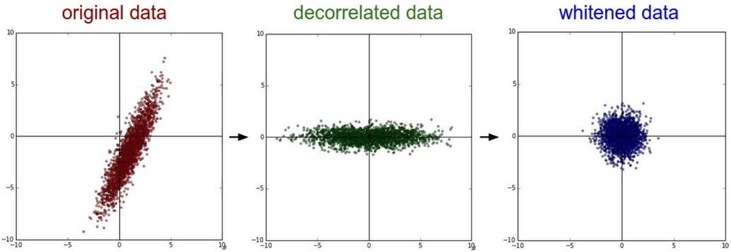

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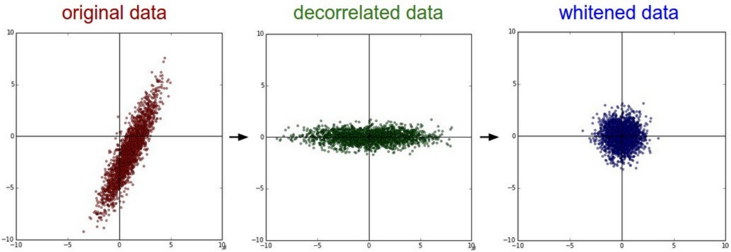

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Summary – Data Preparation

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$$\sum_{t=1}^{T-\tau} \mathbf{x}_t = 0 \qquad \sum_{t=1}^{T-\tau} \mathbf{y}_t = 0$$

- Covariance matrices:

$$\mathbf{C}_{xx} = \frac{1}{T-\tau} \sum_{t=1}^{T-\tau} \mathbf{x}_t \mathbf{x}_t^\top = \frac{1}{T-\tau} \mathbf{X}^\top \mathbf{X}$$

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“Best” Projection of Dynamical Data

- Seek **Encoding** (projection) and **Decoding**:

$$\mathbf{z}_t = \tilde{\mathbf{E}}\tilde{\mathbf{x}}_t$$
$$\tilde{\mathbf{y}}_t^* = \tilde{\mathbf{D}}\mathbf{z}_t = \tilde{\mathbf{K}}_d\tilde{\mathbf{x}}_t$$

with $\tilde{\mathbf{E}} = \mathbb{R}^{m\times n}$, $\tilde{\mathbf{D}} = \mathbb{R}^{n\times m}$ and the rank-d transition matrix:

$$\tilde{\mathbf{K}}_d = \tilde{\mathbf{D}}\tilde{\mathbf{E}}$$

- **Aim**: As for PCA, we can formulate two different optimization strategies: (i) minimizing a suitable error, and (ii) maximizing a suitable variance.
- Here: **minimize prediction error** by solving regression problem:

$$\min_{\tilde{\mathbf{K}}_d} \left\|\tilde{\mathbf{Y}} - \tilde{\mathbf{Y}}^*\right\|_F^2 = \min_{\tilde{\mathbf{K}}_d} \left\|\tilde{\mathbf{Y}} - \tilde{\mathbf{X}}\tilde{\mathbf{K}}_d^\top\right\|_F^2$$

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- Full-rank solution (using $\tilde{\mathbf{X}}^\top\tilde{\mathbf{X}} = (T-\tau)\mathbf{I}$):

$$\tilde{\mathbf{K}}^\top = \left(\tilde{\mathbf{X}}^\top\tilde{\mathbf{X}}\right)^{-1}\tilde{\mathbf{X}}^\top\tilde{\mathbf{Y}} = \frac{1}{T-\tau}\tilde{\mathbf{X}}^\top\tilde{\mathbf{Y}}$$

- Using definition of covariance matrices:

$$\tilde{\mathbf{K}}^\top = \mathbf{C}_{xx}^{-\frac{1}{2}}\mathbf{C}_{xy}\mathbf{C}_{yy}^{-\frac{1}{2}}$$

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$$\tilde{\mathbf{K}}_d^\top = \mathrm{SVD}\left(\mathbf{C}_{xx}^{-\frac{1}{2}}\mathbf{C}_{xy}\mathbf{C}_{yy}^{-\frac{1}{2}}\right) = \tilde{\mathbf{U}}_d\mathbf{\Sigma}_d\tilde{\mathbf{V}}_d^\top$$

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Special case: reversible dynamics: TICA

