Using tICA to identify the Causes of Conformational Changes in Transporters

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MDAnalysis User Group Meeting

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Center for Biological Physics
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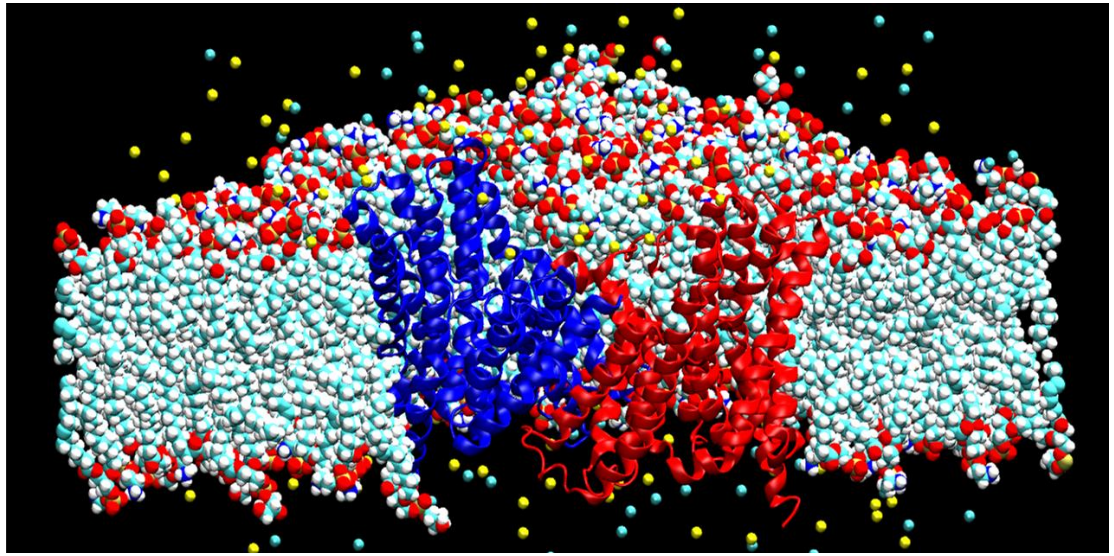
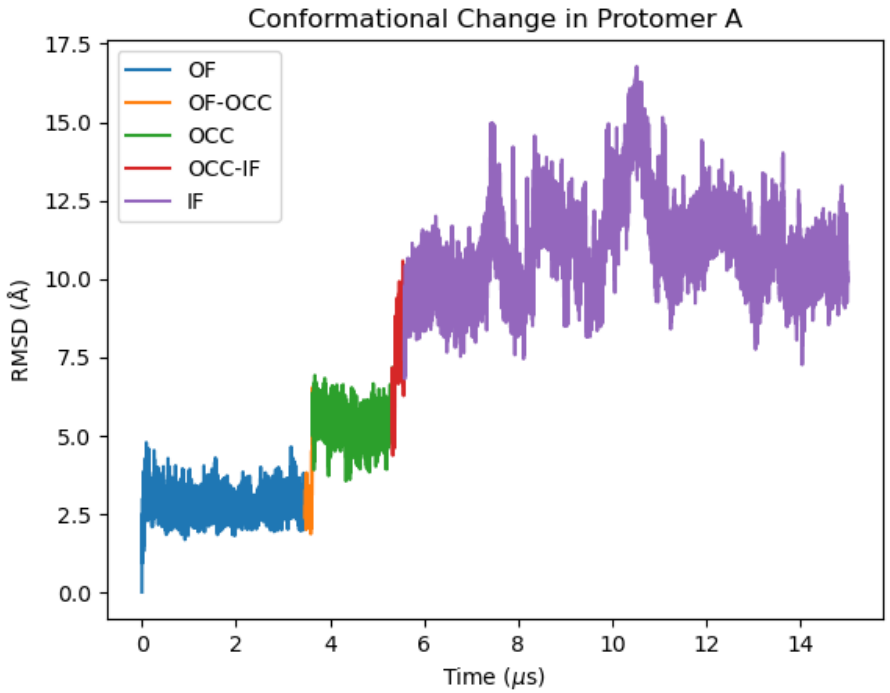
NapA undergo Conformational Changes

NapA





$$\mathrm{RMSD(t)} = \sqrt{\frac{1}{N}\sum_{i=1}^{N}||\mathbf{r}_i(t) - \mathbf{r}_i^{\mathrm{ref}}||^2}$$

Ian Kenney et al *Unpublished*

Time Independent Component Analysis (tICA) can pick up slow modes.

$$\tilde{q}(t) = q(t) - \langle q(t) \rangle$$

$$\mathbf{Q}_{ij}(t+\tau) = \langle \tilde{q}(t)_i \cdot \tilde{q}(t+\tau)_j \rangle$$

