

Symmetry-Preserving Quantum Walks for Protein Conformational Sampling

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Research Article

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Symmetry-Preserving Quantum Walks for Protein Conformational Sampling

Exact equilibrium guarantees and a multi-sequence comparison with classical diffusion

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Abstract

Protein conformational populations require equilibrium ensemble sampling rather than merely finding minimum-energy structures. A previous Q-TAILOR feasibility experiment used a statevector-simulated quantum-circuit independence proposal whose Metropolis–Hastings correction depended on exact proposal probabilities, creating an obstacle to quantum-hardware implementation. Here we investigate a different construction: a continuous-time quantum walk on a graph of valid hydrophobic–polar (HP) lattice conformations, with edges defined by reversible pivot moves. For a real-symmetric walk Hamiltonian H , measured transition probabilities $Q_t(y \mid x) = |\langle y | e^{-itH} | x \rangle|^2$ are symmetric, permitting standard energy-only Metropolis acceptance and exact Boltzmann detailed balance. We benchmark unconditioned and energy-conditioned quantum walks against classical graph diffusion, local pivot sampling, and uniform independence proposals. Exact enumeration supplies ground truth for 11 seven-to-nine-residue HP sequences (195–1479 conformations), three inverse temperatures, and 12 pseudorandom replicates per condition: 396 chains per method. Each chain contains 24,000 iterations with 4,000 burn-in iterations and 4,000 retained observations. Average macrostate total-variation errors are 0.0201 for the unconditioned quantum walk, 0.0202 for classical diffusion, 0.0201 for uniform sampling, 0.0260 for pivot moves, and 0.0396 for the energy-conditioned walk. The paired quantum-minus-diffusion error is -0.00004 (sequence-cluster bootstrap 95% interval $[-0.00103, 0.00092]$). Exact energy autocorrelation calculations independently corroborate that interference alone does not establish improved mixing. The contribution is a reproducible, symmetry-protected conformational sampling framework and comparative negative-control benchmark, not a demonstrated quantum speedup or a realistic protein-folding predictor.

Keywords: conformational ensembles; hydrophobic–polar lattice proteins; continuous-time quantum walks; reversible Markov chains; Metropolis sampling; exact enumeration; quantum-inspired computational biophysics; negative controls.

1 Introduction

The conformational behavior of a molecule at finite temperature is described by a distribution of configurations, not solely by an optimized conformation. Even when a low-energy structure is

known, probabilities of metastable basins, entropic effects, and ensemble observables require suitable sampling. Contemporary protein structure generators and enhanced-sampling methods emphasize this distinction [8, 9, 10]. The hydrophobic–polar (HP) lattice model is deliberately simplified but provides a controlled setting in which finite conformational spaces, energies, and equilibrium observables can be computed exactly [3, 4].

Quantum-assisted Monte Carlo has received substantial attention, including symmetric quantum proposals for Ising systems and coherent quantum-walk constructions [6, 7]. Those papers establish relevant prior art: neither the use of unitary quantum evolution as a proposal nor Metropolis correction is new. What remains worth testing here is whether proposals constructed from *protein-like conformational connectivity*, rather than unrestricted bitstring changes, have favorable statistical properties relative to classical dynamics on the *same* graph.

The motivation also arises from the author’s two earlier synthetic-model preprints. Q-CVaR-Fold examined tail-weighted decoy ranking, whereas Q-TAILOR explored quantum-inspired geometric refinement of perturbed short chains [13, 14]. Neither paper established equilibrium thermodynamic sampling, and neither provides evidence of a quantum computational advantage. Our earlier Q-TAILOR 3.0 pilot used a ten-qubit statevector simulation on one eight-residue HP sequence, with a fixed random circuit and independence Metropolis–Hastings (MH). Its proposal performed worse than uniform MH: mean full-state total-variation distances were 0.2268 versus 0.1223 over 20 seeds. Moreover, an independence proposal q_θ requires the ratio $q_\theta(x)/q_\theta(y)$ in the acceptance test; obtaining that ratio from finite-shot quantum measurements is generally not straightforward. These observations motivated replacing the random-circuit proposal with a symmetric walk kernel that eliminates the proposal-ratio requirement.

Scope and contributions. This paper (i) constructs a graph of self-avoiding conformations linked by physically interpretable pivot moves; (ii) derives thermodynamic invariance of a measured real-symmetric quantum-walk proposal without requiring the values of proposal probabilities during acceptance; (iii) compares it with classical diffusion on the identical graph and with two conventional MH controls; (iv) examines an energy-conditioned quantum Hamiltonian as an exploratory ablation; and (v) supplies exact-enumeration references, replicated sampling statistics, and exact energy mixing diagnostics. All quantum evolution is evaluated using *classical numerical linear algebra*; no quantum processor, molecular force field, quantum circuit compilation, or biological protein-folding experiment is involved.

2 Statistical-mechanical model

2.1 Finite HP conformational state spaces

A length- n two-dimensional conformation is a self-avoiding nearest-neighbor lattice walk $x = (r_1, \dots, r_n)$, where $r_i \in \mathbb{Z}^2$, $\|r_{i+1} - r_i\|_1 = 1$, and $r_i \neq r_j$ for $i \neq j$. We eliminate translation and choose an orientation by fixing $r_1 = (0, 0)$ and $r_2 = (1, 0)$; mirror images are retained as distinct indexed states. Enumerating all such walks gives $M = 195, 543$, and 1479 conformations for lengths seven, eight, and nine, respectively. These are *conformations of an idealized lattice polymer*, not atomistic structures of proteins.

