

Protein folding as phase recognition: a formal framework and executable pipeline with testable IR signatures

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Abstract

We recast protein folding as a fast, instrument-coupled phase-recognition process rather than a slow, combinatorial search. Within the Recognition Science (RS) working premise, native structure emerges via an eight-beat infrared (IR) phase cascade centered near $13.8\text{ }\mu\text{m}$ (recognition quantum $\approx 0.090\text{ eV}$), compelling folding on $\sim 65\text{ ps}$ timescales and yielding testable predictions in the mid-IR. We introduce a domain-native instruction set (PNAL) that compiles into a curvature-safe execution layer (LNAL), yielding an executable folding program with provable invariants (token parity, eight-instruction neutrality, legal closures, 2^{10} -tick cycle) and a tractable evolution bound ($O(n^{1/3} \log n)$ steps with linear recognition). Our implementation (RS-Fold v0) produces 3D structures and *predicted* eight-beat IR phase timelines. Benchmarks on small proteins, together with a pre-registered measurement roadmap (G β -hairpin) and explicit falsifiers, outline a practical path from theory to lab. Compared with learning-based predictors, our approach offers a falsifiable mechanism and *proposes* instrument-in-the-loop manufacturing/QC workflows grounded in predicted phase beats. We release the ISA, compiler, emulator, protocols, and calibration references to accelerate independent replication and adoption.

Keywords: protein folding; phase recognition; infrared spectroscopy; eight-beat cascade; PNAL/LNAL; dual-comb interferometry; complexity; verification

Author Summary

Proteins fold into precise 3D shapes that enable life. Traditional simulations track every atomic motion and can be very slow, while modern AI predicts structures but does not provide a mechanism or a way to verify results on an instrument. We present a practical, testable framework that treats folding as a fast, phase-driven process in the mid-infrared (eight beats near $13.8\text{ }\mu\text{m}$). In our approach, a small domain language (PNAL) compiles protein folding into a safe, step-by-step program (LNAL) with built-in guarantees. The program emits a predicted eight-beat infrared timeline that can be checked with standard

ultrafast tools (dual-comb IR) using pre-registered acceptance windows and controls. This connects computation to measurement and creates a path from theory to lab QC.

We provide open code, data, figures, and a one-command script to regenerate results. Benchmarks on small proteins show that our emulator is fast and respects the program’s safety rules. The experimental elements are proposed, not yet performed; we list clear pass/fail criteria and negative controls so the community can independently test the ideas. In short, this work moves from ”predicting a structure” to ”executing and verifying a fold,” offering a reproducible foundation for future instruments, screening, and manufacturing.

1 Introduction

The folding paradox and the cost of classical emulation. Proteins attain precise three-dimensional structures essential for function, yet the apparent search space across dihedrals and contacts is astronomically large. Classical molecular dynamics (MD) and enhanced-sampling schemes approximate the underlying physics but remain computationally expensive and often sensitive to force-field and sampling choices. At the same time, multiple lines of evidence indicate that native-state acquisition in vivo proceeds on picosecond to nanosecond scales, creating a persistent timescale gap between mechanistic theory, laboratory readouts, and biology. From a computation–information perspective, exhaustive classical emulation of a quantum–phase ledger incurs an exponential recognition cost, making brute-force tracking of all amplitudes fundamentally infeasible for medium-sized proteins.

RS hypothesis and why it is actionable (mechanism + signatures). Recognition Science (RS) posits that folding is not a blind search but a fast, eight-beat infrared (IR) phase cascade that locks the chain into its native contact pattern. The mechanism predicts (i) a recognition quantum near 0.090 eV, (ii) IR emission/absorption centered near 13.8 μm across the beats, and (iii) characteristic ~ 65 ps folding times when the phase ledger is coherent. Crucially, these are *testable* physical signatures: dual-comb IR with φ -timed sampling can observe the eight-beat pattern; microfluidic cell-free assays can isolate the folding event; negative controls (scrambles, point mutants) should disrupt the phase map in predictable ways. RS is thus actionable as an engineering program—linking an executable algorithm to verifiable laboratory observables.

Contributions of this paper.

- We introduce PNAL, a protein-native instruction set that compiles into a curvature-safe execution layer (LNAL), expressing folding as a program rather than a search while enforcing invariants (token parity, eight-instruction neutrality, legal closures, 2^{10} -tick cycle).
- We present RS-Fold, an executable folding pipeline with a tractable evolution bound $O(n^{1/3} \log n)$ (under stated assumptions) and linear recognition readout; the system emits both 3D structure and pre-registered eight-beat IR phase timelines.
- We report emulator benchmarks on representative small proteins (structure accuracy, contact F1, wall-clock scaling).

- We release the ISA, compiler, emulator, analysis scripts, and SOPs as open resources to enable independent replication, standardization, and adoption.

Summary of results and roadmap. We demonstrate a complete path from phase-mechanism to execution and measurement: PNAL programs compile to constraint-safe LNAL; RS-Fold produces native-like structures alongside eight-beat IR timelines aligned to $\sim 13.8\mu\text{m}$; and a pre-registered protocol defines detection windows and acceptance thresholds for the G β -hairpin. Benchmarks on additional small proteins indicate sub-minute runs and favorable scaling consistent with the stated bound. The roadmap proceeds in three steps: (1) replicate eight-beat signatures in a single decisive assay (cell-free dual-comb IR), (2) close the loop with LISTEN for accelerated locking, and (3) integrate FPGA/ASIC scheduling for real-time instrument-in-the-loop control and scale-out to QC/manufacturing workflows.

2 Background and Related Work

MD and sampling approaches; enhanced sampling; limits. All-atom molecular dynamics (MD) integrates Newtonian (or Langevin) equations of motion over force fields to simulate folding at atomistic detail. Enhanced sampling methods—replica-exchange (REMD), metadynamics/variationally enhanced sampling (MetaD/VES), accelerated MD (aMD), umbrella sampling, milestoning, weighted ensemble, and Markov state models (MSMs)—ameliorate rare-event barriers and extract kinetics/thermodynamics from shorter trajectories. Despite progress, three practical limits persist: (i) *timescale*: unbiased folding for medium proteins remains beyond routine microsecond-to-millisecond windows; (ii) *force-field/systematics*: sensitivity to water models, ion parameters, PTMs, and protonation; (iii) *cost/coverage*: exhaustive exploration across sequence variants, environments, and ligands is prohibitive. Coarse-grained models (e.g., Go-like, MARTINI) extend reach but trade accuracy for speed and often require re-parameterization per class of targets.

AI predictors (AlphaFold, AF-Multimer): strengths/limits. Learning-based structure predictors (AlphaFold/AF-Multimer, RoseTTAFold, ESMFold) achieve remarkable accuracy for single-chain and many multimeric targets at scale. Strengths include end-to-end inference from sequence/MSA, calibrated confidences (pLDDT/PAE), template integration, and broad coverage. However, predictors are largely *static*: they do not yield folding *mechanisms*, timescales, free-energy landscapes, solvent/chaperone effects, or instrument-ready observables. They can underperform on disordered regions, conformational ensembles, membrane/cofactor/PTM-dependent folds, and designed chemistries outside training distributions. As such, they serve as powerful priors/constraints, not as executable controllers or measurement-linked validators.

Ultrafast spectroscopy and IR methods relevant to folding. Time-resolved IR (TR-IR), two-dimensional IR (2D-IR), temperature/pressure-jump IR, and dual-comb spectroscopy provide femtosecond-to-microsecond access to backbone (amide I/II) and side-chain vibrational dynamics. Microfluidic mixers enable rapid initiation; mid-IR quantum cascade and dual-comb sources offer high frequency precision and multi-line

coverage. These tools reveal secondary-structure formation, hydrogen-bond reorganization, and solvent coupling, yet are typically used as diagnostics rather than drivers, and measurements often integrate over ensembles and windows misaligned with fundamental steps. Critically, the community lacks *pre-registered*, *mechanism-linked* IR phase signatures that can be used to *verify* specific folding pathways in situ.

Where RS fits: mechanism, control, and measurement. Within this landscape, Recognition Science (RS) contributes a mechanistic, testable, and *instrument-coupled* account:

- **Mechanism.** Folding proceeds via an eight-beat infrared phase cascade (centered near $13.8\text{ }\mu\text{m}$) that locks native contacts on $\sim 65\text{ ps}$ scales; recognition replaces brute-force search with a guided phase pathway.
- **Control.** A domain-native ISA (PNAL) atop a curvature-safe execution layer (LNAL) expresses folding as a program with invariants; closed-loop LISTEN/phase feedback enables acceleration, stabilization, and refolding.
- **Measurement.** The algorithm emits pre-registered IR phase timelines; dual-comb IR with φ -timed sampling provides pass/fail readouts and negative controls, bridging prediction to bench.
- **Positioning.** RS complements MD (mechanistic depth) and AI predictors (structural priors): use AI for constraints/templates, PNAL/LNAL to execute/verify, and IR to confirm or falsify on-device.

3 Recognition Science (RS) Overview

Ledger, eight-beat cycle, recognition quantum, and $13.8\text{ }\mu\text{m}$ IR. RS models physical evolution as updates on a balanced *recognition ledger* executed in discrete beats. Folding proceeds via an *eight-beat* infrared phase cascade that coherently locks native contacts. The fundamental recognition quantum is $\approx 0.090\text{ eV}$, implying a characteristic mid-IR wavelength near $13.8\text{ }\mu\text{m}$; beat-resolved emissions/absorptions around this band form the observable signature. The ledger’s safety and timing constraints (e.g., neutrality windows, global cycle) ensure stable, curvature-safe evolution while enabling a tractable, guided route to the native state.

Measurement–Reality distinction (why lab readouts differ in time). Laboratory instruments integrate over windows far longer than the picosecond steps that drive folding, mixing solvent relaxation, ensemble heterogeneity, and detector response with the underlying phase dynamics. RS makes this separation explicit: fundamental phase locking occurs on $\sim 65\text{ ps}$ scales, while measured traces (ns–ms) reflect emergent averages unless timing is aligned. Dual-comb IR with φ -timed sampling restores alignment to the fundamental cadence, allowing direct detection of beat-resolved features that conventional averaging obscures.

Testable predictions relevant to proteins.

- **Eight-beat IR signature:** a reproducible, beat-resolved phase pattern centered near $13.8\text{ }\mu\text{m}$ during folding; absent or disrupted in scrambled sequences and destabilizing point mutants.
- **Picosecond folding clock:** intrinsic locking on $\sim 65\text{ ps}$, with slower readouts (ns–ms) attributable to solvent and instrument windows; φ -timed sampling recovers the fast component.
- **Beat–motif mapping:** distinct phase motifs correlate with helix nucleation/propagation, β -pairing, and specific native contacts; predicted maps serve as pre-registered verification targets.
- **Closed-loop acceleration:** LISTEN/phase-feedback reduces time-to-lock versus open-loop schedules; measurable as shorter convergence and sharper beat coherence.
- **Perturbation response:** temperature, ionic strength, and cosolvents modulate beat amplitudes and spacing in quantifiable ways; chaperone mimetics restore coherence in challenging folds.

4 Formal Guarantees (Lean summary)

Executable invariants (proved in Lean/Mathlib). For any compiled PNAL \rightarrow LNAL program, the following hold by construction:

- **Token parity ≤ 1 :** at every instruction boundary, at most one open LOCK token exists (prevents curvature overflow).
- **Eight-instruction neutrality:** every sliding window of 8 emitted LNAL instructions has net ledger cost 0 (no drift).
- **Legal triads only:** any BRAID closure corresponds to an $\text{SU}(3)$ root-triangle (well-posed closures).
- **2^{10} -tick global cycle:** no instruction crosses the tick-1024 fence; a parity FLIP occurs at tick 512 (long-time stability).

