Novelty Assessment Report

Paper: Enhancing Diffusion-Based Sampling with Molecular Collective Variables
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Abstract

Diffusion-based samplers learn to sample complex, high-dimensional distributions using energies or log densities alone, without training data. Yet, they remain impractical for molecular sampling because they are often slower than molecular dynamics and miss thermodynamically relevant modes. Inspired by enhanced sampling, we encourage exploration by introducing a sequential bias along bespoke, information-rich, low-dimensional projections of atomic coordinates known as collective variables (CVs). We introduce a repulsive potential centered on the CVs from recent samples, which pushes future samples towards novel CV regions and effectively increases the temperature in the projected space. Our resulting method improves efficiency, mode discovery, enables the estimation of free energy differences, and retains independent sampling from the approximate Boltzmann distribution via reweighting by the bias. On standard peptide conformational sampling benchmarks, the method recovers diverse conformational states and accurate free energy profiles. We are the first to demonstrate reactive sampling using a diffusion-based sampler, capturing bond breaking and formation with universal interatomic potentials at near-first-principles accuracy. The approach resolves reactive energy landscapes at a fraction of the wall-clock time of standard sampling methods, advancing diffusion-based sampling towards practical use in molecular sciences.

Core Task Landscape

This paper addresses: **Enhanced Sampling of Molecular Conformations Using Collective Variables**

A total of **50 papers** were analyzed and organized into a taxonomy with **17 categories**.

Taxonomy Overview

The research landscape has been organized into the following main categories:

- **Collective Variable Design and Discovery**
- **Enhanced Sampling Algorithms and Methodologies**
- **Application Domains and Molecular Systems**
- **Reviews, Tutorials, and Methodological Overviews**

Complete Taxonomy Tree

- Enhanced Sampling of Molecular Conformations Using Collective Variables Survey Taxonomy
- Collective Variable Design and Discovery
  - Machine Learning-Based CV Discovery
  - Deep Learning Architectures for CV Learning (5 papers)
    - [16] Modeling and enhanced sampling of molecular systems with smooth and nonlinear data-driven collective variables. (Behrooz Hashemian, 2013) View paper
    - [18] Molecular enhanced sampling with autoencoders: Onâ□□theâ□□fly collective variable discovery and accelerated free energy landscape exploration (Wei Chen, 2017) View paper
    - [21] A variational conformational dynamics approach to the selection of collective variables in metadynamics (James McCarty, 2017) View paper
    - [43] Descriptor-free collective variables from geometric graph neural networks (Jintu Zhang, 2024) View paper
    - [50] Data-driven collective variables for enhanced sampling (L. Bonati, 2020) View paper
  - Surrogate Models and Interpretable ML CVs (2 papers)
    - [7] Acceleration with interpretability: A surrogate model-based collective variable for enhanced sampling (Sompriya Chatterjee, 2025) View paper
    - [39] Improving the accuracy and convergence of drug permeation simulations via machine-learned collective variables. (Fikret Aydin, 2021) View paper
  - Path-Based and Transition-Focused CV Learning (4 papers)
    - [3] Enhanced sampling of protein conformational changes via true reaction coordinates from energy relaxation (Huiyung Li, 2025) View paper
    - [22] Deep learning path-like collective variable for enhanced sampling molecular dynamics. (Thorben FrÃ¶hlking, 2024) View paper
    - [35] Deep learning collective variables from transition path ensemble. (Dhiman Ray, 2023) View paper
    - [36] Discovering collective variables of molecular transitions via genetic algorithms and neural networks (Antonio Aparicio PÃ©rez, 2021) View paper
  - Physics-Informed and Geometric CV Construction
  - Symmetry-Aware and Permutationally Invariant CVs (1 papers)
    - [5] Permutationally Invariant Networks for Enhanced Sampling (PINES): Discovery of Multimolecular and Solvent-Inclusive Collective Variables. (Nicholas S. M. Herringer, 2023) View paper

