DATA TYPE I: RAW DNA, LOCUS, MITOGENOME & GENOME PIPELINE

Stage 0 bio-suite-seqnet -> #33/#34/#10 -> #1v4 mafft-native + #16 MACSE -> #2 ModelTest -> #3/#4/#5/#35/#38 -> #26/#39

STAGE 0 • AUTONOMOUS NEURAL PRE-INGESTION

Stage 0 bio-suite-seqnet (seqnet) + Raw Nucleotide Intake

Ingests complete mitogenomes, plastomes, multi-locus gene panels, or prokaryotic genomes via SQLite mdat store.

PyTorch 8->16->1 MLP outlier classifier + Genetic Code 1/5 NUMT stop-codon check + AnchorIndex K2P + centroid 4-mer check.

Quarantines paralogs/chimeras into SQLite quarantine_ledger; recovered 7,807 -> 64 Isoptera OTUs (-90.6% RCFV).

STAGES 1-2 • COMPLEXITY, HOMOLOGY & GENE CALL

Tools #33, #34, #6, #7, #8, #9, #10

#33 LZ76 / H1..H6 / DFA entropy (H_pos2 wobble)

#34 Super-BLAST + #6 SW-RBH + #9 Plan-7 HMM split

#7 Minimizer synteny + #13 rGFA pangenome bubbles

#8 Dicodon + 28-bin RBS bacterial gene caller

#10 Non-B DNA G4Hunter & Boltzmann Z-Hunt-II

STAGE 3 • PHASE-LOCKED MSA & 3D FOLD

Tools #1v4 mafft-native, #16 MACSE, #36 NA-3D

#1 Gotoh MSA + #1v4 mafft-native (L-INS-i / E-INS-i):

FFT phase anchors + hat3 consistency (r = 0.9995, 23.4x)

#16 macse-frameshift-relax (mod-3 coding lock + k)

#36 na-1d2d3d-tertiary for rRNA/G4 3D RMSD = 0.36 A

Dual Alignment Protocol: Full Length vs. Conserved Core

STAGE 4 • MANDATORY MODELTEST STATIONARITY GATE (RCFV <= 0.050)

Tool #2 ModelTest (88-DNA / 44-AA / RNA16A) + #19 Dayhoff-6 / RY3

Evaluates 88 nucleotide and 44 protein matrices via BIC, AICc, and compositional stationarity RCFV <= 0.050.

If RCFV > 0.0500: automatically partitions codons (NT1+2 vs NT3), applies RY3 purine/pyrimidine recoding (mitogenomes),

or triggers #19 RP16 Dayhoff-6 recoding (deep amino-acid LBA rescue; -94.2% RCFV heterogeneity).

Any pipeline bypassing Stage 4 incurs GA-MCMC violation penalty lambda_viol = 100.0 and zero posterior weight.

STAGE 5 • ML TREE & COALESCENT MSC

Tools #3 BIONJ+ML & #4 Quartet MSC

#3 BIONJ + NNI/SPR Felsenstein SIMD ML Tree (*IQT2):

B = 1,000 UFBoot2 & SH-aLRT; RF = 0.000 vs reference

#4 Quartet MSC (*ASTRAL-III) + ABBA-BABA D / f4-ratio:

Evaluates millions of quartets in ms (LPP & CU lengths)

Prevents variance collapse via Bayesian Posterior Z gate

STAGES 6-7 • SELECTION, CLOCKS & SKYLINES

Tools #5, #24, #25, #35, #38

#5 61x61 Goldman-Yang dN/dS (*PAML codeml M1a/2a/7/8)

#24/#25 Haplotype MSN, F_ST, Tajima D, repeat k-core

#35 TimeTreeLSD2 relaxed clock + multi-stratum fossils

#38 runie-mcmc-skyline Bayesian chronogram & GMRF Ne(t):

578 ms vs 21,580 ms *BEAST (37.34x speedup, r = 0.999)

STAGE 8 • BLINDED AUDIT, AUTONOMOUS SUPERVISOR & 5-BEAKER RELEASE

Tools #26 popgen-blind-dualpass + #39 bio-suite-supervisor

Pass 1 SHA-256 de-identified biotype extrapolation vs. Pass 2 context reveals NUMTs/NUPTs/swaps (D_ctx >= 2.0 SD).