- Consider both "forward" time $\{\mathbf{x}(1), \ldots, \mathbf{x}(T)\}$ and "backward" time $\{\mathbf{x}(T), \ldots, \mathbf{x}(1)\}$. Thus:

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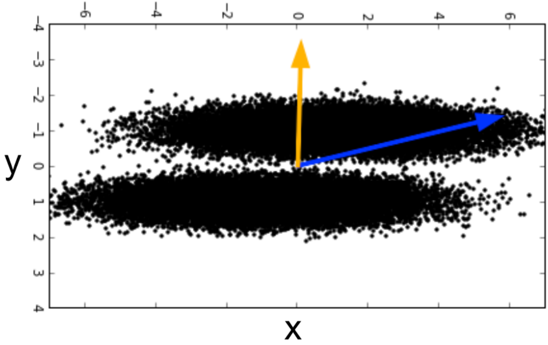
TICA/TCCA vs PCA



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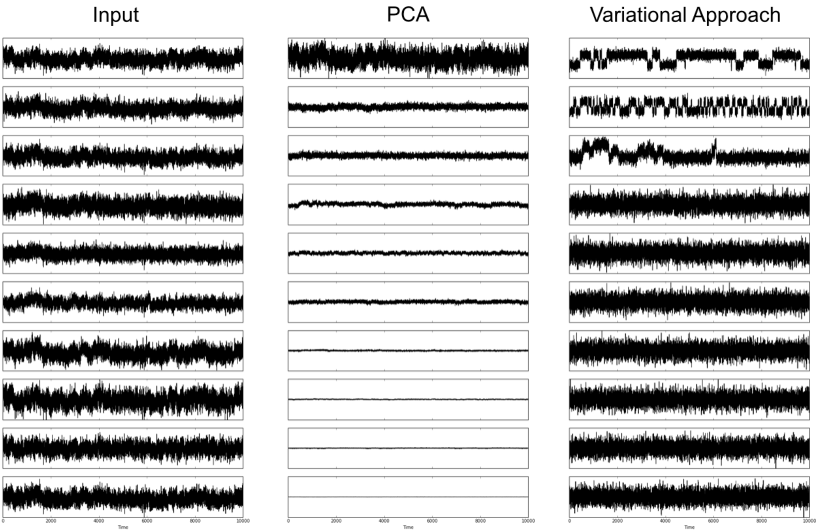
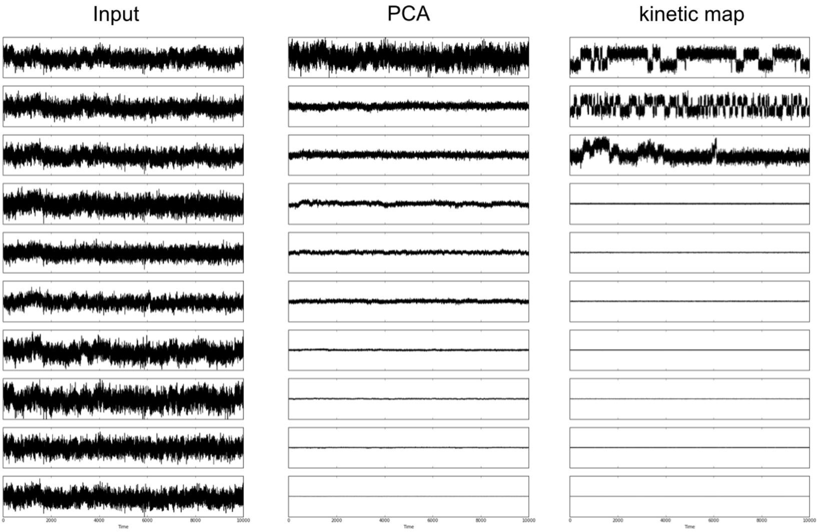
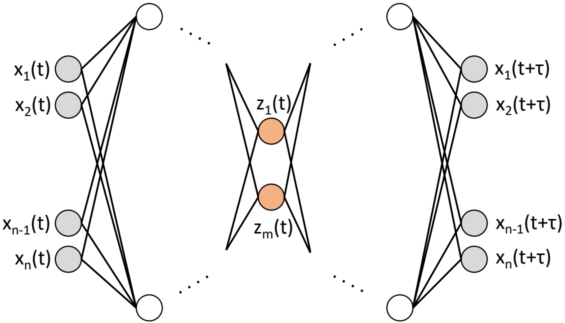