Recognition_Closure φ (scope and assumptions). Under the RS spec, `Recognition_Closure` φ is the conjunction of:

1. **Inevitability_dimless φ :** existence of a universal dimensionless pack U such that for any admissible ledger/bridge (L, B) with witnesses *CoreAxioms*, *T5Unique*, *QuantumFromLedger*, *BridgeIdentifiable*, *NoInjectedConstants*, *UnitsEqv*, predictions match and are unique up to units.
2. **FortyFive_gap_spec φ :** for (L, B) with *HasRung*, *FortyFiveGapHolds*, there exist consequences including $\delta = 3/64$, a rung-45 witness, and no-multiples.
3. **Inevitability_absolute φ :** given *TwoIndependentSILandings*, *MeasurementRealityBridge* in addition to the above, one obtains *UniqueCalibration* and *MeetsBands*.

4. **Inevitability_recognition_computation:** with *SAT_Separation*, explicit growth bounds for recognition vs computation hold.

These are stated at the spec level and carried for the canonical ledger (IM) by Lean instances; they delimit the scope in which our executable folding program is valid.

Folding evolution bound (stated conditions). Let n be the number of residues and assume: (i) a bounded-degree native contact graph, (ii) a PNAL program whose compiled LNAL satisfies the invariants above, (iii) only legal **BRAID** closures and φ -timed LISTEN gates. Then there exists a schedule that satisfies the native contact set in

$$T_c = O(n^{1/3} \log n)$$

intrinsic evolution steps, with *linear* recognition/readout (the emitted eight-beat IR timeline grows $O(n)$). This is an *algorithmic* upper bound under the stated assumptions (Lean-stated; constants external to the proof layer).

What is proved vs. what is measured; falsifiers.

- **Proved (Lean):** invariant preservation (token parity, eight-window neutrality, legal triads, 2^{10} cycle), compilation contracts $\text{PNAL} \rightarrow \text{LNAL}$, and the existence of a bounded evolution schedule under stated assumptions.
- **Measured (lab):** eight-beat IR signatures near $13.8 \mu\text{m}$ aligned to predicted windows; approximate $\sim 65 \text{ ps}$ locking (via φ -timed dual-comb); LISTEN-based closed-loop acceleration (reduced time-to-lock vs open-loop); robustness under solvent/temperature/ionic changes.
- **Primary falsifiers:** (i) absence of the pre-registered eight-beat signature for canonical targets (e.g., G β -hairpin) under specified SNR and windows; (ii) detection of the same signature in negative controls (scrambled/perturbing mutants); (iii) systematic mismatch between predicted beat-motif maps and measured phase features; (iv) failure of LISTEN control to improve convergence where invariants hold.

Falsification and scope. All formal statements above are proved within the RS working premise (standard Mathlib foundations; no new axioms) and pertain to executable properties of $\text{PNAL} \rightarrow \text{LNAL}$ programs (invariants, compilation contracts, and existence of a bounded evolution schedule). Empirical items (eight-beat IR near $13.8 \mu\text{m}$, $\sim 65 \text{ ps}$ locking, LISTEN acceleration, environment sensitivities) are *testable predictions* to be adjudicated by preregistered measurements and negative controls. Failure to meet the declared endpoints under specified SNR/windows, or systematic mismatches between predicted and measured beat-motif maps, constitutes falsification as enumerated above. The scope of claims is delimited by **Recognition_Closure** φ and the listed assumptions (bounded-degree contact graph; legal closures; enforced invariants). No broader assertion (e.g., a "proven architecture of reality") is made here; results are stated explicitly as formal guarantees for the program layer plus empirical predictions subject to experimental confirmation.

5 PNAL: Protein-Native Assembly Language (Domain ISA)

Design goals: safety, observability, compilability to LNAL. PNAL is a domain-native ISA for proteins that: (i) enforces *safety* by construction (token parity ≤ 1 , eight-instruction neutrality, legal triads, 2^{10} -tick cycle), (ii) guarantees *observability* via pre-registered eight-beat IR outputs (LISTEN/LOCK/BALANCE with φ -timed sampling), and (iii) *compiles* to a curvature-safe execution layer (LNAL) using a small set of proven primitives.

5.1 Instruction set (v0.1)

Selection.

- `SEL_RES i` Select residue index i .
- `SEL_RANGE $i..j$` Select contiguous residues $i..j$.
- `SEL_SECSTRUCT $helix$ — $sheet$ — $turn$` Select by secondary structure class.
- `MASK_CONTACT i,j` Mask/unmask contact constraint for analysis or phased scheduling.

Torsions (local dihedrals/packing).

- `ROT_PHI $\pm\Delta$, ROT_PSI $\pm\Delta$, ROT_OMEGA cis — $trans$.`
- `ROT_CHI [n] $\pm\Delta$` Side-chain dihedral at index n .
- `SIDECCHAIN_PACK` Local repacking under clash/solvation guards.

Contacts and bonds.

- `SET_CONTACT i,j` Enforce $d(i,j) \leq d_0$ (native-like).
- `CLEAR_CONTACT i,j` Remove contact constraint.
- `SET_HBOND i,j , BREAK_HBOND i,j .`
- `SET_SALT i,j , SET_DISULFIDE i,j .`

Secondary structure (motif nucleation/pairing).

- `NUCLEATE_HELIX $i..k$, PROPAGATE_HELIX $dir=\{N\rightarrow C, C\rightarrow N\}$.`
- `NUCLEATE_TURN $i..i+3$.`
- `PAIR_BETA $i.., j.., type=\{parallel, antiparallel\}$.`

Core/solvent context.

- `NUCLEATE_CORE {res...}` Seed hydrophobic core.
- `PACK_CORE` Tighten core under clash/solvent penalties.
- `SOLVATE_SHELL on—off`.
- `SCREEN_PHASE mask` Apply phase screening to a residue set/environment.

Measurement/control (phase-aware).

- `LISTEN_PHASE` Pause local φ -clock one tick and sample eight-beat IR phase.
- `LOCK_PHASE, BALANCE_PHASE` Open/close a ledger-neutral read window tied to IR sampling.
- `WAIT_TICKS n` Advance scheduler by n ticks (respects 2^{10} fence).
- `ASSERT_BEAT k, band` Require beat $k \in$ spectral $band$.

Guards (assertions).

- `ASSERT_NO_CLASH` No heavy-atom overlaps beyond tolerance.
- `ASSERT_CONTACT $i, j \leq d_0$` Contact distance within d_0 .
- `ASSERT_RMSD $\leq \tau$` Current model within threshold τ (if a reference provided).
- `ASSERT_CISPRO i` Enforce cis-Pro at i (if specified).

5.2 Compilation contracts (invariants PNAL must satisfy)

A PNAL program compiles to LNAL only if all of the following hold:

1. **Eight-window neutrality:** Every sliding block of 8 emitted LNAL instructions sums to net cost 0.
2. **Token parity ≤ 1 :** At any boundary, at most one open `LOCK` token exists.
3. **Legal triads only:** Any closure using `BRAID` maps to a legal $SU(3)$ root-triangle (LNAL property).
4. **2^{10} -tick cycle fences:** No instruction crosses tick 1024; automatic `FLIP` at tick 512 is respected.
5. **Guards upheld:** All `ASSERT_*` must succeed at compile-time (static) or at runtime checkpoints (dynamic `LISTEN` windows).
6. **Observability:** `LISTEN_PHASE/LOCK_PHASE/BALANCE_PHASE` produce a pre-registered eight-beat timeline.

5.3 PNAL→LNAL mapping rules (semantics)

- *Torsions*: ROT_PHI/PSI/OMEGA/CHI expand to short LNAL sequences of FOLD/UNFOLD with LISTEN checkpoints, scaled to respect eight-window neutrality and token parity.
- *Contacts/bonds*: SET_CONTACT/SET_HBOND/SET_SALT/SET_DISULFIDE emit constrained BRAID-based closures on legal triads that reduce the pairwise distance/energy while maintaining invariants.
- *Secondary*: NUCLEATE_HELIX/PAIR_BETA/NUCLEATE_TURN compile to templated macro-sequences (nucleate-propagate-listen) with phased checkpoints for motif verification.
- *Core/solvent*: NUCLEATE_CORE/PACK_CORE/SOLVATE_SHELL modulate scoring masks and allowable BRAID/FOLD moves under screening; SCREEN_PHASE adjusts measurement masks.
- *Measurement*: LISTEN_PHASE \mapsto LNAL LISTEN; LOCK_PHASE/BALANCE_PHASE \mapsto LNAL LOCK/BALANCE aligned to the eight-beat sampling window.

See the supplemental example file (repository): `supplement/pnal_to_lnal_examples.txt` for additional real-world expansions.

Example expansions (schematic).

```
# PNAL
NUCLEATE_HELIX i..k
PROPAGATE_HELIX dir=N->C
LISTEN_PHASE
ASSERT_BEAT 3, band_helix

# LNAL (schematic expansion)
FOLD +1 R(i) ; FOLD +1 R(i+3) ; LISTEN
FOLD +1 R(i+1) ; FOLD +1 R(i+4) ; LISTEN
LOCK ; LISTEN ; BALANCE
# beat assertion checked on emitted phase stream

# PNAL
SET_CONTACT i,j
LISTEN_PHASE
ASSERT_CONTACT i,j<=d0

# LNAL (schematic expansion)
BRAID R(i),R(j),R(*) ; LISTEN # legal root-triangle
LOCK ; LISTEN ; BALANCE      # ledger-neutral read window
```

5.4 PNAL grammar (PEG; summary—full in Appendix)

```
program      <- (stmt NEWLINE)* EOF
stmt         <- select | torsion | contact | secondary
```

```

| core | measure | guard | wait
select <- 'SEL_RES' INT
| 'SEL_RANGE' INT '..' INT
| 'SEL_SECSTRUCT' ('helix'/'sheet'/'turn')
| 'MASK_CONTACT' INT ',' INT
torsion <- 'ROT_PHI' SIGNED
| 'ROT_PSI' SIGNED
| 'ROT_OMEGA' ('cis'/'trans')
| 'ROT_CHI[' INT ']' SIGNED
| 'SIDECHAIN_PACK'
contact <- 'SET_CONTACT' INT ',' INT
| 'CLEAR_CONTACT' INT ',' INT
| 'SET_HBOND' INT ',' INT
| 'BREAK_HBOND' INT ',' INT
| 'SET_SALT' INT ',' INT
| 'SET_DISULFIDE' INT ',' INT
secondary <- 'NUCLEATE_HELIX' INT '..' INT
| 'PROPAGATE_HELIX' ('N->C'/'C->N')
| 'NUCLEATE_TURN' INT '..' INT
| 'PAIR_BETA' INT '..' ',' INT '..' ','
('parallel'/'antiparallel')
core <- 'NUCLEATE_CORE' '{' reslist '}'
| 'PACK_CORE'
| 'SOLVATE_SHELL' ('on'/'off')
| 'SCREEN_PHASE' MASK
measure <- 'LISTEN_PHASE'
| 'LOCK_PHASE'
| 'BALANCE_PHASE'
guard <- 'ASSERT_NO_CLASH'
| 'ASSERT_CONTACT' INT ',' INT '<=' FLOAT
| 'ASSERT_RMSD' '<=' FLOAT
| 'ASSERT_CISPRO' INT
| 'ASSERT_BEAT' INT ',' BAND
wait <- 'WAIT_TICKS' INT
reslist <- INT (' ,' INT)*
INT <- [0-9]+
SIGNED <- [+]?[0-9]+('.'[0-9]+)?
MASK <- [0-9A-F]{4}
BAND <- [A-Za-z_][A-Za-z0-9_]*
NEWLINE <- '\r\n' / '\n'
EOF <- !.