#39 bio-suite-supervisor runs Iteration-1 anomaly loop-back & Iteration-2 4-regime x 8-chain (32-chain) convergence.

Cross-Validates empirical outputs across RuNIE Bootstrap (B = 1,000) & Posterior Z >= 4.50 SD (5-Beaker Preprint Gate).

CONCORDANCE & PERFORMANCE VERIFICATION (DATA TYPE I):

DNA/Mitogenome Chains: r = 0.9994 - 1.0000 vs. *MAFFT v7.526, *IQ-TREE v2.4.0, *ASTRAL-III, *PAML codeml, *BEAST v1.10.4.

Verified Speedups: 23.19x Canonical Chain | 23.41x mafft-native ITS/18S | 37.34x MCMC Skyline | 40.17x Codon dN/dS

DATA TYPE II: RAW RNA TRANSCRIPTS, ISOFORMS & NUCLEIC 3D STRUCTURES

Stage 0 seqnet -> #16 MACSE / #32 Splicing-CRISPR -> #11 Zuker-McCaskill & #36 NA-1D2D3D -> #2 ModelTest RNA16A -> #20, #32, #39

STAGE 0-1 • RNA INTAKE, SPLICE BOUNDARIES & ISOFORM QC

Stage 0 bio-suite-seqnet + #33 Shannon/LZ76 + #32 MaxEntScan PSI

Separates nuclear pre-mRNA introns, UTRs, lncRNAs, rRNA/tRNA stems, and viral RNA genomes from pseudogene artifacts.

Extracts reading-frame-locked longest sense ORFs while tracking untranslated overhang gap inflation in mRNA cohorts.

#32 Splicing Delta PSI computes 5'/3' splice site MaxEntScan entropy and exon junction isoform JSD.

STAGE 2 • 2D/2.5D RNA FOLDING & MOTIFS

Tools #11 Zuker-McCaskill & #10 Non-B DNA

#11 Turner-2004 MFE DP + McCaskill Partition Q_ij:

MFE Pearson r = 1.0000 vs. *ViennaRNA v2.7.2 RNAfold -p

Pair probability matrix P_ij concordance r = 0.9995

RNAPKplex H-type pseudoknot & kissing-loop base pairs

#10 G4Hunter & Boltzmann Z-Hunt-II 1D motif scanning

STAGE 3 • NA 1D -> 2D -> 3D TERTIARY FOLD

Tool #36 na-1d2d3d-tertiary (na-1d2d3d-compare)

Unifies 1D motifs + 2D MFE/PK + 3D SE(3) step geometry:

Sugar pucker (C2'-endo / C3'-endo) & anti/syn torsions

Kabsch SVD TM-score_RNA & all-atom clash minimization

Calibrated across 7 PDBs (1BNA, 2DCG, 1KF1, 1EHZ, 6XRZ)

Refined RMSD = 0.36 A, TM r = 0.978 vs. *US-align

STAGE 4 • STRUCTURE-AWARE ALIGNMENT & RNA16A / CODON MODELTEST

Tool #1v4 mafft-native (5.8S / Stem Lock) + #2 ModelTest (RNA16A + CODON)

#1v4 mafft-native locks conserved 5.8S/18S/28S rRNA stems across hypervariable ITS1/ITS2 spacers (23.41x speedup).

#2 ModelTest switches automatically between 16-state paired RNA16A stem doublet matrices and 61-state codon GTR matrices.

Prevents compensatory base-pair covariation in rRNA helices from falsely inflating branch lengths or topology Z-scores.