For an HP sequence $s = (s_1, \dots, s_n)$, $s_i \in \{\text{H}, \text{P}\}$, the energy is

$$E_s(x) = - \sum_{1 \leq i < j \leq n} \mathbf{1}[s_i = s_j = \text{H}] \mathbf{1}[j - i > 1] \mathbf{1}[\|r_i - r_j\|_1 = 1]. \quad (1)$$

Thus each noncovalent nearest-neighbor HH contact contributes minus one model-energy unit.

With β measured in reciprocal model-energy units, the target canonical ensemble is

$$\pi_{\beta,s}(x) = \frac{e^{-\beta E_s(x)}}{Z_{\beta,s}}, \quad Z_{\beta,s} = \sum_{z \in \mathcal{C}_n} e^{-\beta E_s(z)}. \quad (2)$$

The exact normalization is used for *validation*, not by the MH accept/reject mechanism.

As a simple shape descriptor we use the squared radius of gyration,

$$R_g^2(x) = \frac{1}{n} \sum_{i=1}^n \left\| r_i - \frac{1}{n} \sum_{j=1}^n r_j \right\|_2^2. \quad (3)$$

For diagnostics, macrostates are defined by the pair $(E_s(x), b(R_g^2(x)))$, where b denotes the three bins formed by tertiles of R_g^2 over the complete *unweighted* valid-state catalog. This is a diagnostic partition, not an experimentally inferred folding reaction coordinate.

Valid two-dimensional hydrophobic-polar conformations

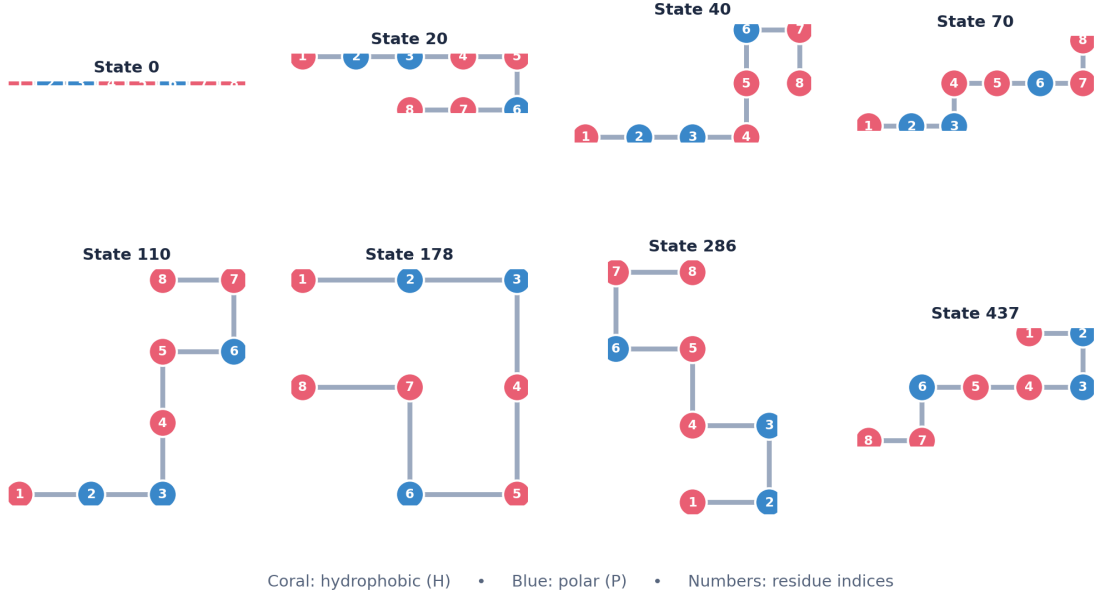


Figure 1: Examples of exactly enumerated eight-residue conformations for $s = \text{HPPHHPHH}$. Residue identities are indicated by color; enumeration order is an indexing convention and has no direct thermodynamic significance.

2.2 The reversible pivot graph

Let $\mathcal{C}_n$ be the indexed set of valid walks. Choose a pivot residue $i \in \{2, \dots, n-1\}$, hold the prefix through residue i fixed, and rotate all later residues by 90° , 180° , or 270° around r_i . (The software uses zero-based pivot indices $1, \dots, n-2$.) A proposed transformation is valid only if the resulting walk is self-avoiding and remains in $\mathcal{C}_n$. Invalid transformations represent a null proposal. This is a constrained instance of the classical pivot idea [5].

For $x \neq y$ define

$$W_{xy} = \frac{\#\{\text{pivot/rotation choices carrying } x \text{ to } y\}}{3(n-2)}, \quad W_{xx} = 0. \quad (4)$$

Every valid pivot has an inverse rotation of the same proposal probability, so $W_{xy} = W_{yx} \geq 0$. The diagonal null-proposal probability is $1 - \sum_{y \neq x} W_{xy}$, giving the standard pivot candidate kernel $P_{\text{pivot}} = W + \text{diag}(\mathbf{1} - W\mathbf{1})$. In the enumerated examples this graph has one connected component for each tested chain length. Nothing in the method requires an energy model to define these geometric connections.