- Geometric and Structural Descriptors (4 papers)
  - [25] Conformational sampling of seven-membered rings using extended puckering collective variables in metadynamics. (Mert Sagiroglugil, 2025) View paper
  - [40] Collective variables for conformational polymorphism in molecular crystals (Oren Elishav, 2023) View paper
  - [41] A Collective Variable for Controlling Occupation in Flexible Confined Volumes (Konstantin Stracke, 2025) View paper
  - [48] Residue Folding Degreeâ□□Relationship to Secondary Structure Categories and Use as Collective Variable (Vladimir Sladek, 2021) View paper
- Dimensionality Reduction-Based CVs (2 papers)
  - [24] Structural generation by inverse transformation using principal component analysis enhances conformational sampling of protein (Rikuri Morita, 2024) View paper
  - [37] Investigating protein dynamics in collective coordinate space (A. Kitao, 1999) View paper

• Enhanced Sampling Algorithms and Methodologies
- Biased Sampling Methods
- Metadynamics and Variants (4 papers)
  - [4] Advanced simulations with PLUMED: OPES and Machine Learning Collective Variables (Trizio, 2024) View paper
  - [10] Enhanced Sampling with Suboptimal Collective Variables: Reconciling Accuracy and Convergence Speed. (Dhiman Ray, 2024) View paper
  - [13] Advances in enhanced sampling along adaptive paths of collective variables. (A. Perez De Alba Ortiz, 2018) View paper
  - [14] Overcoming Sampling Issues and Improving Computational Efficiency in Collective-Variable-Based Enhanced-Sampling Simulations: A Tutorial (Haohao Fu, 2024) View paper
- Adaptive Biasing and Reweighting Techniques (2 papers)
  - [1] Enhanced sampling of robust molecular datasets with uncertainty-based collective variables (Aik Rui Tan, 2024) View paper
  - [11] Girsanov Reweighting Enhanced Sampling Technique (GREST): On-the-Fly Data-Driven Discovery of and Enhanced Sampling in Slow Collective Variables. (Kirill Shmilovich, 2023) View paper
- Unbiased and Temperature-Based Methods (4 papers)
- [20] Unconstrained enhanced sampling for free energy calculations of biomolecules: a review (Yinglong Miaoa, 2016) View paper
- [42] An interoperable implementation of collectiveâ□□variable based enhanced sampling methods in extended phase space within the OpenMM package (Shitanshu Bajpai, 2023) View paper
- [46] Efficient conformational sampling of collective motions of proteins with principal component analysis-based parallel cascade selection molecular dynamics (Takunori Yasuda, 2020) View paper
- [47] Accelerating the conformational sampling of intrinsically disordered proteins (Trang Nhu Do, 2014) View paper
- Multi-CV and Adaptive Sampling Strategies (3 papers)
- [30] Efficient sampling of conformational space via unbiased molecular dynamics in multiple low-dimensional collective variable spaces (Wentao Zhu, 2025) View paper
- [31] Unbiased Enhanced Sampling in Molecular Dynamics via Simultaneously Accelerating Diffusion in Multiple Low-Dimensional Collective Variable Spaces. (Wentao Zhu, 2025) View paper
- [32] Unsupervised learning of collective variables for conformational sampling of cyclic peptides. (Jiayuan Miao, 2025) View paper
- Diffusion-Based and Generative Sampling ★ (1 papers)
- [0] Enhancing Diffusion-Based Sampling with Molecular Collective Variables (Anon et al., 2026) View paper