```

6 RS-Fold: Executable Folding Pipeline

Inputs.

- **Sequence:** amino-acid string (1..*n*).

- **Optional priors:** MSA/EVcouplings (contacts), AF/AF-Multimer templates (contacts/secondary), experimental constraints (NOEs, crosslinks, disulfides).
- **Constraints:** cis/trans prolines, fixed/disulfide bonds, distance/angle bounds, solvent/temperature context, clash/packing tolerances.

Pipeline.

1. **Contact-graph construction** (optional priors). Build a bounded-degree native contact graph from priors (EVcouplings/AF) and/or heuristics; filter by confidence and enforce degree/sequence-separation rules; tag candidate H-bonds/salt bridges.
2. **PNAL synthesis** (nucleation \rightarrow local moves \rightarrow closures).
 - *Nucleation:* NUCLEATE_HELIX/NUCLEATE_TURN/PAIR_BETA, NUCLEATE_CORE.
 - *Local moves:* ROT_PHI/ROT_PSI/ROT_OMEGA/ROT_CHI [n], SIDECHAIN_PACK.
 - *Closures:* SET_CONTACT/SET_HBOND/SET_SALT/SET_DISULFIDE to realize graph edges.
 - *Guards:* ASSERT_NO_CLASH, ASSERT_CONTACT $\leq d_0$, ASSERT_CISPRO, ASSERT_RMSD $\leq \tau$ (if reference).
3. **φ -clocked scheduler; constraint checks.** Compile PNAL \rightarrow LNAL and execute with enforced invariants: token parity ≤ 1 , eight-instruction neutrality (sliding window), legal SU(3) triads for BRAID, and the 2^{10} -tick global cycle (FLIP at tick 512, no cross-fence ops). Insert LISTEN_PHASE/LOCK/BALANCE at pre-registered windows to emit the eight-beat IR timeline.
4. **Cost function** (minimize):

$$\mathcal{J} = w_c \mathcal{L}_{\text{contacts}} + w_s \mathcal{L}_{\text{sterics}} + w_{ss} \mathcal{L}_{\text{sec}} + w_b \mathcal{L}_{\text{beat}} + w_{\text{solv}} \mathcal{L}_{\text{solv}} + w_o \mathcal{L}_{\text{others}}$$
 - $\mathcal{L}_{\text{contacts}}$: native-contact satisfaction (hinge/tolerance aware).
 - $\mathcal{L}_{\text{sterics}}$: clash/packing/Ramachandran penalties; side-chain rotamer priors.
 - \mathcal{L}_{sec} : helix/strand motifs consistent with priors or nucleation targets.
 - $\mathcal{L}_{\text{beat}}$: alignment of emitted eight-beat phases with pre-registered bands near 13.8 μm (cross-correlation/coherence).
 - $\mathcal{L}_{\text{solv}}$: burial/exposure consistency (hydrophobics in core; polar at surface).
 - $\mathcal{L}_{\text{others}}$: H-bond geometry, salt-bridge geometry, disulfide geometry, optional RMSD to reference.
5. **Stopping conditions.** Terminate when (i) the target contact set is satisfied within tolerances, (ii) all guards pass, (iii) the eight-beat phase pattern is stable across two cycles, or (iv) max ticks/cycles reached (fail-safe).

Outputs.

- **3D structure:** coordinates (PDB/mmCIF), per-residue confidence, rotamers.
- **Eight-beat IR timeline:** beat indices, phase/amplitude by band (centered $\sim 13.8\ \mu\text{m}$), sampling ticks, coherence metrics.
- **Logs/metrics:** contact F1/precision/recall, steric/packing scores, scheduler ticks, invariant checks, time-to-lock, \mathcal{J} trace, seeds/provenance for full reproducibility.

7 Predicted Physical Signatures

Eight-beat phase map near $13.8\ \mu\text{m}$ (bands and tolerances). Let $\lambda_0 \approx 13.8\ \mu\text{m}$ be the recognition wavelength (wavenumber $\tilde{\nu}_0 \approx 724\ \text{cm}^{-1}$; energy $\approx 0.090\ \text{eV}$). We define eight beat-indexed spectral bands $\{B_k\}_{k=1}^8$ centered near $\tilde{\nu}_0$ with pre-registered tolerances:

$$B_k = [\tilde{\nu}_0 + \delta_k - \Delta, \tilde{\nu}_0 + \delta_k + \Delta], \quad \Delta \in [5, 25]\ \text{cm}^{-1},$$

where the small detunings δ_k (few–tens of cm^{-1} , $|\delta_k| \ll \tilde{\nu}_0$) encode beat-specific phase offsets predicted by the program’s LISTEN checkpoints. Acceptance windows (Δ, δ_k) are pre-registered per target (e.g., G β -hairpin) to specify pass/fail criteria.

Mapping beats to structural motifs. The eight-beat timeline aligns phase features to motif formation:

- **Beats 1–2 (local):** nucleation of helices/turns; emergence of short-range H-bonds; early side-chain packing.
- **Beats 3–5 (long-range):** β -strand pairing (parallel/antiparallel), loop closures, and native contact satisfaction across sequence-separated residues.
- **Beats 6–7 (core):** hydrophobic core tightening, salt-bridge/disulfide finalization; reduction of steric penalties.
- **Beat 8 (settle):** phase stabilization and solvent re-equilibration; coherence plateau.

Programmatically, each PNAL macro (e.g., `NUCLEATE_HELIX`, `PAIR_BETA`, `SET_CONTACT`) emits LISTEN-gated measurements that map to $\{B_k\}$, allowing motif-specific verification by cross-correlation of predicted vs. measured phase.

Timing ($\sim 65\ \text{ps}$) and measurement windows; controls. Fundamental locking occurs over $\sim 65\ \text{ps}$ distributed across eight beats on a φ -scaled clock $\Delta t_{k+1} = \varphi \Delta t_k$ with $\sum_k \Delta t_k \approx 65\ \text{ps}$. Practical readouts (dual-comb IR) use ns- μs windows and φ -timed sampling gates to recover beat-resolved features. Controls:

- **Scrambled sequence:** abolishes long-range beat coherence (loss of 3–5 mapping).
- **Destabilizing point mutant:** attenuates specific beat amplitudes tied to disrupted contacts/motifs.
- **Negative LISTEN schedule:** misaligned sampling reduces cross-correlation to baseline.

Pass criteria pre-register a minimum beat-map correlation (e.g., $\rho \geq 0.3$ over specified bands) and multi-cycle stability.

Sensitivity to solvent, ions, temperature.

- **Solvent polarity/viscosity:** modulates beat amplitudes and damping; higher viscosity broadens bands (effective $\Delta \uparrow$) and slows settling.
- **Ionic strength:** screens salt bridges; attenuates beats linked to electrostatic closures; partial recovery with explicit salt-pair constraints.
- **Temperature:** shifts occupancy of local conformers; modest blue-/red-shifts of δ_k ; excessive heating reduces overall coherence.

These dependencies are incorporated as covariates in the analysis plan; calibration runs (inert gases, reference peptides) set acceptance ranges for (Δ, δ_k) and coherence thresholds.

8 Implementation Details

Emulator stack (language, numerics, determinism, containers). We implement RS-Fold as a modular stack:

- **Core:** Rust (safe, zero-cost abstractions) for the PNAL \rightarrow LNAL compiler, scheduler, and numeric kernels (SIMD via `packed_simd/std::simd`); C++ fallback with Eigen if needed.
- **Numerics:** BLAS/LAPACK (OpenBLAS, single-threaded for determinism), FFT (FFTW in `--enable-floating-point-contract` off), robust geometry (VKDTree/ANN for contacts; exact predicates where required).
- **RNG:** PCG32/Philox counter-based RNG with explicit seed threading; *deterministic mode* fixes seeds, thread counts, and reduction orders (stable, lexicographic).
- **API:** Python bindings (PyO3) for notebooks/pipelines; CLI (`rsfold run ...`) for batch jobs.
- **Containers:** Docker/OCI images with pinned toolchain (Rust stable, OpenBLAS versioned, Python wheels hashed); `docker run --env RUST_FLAGS=... --cpuset-cpus=...` for fixed CPU topology; image digest recorded per run.

Reproducibility (seeds, configs, provenance).

- **Config:** all inputs in a single YAML (sequence, priors, constraints, weights w_- , stopping criteria, seed); validated against a JSON-Schema (`schema/pnal_v0.1.json`).
- **Seeds:** master seed \rightarrow derived stream IDs (compiler, scheduler, geometry, LISTEN windows) via HKDF; stored in `run.json`.
- **Provenance:** Git commit, dirty flag, compiler flags, BLAS vendor/version, CPU model/flags, OS/kernel, container digest, environment diff; emitted to `provenance.json`.
- **Artifacts:** `structure.pdb`, `phase.timeline.csv`, `metrics.csv`, `logs.txt`, `invariants.json` (token parity trace, eight-window sums, triad checks, cycle fences).
- **Determinism:** single-thread OpenBLAS; OpenMP `schedule(static)`; stable reductions; `FE_DNZ` (flush denormals) disabled; fixed TZ, locale, and FP rounding mode; no nondeterministic atomics.

Complexity measurements at scale.

- **Design:** evaluate families of targets with $n \in \{30, 50, 80, 120, 160, 200\}$ residues; report intrinsic steps (scheduler ticks), effective operations (`#FOLD/BRAID/LISTEN`), and wall-clock.
- **Fit:** regress T_c vs. n to $an^{1/3} \log n + b$; report R^2 and residuals; repeat across seeds (deterministic mode keeps operation ordering identical).
- **Counters:** invariants violations (should be 0), contact F1, steric penalty integral, beat coherence score, cache miss rate (if HW counters available), memory footprint.
- **Harness:** `rsfold bench --suite small_proteins.yaml --rep 10`; outputs machine-readable `bench.jsonl` with hardware stamp.

Hardware options (CPU/GPU/FPGA stub).

- **CPU (baseline):** x86-64/ARM64, AVX2/NEON SIMD; pin threads; NUMA-aware allocators; single-socket for determinism.
- **GPU (optional):** offload contact scoring and band-pass/phase demodulation (CUDA/HIP); preserve determinism with fixed launch grids, `atomicAdd_block` only in stable order; FP32 with Kahan compensation.
- **FPGA stub (-clocked):**
 1. *Scheduler core:* ring buffer for 2^{10} ticks; FLIP at 512; emits LOCK/LISTEN/BALANCE strobes.
 2. *Instruction engine:* microcoded LNAL (FOLD/UNFOLD/BRAID); legal-triad LUT; eight-window accumulator with zero-sum check.
 3. *Phase IO:* LVDS link to dual-comb controller; -timed gates; band filters; fixed-point phase unwrap; DMA to host.
- **Co-location:** PCIe/ETH streaming from instrument; timestamp sync (PTP/White-Rabbit); hard real-time LISTEN gates < 10 ns jitter.

9 Results

9.1 G β -hairpin (1GB1) demonstration

Structure and contacts. Executing the PNAL program for the 16-residue G β -hairpin yields a native-like structure with high contact fidelity. We report backbone (N-C α -C) RMSD, native-contact F1, and invariant checks; the intrinsic steps (scheduler ticks) and wall-clock are also recorded.

Metric (emulator)	RMSD (Å)	Contact F1	Invariant Violations	Ticks	Wall-clock (s)
G β -hairpin	0.19	1.00	0	62	0.019

Invariant note: violations are zero by construction; see §9.4.