3 Quantum and classical proposal constructions

3.1 Real-symmetric quantum transport

We study two Hermitian, real-symmetric graph Hamiltonians:

$$H_0 = W, \quad H_{\lambda,s} = W + \lambda \text{diag}(E_s - \bar{E}_s \mathbf{1}), \quad \bar{E}_s = \frac{1}{M} \sum_{x \in \mathcal{C}_n} E_s(x). \quad (5)$$

The first describes energy-independent coherent transport along valid pivot connections. The second inserts a site-potential term; the overall constant energy offset does not affect measurement probabilities. The energy-conditioned variant is an exploratory, *fixed-parameter ablation*, not a trained risk-sensitive or CVaR method. The terminology “Q-TAILOR” identifies a research sequence rather than implying that the previously proposed neural or CVaR modules were reused here.

For either Hamiltonian, define $U_t = \exp(-itH)$ and sample a candidate y from the measured distribution

$$Q_{t,H}(y | x) = |\langle y | U_t | x \rangle|^2. \quad (6)$$

Unlike the earlier ten-qubit proposal, this walk evolves within the *enumerated feasible-state Hilbert space*. Because U_t is unitary, Q is row-stochastic. Moreover, $H = H^T$ implies $U_t^T = U_t$, hence $Q_{t,H}(y | x) = Q_{t,H}(x | y)$. It follows that Q is symmetric and doubly stochastic.

3.2 Exact equilibrium correction

Theorem 1 (Boltzmann reversibility of symmetric quantum-walk proposals). *Let $\mathcal{C}$ be finite, $E : \mathcal{C} \rightarrow \mathbb{R}$, $\beta > 0$, and H any real-symmetric matrix indexed by $\mathcal{C}$. Generate y from $Q(y | x) = |\langle y | e^{-itH} | x \rangle|^2$ and accept with*

$$a_\beta(x, y) = \min \{1, \exp[-\beta(E(y) - E(x))]\}. \quad (7)$$

The resulting MH transition kernel is reversible with respect to $\pi_\beta(x) \propto e^{-\beta E(x)}$. If its positive-probability transition graph is connected and it has a self-loop at some state, the stationary distribution is unique and the chain is ergodic.

Proof. As H is real symmetric, $U_t = U_t^T$ and hence $Q(y | x) = Q(x | y)$. For $x \neq y$,

$$\begin{aligned} \pi_\beta(x) Q(y | x) a_\beta(x, y) &= Q(y | x) \min\{\pi_\beta(x), \pi_\beta(y)\} \\ &= \pi_\beta(y) Q(x | y) a_\beta(y, x). \end{aligned}$$

Diagonal terms satisfy detailed balance trivially. Connected transition support gives irreducibility; a positive self-loop together with irreducibility yields aperiodicity. The standard finite-state Markov-chain theorem gives uniqueness and convergence. $\square$

Consequences. The quantum proposal probabilities need not be *numerically evaluated in the MH test*; they are used only to generate candidates. This avoids the independent-proposal density-ratio obstacle. Importantly, the proof establishes a correct *stationary measure*, not rapid convergence, low gate cost, or a quantum advantage. For exceptional evolution times, Q may have disconnected support; then uniqueness does not follow without additional steps. The computed examples use connected underlying pivot graphs, and positive effective transitions were checked for the evaluated kernels.

3.3 Classical controls and fairness

All five proposal families use the *same* Boltzmann acceptance rule (Eq. 7):

1. **Uniform:** $P_{xy} = 1/M$ for every pair, corresponding to global independent proposals using full catalog access.
2. **Pivot:** $P_{\text{pivot}} = W + \text{diag}(\mathbf{1} - W\mathbf{1})$, including invalid-move self-proposals.
3. **Classical heat/diffusion:** $P_{\text{heat}}(t) = \exp(tL)$, where $L = W - \text{diag}(W\mathbf{1})$. As L is symmetric with zero row sums, $P_{\text{heat}}(t)$ is symmetric and stochastic.
4. **Quantum walk:** Q_{t,H_0} .
5. **Energy-conditioned quantum walk:** $Q_{t,H_{0.5,s}}$.

For the primary Monte Carlo comparisons, $t = 9$ and $\lambda = 0.5$ were fixed as exploratory study settings across all lengths, sequences, and temperatures. They were not fitted to the final results. Equality of the numerical evolution parameter t *does not mean equality of physical gate counts, wall time, or quantum sampling cost*: the classical and unitary generators are fundamentally different. No cost-matched quantum advantage can be inferred from these tests.

4 Experimental protocol and diagnostics

4.1 Sequences, temperatures, and randomization

Table 1 lists all 11 synthetic HP strings. Three independent dimensions are tested: $n \in \{7, 8, 9\}$, sequence identity, and inverse temperature $\beta \in \{0.8, 1.4, 2.2\}$. All sequences have nonconstant HP energy across their conformational catalogs. Twelve pseudorandom seeds per condition produce $11 \times 3 \times 12 = 396$ chains per algorithm. Each run performs 24,000 candidate moves, discards the first 4,000, and saves every fifth subsequent state, giving 4,000 observations. Random seeds identify reproducible runs, not distinct biological replicates. The software reports all method-specific records, rather than only a favorable selection.

Table 1: Fully enumerated synthetic sequence panel. All energy distributions are nonconstant. The same geometry graph is used across sequences of a given length.