• Application Domains and Molecular Systems
- Protein Conformational Dynamics (2 papers)
- [26] Exploring kinase Asp-Phe-Gly (DFG) loop conformational stability with AlphaFold2-RAVE (Bodhi P. Vani, 2023) View paper
- [28] Deep-Learning-Assisted Enhanced Sampling for Exploring Molecular Conformational Changes. (Haohao Fu, 2023) View paper
- Nucleic Acids and RNA Dynamics (2 papers)
- [6] Enhanced sampling strategies for molecular simulation of DNA (Bernadette Mohr, 2024) View paper
- [29] HB-CUFIX: Force field for accurate RNA simulations (Akshaya Kumar Das, 2025) View paper
- Molecular Recognition and Binding (4 papers)
- [9] Enhanced Sampling Simulations of RNAâ□□Peptide Binding Using Deep Learning Collective Variables (Nisha Kumari, 2025) View paper
- [15] Improved free-energy estimates for the permeation of bulky antibiotic molecules through porin channels using temperature-accelerated sliced sampling (Abhishek Acharya, 2025) View paper
- [33] Machine learning derived collective variables for the study of protein homodimerization in membrane (Ayan Majumder, 2024) View paper
- [44] Studying the Collective Functional Response of a Receptor in Alchemical Ligand Binding Free Energy Simulations with Accelerated Solvation Layer Dynamics. (Wei Jiang, 2024) View paper
- Crystallization and Phase Transitions (4 papers)
- [12] â□¦ external electric-field-induced crystallization of TKX-50 from solution by finite-temperature string with order parameters as collective variables for ionic crystals (F Ren, 2024) View paper
- [17] Finite temperature string by K-means clustering sampling with order parameters as collective variables for molecular crystals: application to polymorphic â□¦ (F Ren, 2024) View paper
- [19] Finite temperature string by K-means clustering sampling with order parameters as collective variables for molecular crystals: application to polymorphic transformation between Î²-CL-20 and Îµ-CL-20. (Fu-de Ren, 2024) View paper
- [49] Polymorph sampling with coupling to extended variables: enhanced sampling of polymorph energy landscapes and free energy perturbation of polymorph ensembles (Eric J. Chan, 2024) View paper
- Chemical Reactions and Catalysis (2 papers)
- [27] Ultrafast dynamics in spatially confined photoisomerization: accelerated simulations through machine learning models. (Weijia Xu, 2024) View paper
- [45] A Molecular View of Methane Activation on Ni(111) through Enhanced Sampling and Machine Learning. (Xu Yinan, 2024) View paper

• Reviews, Tutorials, and Methodological Overviews (5 papers)
- [2] Enhanced sampling in molecular dynamics (Yi Isaac Yang, 2019) View paper
- [8] Enhanced Sampling in the Age of Machine Learning: Algorithms and Applications (Zhu Kai, 2025) View paper
- [23] Enhanced Sampling Based on Collective Variables (Haohao Fu, 2023) View paper
- [34] Collective Variable-Based Enhanced Sampling: From Human Learning to Machine Learning. (Haohao Fu, 2024) View paper

- [38] CHARMMâ□□GUI Enhanced Sampler for various collective variables and enhanced sampling methods (Donghyuk Suh, 2022) View paper

Narrative

Core task: Enhanced sampling of molecular conformations using collective variables. The field organizes around four main branches that reflect distinct but interconnected challenges. Collective Variable Design and Discovery focuses on identifying low-dimensional coordinates that capture essential molecular motions, employing techniques ranging from data-driven dimensionality reduction (e.g., Autoencoder CV Discovery[18], Nonlinear Data Driven CVs[16]) to machine learning approaches that learn optimal representations from simulation data (e.g., ML Enhanced Sampling[8], Deep Learning Path CV[22]). Enhanced Sampling Algorithms and Methodologies develops computational strategies to accelerate exploration of conformational space along these variables, including diffusion-based and generative methods, adaptive schemes, and temperature-based protocols. Application Domains and Molecular Systems demonstrates these techniques across diverse targets such as proteins, nucleic acids, and small molecules, while Reviews, Tutorials, and Methodological Overviews provide pedagogical resources and critical assessments of best practices (e.g., CV Enhanced Sampling Tutorial[14]).

Recent work highlights a tension between interpretability and expressiveness in CV design: traditional geometric descriptors offer physical insight but may miss complex reaction coordinates, whereas deep learning methods can capture intricate patterns yet remain opaque. Within the Enhanced Sampling Algorithms branch, diffusion-based and generative approaches represent an emerging direction that leverages probabilistic models to guide sampling. Diffusion Molecular CVs[0] sits squarely in this subfield, employing diffusion models to construct collective variables that facilitate conformational exploration. This contrasts with uncertainty-driven strategies like Uncertainty Based CVs[1], which prioritize regions of high model uncertainty, and surrogate-based methods such as Surrogate Model CV[7], which build approximate energy landscapes. The original paper's emphasis on generative modeling aligns it with broader trends integrating modern machine learning into molecular simulation, offering a complementary perspective to variational and autoencoder-based CV discovery methods.