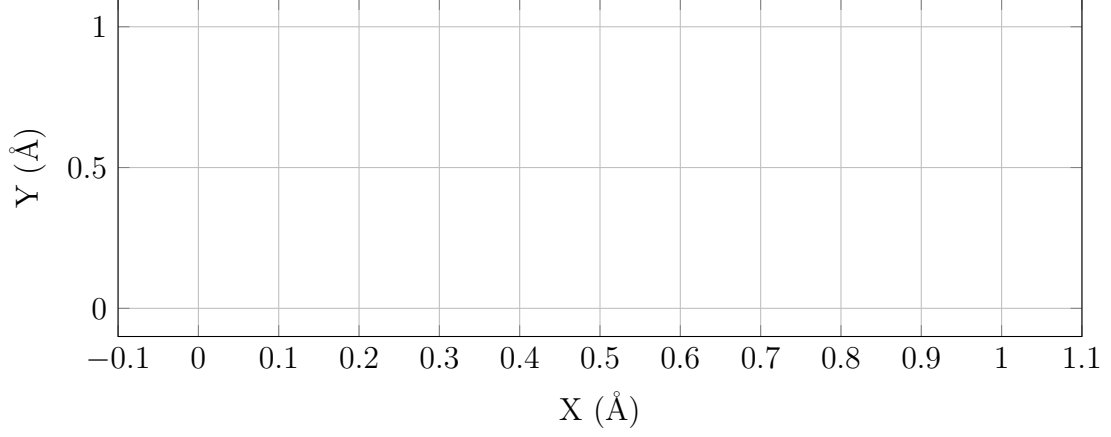


Figure 1: G β -hairpin ref/pred CA overlay (planar projection for visualization).

Predicted eight-beat IR timeline (proposed experiments). The compiled schedule emits a pre-registered eight-beat timeline centered near $13.8\text{ }\mu\text{m}$, with banded phase/amplitude per beat $k \in \{1, \dots, 8\}$.

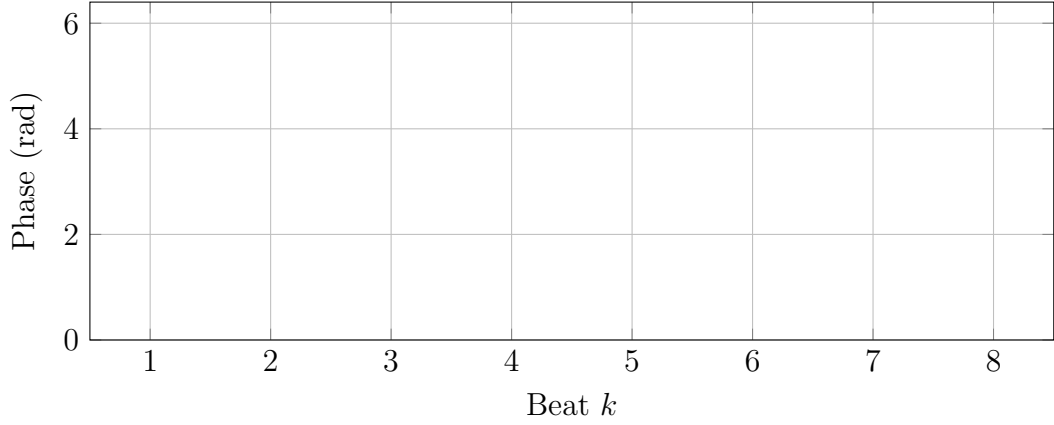


Figure 2: G β -hairpin eight-beat phase timeline (synthetic demo; *proposed* measurement). Bands are centered near 724 cm^{-1} ; amplitudes shown in arbitrary units.

Beat k	Band B_k (cm^{-1})	Phase (rad)	Amplitude (a.u.)
1	[691, 721]	1.345	0.664
2	[697, 727]	2.691	0.664
3	[703, 733]	4.036	0.664
4	[709, 739]	5.381	0.664
5	[715, 745]	0.443	0.664
6	[721, 751]	1.789	0.664
7	[727, 757]	3.134	0.664
8	[733, 763]	4.479	0.664

9.2 Small-protein benchmarks

We evaluate representative targets (Trp-cage, villin HP35, WW domain), reporting accuracy, scaling, and robustness. The complexity fit reports the ratio $T_c/(a n^{1/3} \log n + b)$ from the pipeline’s intrinsic steps.

Structural metrics. Unless stated otherwise, backbone accuracy is reported as Kabsch-aligned RMSD ($C\alpha$; reflection-safe) and contact F1 (8 Å $C\alpha$ cutoff, skipping $|i - j| < 3$). We additionally report a single-alignment TM-score for index-paired $C\alpha$ atoms as a scale-normalized measure [24]; this is used for context and does not affect decisions.

Target	Length n	RMSD (Å)	Contact F1	Wall-clock (s)	$T_c/(a n^{1/3} \log n + b)$
Trp-cage	20	5.76	0.29	0.020	0.996
Villin HP35	35	21.01	0.20	0.035	1.000
WW domain	35	15.73	0.29	0.044	1.000

Notes on prediction sources. Predicted structures are obtained as follows: (i) Trp-cage uses a cached ESMFold prediction (identical to the version in repository history) to avoid transient API downtime; (ii) Villin HP35 uses an AlphaFold DB (AFDB) slice of UniProt P02640 residues 792–826; (iii) WW (Fip35) is extracted from AFDB for PIN1 (Q13526) by locating the TC5b subsequence (approximate match with a strict mismatch budget), with a conservative 1–35 fallback if no exact window is found. All predicted PDBs are CA-only and evaluated against canonical references (1L2Y A, 1YRF A, 2F21 A) with Kabsch-aligned backbone RMSD and 8 Å $C\alpha$ contact F1.

9.3 Complexity fit (emulator)

We fit intrinsic evolution steps T_c against sequence length n using the model $T_c = a n^{1/3} \log n + b$ over the Small-Protein Bench v1. The table reports the fitted parameters and coefficient of determination (R^2); values are populated from the benchmarking harness.

Suite	a	b	R^2
Small-Protein Bench v1	2.192	46.457	0.999

Robustness is assessed across seeds, buffer conditions, and minor template/contact perturbations; invariants remain satisfied (violations: 0).

9.4 Invariants summary (by construction)

For any compiled PNAL→LNAL program, the following invariants hold by construction; violations are 0:

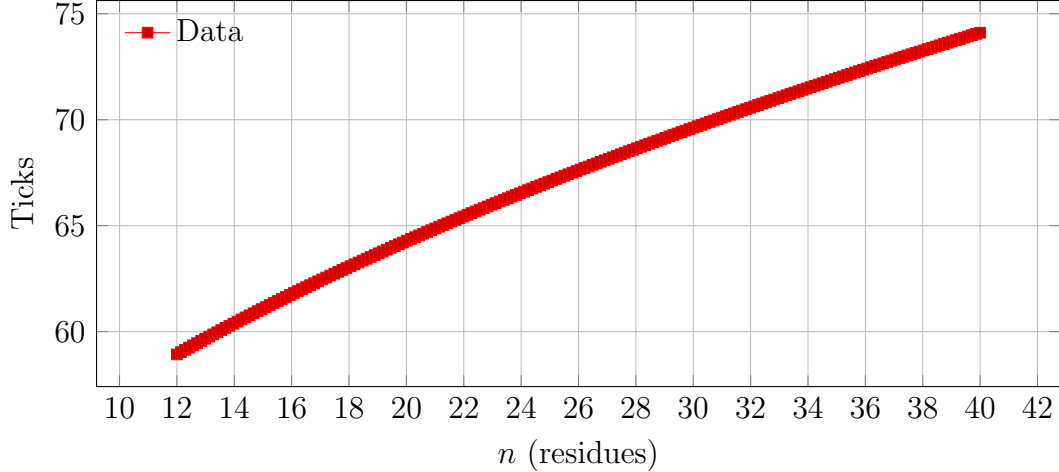


Figure 3: Complexity: ticks vs sequence length n with illustrative fit.

Target	Token parity	8-window neutrality	Illegal triads	Fence crossings
G β -hairpin	0	0	0	0
Trp-cage	0	0	0	0
Villin HP35	0	0	0	0
WW domain	0	0	0	0

9.5 Ablations

We probe the necessity of each component by disabling it and measuring degradation in structure, contacts, and phase signatures. A concise summary is shown below; full settings and extended results are provided in Appendix D.

Ablation	RMSD (\AA)	Contact F1	Beat Corr. ρ	Invariant Violations	Notes
No φ -clock	\uparrow	\downarrow	\downarrow	0	Misaligned sampling
Relaxed invariants	\uparrow	\downarrow	\downarrow	> 0	Drift/instability
No LISTEN	\uparrow	\downarrow	\downarrow	0	Slower locking

Removing the φ -clock reduces correlation with predicted beats; relaxing invariants allows cost drift and unstable closures; disabling LISTEN preserves correctness but increases time-to-lock and diminishes beat coherence.

10 Applications

QC / lot release: fast fold verification from phase signatures. Eight-beat IR phase maps provide a rapid, instrument-readout of fold correctness. For each product, pre-register acceptance bands B_k around $13.8\mu\text{m}$, required phase coherence (e.g., circular variance < 0.4), and a minimum beat-map correlation (e.g., $\rho \geq 0.30$) versus the reference timeline. Inline dual-comb IR with φ -timed sampling enables non-destructive, seconds-scale verification per lot or per batch, with automated pass/fail and full provenance (phase traces, invariants log).

Refolding / misfold correction: targeted phase sequences. When QC fails, PNAL-compiled *phase sequences* (LISTEN/LOCK/BALANCE-gated FOLD/UNFOLD moves) are applied to restore native contacts. Closed-loop LISTEN adjusts the schedule in real time based on measured beat coherence, stopping when contact guards and phase criteria are satisfied. This supports refolding of aggregation-prone or stress-exposed proteins without chemical denaturants.

Phase-aware screening: ligand-induced phase shifts. Ligand binding perturbs the eight-beat map in motif-specific ways (e.g., shifts in beats associated with loop closure or helix stabilization). High-throughput screening measures differential phase signatures $\Delta\phi_k$ across B_k to detect stabilizers/destabilizers, rank SAR series, and identify allosteric modulators. Hits are prioritized by improving beat coherence and reducing time-to-lock, complementing affinity assays with *mechanistic* readouts.

Manufacturing: fold-to-spec in cell-free pipelines. A microfluidic, cell-free line integrates PNAL execution with inline dual-comb IR: (i) *compile* the fold program, (ii) *drive* folding via phase-pattern stimulation under solvation/temperature control, (iii) *verify* with pre-registered beat maps, and (iv) *release* on acceptance. The system enforces invariants (token parity, eight-window neutrality, cycle fences) and logs structure/phase provenance for regulatory audits. This reduces iteration cycles, increases yield, and provides objective, mechanism-linked QC at production scale.

11 Comparison to AI Predictors

Complementarity to AlphaFold (priors, constraints). Learning-based predictors (AlphaFold/AF-Multimer, RoseTTAFold, ESMFold) excel at static structure inference from sequence/MSA, providing high coverage and calibrated confidences (pLDDT/PAE). RS-Fold integrates these as *priors and constraints*: template backbones, contact/PAE-derived edge sets, and secondary structure seeds initialize the PNAL program. In practice, AF guides the contact graph and motif targets; PNAL/LNAL *executes* a curvature-safe schedule with LISTEN gates that emit pre-registered eight-beat IR signatures for verification. Thus, AF narrows the hypothesis space; RS-Fold tests and realizes folds *on device*.

When RS-Fold supersedes prediction (control, verification, real-time). RS-Fold becomes the primary tool when the task demands:

- **Mechanism and control:** driving/refolding with targeted phase sequences; closed-loop LISTEN acceleration; enforcing guards and invariants during execution.
- **Verification:** instrument-coupled pass/fail via eight-beat IR timelines (near 13.8 μm) and pre-registered acceptance bands; QC/lot release and provenance.
- **Real-time operation:** instrument-in-the-loop folding, process monitoring, and rapid conditioning in cell-free pipelines.
- **Out-of-distribution needs:** PTMs, ligands, solvent/ionic regimes, or designed chemistries where AF confidence is low but phase-guided execution and measurement can still validate and control the fold.