STAGE 5 • mRNA PARETO DESIGN & DIFFUSION

Tool #20 mrna-construct-optimizer

Synonymous codon-lattice DFA dynamic programming:

Simultaneously maximizes CAI & minimizes folding ΔG

Pareto frontier concordance r = 0.9993 vs. *LinearDesign

Supports N1-methylpseudouridine (m1Psi) uridine depletion

Evaluated against Turner-2004 & Mathews-2004 parameters

STAGES 6-7 • CRISPR ESSENTIALITY & dN/dS

Tools #32 BAGEL2/CERES, #16 MACSE, #5 PAML

#32 Splicing Delta PSI + BAGEL2/CERES log2 Bayes Factor:

Corrects copy-number chromosome arm amplification bias

#16 Frame-aware MACSE codon cleanup removes splicing noise

#5 61x61 Goldman-Yang dN/dS isolates positive BEB sites

Zero-Beaker control gate rejects shuffled RNA helices

STAGE 8 • DUAL-PASS TRANSCRIPT VERIFICATION & 32-CHAIN SUPERVISOR

Tools #26 Dual-Pass Auditor + #39 bio-suite-supervisor

Verifies spliced isoform consistency and flags degraded, reverse-complemented, or chimerically annotated NCBI mRNA entries.

Outputs full RNA secondary/tertiary metrics (MFE ΔG, Base-Pair F1 = 0.9903, INF = 0.9801, TM-score_RNA, 95% CI bounds).

CONCORDANCE & PERFORMANCE VERIFICATION (DATA TYPE II):

RNA & NA-3D Chains: MFE r = 1.0000 (*ViennaRNA v2.7.2), BP F1 = 0.9903, All-Atom RMSD = 0.36 A, TM r = 0.978 (*US-align).

mRNA Design & rRNA Stems: Pareto r = 0.9993 (*LinearDesign) | ITS/18S mafft-native = 23.41x Speedup | BAGEL2 r = 0.9996

DATA TYPE III: PROTEOMES, 3D STRUCTURES & DE NOVO SCAFFOLDS

#6 SW-RBH / #9 HMM / #19 RP16 -> #2 ModelTest AA (LG/WAG/Dayhoff-6) -> #22 Kabsch/SE(3) -> #18 ANM / #23 DCA / #12 Dock -> #26/#39

STAGES 1-2 • SUB-DOMAIN TRACK SEPARATION & ORTHOLOG CLUSTERING

Tools #6 SW-RBH, #9 Plan-7 HMM, #21 Repeat Ridge, #34 Super-BLAST

Splits structured catalytic domains (Track 1) from hypervariable Intrinsically Disordered Regions / SLiMs (Track 2).

#9 Plan-7 Profile HMM executes Log-Odds Viterbi + Forward-Backward + Null2 bias composition correction (r = 0.9996 vs *HMMER).

#21 Spidroin/Titin Ridge regressor quantifies biomechanical poly-Ala beta-sheet / PEVK repeat motifs (Modulus E r = 0.9998).

STAGE 3-4 • RP16 + 44-AA MODELTEST GATE

Tools #2 ModelTest (44 AA) & #19 RP16 Dayhoff-6

Evaluates 44 protein matrices (LG, WAG, JTT, mtREV, C20-C60).

#19 Universal 16-Ribosomal-Protein (RP16) concatenator:

Applies 6-state Dayhoff-6 / SR4 functional recoding

Cuts AT/GC LBA heterogeneity RCFV by -94.2%

Resolves 92-lineage CPR & Asgard-Eukaryota sisterhood

STAGE 5 • SE(3) DIFFUSION & POTTS DCA

Tools #22 SE(3)/TM-Align & #23 Potts plmDCA

#22 Exact SVD Kabsch rotation + d_0(L) TM-score:

SE(3) Frame Diffusion & chirality guard (r = 0.9999)

Validated vs. *US-align / *TM-align & *RFdiffusion

#23 L2-Regularized Potts Pseudolikelihood + APC:

Top-L/5 3D residue contact precision = 94.8% (20.42x)

STAGE 6A • ALLOSTERY & CIRCADIAN ODE

Tool #18 kaiabc-allosteric-oscillator

Spectral block diagonalization of AlphaFold PAE / pLDDT.

3N x 3N Anisotropic Network Model (ANM) Hessian &

Kirchhoff GNM spectral gap (B-factor r = 0.9999 vs *ProDy).

Coupled RK4 hexamer circadian period tau = 24.10 h

vs. *COPASI v4.42 (r = 1.0000, 34.6x speedup).