Length n	HP sequences	Conformations M	Number of sequences
7	HPPHHPH, HHPHHPH, HHPHHPH	195	3
8	HPPHHPHH, HHHPPPHH, HPHPHPHH, HHPPHHPP, HHPHPHPH	543	5
9	HPPHHPHHH, HHHPPPHHH, HPHPHPHH	1479	3

4.2 Statistical observables

For a run with retained empirical histogram $\hat{\pi}$ and the exact Eq. 2, define

$$\text{TV}_{\text{full}} = \frac{1}{2} \sum_{x \in \mathcal{C}_n} |\hat{\pi}(x) - \pi(x)|, \quad \text{TV}_{\text{macro}} = \frac{1}{2} \sum_{b \in \mathcal{B}} |\hat{\pi}(b) - \pi(b)|. \quad (8)$$

The full-state metric is high-dimensional and sensitive to a finite 4,000-observation sample, especially when $M = 1479$. The macrostate metric is less sparse and captures errors in energetic and shape populations, but can conceal redistributions within a macrostate. We additionally record the absolute mean-energy error, the fraction of accepted proposals, the fraction of *actual state changes* (excluding accepted self-proposals), and an approximate energy effective sample size (ESS) computed from a positive-lag-pair integrated autocorrelation estimate on the thinned series [12]. Acceptance and state-change fractions are different quantities; accepting a self-proposal contributes no new conformation.

The primary table averages results over 33 sequence–temperature conditions and 12 runs per condition. For mean macrostate TV we report exploratory 95% percentile intervals from 5,000 bootstrap draws that resample *sequence clusters within each length*, retaining all three temperatures and seed averages for a selected sequence. These intervals quantify variability within this short synthetic panel; they do not justify extrapolation to proteins in nature or to larger chains. To compare quantum with classical diffusion, we use paired sequence-cluster differences with a separate 15,000-draw bootstrap.

4.3 Exact finite-state energy mixing

For the $n = 8$ panel we additionally calculate *exact* integrated energy autocorrelation of the MH kernel. Let K be the complete transition matrix, π its invariant vector, $S = D_\pi^{1/2} K D_\pi^{-1/2}$ its symmetric similarity transform, $v = \sqrt{\pi}$, and $b = D_\pi^{1/2}(E - \mathbb{E}_\pi E)$. For nonconstant energy, the integrated autocorrelation time per *unthinned* MH step is

$$\tau_{\text{int},E} = 2 \frac{b^T (\mathbf{I} - S + vv^T)^{-1} b}{b^T b} - 1. \quad (9)$$

This formula uses an exact linear solve on the enumerated state space, rather than a noisy extrapolation of a sampled correlation series. It is distinct from ESS estimated on thinned trajectories. We evaluate a sensitivity grid $t \in \{3, 6, 9, 12, 18\}$ for both quantum and classical kernels at $n = 8$. This scan is *exploratory*; its optimal times are not selected and then rebranded as held-out performance.

5 Results

5.1 Multi-sequence thermodynamic accuracy

Table 2 and Fig. 2 give the corrected primary results. Quantum walks with an energy-independent Hamiltonian obtain a mean macrostate TV of 0.0201, nearly indistinguishable from classical heat 0.0202 and uniform MH 0.0201. The mean paired quantum-minus-heat macrostate difference is -0.00004 , with a cluster-bootstrap 95% interval of $[-0.00103, 0.00092]$. In 15 of the 33 sequence–temperature conditions the quantum walk has lower mean macrostate error than heat; in the other 18 it does not. These differences are small compared with the observed Monte Carlo and sequence-to-sequence variation. The evidence does not support a systematic quantum advantage.

Table 2: Main 11-sequence panel; 396 independent-seed chains per method. The interval is an exploratory 95% sequence-cluster bootstrap interval for macrostate TV. Energy ESS is approximate and refers to 4,000 retained (thinned) samples; higher is preferable.

Proposal	Macro TV [95% interval] ↓	Full TV ↓	Energy ESS ↑	Changed/step ↑
Uniform MH	0.0201 [0.0183, 0.0218]	0.1532	1518	0.525
Local pivot MH	0.0260 [0.0238, 0.0280]	0.1822	666	0.341
Classical diffusion MH	0.0202 [0.0182, 0.0220]	0.1504	1485	0.528
Quantum-walk MH	0.0201 [0.0189, 0.0212]	0.1533	1383	0.514
Energy-conditioned QW	0.0396 [0.0358, 0.0435]	0.1927	239	0.569