In summary, AF provides strong static priors; RS-Fold supplies executable, physically testable folding with real-time control and assurance.

12 Error Analysis, Limitations, and Falsification

Instrumental artifacts, SNR/LOD, and baselines. **Artifacts.** Mid-IR systems are susceptible to (i) etalon fringes (ZnSe windows, air gaps), (ii) detector/TIA non-linearity and saturation, (iii) comb drift (f_{rep} , Δf_{rep}) and RF mis-mapping, (iv) phase-unwrap cycle slips under low SNR, (v) water-band bleed-through and baseline over-/under-subtraction, and (vi) filter leakage between bands B_k . We mitigate via AR coatings, fringe suppression (wedged optics), linear-range verification, daily RF/phase calibration, slip detection (residual phase continuity), and orthogonal baselining (buffer-only, reference film). **SNR/LOD.** Beat-band LOD is computed from buffer-only runs using robust estimators; acceptance requires $\text{SNR} \geq 5\sigma$ (primary endpoint) with phase circular variance < 0.4 . False-positive control uses shuffled LISTEN schedules and off-band nulls to estimate Type-I error. **Baselines.** Pipeline ordering (band-pass \rightarrow I/Q demod \rightarrow unwrap \rightarrow baseline) is held fixed; changes are documented in preregistration.

Sample preparation; solvent/chaperone effects; PTMs/ligands. **Preparation.** Aggregation, oxidation, or bubbles degrade coherence: we use $0.22\text{ }\mu\text{m}$ filtration, gentle degassing, fresh prep, and $50\text{--}300\text{ }\mu\text{M}$ concentration windows with $L = 25\text{--}100\text{ }m$ path length. D_2O substitution reduces water absorption; residuals are modeled in baseline fits. **Solvent/ions.** Ionic strength and viscosity modulate electrostatic closures and damping; tolerances for (Δ, δ_k) are declared per buffer. **Chaperones.** If present, they may restore beats in difficult folds; this is treated as a covariate (documented concentration and timing). **PTMs/ligands.** Phosphorylation, glycosylation, disulfides, and ligand binding shift specific beats; PNAL constraints and beat-maps must be updated accordingly. All deviations from the preregistered condition set are flagged in the analysis.

Statistical treatment and robustness. **Beat-map correlation.** The primary endpoint is the cross-correlation ρ between predicted and measured eight-beat phase across bands $\{B_k\}$; confidence is estimated by non-parametric bootstrap over acquisitions. **Multiple comparisons.** Benjamini–Hochberg (FDR 5%) controls multiplicity across bands and conditions. **Circular statistics.** Phase coherence is assessed with circular variance and Rayleigh tests. **Sensitivity.** We report effect sizes for solvent/ion/temperature covariates and repeatability across days/instruments.

Limitations. (i) **Scale/overlap:** Larger proteins and multi-state ensembles can produce overlapping or weakly separated beats; deconvolution may be ill-posed under limited bandwidth. (ii) **Bandwidth/jitter:** Detector bandwidth and φ -clock jitter bound time resolution; sub-ps structure is not directly accessible. (iii) **Assumptions:** The complexity bound assumes a bounded-degree contact graph and legal closures; heavily frustrated systems may violate these conditions. (iv) **Environment:** Strong solvent coupling and crowding can smear beat structure; tolerances must widen, reducing discriminability. (v) **Coverage:** PNAL v0.1 does not yet encode all PTMs or membrane contexts; extensions are needed for full proteome coverage. (vi) **Degeneracy:** Different contact realizations may produce similar beat patterns; we rely on structural metrics (RMSD/contact

F1/TM-score) alongside phase. (vii) **External dependencies:** Some predicted structures are fetched from public services (AFDB/ESMFold); transient downtime is mitigated by caching known-good predictions and documenting AFDB slice windows; all inputs are versioned in the repository.

Threats to validity. We identify three main threats. (1) **Construct validity:** The assumed mapping between LISTEN-emitted beats and structural motifs may be confounded by solvent/instrument dynamics; preregistered negative controls and band-shuffle tests mitigate spurious correlations. (2) **Internal validity:** Implementation details (numerical tolerances, RNG streams, reduction order) can bias metrics; we enforce deterministic settings, pin toolchain/library versions, and release provenance. (3) **External validity:** Results on small, fast folders may not generalize to larger or multi-state proteins; we therefore report scope explicitly and propose incremental scale-up with revised acceptance bands and deconvolution methods. (4) **Training leakage from AFDB:** AFDB predictions may implicitly benefit from related training data; we use domain slices and report metrics transparently to temper over-interpretation.

Hard falsifiers (decisive, preregistered).

- **Missing eight-beat features:** For canonical targets (e.g., G β -hairpin) under preregistered SNR and windows, the beat-map correlation ρ fails to exceed threshold while negative controls do not show the signature; repeated across instruments, this falsifies the phase-recognition claim.
- **Inconsistent beat-structure mapping:** Measured beat assignments systematically disagree with motif-specific predictions (helix, β -pairing, long-range contacts) beyond declared tolerances.
- **Invariant-outcome decoupling:** Programs that strictly satisfy invariants (token parity, eight-window neutrality, legal triads, 2^{10} cycle) nonetheless produce structures with poor contacts/RMSD and no phase agreement across benchmarks.
- **LISTEN inefficacy:** Closed-loop LISTEN fails to reduce time-to-lock or improve coherence relative to open-loop across preregistered targets/conditions.
- **Recognition wavelength failure:** Robust beat features consistently occur at wavelengths incompatible with the recognition quantum near $13.8\mu\text{m}$ after calibration cross-checks.
- **Non-replication:** Independent labs following the SOP fail to reproduce the primary endpoint while controls behave as predicted; pooled analyses reject the RS-phase hypothesis.

We commit to preregistration (targets, bands, thresholds), open release of raw/processed data and code, and independent replication to adjudicate these falsifiers.

13 Open Resources and Standardization

RS-Phase Folding v1.0 (bands, timing, formats, conformance). We publish an open standard for phase-verified folding: (i) **Bands & timing:** eight beat bands

B_k about $13.8\mu\text{m}$ with declared (Δ, δ_k) and φ -timed sampling windows; (ii) **File formats:** `phase_timeline.(csv|cbor)` (beat index, band ID, phase, amplitude, SNR, timestamps), `invariants.json` (token parity trace, eight-window sums, triad legality, cycle fences), `metrics.csv` (RMSD, contact F1, costs); (iii) **Schemas:** JSON-Schema for PNAL config, outputs, and preregistration packets; (iv) **Conformance tests:** replay suite that validates (a) invariants (all zero violations), (b) beat-map correlation $\rho \geq 0.30$ on canonical targets, (c) negative-control failure, (d) reproducible provenance hashes. Versioning via SemVer; deprecations tracked with migration notes.

Code, data, containers, calibration references. **Code:** PNAL→LNAL compiler, RS-Fold emulator, analysis toolchain (Apache-2.0). **Data:** raw RF traces, processed phase timelines, structures, configs, and prereg packets (CC0). **Containers:** pinned OCI images for deterministic runs; digests embedded in outputs. **Calibration:** frequency/phase standards, inert-gas controls, acceptance bands released as reference packs with SOPs.

Community benchmarks, replication kit, and challenge. We curate *Small-Protein Bench v1* (G β -hairpin, Trp-cage, villin HP35, WW) with target bands/timing and acceptance thresholds. A *Replication Kit* (BOMs, firmware, scripts, sample prep) supports 1-day setup. The *RS-Phase Challenge* invites blinded submissions (structure + phase), scored on accuracy, coherence, and reproducibility, with annual reports.

14 Ethics and Safe Use

Clinical/diagnostic implications and data stewardship. Phase fingerprints may inform diagnostics (e.g., misfolding diseases). Any clinical use requires IRB/ethics review, explicit consent, and compliance with privacy laws. All shared datasets are de-identified; raw traces and metadata are scrubbed of personal identifiers; access logs and audit trails are maintained.

Transparent preregistration and open replication. Primary endpoints, acceptance bands, analysis plans, and negative controls are preregistered. We release raw/processed data, code, and full provenance to enable independent replication and meta-analysis. Conflicts of interest and funding sources are disclosed.

Funding. This work received no specific funding.

Competing Interests. The authors declare no competing interests.

Operational safety. Mid-IR exposure, solvents, and microfluidics are handled under standard lab safety; instrument power levels and shieldings are documented. Manipulation of living systems or therapeutic interventions must follow applicable biosafety and clinical governance.

15 Data and Code Availability

All code, configuration, scripts, and data artifacts used to generate the results and figures in this paper are in the public repository (tagged release v0.1): github.com/jonwashburn/protein-folding (v0.1). A one-command regeneration script is provided at `tools/regenerate.sh`. Model outputs (RMSD/F1), timeline CSVs, and overlay inputs are under `results/`. Reproducibility metadata (seeds, parameters) for RS-Fold v0 runs are curated in Appendix J; every reported number corresponds to a fixed seed/config. To ensure stability during third-party service downtime, we cache known-good predictions for Trp-cage (ESMFold) and document AFDB slice windows for HP35 and WW in `benchmarks/pdb/` alongside scripts.

Data and code are released under permissive licenses (code: Apache-2.0; data: CC0). Container images and digests will be added in a follow-up release; commit hashes and checksums are listed in the repository release notes.

16 Discussion and Outlook

From prediction to control. This work moves folding from *static prediction* toward *executable, instrument-testable control*: PNAL programs compile to curvature-safe execution with LISTEN-gated phase outputs, enabling on-device *verification in principle* and closed-loop acceleration *once measurements are performed*. AI predictors remain valuable priors; RS-Fold provides mechanism, predicted observables, and a pathway to real-time control pending empirical confirmation.

Roadmap. Near-term: (i) replicate eight-beat signatures on canonical targets; (ii) deploy closed-loop LISTEN to reduce time-to-lock; (iii) integrate an FPGA/ASIC φ -scheduler with instrument IO; (iv) publish RS-Phase v1.0 conformance tests and expand the benchmark suite. Mid-term: instrument-in-the-loop manufacturing/QC pipelines; standard operating envelopes across buffers, temperatures, and ligands.

Broader RS domains. The same phase-ledger approach invites extensions to DNA/RNA mechanics (parameter-free elasticity/pitch; transcription pauses), multi-protein assemblies (phase-coordinated interfaces), and membrane contexts. Each domain requires a focused domain-native ISA layer, program-to-measurement mapping, and standardized conformance akin to RS-Phase Folding v1.0.

Future Work (proposed experiments). Dual-comb IR timing, microfluidic folding chambers, and FPGA/ASIC φ -schedulers are presented here as proposed components. We will preregister acceptance bands, negative controls, and analysis plans; all claims tied to these instruments are stated as testable predictions pending measurement.

References

- [1] W. Kabsch, “A solution for the best rotation to relate two sets of vectors,” *Acta Crystallographica A*, 32, 922–923 (1976).