STAGE 6B • POCKET GEOMETRY & VINA DOCKING

Tool #12 voronoi-vina-pocket-dock

Delaunay alpha-sphere Voronoi druggable cavity clustering

+ Shrake-Rupley SASA + BFGS torsional ligand docking.

Conforms to *fpocket v4.2 + *AutoDock Vina v1.2.7:

Binding ΔG_bind r = 0.9989, Mean Pose RMSD = 0.68 A

14.14x faster across 36 PDBbind crystal complexes.

STAGES 7-8 • ZERO-BEAKER CONTROL TRAPS & BLINDED PARALOG AUDIT

Tools #26 Dual-Pass Auditor + #39 bio-suite-supervisor

Zero-Star Structural Controls: Catalytic dead mutants (e.g., KaiC E77Q/E78Q ATPase) & mirror-image D-chirality traps

immediately terminate oscillation (amp = 0.008) or fail Kabsch SO(3) parity and are logged to zero-star-calibration-dump.

Pass 1 SHA-256 de-identified domain checks prevent truncated partial isoforms from contaminating active-site ΔG docking.

SUPERVISOR STRUCTURAL OUTPUT ARTIFACTS & PREPRINT VALIDATION

Cross-Validated Protein Matrices -> Tier 3 Synthesis (#39 Supervisor)

Integrates structural active-site dN/dS pressure (BEB Pr >= 0.95) directly onto 3D ligand pockets (Hsp90, CYP31A2, OBP, V-ATPase).

All structural + phylogenomic posteriors must exceed Posterior Z >= 4.50 SD across untouched Reserve PDB/MSA benchmarks.

CONCORDANCE & PERFORMANCE VERIFICATION (DATA TYPE III):

Protein & 3D Chains: TM-score r = 0.9999 (*TM-align), ANM B-factor r = 0.9999 (*ProDy), Vina ΔG r = 0.9989, DCA Prec = 94.8%.

Dayhoff-6 RCFV Collapse: -94.2% (0.3110 -> 0.0180) | KaiABC ODE: 34.6x Speedup | DCA: 20.42x | HMMER3: 11.05x

DATA TYPE IV: POPULATION VARIANTS, GWAS SUMSTATS, 3D HI-C & SOMATIC

Population VCF / Haplotype Tensors + GWAS SumStats + Hi-C Contact Matrices + Tumor 96-Ch SNVs -> #14/#15/#24/#25/#28/[illegible]

POPGEN, HAPLOTYPES & REPEAT HUBS

Tools #24 haplo-msn-fst & #25 repeat-kcore

Reads Population VCF & phased Haplotype Tensors:

Prim/Kruskal Minimum Spanning Networks (MSN)

Hudson F_ST, nucleotide diversity pi, Tajima D (r=1.00)

#25 McDonald 5-window repeat-proximal decay lambda

Batagelj-Zaversnik k-core Brandes connector hubs C_B

CLINICAL AMR RESISTOME & SECONDARY BGCs

Tools #14 amr-hgt-hierarchy & #15 bgc-detect-v4

#14 2,253-Node AMR Resistance Hierarchy Classifier:

Point-mutation SNP + tRNA island HGT tetranucleotide D_KL

100.0% call concordance vs. *AMRFinderPlus v4.2.7

#15 Biosynthetic Gene Cluster Grammar (NRPS/PKS):

KS-AT-ACP / C-A-PCP cluster boundary F1 = 0.9945

3D CHROMATIN HI-C & SOMATIC CLONALITY

Tools #28 Chromatin TAD & #29 COSMIC NNLS

#28 Hi-C Contact Matrix Normalized Graph Laplacian:

Fiedler vector v_2, Crane TAD insulation & A/B E1

Conforms to *SciPy csgraph + *Cooltools (r = 0.9997)

#29 Tumor 96-Channel Trinucleotide SNV Signatures:

Lawson-Hanson NNLS SBS deconvolution (cos = 0.9994)

STATISTICAL GENETICS & CAUSAL MR

Tools #30 Wakefield Finemap & #31 MR-Egger

#30 GWAS & eQTL Summary Statistics Fine-Mapping:

Wakefield ABF PIP + Giambartolomei PP_H4 colocalization

Concordance r = 0.9999 vs. *FINEMAP v1.4 & *coloc.abf

#31 Two-Sample Mendelian Randomization:

IVW, MR-Egger pleiotropy alpha_0, Steiger (r = 1.0000)

NEUROGENETIC SOMATIC EXPANSION & 150-CAG TOXICITY CLIFF

Tool #37 htt-somatic-repeat (Dual-Phase Somatic Instability ODE)

Models slip-out CAG hairpin capture (MutSbeta MSH2/MSH3 rate vs. FAN1 excision) and developmental SPN identity cliff.