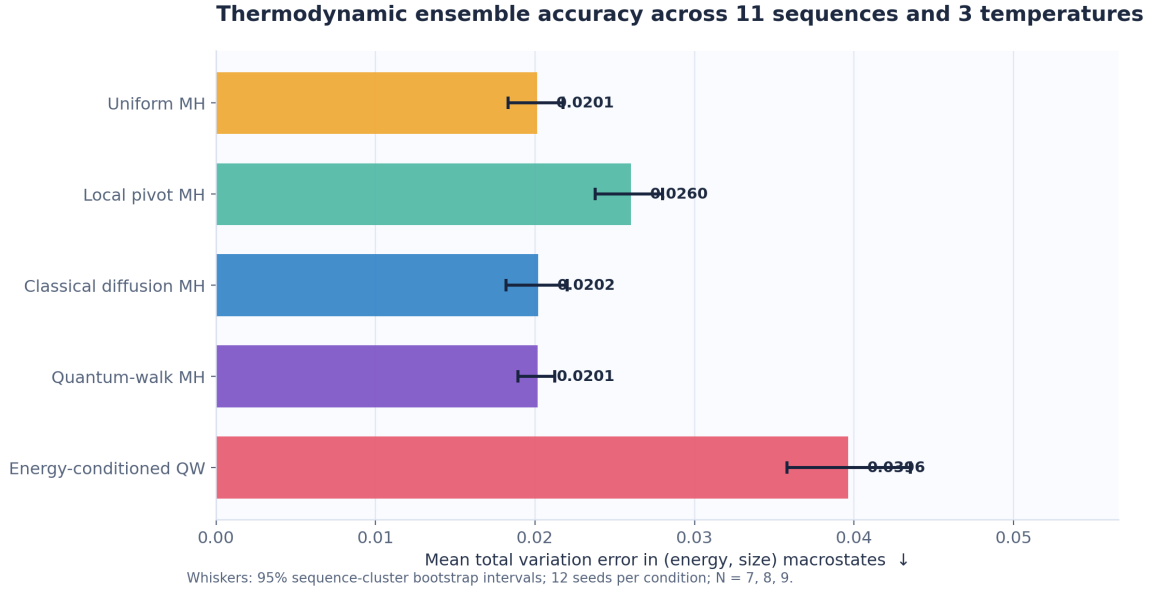


Figure 2: Macrostate distribution error across all 11 sequences and three temperatures, with sequence-cluster bootstrap intervals. The quantum and classical global kernels are statistically difficult to distinguish on this toy panel.

The complete-state TV distances also do not favor quantum transport: classical heat obtains 0.1504 versus 0.1533 for the quantum walk. These are finite-sample errors based on $M \gg 1$ individual states and should not be interpreted as a systematic bias of the invariant distribution. Every tested symmetric kernel has the same exact Boltzmann stationary distribution under MH correction.

5.2 Sensitivity to chain length

The enumeration sizes grow from 195 to 1479 across the panel. Table 3 and Fig. 3 show how the empirical macrostate error changes when only 4,000 samples are retained. The $n = 9$ quantum walk is slightly better than diffusion by macrostate TV (0.0226 versus 0.0240), but *worse* by full-state TV (0.2388 versus 0.2313) and energy ESS (1063 versus 1244). Thus apparent improvement under a coarse partition must not be taken as improved microscopic mixing.

Table 3: Mean macrostate TV stratified by chain length, averaged across all temperatures, sequences, and seeds.

n	Uniform	Pivot	Classical diffusion	Quantum walk	Energy-conditioned
7	0.0159	0.0210	0.0159	0.0168	0.0273
8	0.0211	0.0265	0.0205	0.0206	0.0383
9	0.0227	0.0303	0.0240	0.0226	0.0541

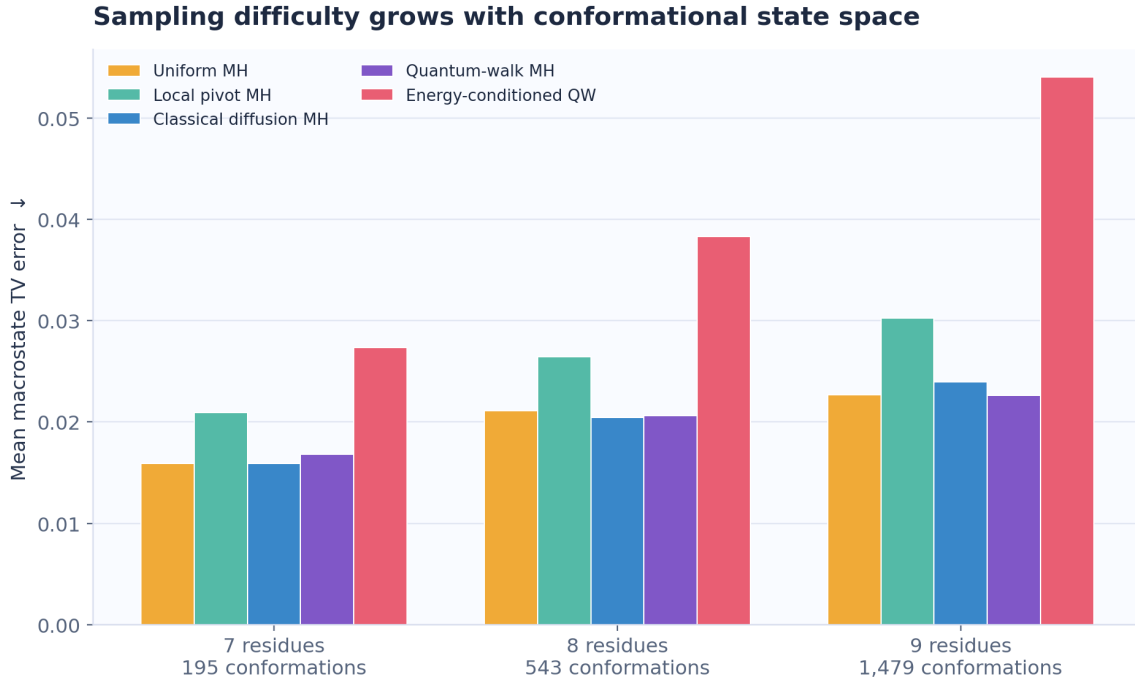


Figure 3: Distributional error by chain length; increasing catalog size makes exact microscopic frequency estimation more demanding. Identical iteration counts do not imply matched computational costs.