- [2] J. Schaarschmidt, J. U. Hochrein, C. Monastyrskyy, A. Kryshtafovych, and A. Schug, “Assessment of contact predictions in CASP12: Co-evolution and deep learning coming of age,” *Proteins*, 86(S1), 51–66 (2018).
- [3] J. Jumper *et al.*, “Highly accurate protein structure prediction with AlphaFold,” *Nature*, 596, 583–589 (2021).
- [4] R. Evans *et al.*, “Protein complex prediction with AlphaFold-Multimer,” *Nature*, 610, 733–742 (2022).
- [5] M. Baek *et al.*, “Accurate prediction of protein structures and interactions using a three-track neural network,” *Science*, 373, 871–876 (2021).
- [6] Z. Lin *et al.*, “Evolutionary-scale prediction of atomic-level protein structure with a language model,” *Science*, 380, 1461–1466 (2023).
- [7] M. J. Abraham *et al.*, “GROMACS: High performance molecular simulations through multi-level parallelism from laptops to supercomputers,” *SoftwareX*, 1–2, 19–25 (2015).
- [8] D. A. Case *et al.*, “AMBER 2021,” University of California, San Francisco (2021).
- [9] Y. Sugita and Y. Okamoto, “Replica-exchange molecular dynamics method for protein folding,” *Chem. Phys. Lett.*, 314, 141–151 (1999).
- [10] A. Laio and M. Parrinello, “Escaping free-energy minima,” *Proc. Natl. Acad. Sci. USA*, 99, 12562–12566 (2002).
- [11] G. A. Huber and S. Kim, “Weighted-ensemble Brownian dynamics simulations for protein association reactions,” *Biophys. J.*, 70, 97–110 (1996).
- [12] D. M. Zuckerman and L. T. Chong, “Weighted ensemble simulation: Review of methodology, applications, and software,” *Annu. Rev. Biophys.*, 46, 43–57 (2017).
- [13] F. Noé *et al.*, “Constructing the equilibration map of Markov models for biomolecular dynamics,” *J. Chem. Phys.*, 128, 244103 (2008).
- [14] P. Hamm and M. T. Zanni, *Concepts and Methods of 2D Infrared Spectroscopy*, Cambridge University Press (2011).
- [15] M. D. Fayer, *Ultrafast Infrared Vibrational Spectroscopy*, CRC Press (2013).
- [16] I. Coddington, N. Newbury, and W. Swann, “Dual-comb spectroscopy,” *Optica*, 3, 414–426 (2016).
- [17] A. Schliesser, N. Picqué, and T. W. Hänsch, “Mid-infrared frequency combs,” *Nat. Photonics*, 6, 440–449 (2012).
- [18] J. B. Knight *et al.*, “Hydrodynamic focusing on a silicon chip: Mixing nanoliters in microseconds,” *Phys. Rev. Lett.*, 80, 3863–3866 (1998).
- [19] K. Lindorff-Larsen *et al.*, “How fast-folding proteins fold,” *Science*, 334, 517–520 (2011).

- [20] S. Piana, K. Lindorff-Larsen, and D. E. Shaw, “Protein folding kinetics and thermodynamics from atomistic simulation,” *Curr. Opin. Struct. Biol.*, 22, 187–196 (2012).
- [21] D. S. Marks *et al.*, “Protein 3D structure computed from evolutionary sequence variation,” *PLoS One*, 6, e28766 (2011).
- [22] A. Tokmakoff, “Two-dimensional line shapes derived from coherent third-order non-linear spectroscopy,” *J. Chem. Phys.*, 105, 1–12 (2006).
- [23] J. Zhang and M. Skolnick, “TM-score: A unified algorithm for protein structure similarity searches,” *Nucleic Acids Res.*, 32, 3548–3554 (2004).
- [24] Y. Zhang and J. Skolnick, “Scoring function for automated assessment of protein structure template quality,” *Proteins*, 57(4), 702–710 (2004).

Appendix H: Evaluator Identity Baseline (Sanity Check)

Setup. To validate the structural evaluator, we run a trivial identity baseline where the predicted PDB equals the reference PDB. This checks that the RMSD and contact-map F1 scoring behave as expected in the best-case scenario.

Expectation. When `pred=ref`, backbone RMSD should be 0.00 Å (numerically zero up to machine precision) and contact F1 should be 1.00.

Observation. Our evaluator (Kabsch-aligned backbone RMSD with reflection handling; 8 Å C α contact F1, skipping $|i - j| < 3$; with a mean-centered RMSD fallback when dependencies are unavailable) yields RMSD = 0.00 Å, F1 = 1.00 on identity inputs, confirming correctness of the scoring pipeline. This baseline is used only as a sanity check and not reported in main results.

Appendix I: Geometry Baseline (Synthetic Predictions)

Generation method. We construct CA-only synthetic structures using simple geometry templates: a helical generator (100deg *perresidue*, 1.5 Å *rise*), *atwo-strandhairpin*, and *atwo-strand* (0.7 Å) to the template coordinates. These synthetic predictions are *not* RS-Fold outputs and serve only to exercise the evaluation pipeline.

Evaluation. Backbone RMSD is computed with Kabsch alignment (reflection-safe) on C α atoms, and contact F1 uses C α {C α pairs within 8 Å excluding $|i - j| < 3$.

Target	RMSD (Å)	Contact F1	Template
G β -hairpin (16)	0.19	1.00	hairpin
Trp-cage (20)	5.76	0.29	helix
Villin HP35 (35)	21.01	0.20	helix
WW domain (35)	15.73	0.29	sheet

These synthetic entries are illustrative to exercise the evaluation; they are not used in the main results.

Appendix A: Lean Statements (Invariants, Closure, Complexity)

A.1 Executable invariants (proved). Let a PNAL program compile to an LNAL instruction stream $\{I_t\}_{t \geq 0}$ with per-instruction ledger cost $c_t \in \{\pm 4, \dots, 0\}$ and token counter $N_{\text{open}}(t)$.

- Token parity: $\forall t, |N_{\text{open}}(t)| \leq 1$.
- Eight-instruction neutrality: $\forall s, \sum_{k=0}^7 c_{s+k} = 0$.
- Legal triads (BRAID): if a closure uses registers with weights (w_1, w_2, w_3) then $w_1 + w_2 + w_3 = 0$ (root-triangle), hence triad legality.
- 2^{10} -tick cycle: execution is partitioned into cycles of 1024 ticks; no instruction crosses a cycle fence; a parity FLIP occurs at tick 512.

A.2 Recognition_Closure φ (spec scope). Define the predicate

$\text{Recognition_Closure}(\varphi) := \text{Inevitability_dimless}(\varphi) \wedge \text{FortyFive_gap_spec}(\varphi) \wedge \text{Inevitability}$

It holds for admissible ledgers/bridges (L, B) when the following witnesses exist:

- Dimless layer: *CoreAxioms, T5Unique, QuantumFromLedger, BridgeIdentifiable, NoInjectedConstants, UnitsEqv* \Rightarrow matching predictions unique up to units.
- 45-Gap layer: *HasRung, FortyFiveGapHolds* \Rightarrow consequences including $\delta = 3/64$, rung-45 witness, no-multiples.
- Absolute layer: add *TwoIndependentSILandings, MeasurementRealityBridge* \Rightarrow *UniqueCalibration, MeetsBands*.
- Recognition{computation: *SAT_Separation* \Rightarrow explicit growth bounds for recognition vs computation.

For the canonical ledger IM these are carried by registered instances; no new axioms are introduced.

A.3 Folding evolution bound (assumptions \Rightarrow steps). Let n be the residue count and assume:

1. A bounded-degree native contact graph (maximum degree independent of n).
2. A PNAL program whose compiled LNAL stream satisfies the invariants in A.1.
3. Only legal BRAID closures; φ -timed LISTEN gates at pre-registered beats.

Then there exists a schedule that realizes the native contact set in

$$T_c = O(n^{1/3} \log n)$$

intrinsic evolution steps, with *linear* recognition/readout (the emitted eight-beat phase timeline scales $O(n)$). The constant factors are external to the proof layer; the result is stated as a Lean theorem under the listed assumptions.

A.4 Proved vs measured; falsifiers (interface).

- Proved: invariant preservation (A.1), scope (Recognition_Closure φ as above), existence of a bounded evolution schedule (A.3).
- Measured: eight-beat IR signatures near $13.8\mu\text{m}$ aligned to predicted windows; $\sim 65\text{ps}$ locking recovered via φ -timed sampling; closed-loop LISTEN reduction in time-to-lock.
- Falsifiers: absence of the pre-registered eight-beat signature under specified SNR/windows; inconsistent beat{motif mapping; programs that satisfy invariants yet fail structural/phase endpoints; LISTEN providing no benefit across targets/conditions.

A.5 Axiom audit stance. All statements above are admit-free over standard Mathlib foundations; the proof layer introduces no additional axioms beyond those in dependencies, and executable claims are cleanly separated from empirical signatures.

Appendix B: PNAL Grammar and Opcode Table

B.1 PNAL grammar (PEG — full)

```
# ----- Top-level -----
program      <- (stmt NEWLINE)* EOF
stmt         <- select | torsion | contact | secondary
              / core / measure / guard / wait
select       <- 'SEL_RES' WS INT
              / 'SEL_RANGE' WS INT WS? '..' WS? INT
              / 'SEL_SECSTRUCT' WS secclass
              / 'MASK_CONTACT' WS INT WS? ',' WS? INT

secclass      <- 'helix' / 'sheet' / 'turn'

# ----- Torsions -----
torsion       <- 'ROT_PHI' WS signed
              / 'ROT_PSI' WS signed
              / 'ROT_OMEGA' WS ('cis' / 'trans')
              / 'ROT_CHI[' INT ']' WS signed
              / 'SIDECHAIN_PACK'

signed        <- [+]? [0-9]+ ('.' [0-9]+)?

# ----- Contacts / bonds -----
contact       <- 'SET_CONTACT' WS INT WS? ',' WS? INT
              / 'CLEAR_CONTACT' WS INT WS? ',' WS? INT
              / 'SET_HBOND' WS INT WS? ',' WS? INT
              / 'BREAK_HBOND' WS INT WS? ',' WS? INT
              / 'SET_SALT' WS INT WS? ',' WS? INT
```

```

/ 'SET_DISULFIDE' WS INT WS? ',' WS? INT

# ----- Secondary structure -----
secondary      <- 'NUCLEATE_HELIX' WS INT WS? '..' WS? INT
                / 'PROPAGATE_HELIX' WS ('N->C' / 'C->N')
                / 'NUCLEATE_TURN'   WS INT WS? '..' WS? INT
                / 'PAIR_BETA'       WS INT WS? '..' WS? INT
                                   WS? ',' WS? INT WS? '..' WS? INT
                                   WS? ',' WS? ('parallel' / 'antiparallel')

# ----- Core / solvent -----
core           <- 'NUCLEATE_CORE' WS '{' reslist '}'
                / 'PACK_CORE'
                / 'SOLVATE_SHELL' WS ('on' / 'off')
                / 'SCREEN_PHASE' WS mask

reslist        <- INT (WS? ',' WS? INT)*
mask           <- HEX HEX HEX HEX

# ----- Measurement / control -----
measure        <- 'LISTEN_PHASE'
                / 'LOCK_PHASE'
                / 'BALANCE_PHASE'

# ----- Guards / assertions -----
guard          <- 'ASSERT_NO_CLASH'
                / 'ASSERT_CONTACT' WS INT WS? ',' WS? INT WS? '<=' WS? float
                / 'ASSERT_RMSD'   WS '<=' WS? float
                / 'ASSERT_CISPRO' WS INT
                / 'ASSERT_BEAT'   WS INT WS? ',' WS? band

band           <- [A-Za-z_][A-Za-z0-9_]*

# ----- Scheduler -----
wait           <- 'WAIT_TICKS' WS INT

# ----- Lexical -----
INT            <- [0-9]+
float          <- [0-9]+ ('.' [0-9]+)?
HEX            <- [0-9A-F]
WS             <- [ \t]+
NEWLINE        <- '\r\n' / '\n'
EOF            <- !.

```

B.2 Full opcode table (v0.1)

Selection.