TICA/TCCA vs PCA



F. Noé, C. Clementi: Kinetic distance and kinetic maps from molecular dynamics simulation. J. Chem. Theory Comput. 11, 5002-5011 (2015)

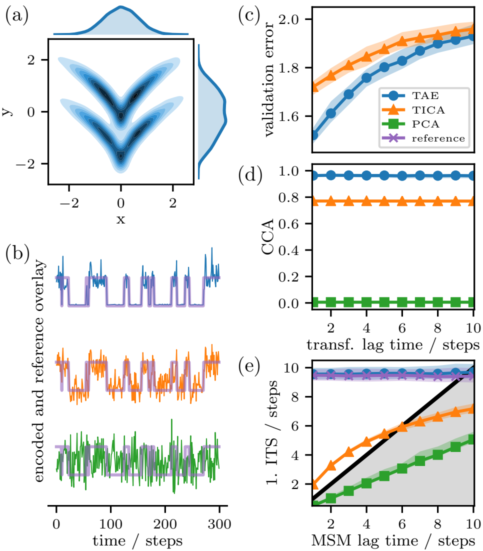
Time-Autoencoder Network



$$\min_{\theta_E,\theta_D} \|\mathbf{Y} - D(E(\mathbf{X};\theta_E);\theta_D)\|_F^2 = \min \sum_{t=1}^{T-\tau} \|\mathbf{x}_{t+\tau} - D(E(\mathbf{x}_t;\theta_E);\theta_D)\|^2$$

C. Wehmeyer and F. Noé: **Time-lagged autoencoders**: Deep learning of slow collective variables for molecular kinetics. J. Chem. Phys. 148, 241703 (2018)

Time-Autoencoder Network



TCCA maximizes correlation between vectors

- **Single collective coordinate**: TCCA maximizes

$$\tilde{\mathbf{u}}, \tilde{\mathbf{v}} = \arg\max_{\mathbf{u},\mathbf{v}} \frac{\mathbf{u}^\top \mathbf{C}_{xy} \mathbf{v}}{\sqrt{\mathbf{u}^\top \mathbf{C}_{xx} \mathbf{u}} \sqrt{\mathbf{v}^\top \mathbf{C}_{yy} \mathbf{v}}} = \arg\max_{\mathbf{u},\mathbf{v}} \frac{c_{\mathbf{uv}}(\tau)}{\sqrt{c_{\mathbf{uu}} c_{\mathbf{vv}}}}$$

- **Multiple collective coordinate** $\mathbf{u}_1, \ldots, \mathbf{u}_n$, $\mathbf{v}_1, \ldots, \mathbf{v}_n$:

$$\tilde{\mathbf{u}}_1, \ldots, \tilde{\mathbf{u}}_n, \tilde{\mathbf{v}}_1, \ldots, \tilde{\mathbf{v}}_n = \arg\max \sum_{i=1}^{n} \frac{c_{\mathbf{u}_1\mathbf{v}_1}(\tau)}{\sqrt{c_{\mathbf{u}_1\mathbf{u}_1} c_{\mathbf{v}_1\mathbf{v}_1}}}$$

$$s.t. \sum_t \mathbf{u}_i^\top \mathbf{x}_t \mathbf{v}_j^\top \mathbf{x}_{t+\tau} = \delta_{ij}$$

$$= \arg\max \left\| \mathbf{C}_{uu}^{-\frac{1}{2}} \mathbf{C}_{uv} \mathbf{C}_{vv}^{-\frac{1}{2}} \right\|_{tr}$$

$$= \arg\max \left\| \mathbf{C}_{uu}^{-\frac{1}{2}} \mathbf{C}_{uv} \mathbf{C}_{vv}^{-\frac{1}{2}} \right\|_{F}^{2}$$

- Trace norm and Frobenius norm:

$$\left\| \mathbf{C}_{uu}^{-\frac{1}{2}} \mathbf{C}_{uv} \mathbf{C}_{vv}^{-\frac{1}{2}} \right\|_{tr} = \sum_{i=1}^{n} \sigma_i \qquad \left\| \mathbf{C}_{uu}^{-\frac{1}{2}} \mathbf{C}_{uv} \mathbf{C}_{vv}^{-\frac{1}{2}} \right\|_{F}^{2} = \sum_{i=1}^{n} \sigma_i^2$$

with σ_i singular values of $\mathbf{C}_{uu}^{-\frac{1}{2}} \mathbf{C}_{uv} \mathbf{C}_{vv}^{-\frac{1}{2}}$.