Related Works in Same Category

No sibling papers were found in the same taxonomy leaf. A taxonomy-subtopic-level comparison will be produced instead.

Taxonomy-Level Summary

The original leaf focuses on modern machine learning approaches (diffusion models, generative methods) for sampling molecular configurations, representing a departure from traditional molecular dynamics. The sibling subtopics cover complementary enhanced sampling strategies: one addressing how to intelligently combine and adapt collective variables during sampling, and another focusing on unbiased methods that manipulate temperature or use replica exchange rather than applying bias potentials.

Similarities: - All three subtopics aim to enhance sampling efficiency of molecular conformations beyond standard MD - All operate within the framework of collective variables or reduced representations of molecular configuration space - Each addresses the challenge of exploring rare events or overcoming energy barriers in molecular systems

Differences: - Diffusion-Based methods use generative ML models to directly sample configurations, while siblings rely on MD-based dynamics - Multi-CV Adaptive focuses on CV selection and combination strategies during sampling, whereas the original leaf uses CVs/energy functions as guidance for generation - Unbiased Temperature-Based methods explicitly avoid bias potentials and instead manipulate thermodynamic parameters, contrasting with both the generative approach and adaptive biasing schemes - The original leaf represents a data-driven, learning-based paradigm while siblings employ physics-based simulation strategies

Suggested Search Directions: - Hybrid methods combining generative models with adaptive CV selection - Diffusion models trained on replica exchange or temperature-accelerated trajectories - Comparison studies of sampling efficiency between generative and traditional enhanced sampling methods

Sibling Subtopics

- **Multi-CV and Adaptive Sampling Strategies** (leaves: 1, papers: 3)
- Scope: Frameworks combining multiple CVs, dynamically selecting CVs, or adaptively balancing exploration across CV spaces.
- Exclude: Excludes single-CV methods and specific biasing schemes; see Biased Sampling Methods and Unbiased Methods.
- **Unbiased and Temperature-Based Methods** (leaves: 1, papers: 4)
- Scope: Enhanced sampling without external biasing potentials including temperature acceleration, replica exchange, and parallel cascade selection.
- Exclude: Excludes methods applying bias potentials along CVs; see Biased Sampling Methods.

Contributions Analysis

Overall novelty summary. The paper introduces a diffusion-based sampler that incorporates collective variables (CVs) with a repulsive bias to enhance molecular conformational sampling. It occupies the 'Diffusion-Based and Generative Sampling' leaf within the Enhanced Sampling Algorithms branch, where it is currently the sole paper in this taxonomy node. This positioning reflects an emerging research direction that applies generative probabilistic models to molecular sampling, contrasting with the more populated branches of metadynamics variants and adaptive biasing techniques that dominate the Enhanced Sampling Algorithms category.

The taxonomy reveals that neighboring leaves contain established methods: 'Metadynamics and Variants' includes four papers on history-dependent biasing, while 'Adaptive Biasing and Reweighting Techniques' contains two papers on density-based adjustments. The paper's approach diverges from these traditional MD-based enhanced sampling methods by leveraging diffusion models rather than iterative bias accumulation. Its connection to the 'Machine Learning-Based CV Discovery' branch is indirect—while those methods focus on learning CVs from data, this work assumes CVs are given and uses them to guide a generative sampler, bridging algorithmic innovation with CV-based exploration.

Among 29 candidates examined across three contributions, none were identified as clearly refuting the work. The 'Well-Tempered Adjoint Schrödinger Bridge Sampler' examined 10 candidates with zero refutable matches, suggesting limited direct overlap in the sampled literature. Similarly, the protocol and convergence guarantee contributions each examined 9-10 candidates without refutation. This absence of refutable prior work within the limited search scope indicates that the specific combination of diffusion-based sampling, CV-guided biasing, and reweighting for molecular systems has not been extensively documented in the top-30 semantic matches and their citations.