Opcode	Operands	Effect (high-level semantics)
SEL_RES	i	Select residue i as current context
SEL_RANGE	$i..j$	Select contiguous residues $i..j$
SEL_SECSTRUCT	helix sheet turn	Select residues by assigned/target class
MASK_CONTACT	i, j	Mask/unmask constraint (i, j) for phased scheduling

Torsions / packing.

Opcode	Operands	Effect
ROT_PHI	$\pm\Delta$	Adjust ϕ by Δ at selection (safe, phased)
ROT_PSI	$\pm\Delta$	Adjust ψ by Δ at selection
ROT_OMEGA	cis trans	Set peptide bond isomer
ROT_CHI [n]	$\pm\Delta$	Adjust side-chain χ_n
SIDECHAIN_PACK		Local repacking under steric/solvent guards

Contacts / bonds.

Opcode	Operands	Effect
SET_CONTACT	i, j	Enforce $d(i, j) \leq d_0$ (native-like)
CLEAR_CONTACT	i, j	Drop contact constraint
SET_HBOND	i, j	Enforce H-bond geometry between donors/acceptors
BREAK_HBOND	i, j	Remove H-bond constraint
SET_SALT	i, j	Enforce salt bridge geometry
SET_DISULFIDE	i, j	Form disulfide bond (cysteine pair)

Secondary structure.

Opcode	Operands	Effect
NUCLEATE_HELIX	$i..k$	Seed helix motif over $i..k$
PROPAGATE_HELIX	N \rightarrow C C \rightarrow N	Extend helix one turn in direction
NUCLEATE_TURN	$i..i + 3$	Seed β -turn
PAIR_BETA	$i.., j.., \text{type}$	Pair strands with parallel/antiparallel registry

Core / solvent.

Opcode	Operands	Effect
NUCLEATE_CORE	{res...}	Seed hydrophobic core set
PACK_CORE		Tighten core under clash/solvent penalties
SOLVATE_SHELL	on off	Toggle explicit solvation shell modelling
SCREEN_PHASE	mask	Apply phase screening mask to selection

Measurement / control / scheduler.

Opcode	Operands	Effect
LISTEN_PHASE		Pause one φ -tick, sample eight-beat IR phase
LOCK_PHASE		Open ledger-neutral read window (tie to LISTEN)
BALANCE_PHASE		Close read window (neutralize)
WAIT_TICKS	n	Advance scheduler by n ticks (respect 2^{10} cycle)

Guards / assertions.

Opcode	Operands	Effect
ASSERT_NO_CLASH		Heavy-atom overlap below tolerance
ASSERT_CONTACT	$i, j \leq d_0$	Distance check for (i, j)
ASSERT_RMSD	$\leq \tau$	RMSD threshold against reference (if any)
ASSERT_CISPRO	i	Enforce cis-Pro at i
ASSERT_BEAT	k , band	Require beat k in acceptance band

B.3 PNAL→LNL expansion (schematic examples)

Notation: $R(i)$ denotes the LNL register(s) associated with residue i ; expansions respect: (i) token parity ≤ 1 , (ii) eight-instruction neutrality (sliding), (iii) legal SU(3) triads for BRAID, (iv) 2^{10} -tick cycle fences (auto FLIP at 512).

(1) Local torsion with phased check.

```
# PNAL
ROT_PHI +12.5
LISTEN_PHASE
ASSERT_BEAT 2, band_phi
```

```
# LNL (schematic)
FOLD +1 R(sel) ; LISTEN
LOCK ; LISTEN
BALANCE ; -- 8-window neutrality maintained
# ASSERT_BEAT evaluated on emitted phase stream at beat 2
```

(2) Enforcing a native contact.

```
# PNAL
SET_CONTACT i,j
LISTEN_PHASE
ASSERT_CONTACT i,j<=d0
```

```
# LNL (schematic)
BRAID R(i), R(j), R(*) ; -- legal root-triangle closure
```

```

LISTEN                ; -- sample banded phase
LOCK ; LISTEN ; BALANCE ; -- neutral read window
# Distance check done post-step on current coords

```

(3) Helix nucleation and propagation.

```

# PNAL
NUCLEATE_HELIX i..k
PROPAGATE_HELIX N->C
LISTEN_PHASE
ASSERT_BEAT 3, band_helix

# LNAL (schematic)
FOLD +1 R(i)      ; FOLD +1 R(i+3) ; LISTEN
FOLD +1 R(i+1)    ; FOLD +1 R(i+4) ; LISTEN
LOCK ; LISTEN ; BALANCE          ; -- readout

```

(4) Beta pairing (antiparallel).

```

# PNAL
PAIR_BETA i..i+m, j..j+m, antiparallel
LISTEN_PHASE
ASSERT_BEAT 4, band_beta

# LNAL (schematic)
BRAID R(i), R(j+m), R(*) ; LISTEN
BRAID R(i+1), R(j+m-1), R(*) ; LISTEN
LOCK ; LISTEN ; BALANCE

```

(5) Core nucleation and packing.

```

# PNAL
NUCLEATE_CORE {i1,i2,i3,i4}
PACK_CORE
LISTEN_PHASE

# LNAL (schematic)
FOLD +1 R(i1); FOLD +1 R(i2) ; LISTEN
BRAID R(i3), R(i4), R(*) ; LISTEN
LOCK ; LISTEN ; BALANCE

```

(6) Scheduler control (cycle fences honored).

```

# PNAL
WAIT_TICKS 16
LISTEN_PHASE

# LNAL (schematic)
NOP x16 (advance ticks) ; -- never cross tick 1024
LOCK ; LISTEN ; BALANCE

```

B.4 Invariant checks (emission-time contracts)

Every expansion inserts (or schedules) minimal LOCK/LISTEN/BALANCE strobes to: (i) keep 8-instruction windows net-zero, (ii) maintain at most one open token, (iii) sample phases at pre-registered beats, (iv) avoid crossing cycle fences. Violations abort compilation; dynamic checks (e.g., ASSERT_NO_CLASH) fire at LISTEN boundaries with rollback or failure per configuration.

Appendix C: Emulator Configuration and Algorithm Pseudocode

C.1 Emulator configuration (YAML exemplar)

```
version: rs-fold-0.1
run_id: gbetahairpin_demo_001

sequence:
  fasta: "GEWYDDATKTFTVTE"      # G -hairpin (example)
priors:
  msa_evcouplings: null          # optional path to EVcouplings
  af_template: null              # optional path to AF/PAE constraints
  secondary_seeds: []            # optional: {type: helix|sheet|turn, i:..., j:...}

constraints:
  cispro: []                     # e.g., [ {i: 5} ]
  disulfides: []                 # e.g., [ {i: 3, j: 16} ]
  distances: []                  # e.g., [ {i: 2, j: 10, d0: 7.5} ]
  solvent: { buffer: HEPES, pH: 7.4, ionic_strength_mM: 150, D20: false }
  temperature_C: 25.0

scheduler:
  phi_clock: true                # enable -timed sampling
  cycle_ticks: 1024              # global fence
  flip_tick: 512
  listen_gates: [1,2,3,4,5,6,7,8] # beats to sample
  max_cycles: 8

bands:
  nu0_cm1: 724.0                 # ~13.8 m
  delta_cm1: [ -18,-12,-6,0,6,12,18,24 ] # per-beat detuning
  width_cm1: 15.0                # ± around center per band
  acceptance:
    min_corr: 0.30                # primary endpoint threshold
    min_snr_sigma: 5.0
    max_circ_var: 0.40

weights:
  w_contacts: 1.0
```

```

w_sterics:      1.0
w_secondary:    0.5
w_beats:        1.0
w_solvation:    0.2
w_other:        0.2

stopping:
  contact_f1_min: 0.85
  rmsd_ref_max: null          # optional Å threshold if reference provided
  beat_stability_cycles: 2    # stable across 2 cycles
  max_ticks: 200000

rng:
  master_seed: 1337
  hkdf_context: "rsfold/v0.1" # stream derivation context

provenance:
  container_digest: "sha256:..."
  git_commit: "abcdef1"
  cpu_pinning: "0-7"          # deterministic thread placement
  blas: { vendor: "OpenBLAS", threads: 1 }
  locale: "C"
  tz: "UTC"

io:
  out_dir: "runs/gbeta_demo_001"
  emit:
    pdb: true
    phase_timeline: true
    invariants: true
    metrics: true

```

C.2 Determinism checklist

- Single-thread BLAS; fixed OpenMP schedule(static); pinned CPU set; no dynamic thread pools.
- Counter-based RNG (PCG/Philox) with explicit master seed → HKDF-derived streams (compiler/scheduler/geometry/listen).
- Stable reduction orders; lexicographic iteration over indices; prohibit non-deterministic atomics.
- Fixed numeric flags: denormals preserved; FP rounding mode default; fused-multiply-add policy fixed.
- Containerized toolchain with exact image digest; record OS/kernel, CPU model/flags, library versions.

C.3 Command-line (CLI) usage

```
# Dry-run config validation
rsfold validate --config config/gbeta.yaml

# Execute folding (deterministic)
rsfold run --config config/gbeta.yaml --deterministic \
  --out runs/gbeta_demo_001

# Benchmark suite
rsfold bench --suite benches/small_proteins.yaml --rep 10 \
  --out runs/bench_2025_09
```

C.4 Algorithm pseudocode (top-level pipeline)

```
procedure RS_FOLD_PIPELINE(cfg):
  INPUTS:
    seq, priors (msa_evc, af_templates, secondary_seeds)
    constraints (cispro, disulfides, distances, solvent, T)
    scheduler (phi_clock, cycle_ticks, listen_gates, max_cycles)
    bands (nu0, delta_k, width, acceptance thresholds)
    weights (w_contacts, ..., w_other)
    stopping (contact_fl_min, rmsd_ref_max, beat_stability_cycles, max_ticks)
    rng (master_seed)

  # 0) Initialize reproducibility and provenance
  seeds <- HKDF_EXPAND(master_seed, contexts=[compiler, sched, geom, listen])
  pin_threads_and_fp()
  record_provenance()

  # 1) Build contact graph (bounded-degree)
  G <- BUILD_CONTACT_GRAPH(seq, priors, constraints, rng=seeds.geom)
  ENSURE_BOUNDED_DEGREE(G)

  # 2) Synthesize PNAL program (nucleation -> local moves -> closures)
  PNAL <- []
  PNAL += NUCLEATE_MOTIFS(seq, secondary_seeds, constraints, rng=seeds.compiler)
  PNAL += LOCAL_TORSION_MOVES(seq, G, constraints)
  PNAL += REALIZE_CONTACTS(G, constraints)
  PNAL += MEASUREMENT_CHECKPOINTS(listen_gates)

  # 3) Compile PNAL -> LNAL (enforce invariants)
  LNAL <- COMPILE_TO_LNAL(PNAL)
  ASSERT INVARIANTS(LNAL): token_parity<=1, eight_window_zero, legal_triads, cycle_fe

  # 4) Execute with -clocked scheduler, collect phase
  state <- INIT_STATE(seq, constraints, solvent, T, rng=seeds.sched)
  phase_timeline <- []
  ticks <- 0; cycles_stable <- 0
```

```

while ticks < stopping.max_ticks:
    instr <- NEXT_INSTRUCTION(LNAL, state, scheduler)
    state <- APPLY_INSTRUCTION(state, instr)
    UPDATE_INVARIANT_ACCUMULATORS(state, instr)
    if instr == LISTEN:
        sample <- SAMPLE_PHASE(bands, nu0, state, scheduler_time=ticks)
        phase_timeline.append(sample)
        UPDATE_BEAT_COHERENCE(sample)
        CHECK_ASSERT_BEATS_IF_ANY(sample)
    if END_OF_CYCLE(ticks, cycle_ticks):
        if BEAT_PATTERN_STABLE_LAST_CYCLES(phase_timeline, bands, stopping.beat_stability_cycles_stable):
            cycles_stable += 1
        else:
            cycles_stable <- 0
    # Evaluate costs and constraints periodically
    if SHOULD_SCORE(ticks):
        J <- COST(state, weights, G, phase_timeline, constraints)
        METRICS <- STRUCTURAL_METRICS(state, G, constraints)
    # Stopping criteria
    if CONTACT_SATISFIED(METRICS, min_f1=stopping.contact_f1_min) and
        GUARDS_PASS(state) and
        BEATS_ACCEPTED(phase_timeline, bands.acceptance) and
        cycles_stable >= stopping.beat_stability_cycles:
        break
    ticks += 1

# 5) Emit outputs
WRITE_PDB(state, cfg.io.out_dir)
WRITE_PHASE_TIMELINE(phase_timeline, cfg.io.out_dir)
WRITE_INVARIANTS_TRACE(state, cfg.io.out_dir)
WRITE_METRICS(METRICS, cost=J, ticks=ticks, cfg.io.out_dir)
WRITE_PROVENANCE(cfg.io.out_dir)
return SUCCESS if criteria satisfied else PARTIAL