TCCA maximizes correlation between vectors

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TICA maximizes autocovariances

- **Single collective coordinate**: TICA maximizes

$$\tilde{\mathbf{u}} = \arg\max_{\mathbf{u}} \frac{\mathbf{u}^\top \mathbf{C}_{xy}\mathbf{u}}{\sqrt{\mathbf{u}^\top \mathbf{C}_{xx}\mathbf{u}}} = \frac{c_{uu}(\tau)}{c_{uu}}$$

- Multiple directions $\tilde{\mathbf{u}}_1, \ldots, \tilde{\mathbf{u}}_n$

$$\tilde{\mathbf{u}}_1, \ldots, \tilde{\mathbf{u}}_n = \arg\max \sum_{i=1}^{n} \frac{c_{\mathbf{u}_1\mathbf{u}_1}(\tau)}{\sqrt{c_{\mathbf{u}_1\mathbf{u}_1} c_{\mathbf{v}_1\mathbf{v}_1}}}$$

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- TICA components are *white*:

$$\mathbf{Z}^\top \mathbf{Z} = \left(\mathbf{X}\mathbf{C}_{xx}^{-\frac{1}{2}} \tilde{\mathbf{U}}_d \right)^\top \mathbf{X}\mathbf{C}_{xx}^{-\frac{1}{2}} \tilde{\mathbf{U}}_d = \tilde{\mathbf{U}}_d^\top \tilde{\mathbf{U}}_d = \mathbf{I}$$

- The autocorrelations of IC's are identical to the Eigenvalues:

$$\left(\mathbf{X}\mathbf{C}_{xx}^{-\frac{1}{2}} \tilde{\mathbf{U}}_d \right)^\top \mathbf{Y}\mathbf{C}_{xx}^{-\frac{1}{2}} \tilde{\mathbf{U}}_d = \tilde{\mathbf{U}}_d^\top \mathbf{C}_{xx}^{-\frac{1}{2}} \mathbf{C}_{xy} \mathbf{C}_{xx}^{-\frac{1}{2}} \tilde{\mathbf{U}}_d = \mathbf{\Sigma}$$

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Special case: Markov State Model

- Choose characteristic functions

$$1_i(\mathbf{x}) = \begin{cases} 1 & \mathbf{x} \in S_i \\ 0 & \mathbf{x} \neq S_i \end{cases}$$

with sets $S_1, ..., S_n$ that partition the state space $\Omega = \cup_i S_i$

- Covariance matrices using $\pi_i = \mathbb{P}[\mathbf{x} \in S_i]$:

$$(\mathbf{C}_{xx})_{ij} = \mathbb{E}_t \left[1_i(\mathbf{x}_t) \cdot 1_j(\mathbf{x}_t)\right] = \delta_{ij}\pi_i$$
$$\mathbf{C}_{xx} = \mathbf{\Pi}$$

- And

$$(\mathbf{C}_{xy})_{ij} = \mathbb{E}\left[1_i(\mathbf{x}_t) \cdot 1_j(\mathbf{x}_{t+\tau})\right] = \pi_i p_{ij}$$

with $p_{ij} = \mathbb{P}\left[\mathbf{x}_{t+\tau} \in S_j \mid \mathbf{x}_t \in S_i\right]$.

- Thus we get an ordinary eigenvalue problem with the transition matrix:

$$\mathbf{C}_{xx}^{-\frac{1}{2}} \mathbf{C}_{xy} \mathbf{C}_{xx}^{-\frac{1}{2}} \mathbf{U} = \mathbf{U}\mathbf{\Lambda}$$
$$\mathbf{P}\mathbf{\Pi}^{-\frac{1}{2}} \tilde{\mathbf{U}} = \mathbf{\Pi}^{-\frac{1}{2}} \tilde{\mathbf{U}}\mathbf{\Lambda}$$
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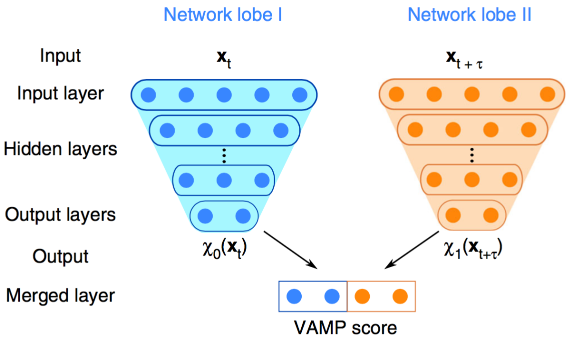