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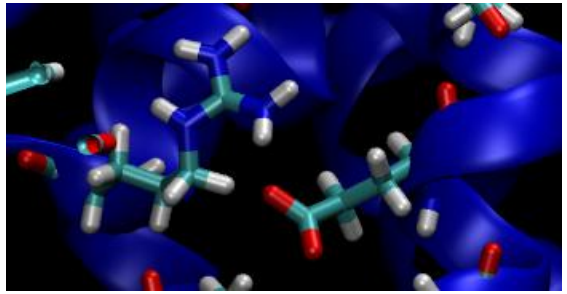
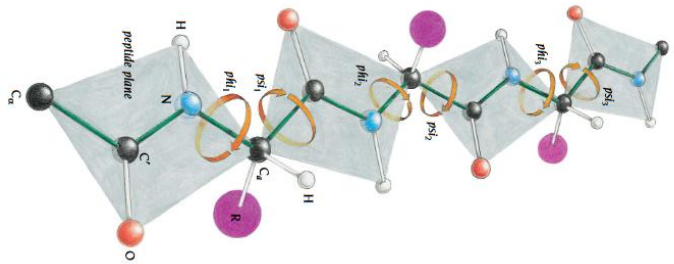
Salt Bridge



Dihedral Angles



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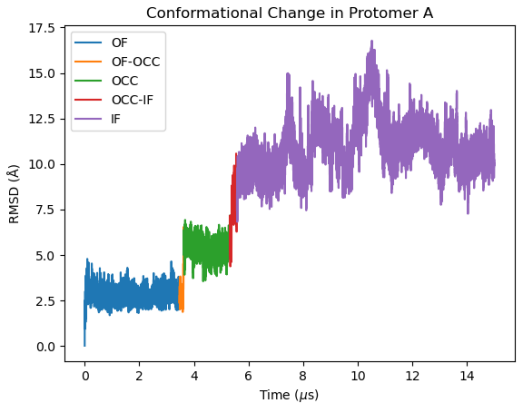
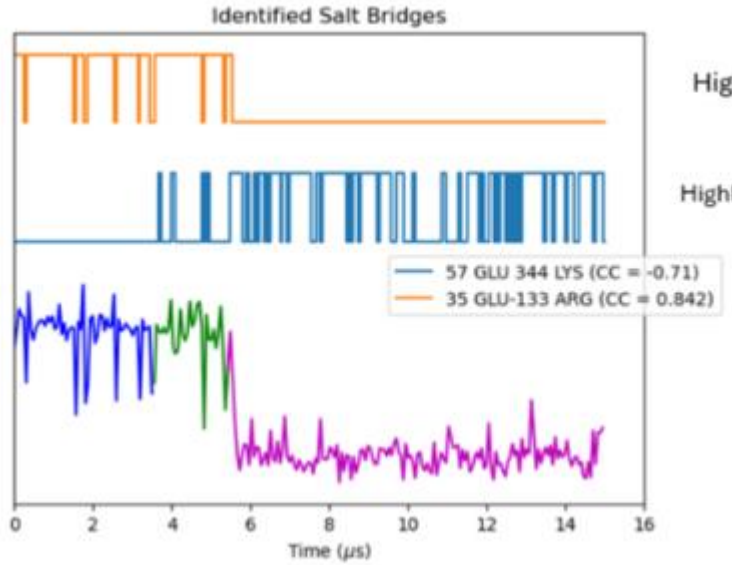
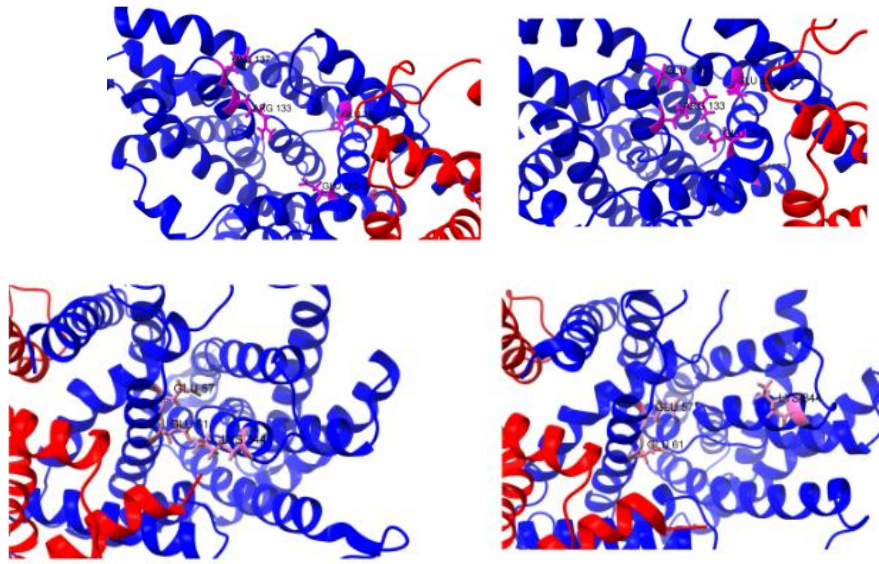
tICA Slow Modes are associated with conformations







1. Can calculate modes from the combination of all possible salt bridges
2. Cross Correlations (CC) between mode shows association with conformations
3. Acts as a "filter" for input time series (features).

$$R = \int_{-\infty}^{\infty} q_{sb}(t) \cdot u_{\text{mode}}(t)\ dt$$

Appendix

$$\lambda_i = \exp\left(\frac{\Delta t}{\tau}\right)$$