ConformaLens: conformational states in Adaptive Molecular Dynamics

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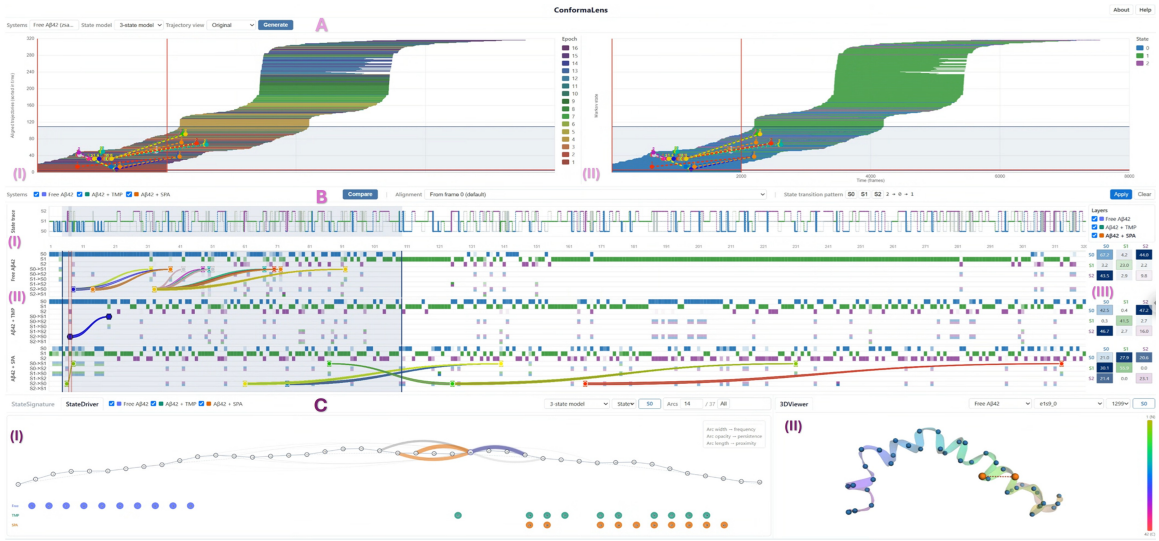


Figure 1: ConformaLens: Interactive visual analysis of adaptive molecular state ensembles. (A) Overlaid trajectory timelines summarize ensemble evolution and state transitions. (B) Comparative pattern matrices summarize state occupancy, transition patterns, and transition rates. (C) Residue interaction matrices, glyphs, and coordinated 3D views support structural reasoning.

Abstract

Adaptive molecular dynamics (MD) ensembles capture complex conformational behavior, but interpreting Markov State Model (MSM) assignments across many trajectories, frames, states, and ligand conditions remains challenging. We present *ConformaLens*, a linked visual analytics application for comparing free, TMP-bound, and SPA-bound Aβ42 simulations. Its coordinated timeline, transition footprints, interaction glyphs, and 3D structural views connect ensemble-level MSM dynamics with ligand effects and residue-level evidence, revealing representative states and residue–residue or residue–ligand differences across trajectories and frames.

Index Terms: Molecular Dynamics (MD), Markov State Models (MSMs), Interactive Visual Analytics, Molecular Visualization.

1 Introduction

Adaptive MD generates large trajectory ensembles that capture how Aβ42 explores different conformational states under free, TMP-bound, and SPA-bound conditions. However, Markov-state labels and existing static or single-trajectory views provide limited support for comparing these ensembles and linking state behavior to representative frames, residue motions, interaction patterns, and 3D molecular structures. The challenge lies in exploring large and complex ensemble data comprising hundreds of adaptive trajectories, thousands of frames, and evolving Markov-state assignments across multiple molecular conditions. Effective analysis requires scalable ensemble-level overviews and comparisons, temporal exploration, and coordinated interpretation of state dynamics, residue interactions, and 3D structural changes. We therefore define three analysis tasks: obtaining an overview of trajectory and state evolution (**T1**), grouping and comparing state-transition patterns across trajectories and molecular conditions (**T2**), and reasoning about state assignments through representative frames, residue interactions, and 3D structural evidence (**T3**). We present **ConformaLens**, an interactive visual analytics system for adaptive molecular state ensembles. It introduces linked trajectory–state timelines, state-footprint comparison matrices, global and local state-transition summaries, representative-frame and state-deviation analysis, residue-state signatures, inter– and intra-residue interaction-driver glyphs, and coordinated 3D views to reveal ligand effects across trajectories and frames.

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2 Related Work

VAMPnets, CoVAMPnet, and related methods identify conformational states and transitions in molecular dynamics trajectories [3, 4], while molecular visualization systems support structural and residue-level analysis [5]. Residue and protein–ligand interactions are characterized using spatial proximity, atom-level geometry, and ligand-binding patterns [1]. However, state assignments remain abstract, existing interfaces often focus on individual trajectories, and fixed contact views provide limited comparison across states, frames, and ligand conditions. *ConformaLens* addresses these limitations through coordinated ensemble timelines, transition analysis, temporal brushing, pattern search, representative structures, residue-interaction measures, and 3D views.