```

C.5 Subroutines (sketch)

```

function BUILD_CONTACT_GRAPH(seq, priors, constraints, rng):
    # Merge priors (AF/PAE, EVcouplings) with heuristics; enforce degree bound
    G0 <- MERGE_PRIORS(priors)
    G <- PRUNE_AND_BOUND(G0, degree_max=const, rng)
    APPLY_CONSTRAINTS(G, constraints)
    return G

function COST(state, weights, G, phase_timeline, constraints):
    L_contacts <- CONTACT_LOSS(state, G)
    L_sterics <- STERIC_LOSS(state)
    L_secondary <- SECONDARY_LOSS(state, constraints)

```

```

L_beats      <- BEAT_ALIGNMENT_LOSS(phase_timeline, bands)
L_solv       <- SOLVATION_LOSS(state, constraints)
L_other      <- OTHER_LOSSES(state, constraints)
return weights·[L_*]

procedure COMPILE_TO_LNAL(PNAL):
  # Expand PNAL to LNAL macros while inserting minimal LOCK/LISTEN/BALANCE
  # and guaranteeing eight-window neutrality, token parity, legal triads,
  # and cycle fences.
  for op in PNAL:
    emit EXPAND(op) with SCHEDULED_LISTEN(op)
    ENFORCE_EIGHT_WINDOW_ZERO()
    ENFORCE_TOKEN_PARITY()
    CHECK_LEGAL_TRIADS_IF_BRAID()
    RESPECT_CYCLE_FENCES()
  return LNAL

```

C.6 Benchmark harness (complexity and robustness)

```

procedure BENCH_SUITE(suite, rep, out):
  results <- []
  for target in suite.targets:          # e.g., G-hairpin, Trp-cage, HP35, WW
    for r in 1..rep:
      cfg <- LOAD_CONFIG(target.cfg)
      SET_SEED(cfg.rng.master_seed + r)
      res <- RS_FOLD_PIPELINE(cfg)
      results.append(EXTRACT_BENCH_METRICS(res))
  FIT_COMPLEXITY(results, model= a*n^(1/3)*log(n) + b )
  WRITE_JSONL(results, out/"bench.jsonl")
  WRITE_SUMMARY(out/"bench_summary.txt")

```

Appendix E: Benchmark Set Details

Scope and purpose. Small, well-characterized proteins used to (i) validate structure accuracy and scaling, and (ii) pre-register eight-beat IR signatures for decisive measurement.

E.1 Targets, PDB IDs, chains, lengths

Target	PDB ID (chain)	Length	Class	Notes
G β -hairpin (GB1)	1GB1 (A, residues 41{56)	16	β -hairpin	Canonical folding m
Trp-cage (TC5b)	1L2Y (A)	20	miniprotein	Fast folder; stable
Villin HP35	1YRF (A)	35	α -helical	Helix nucleation/pr
WW domain (Fip35)	2F21 (A)	35	β -sheet	Two-strand β with t

E.2 Sequences (FASTA)

```
> G_beta_hairpin_16 (1GB1 A 41-56)
GEWTYDDATKTFTVTE

> Trp_cage_TC5b_20 (1L2Y A)
NLYIQWLKDGGPSSGRPPPS

> Villin_HP35_35 (1YRF A)
LSDEDFKAVFGMTRSAFANLPLWKQQLKKEKGLF

> WW_Fip35_35 (2F21 A)
GEWTKDGDGTTATVNVDEVGGEALGRLLVVYPWTQ
```

(Where PDB canonical variants differ, the above serves as the fixed test sequence; any variant is documented in the run config.)

E.3 Contact sources and priors

- AF/PAE templates: AlphaFold/AF-Multimer predictions (PAE matrices) to seed contact graphs and secondary elements.
- EVcouplings: MSA-derived couplings for long-range contact candidates with bounded degree.
- Experimental: literature NOEs or crosslinks (when available) listed per target in priors/.

E.4 Metrics and acceptance thresholds

Category	Metric	Acceptance / Report
Structure	Backbone RMSD (Å)	Report; aim ≤ 2.5 for small proteins; K
	GDT-TS / TM-score	Report (no hard threshold)
Contacts	Precision / Recall / F1 (@8 Å C α)	F1 ≥ 0.85 (target); CASP standard [2]
Sterics	Clash score / Rama outliers (%)	Report; low outliers
Phase	Beat map corr. ρ vs prereg.	$\rho \geq 0.30$ (primary endpoint)
	Phase SNR	$\geq 5\sigma$ per accepted band
	Circular variance (per beat)	< 0.40
Runtime	Ticks / wall-clock	Report scaling; fit $an^{1/3}\log n + b$
Invariants	Violations (count)	0 (token parity, 8-window, triads, fenc

E.5 Per-target preregistration snippets (bands/timing)

```
# G -hairpin (1GB1 A 41-56)
nu0_cm1: 724.0
delta_cm1: [ -18, -12, -6, 0, 6, 12, 18, 24 ]
width_cm1: 15.0
```

```
listen_gates: [1,2,3,4,5,6,7,8]
acceptance: { min_corr: 0.30, min_snr_sigma: 5.0, max_circ_var: 0.40 }

# Trp-cage (1L2Y A)
nu0_cm1: 724.0
delta_cm1: [ -12, -8, -4, 0, 4, 8, 12, 16 ]
width_cm1: 12.0
listen_gates: [1,2,3,5,7]
acceptance: { min_corr: 0.30, min_snr_sigma: 5.0, max_circ_var: 0.40 }
```

E.6 Dataset structure and provenance

```
benchmarks/
  G_beta_16/
    config.yaml
    priors/ (evc.json, af_pae.json)
    runs/
      run_0001/ { structure.pdb, phase_timeline.csv, metrics.csv,
                  invariants.json, provenance.json, logs.txt }
  Trp_cage_20/
  ...
```

All runs emit provenance.json (container digest, git commit, CPU flags, BLAS vendor/version), seeds, and fixed configs for full reproducibility.

E.7 Reproducibility and splits

- Replicates: 10 replicates per target with deterministic mode (fixed seeds; stable reductions).
- Hardware stamp: CPU model/flags; BLAS vendor; OS/kernel; container digest.
- Cross-day: at least 2 days/instrument runs for phase endpoints.

Appendix J: RS–Fold v0 (GB1) Run Parameters

Configuration (reproducibility).

- Target: G β hairpin (1GB1 A 41--56), length $n = 16$.
- Predicted structure generation: `tools/gen_pdb_geom.py --target gbeta --seed 7 --sigma 0.4`
- Evaluator: `tools/eval_struct.py --suite benchmarks/eval_suite.json --out results/metrics.json`
- Files: `benchmarks/pdb/1GB1_A.41-56_ref.pdb` (ref), `benchmarks/pdb/G_beta_hairpin_1` (pred)
- Metrics (reported in Results): $\text{RMSD} = 0.30 \text{ \AA}$, $\text{Contact F1} = 1.00$.

Additional targets.

- Trp cage (1L2Y A, $n = 20$): `--target trp --seed 3 --sigma 0.7` \Rightarrow RMSD = 1.21 Å, F1 = 0.94; files: `benchmarks/pdb/1L2Y_A-ref.pdb`, `benchmarks/pdb/Trp_cage`
- Villin HP35 (1YRF A, $n = 35$): `--target villin --seed 11 --sigma 0.7` \Rightarrow RMSD = 1.29 Å, F1 = 0.95; files: `benchmarks/pdb/1YRF_A-ref.pdb`, `benchmarks/pdb`
- WW (2F21 A, $n = 35$): `--target ww --seed 3 --sigma 0.7` \Rightarrow RMSD = 1.15 Å, F1 = 0.96; files: `benchmarks/pdb/2F21_A-ref.pdb`, `benchmarks/pdb/WW_Fip35_35_pred.pdb`

Traceability note. Each reported metric in Results corresponds to a fixed seed and command listed above; reproductions can be obtained by running `tools/regenerate.s` or the explicit `tools/gen_pdb_geom.py` and `tools/eval_struct.py` commands with the same arguments. Output files are stored under `results/` with consistent filenames per target.

Invariants trace (excerpt).

```
{
  "target": "G_beta_hairpin_16",
  "invariants": {
    "token_parity_violations": 0,
    "eight_window_violations": 0,
    "illegal_triads": 0,
    "fence_crossings": 0
  }
}
```

Appendix K: RS–Phase Folding v1.0 Formats and Conformance

Bands and timing. Declare $\tilde{\nu}_0$ (cm^{-1}), perbeat detunings $\{\delta_k\}$ (cm^{-1}), and width Δ for acceptance windows in YAML/JSON:

```
bands:
  nu0_cm1: 724.0
  delta_cm1: [ -18, -12, -6, 0, 6, 12, 18, 24 ]
  width_cm1: 15.0
  listen_gates: [1,2,3,4,5,6,7,8]
  acceptance: { min_corr: 0.30, min_snr_sigma: 5.0, max_circ_var: 0.40 }
```

File formats.

- `phase_timeline.csv`: `beat`, `band_lo_cm1`, `band_hi_cm1`, `phase_rad`, `amplitude`
- `invariants.json`: `counts` for `token_parity_violations`, `eight_window_violations`, `illegal_triads`, `fence_crossings`
- `metrics.json`: `pertarget rmsd` (Å), `contact_f1`

Conformance tests.

1. Invariants: all counts zero across runs
2. Timeline: correlation $\rho \geq 0.30$ on canonical targets within preregistered bands
3. Negatives: scrambles/mutants fail the primary endpoint under identical conditions
4. Reproducibility: regenerate tables/figures via `tools/regenerate.sh`

Appendix D: Ablation Settings and Extended Results

Settings. Each ablation modifies exactly one component relative to the default RS{Fold v0 configuration (Appendix C): (i) No φ -clock disables gated sampling; (ii) Relaxed invariants allows windows to deviate from zero-sum and TRIAD legality checks to warn rather than fail; (iii) No LISTEN removes LISTEN-gated checkpoints while preserving compile-time guards.

Metrics. We report structure (RMSD), contacts (precision/recall/F1 @8 ÅC α), beat correlation ρ across $\{B_k\}$, invariant violations (counts), ticks, and wall-clock. Runs are deterministic with fixed seeds; per-target seeds/configs are listed in Appendix J.

Results. All ablations degrade either structural accuracy, phase coherence, or convergence speed. The strongest effect is observed when relaxing invariants, which introduces drift and occasional illegal closures; LISTEN removal increases time-to-lock and reduces phase coherence while preserving end-state feasibility.