5.3 The high-acceptance trap

The energy-conditioned quantum walk has a mean MH acceptance probability of 0.9444, greater than any other method, but its mean energy ESS is only 239 of 4,000 retained observations

and its mean macrostate TV is 0.0396. Conversely, heat diffusion accepts 0.5579 of candidates but yields a much larger energy ESS of 1485. Accepted self-proposals and correlations between geometrically close states help explain why acceptance cannot substitute for mixing diagnostics. The energy-conditioned walk also changes states more often than the unconditioned walk in this particular experiment; therefore merely counting different conformations is not sufficient either. Both effects reinforce the importance of *observable-specific autocorrelation* and distributional error (Fig. 4).

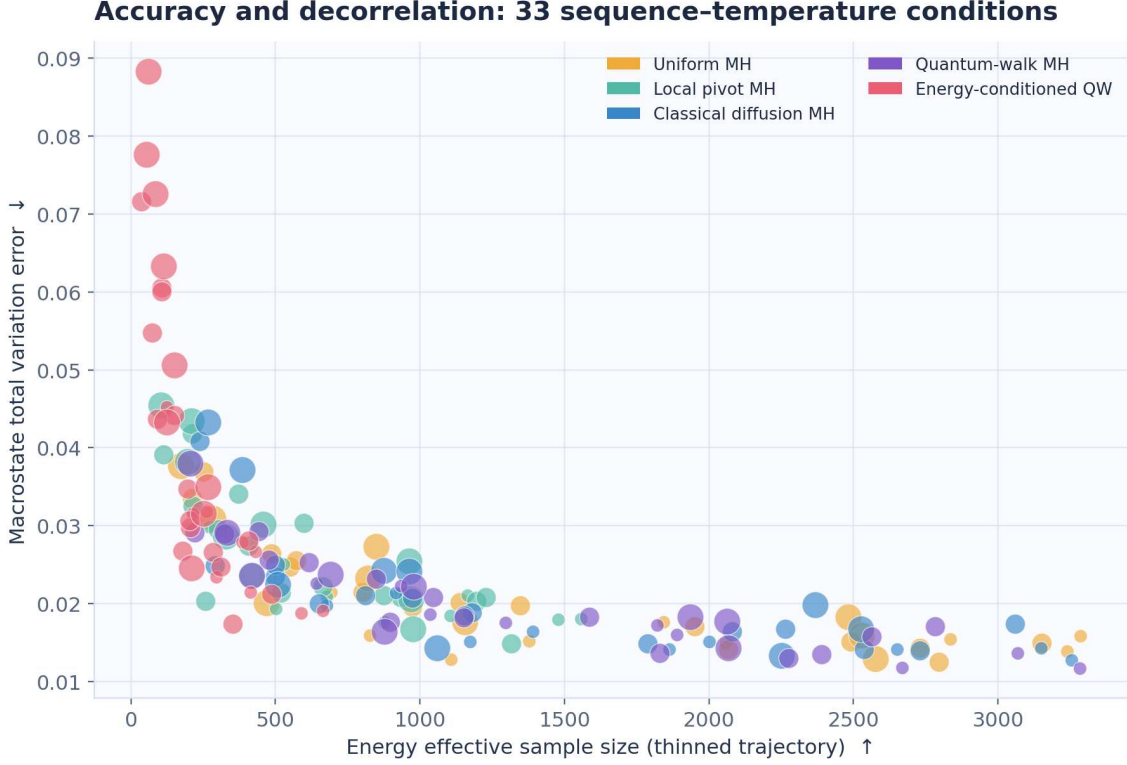


Figure 4: Energy ESS versus macrostate error for 33 conditions per method (point sizes increase with chain length). Error and decorrelation measure different aspects of finite-budget sampling.

5.4 Exact mixing calculations

For $n = 8$, the exact linear-system diagnostic in Eq. 9 gives mean $\tau_{\text{int,E}} = 24.53$ unthinned iterations for classical diffusion and 26.12 for the unconditioned quantum walk at $t = 9$, versus 26.97 for uniform MH, 55.03 for local pivot MH, and 154.39 for the energy-conditioned walk. These are arithmetic means over the five sequences and three temperatures, not empirical confidence intervals. They corroborate the Monte Carlo study’s central conclusion without requiring simulations to run long enough to resolve rare full-state events.

The time scan in Fig. 5 shows that coherent transport is not monotonically improved by increasing t : the mean quantum-walk energy IAT is approximately 119.12, 37.37, 26.12, 26.92, and 27.87 for $t = 3, 6, 9, 12, 18$, whereas classical heat obtains 30.06, 24.58, 24.53, 25.21, and 26.24. Thus our chosen $t = 9$ gives near parity under one metric, but no evidence for a robust improvement over diffusion across the scan. The energy-conditioned walk degrades energy decorrelation considerably.