The analysis suggests the work occupies a relatively sparse intersection of diffusion models and CV-based enhanced sampling, though the limited search scope (29 candidates) means broader literature may exist outside this sample. The taxonomy structure shows diffusion-based methods are underrepresented compared to metadynamics and temperature-based approaches, positioning this contribution in a less crowded methodological niche. However, the reactive sampling demonstration and free energy estimation capabilities connect it to established application domains, particularly chemical reactions and protein conformational dynamics, where enhanced sampling is well-developed.

This paper presents **3 main contributions**, each analyzed against relevant prior work:

Contribution 1: Well-Tempered Adjoint Schrödinger Bridge Sampler (WT-ASBS)

Description: The authors introduce WT-ASBS, a method that enhances the ASBS diffusion-based sampler by incorporating a well-tempered bias along collective variables (CVs). This bias is updated online during training to encourage exploration of rare modes and enables accurate estimation of free energy differences while preserving the ability to recover the Boltzmann distribution through reweighting.

This contribution was assessed against **10 related papers** from the literature. Papers with potential prior art are analyzed in detail with textual evidence; others receive brief assessments.

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1. Local and global perspectives on diffusion maps in the analysis of molecular systems

URL: View paper

Brief Assessment

Diffusion Maps Analysis[59] focuses on using diffusion maps to identify metastable sets and committor functions from simulation data, not on diffusion-based samplers with well-tempered biasing mechanisms for enhanced exploration during training.

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2. Hamiltonian replica exchange augmented with diffusion-based generative models and importance sampling to assess biomolecular conformational basins and â□¦

URL: View paper

Brief Assessment

Hamiltonian Replica Diffusion[51] focuses on combining replica exchange methods with diffusion models for biomolecular sampling, rather than introducing well-tempered biasing mechanisms into diffusion-based samplers for molecular enhanced sampling as in the original paper.

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3. Mitigating Exposure Bias in Score-Based Generation of Molecular Conformations

URL: View paper

Brief Assessment

Exposure Bias Mitigation[60] addresses exposure bias in score-based molecular conformation generation through input perturbation during training. This is fundamentally different from WT-ASBS, which introduces a well-tempered bias along collective variables during diffusion-based sampling to enhance exploration of rare modes in molecular systems.

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4. Protein-ligand interaction prior for binding-aware 3d molecule diffusion models

URL: View paper

Brief Assessment

Protein Ligand Diffusion[53] focuses on protein-ligand binding for drug design using diffusion models with interaction priors, not on general molecular sampling with collective variable biasing for enhanced exploration and free energy estimation.

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5. On scalable and efficient training of diffusion samplers

URL: View paper

Brief Assessment

Diffusion Sampler Training[52] focuses on scalable training of diffusion samplers using MCMC-based exploration with novelty rewards, not on well-tempered biasing along collective variables for molecular sampling.

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6. Fine-Tuning Diffusion Models via Intermediate Distribution Shaping

URL: View paper

Brief Assessment

Intermediate Distribution Shaping[58] focuses on fine-tuning diffusion models for generative tasks using rejection sampling and intermediate distribution shaping, not on molecular sampling with collective variables and enhanced exploration for thermodynamic properties.

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7. Target-aware 3D molecular generation based on guided equivariant diffusion

URL: View paper

Brief Assessment

Target Aware Diffusion[55] focuses on target-aware 3D molecular generation for structure-based drug design, not on general molecular sampling with enhanced exploration mechanisms. The candidate addresses a different problem domain (drug discovery with protein targets) using diffusion models, whereas the original contribution concerns enhanced sampling for molecular conformations and reactive landscapes with well-tempered bias mechanisms.

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8. Transition Path Sampling with Improved Off-Policy Training of Diffusion Path Samplers

URL: View paper

Brief Assessment

Transition Path Diffusion[56] focuses on transition path sampling between metastable states without collective variables, while WT-ASBS enhances equilibrium sampling with well-tempered bias along CVs for rare mode exploration and free energy estimation.

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9. DiSCO: Diffusion SchrÃ¶dinger Bridge for Molecular Conformer Optimization

URL: View paper

Brief Assessment

DiSCO[57] focuses on molecular conformer optimization using a Schrödinger bridge for conformer-to-conformer translation in drug discovery, not on enhanced sampling with biasing mechanisms for rare event exploration in molecular dynamics.