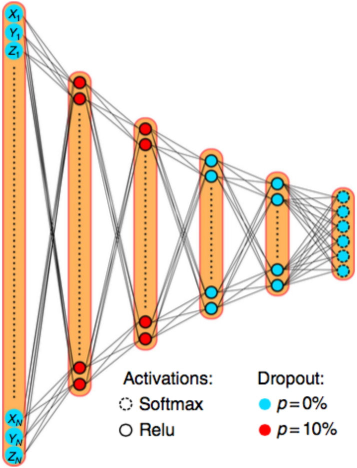
Objective: maximize VAMP-2 score.

$$\arg\max_{\chi_0,\chi_1} \left\| \mathbf{C}_{00}^{-\frac{1}{2}} \mathbf{C}_{01} \mathbf{C}_{11}^{-\frac{1}{2}} \right\|_F^2$$

with covariance matrices (can be computed in minibatches):

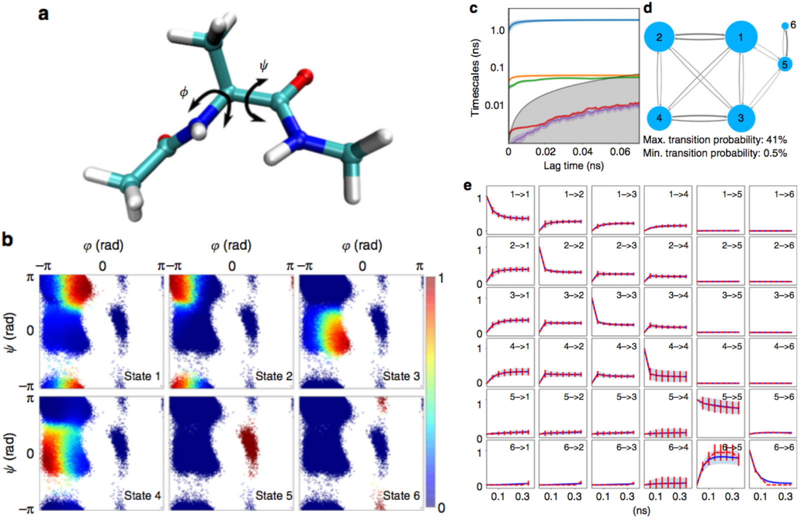
$$\mathbf{C}_{00} = \sum_t \chi_0(\mathbf{x}_t)\chi_0^\top(\mathbf{x}_t) \quad \mathbf{C}_{01} = \sum_t \chi_0(\mathbf{x}_t)\chi_1^\top(\mathbf{x}_{t+\tau}) \quad \mathbf{C}_{11} = \sum_t \chi_1(\mathbf{x}_{t+\tau})\chi_1^\top(\mathbf{x}_{t+\tau}).$$

VAMPnet



A. Mardt, L. Pasquali, H. Wu, F. Noé: **VAMPnets** for deep learning of molecular kinetics Nat. Commun. 9, 5 (2018)

VAMPnet



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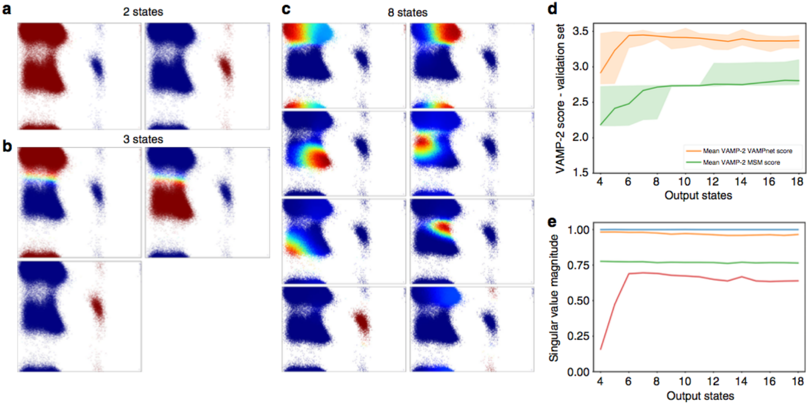

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