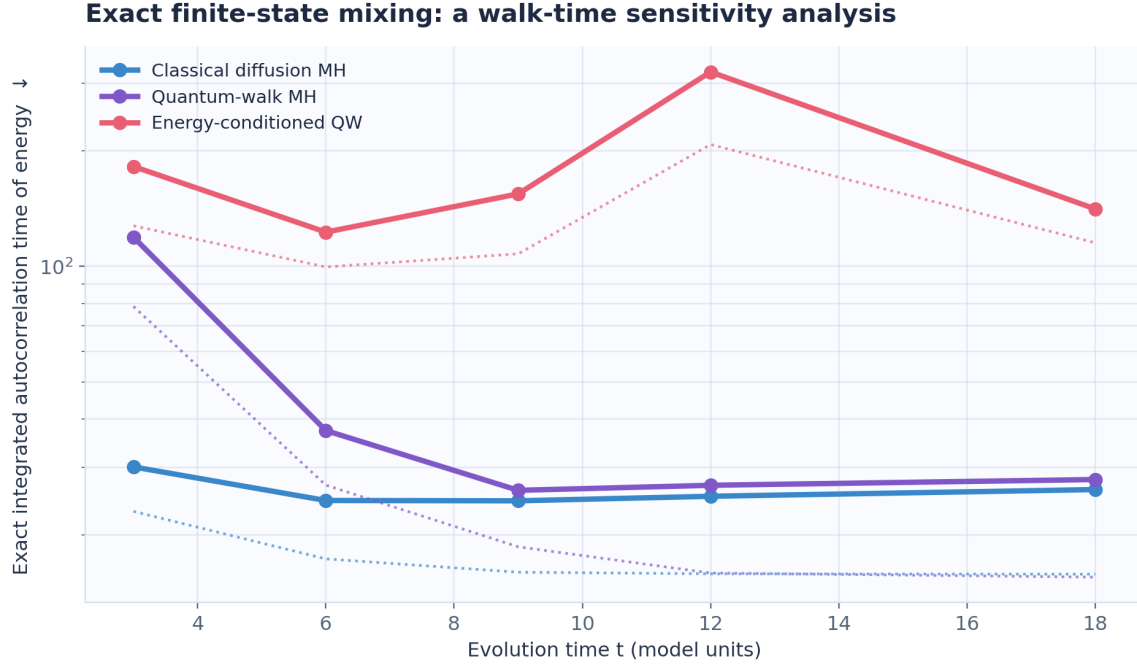


Figure 5: Mean (solid) and median (dotted) exact energy integrated autocorrelation time at $n = 8$ as a function of evolution time. Both axes represent *model-level* quantities, not hardware runtime or circuit depth.

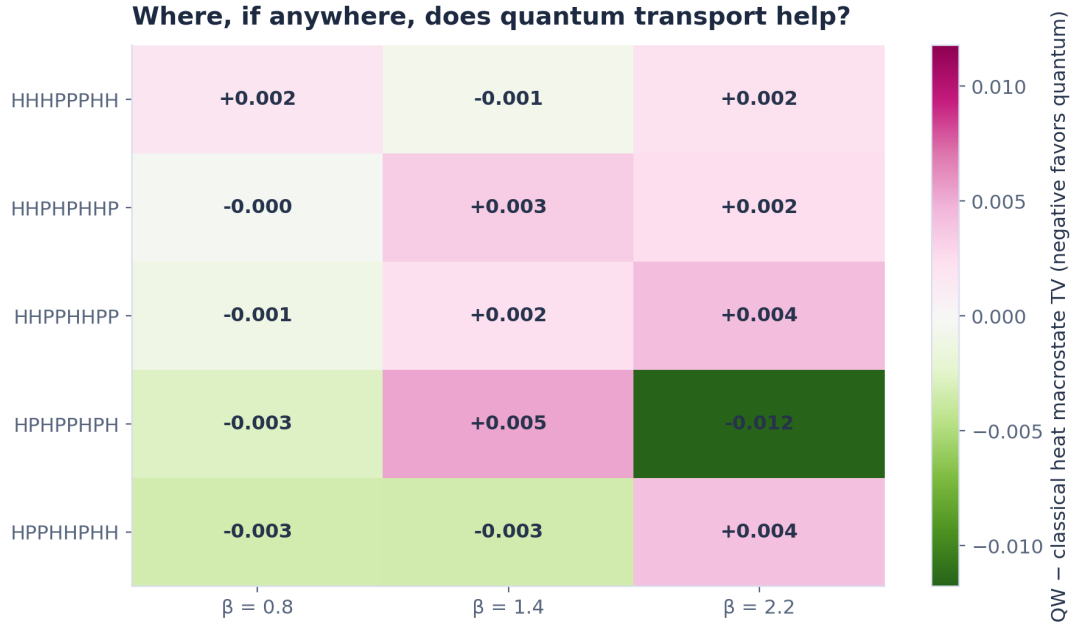


Figure 6: Condition-wise quantum-minus-classical mean macrostate TV for the $n = 8$ sequence panel. Negative cells favor quantum proposals; positive cells favor classical diffusion. Differences change sign across sequences and temperatures.

6 Discussion

6.1 What was demonstrated

The mathematical result is exact: a real-symmetric conformation-graph Hamiltonian generates symmetric measured proposal probabilities, and Metropolis correction preserves canonical equilibrium populations irrespective of the interference pattern. This construction avoids the need to *estimate* the ratio of quantum proposal probabilities for an independence-MH correction. It also restricts the Hilbert-space dynamics to valid conformational labels in the abstract model, rather than allocating amplitudes to impossible bitstrings and discarding them afterward.