3 Method

Analyzing the challenge tasks requires both ensemble-level descriptions of state behavior and molecular evidence explaining the structural differences among states. The provided data include processed Markov-state assignments, trajectory ordering, and concatenated trajectory paths for free and ligand-bound Aβ42 systems,

but they do not directly encode structural geometry, residue interactions, or ligand contacts. We therefore construct additional analysis-ready datasets by mapping frames to molecular structures and computing representative frames, structural descriptors, residue- and atom-distance summaries, and ligand-contact statistics. These derived measures are linked to the original state and trajectory data through shared system, trajectory, state, and frame identifiers. Using these connected datasets, *ConformaLens* supports an ensemble-to-structure workflow that progresses from global MSM behavior to residue-level explanations. Users first examine state occupancy and transitions through aligned epoch and state timelines, then compare occupancy, transition rates, and temporal footprints across systems. Selected states and trajectory patterns are then linked to representative frames, residue distances, ligand contact glyphs, interaction drivers, and coordinated 3D structures to explain the effects of TMP and SPA on molecular structure.

4 Design and Result

ConformaLens comprises three coordinated sections designed to support ensemble overview, comparative state analysis, and structure-guided reasoning. To provide a scalable overview of simulation ensembles, we designed the overview section (Fig. 1(A)) to compare molecular systems across epochs, trajectories, concatenated paths, and MSM states. Overlaid timelines encode simulation duration, epoch progression, state persistence, and switching for original and concatenated trajectories. Transition patterns identified in the comparative view are highlighted on the corresponding trajectories and frames, supporting inspection of temporal and ligand-dependent differences. The overview helps users recognize global sampling coverage, persistent states, and recurring transition patterns across entire simulation ensembles.

To support interactive comparison of transition behavior, we designed the comparative state-dynamics view (Fig. 1(B)) for global and local analysis across free and ligand-bound Aβ42 systems. Each trajectory is represented by a transition-footprint matrix (Fig. 1(B-I)) encoding state occupancy (Fig. 1(B-II)) and directed transition rates (Fig. 1(B-III)). Gray indicates similar behavior, while colorful highlights deviations from the free-system baseline. Trajectories aligned by state entries or transitions trace repeated patterns through Sankey-like in glyphs design [6, 2], and compare local rates using heatmaps. Brushing selects trajectory windows, updates rate summaries, highlights corresponding timeline regions, and provides context for structural analysis and helping to group similar trajectories to compare transition treat across time and ligand conditions.

To facilitate structural reasoning in T3, coordinated StateSignature, StateDriver, and 3D views link Markov states to representative frames, residue interactions, ligand contacts, and their spatial locations. StateSignature (Fig. 2(A)) combines a residue-pair matrix of heavy-atom distance stability with a frame-distribution view (Fig. 2(B)) to identify representative and peripheral conformations. Selecting a matrix cell or frame loads the corresponding structure and highlights the relevant residues in 3D. StateDriver (Fig. 1(C-I)) reveals non-local residue–residue contacts and residue–ligand atomic proximities that characterize each state and distinguish molecular systems. Glyph height, width, and opacity encode proximity, frequency, and persistence, respectively, while color indicates the system.

Together, these linked views reveal which conformational and interaction changes contribute to state assignments and where they occur in the molecular structure. To spatially validate the identified patterns, the 3D Viewer (Fig. 1(C-II)) synchronizes selections from timelines, matrices, StateSignature, and StateDriver. It displays the selected system, trajectory, frame, and state using a sequence-colored ribbon and state-colored markers. Highlighted residues and dashed contact links translate abstract state patterns into molecular structures without recomputing trajectories in the browser.

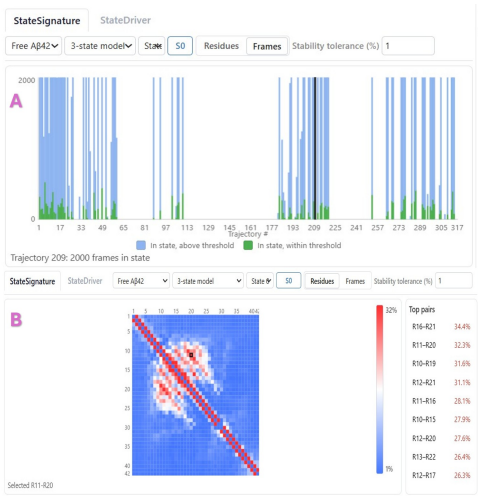


Figure 2: (A) Frame occupancy by state bars. (B) Residue-pair proximity, frequency, and persistence heatmap.

5 Evaluation

We evaluated *ConformaLens* with five visualization researchers from the EVL at the University of Illinois Chicago. Participants completed the three analysis tasks (**T1–T3**) and rated ten statements covering trajectory and state overviews, cross-state comparison, temporal alignment, transition, residue reasoning, interface clarity, usability, and the learnability workflow. Ratings were consistently positive (mean: 4.0–4.8/5). Participants particularly valued the coordinated views and linked interactions for tracing patterns across trajectories, states, residues, and 3D structures, while the timeline and comparison views were rated highly for supporting ensemble-level exploration. The full protocol, questionnaire, and detailed results are provided in the supplementary material.

6 Conclusion

ConformaLens supports interactive exploration of adaptive MD ensembles through coordinated trajectory, state-transition, residue-interaction, and 3D structural views. A task-based evaluation with visualization researchers assessed the clarity, usability, and analytical effectiveness of the system ratings and qualitative feedback. Precomputed structural descriptors enable responsive exploration of large free, TMP-bound, and SPA-bound Aβ42 datasets. The source code and interactive interface are publicly available.

Acknowledgments

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