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10. Conditional diffusion models for molecular dynamics conformation sampling

URL: View paper

Brief Assessment

Conditional Diffusion MD[54] focuses on generating initial configurations for molecular dynamics simulations with relaxation constraints, not on enhanced sampling with well-tempered biasing mechanisms for exploring rare modes in equilibrium sampling.

Contribution 2: Protocol for applying WT-ASBS to molecular systems

Description: The authors present a practical protocol for deploying WT-ASBS to molecular sampling tasks. This includes strategies for data-based pretraining, CV selection, restraint potentials, and post-training reweighting. The protocol is demonstrated on peptide conformational sampling and, for the first time, on reactive chemical landscapes using diffusion-based samplers.

This contribution was assessed against **10 related papers** from the literature. Papers with potential prior art are analyzed in detail with textual evidence; others receive brief assessments.

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1. Metalorian: De Novo Generation of Heavy Metal-Binding Peptides with Classifier-Guided Diffusion Sampling

URL: View paper

Brief Assessment

Metalorian[74] focuses on generating heavy metal-binding peptides using conditional diffusion models for protein design, not on enhanced sampling protocols for molecular dynamics or reactive chemical landscapes in Cartesian coordinates.

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2. Full-atom peptide design with geometric latent diffusion

URL: View paper

Brief Assessment

Geometric Latent Diffusion[73] focuses on peptide design using latent diffusion models for full-atom geometry, not on enhanced sampling protocols for molecular conformational sampling or reactive landscapes in Cartesian coordinates.

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3. Consistent sampling and simulation: Molecular dynamics with energy-based diffusion models

URL: View paper

Brief Assessment

Energy Based Diffusion[72] focuses on diffusion-based sampling for molecular dynamics with energy-based models and Fokker-Planck regularization, not on well-tempered metadynamics-style biasing protocols for peptide conformational sampling or reactive landscapes in Cartesian coordinates as described in the original paper.

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4. Sparks of function by de novo protein design

URL: View paper

Brief Assessment

De Novo Protein[70] focuses on de novo protein design and structure generation, not on diffusion-based sampling protocols for molecular dynamics or reactive chemical landscapes in Cartesian coordinates.

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5. Direct conformational sampling from peptide energy landscapes through hypernetwork-conditioned diffusion

URL: View paper

Brief Assessment

Hypernetwork Conditioned Diffusion[75] focuses on peptide conformational sampling using hypernetwork-conditioned diffusion models, not on the WT-ASBS protocol with CV-based biasing, restraint potentials, and reweighting strategies described in the original paper.

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6. Towards Unraveling Biomolecular Conformational Landscapes with a Generative Foundation Model

URL: View paper

Brief Assessment

Generative Foundation Model[78] focuses on diffusion-based sampling for biomolecular conformational ensembles using a multi-level graph architecture, not on enhanced sampling protocols with collective variables and restraint potentials for molecular systems.

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7. CPLâ□□Diff: A Diffusion Model for De Novo Design of Functional Peptide Sequences with Fixed Length

URL: View paper

Brief Assessment

CPL-Diff[71] focuses on de novo design of functional peptide sequences with controlled length using diffusion models for sequence generation, not on molecular sampling protocols for conformational exploration or reactive landscapes in Cartesian coordinates.

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8. Fast and Accurate Peptideâ□□MHC Structure Prediction via an Equivariant Diffusion Model

URL: View paper

Brief Assessment

Peptide MHC Diffusion[79] focuses on structure prediction for peptide-MHC complexes using diffusion models, not on enhanced sampling protocols for molecular dynamics or reactive landscapes in Cartesian coordinates.

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9. Data-Driven Approaches for Molecular Design and Simulation: From Self-Assembling Peptides to Enhanced Sampling Techniques and Atomistic Structure Generation

URL: View paper

Brief Assessment

Data Driven Molecular Design[77] focuses on a machine learning-enabled enhanced sampling technique with adaptive sampling workflows for molecular simulation, but does not describe the specific WT-ASBS protocol involving data-based pretraining, CV selection, restraint potentials, and post-training reweighting for diffusion-based samplers as presented in the original paper.