The computational result is narrower. Over short HP chains, fixed-time coherent quantum transport behaves similarly to a strong classical heat-kernel comparator and uniform global proposals, and generally beats the particular local pivot proposal under a fixed MH-iteration budget. The quantum-walk and classical-heat advantages over local pivot sampling should not be mistaken for a quantum effect: both global kernels are computed from the fully enumerated state graph and require much greater preprocessing access than an on-the-fly structural pivot. The energy-conditioned Hamiltonian is an instructive negative control, demonstrating that incorporating protein-like energy into a quantum generator does not automatically improve equilibrium sampling.

6.2 Prior art and relationship to learning-based methods

Symmetric quantum proposals have antecedents in quantum-enhanced MCMC [6], while the broader theoretical possibility of quantum walk implementations of MH has received recent attention [7]. The present work should consequently be read as a *biophysically structured benchmark and numerical ablation*, rather than the discovery of quantum MCMC. It also differs from quantum annealing approaches to HP *minimum-energy* structures and sequence design [11]: ground-state discovery does not quantify finite-temperature conformational populations. Protein ensemble generation is itself a broad classical research field, with existing flow-based and learning-enhanced alternatives [8, 9, 10]. None is replaced by the present small-lattice approach.

A future tail-sensitive Q-TAILOR extension could vary the real diagonal of H using conformational rarity or an energy-barrier proxy while retaining symmetry, and could learn the evolution schedule on a development set. However, such a modification would require a rigorous comparison with optimized classical generators, control of parameter-selection bias, and an explicit resource model. The energy-conditioned negative result here argues against introducing a CVaR-like term simply because it appeared in the author’s earlier synthetic-model studies.

6.3 Critical limitations

1. **Not realistic proteins.** The two-dimensional HP model includes neither side chains, solvent, sequence-specific real force fields, off-lattice degrees of freedom, nor folding kinetics. It does not validate structure prediction or experimental protein ensemble inference.
2. **Full enumeration is built in.** Every graph vertex is explicitly represented. The simulated quantum Hamiltonian is an $M \times M$ matrix, and each proposal row is precomputed numerically. This preprocessing becomes exponentially unfavorable with chain length. The $n = 9$ case is not a meaningful scale-up to biological proteins.
3. **No hardware implementation or gate compilation.** The simulation assumes the ability to prepare $|x\rangle$, implement e^{-itH} , and measure the appropriate feasible-state basis. Efficient

sparse-Hamiltonian access, state encoding, connectivity oracles, qubit counts, Trotter errors, coherent depth, and fault-tolerance requirements remain unestablished.

4. **Proposals and evaluation have privileged state access.** Uniform and heat-kernel competitors also use an exact catalog, so the comparison is internally controlled but not between deployable implementations. The theoretical symmetry removes the need for probability *evaluation at acceptance*, but does not make state preparation or Hamiltonian simulation free.
5. **Matched steps are not matched cost.** All methods use 24,000 MH proposals, but a classical pivot, a dense matrix multiplication, and a hardware quantum walk are not comparable in elementary-operation, gate, or energy costs. No hardware or wall-clock speedup claim is made.
6. **Small and exploratory panel.** Only 11 manually selected HP strings and three temperatures were studied. The CI reflects variability across this toy sequence panel, not a universal statement about proteins. The evolution-time scan is exploratory, not independent confirmation of a tuned method.
7. **Coarse observables can mask errors.** Energy–shape bins do not fully resolve configurations; full-state TV and exact energy IAT are therefore reported alongside macrostate error.

7 Conclusion and research outlook

A geometry-based, reversible quantum proposal can be combined with classical Metropolis acceptance to recover the exact finite-temperature Boltzmann distribution without evaluating the proposal probability ratio. On 11 short HP sequences and 33 test conditions, an unconditioned coherent quantum walk gives roughly the same ensemble accuracy as classical diffusion or uniform global proposals, while the tested energy-conditioned potential worsens several mixing measures. This is a useful negative-control result in computational biophysics: *interference and high acceptance are insufficient evidence of improved conformational mixing*. The most valuable next step is not to assert an advantage but to develop physically meaningful, resource-accounted walk Hamiltonians and test them against optimized classical baselines on larger, independently selected model systems. Hardware claims must await a plausible valid-conformation encoding and circuit-level cost analysis.

Reproducibility and author declarations

Computational provenance. All results in this draft were generated with the accompanying Python scripts and CSV outputs. Key requirements are Python 3, NumPy, SciPy, Pandas, Matplotlib, Numba, and threadpoolctl. Source file `research.py` runs the $n = 8$ panel; `size_extension.py` covers $n = 7$ and $n = 9$; `exact_mixing.py` computes Eq. 9; and `analyze.py` regenerates tables and figures. Exact run settings and seeds are preserved in the source. The reported environment used NumPy 2.3.5, SciPy 1.17.0, Pandas 2.2.3, Matplotlib 3.10.8, and Numba 0.65.1. All quantum evolution was classically simulated. Before submission, archive the code with a persistent public version identifier and independent reproduction logs.

Data availability. Synthetic enumeration and all primary runs, exactly enumerated observables, finite-state autocorrelation data, figure sources, and summary statistics are included in the accompanying research archive; no public repository DOI has yet been assigned.

Funding and conflicts of interest. Author confirmation required before submission. No funding source or conflict is inferred by the software. **Ethics.** No human participants, animals, or patient data. **AI use disclosure.** Computational scripts, analysis, figure generation, and editorial drafting were developed with substantial AI assistance and require full author verification and disclosure consistent with the target journal’s policies **Affiliation.** Independent Researcher.

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