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10. Determination of reaction coordinates via locally scaled diffusion map

URL: View paper

Brief Assessment

Locally Scaled Diffusion[76] focuses on determining collective variables using diffusion maps from Boltzmann-sampled configurations, not on diffusion-based sampling protocols with well-tempered biasing for molecular systems.

Contribution 3: Convergence guarantee for WT-ASBS

Description: The authors provide a theoretical convergence result (Proposition 3.1) proving that the bias potential in WT-ASBS converges almost surely to the well-tempered target distribution. This ensures that the potential of mean force along the CVs can be recovered from the final bias, establishing the method's theoretical soundness.

This contribution was assessed against **9 related papers** from the literature. Papers with potential prior art are analyzed in detail with textual evidence; others receive brief assessments.

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1. Finite-time convergence rates of nonlinear two-time-scale stochastic approximation under Markovian noise

URL: View paper

Brief Assessment

Nonlinear Two-Timescale Convergence[65] focuses on two-time-scale stochastic approximation under Markovian noise for finding roots of coupled nonlinear operators, not on biased sampling methods for molecular systems or well-tempered metadynamics convergence.

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2. A two-time-scale adaptive search algorithm for global optimization

URL: View paper

Brief Assessment

Adaptive Search Algorithm[67] addresses deterministic optimization via two-time-scale stochastic approximation for parameter updates, not biased molecular sampling with convergence to well-tempered distributions along collective variables.

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3. Finite-sample analysis of two-time-scale natural actorâ□□critic algorithm

URL: View paper

Brief Assessment

Two-Time-Scale Actor-Critic[63] focuses on reinforcement learning policy optimization with two-time-scale stochastic approximation, not on biased sampling methods for molecular systems or well-tempered metadynamics convergence.

---

4. Revisiting experience replay in non-stationary environments

URL: View paper

Brief Assessment

Experience Replay Revisited[66] focuses on experience replay sampling strategies in reinforcement learning, not on convergence guarantees for biased sampling methods in molecular dynamics or diffusion-based samplers.

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5. A two-time-scale stochastic optimization framework with applications in control and reinforcement learning

URL: View paper

Brief Assessment

Two-Time-Scale Optimization[62] focuses on two-time-scale stochastic gradient methods for general optimization with auxiliary variables, not specifically on well-tempered bias convergence in molecular sampling contexts.

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6. Two-timescale linear stochastic approximation: Constant stepsizes go a long way

URL: View paper

Brief Assessment

Two-Timescale Linear SA[64] focuses on two-timescale stochastic approximation with constant stepsizes in a different algorithmic context (linear SA with Markovian noise), not on well-tempered biased sampling methods for molecular dynamics.

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7. Fast Nonlinear Two-Time-Scale Stochastic Approximation: Achieving Finite-Sample Complexity

URL: View paper

Brief Assessment

Fast Two-Time-Scale[61] focuses on two-time-scale stochastic approximation for finding roots of coupled nonlinear operators, not on biased sampling methods for molecular dynamics or well-tempered metadynamics convergence.

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8. Convex Potential Mirror Langevin Algorithm for Efficient Sampling of Energy-Based Models

URL: View paper

Brief Assessment

Mirror Langevin EBM[68] focuses on sampling from energy-based models using mirror Langevin dynamics with convex potential flows, not on biased sampling methods with two-time-scale update schemes for molecular dynamics.

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9. Energy-based Model Training Objective Robust to Inaccurate SGLD Samples

URL: View paper

Brief Assessment

EBM Training Objective[69] focuses on training energy-based models with stochastic gradient Langevin dynamics (SGLD) samples and addresses stability through reweighting schemes. It does not provide convergence guarantees for biased sampling methods under two-time-scale update schemes as in WT-ASBS.

Appendix: Text Similarity Detection

No high-similarity text segments were detected across any compared papers.

References

- [0] Enhancing Diffusion-Based Sampling with Molecular Collective Variables View paper
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