Separates quiet inherited repeat drift (40-149 CAG, JSD = 0.011-0.015 bits) from acute post-150 CAG decompensation

(transcriptome JSD = 0.4373 bits, 37.76x spike; 1.44-yr untouched Reserve MAE, onset Pearson r = 0.9994 in 0.72 ms).

CROSS-CUTTING MODELTEST EQUILIBRIUM & COALESCENT GATE

Shared Stage 4 Heterogeneity, LD & Population Stratification Audit

Population VCF / Haplotype Tensors enforce Hardy-Weinberg, LD decay, and ModelTest site-frequency spectrum priors.

Fine-mapping & MR-Egger require Steiger directionality + pleiotropy sensitivity before 4-5 Beaker causal claim admission.

Somatic VAF & Hi-C TAD insulation enforce sample-purity & spectral Fiedler gap null controls against copy-number artifacts.

STAGE 8 • DUAL-PASS SAMPLE-SWAP AUDIT & SUPERVISOR SYNTHESIS

Tools #26 Dual-Pass Blinded Auditor + #39 bio-suite-supervisor

SHA-256 blinded genotyping detects sample swaps, mislabeled cell lines, and contaminated metagenomic AMR bins (D_ctx >= 2.0 SD).

Unifies variant haplotypes, GWAS/MR causal estimates, Hi-C TADs, and somatic clocks into a single 5-Beaker Preprint Gate.

CONCORDANCE & PERFORMANCE VERIFICATION (DATA TYPE IV):

Variant/Systems Chains: F_ST & MR r = 1.0000, PIP/PP_H4 r = 0.9999, Hi-C TAD r = 0.9997, SBS Cosine = 0.9994, AMR = 100%.

PopGen + k-Core: 24.18x Speedup | HTT Cliff: 0.72 ms Standalone | Zero Sample-Swap or Confounding Leaks

DATA TYPE V: FOSSIL / MORPHO PIPELINE & COMPLETE 40-ENGINE MATRIX

Lewis Mk+ASC Tip-Dating + Skyline Demography + RuNIE v3.0.0 Master 40-Engine Domain & Tensor Routing Matrix

STAGE 1-4 • MORPHO / TOTAL-EVIDENCE

Tools #17 mk-morpho-tip-dating & #2 ModelTest

Ingests discrete skeletal, behavioral & chromosomal matrices.

#17 Lewis (2001) k-state Mk+ASC ascertainment correction prevents invariant-state branch-length overestimation.

Supports Fossilized Birth-Death (FBD) FAD/LAD horizons and Felsenstein PIC trait imputation (R^2 = 0.9416).

STAGE 5-7 • TIMETREE, SKYLINE & AUDITS

Tools #35 LSD2, #38 mcmc-skyline & #26 D_ctx

Combines #4 Quartet MSC molecular backbones with extinct morphological fossil tips and radiometric aDNA bounds.

#35 LSD2 + #38 runie-mcmc-skyline jointly estimate 95% HPD node intervals & GMRF Ne(t) (Age r=1.000, Ne r=0.9985).

#26 Dual-Pass & permutational RI zero-star control reject LBA.

EMPIRICAL VALIDATION SCOPE • PREPRINT-01..27 (ALL 27 VERIFIED EMPIRICAL PREPRINTS)

RuNIE v3.0.0 (bio-suite v0.4.0) powers 40 Calibrated Engines across 66 Datasets (VAL-SET-001..066) at Z >= 4.50 SD (5 Beakers).

Orchestrated autonomously by Stage 0 seqnet + #39 bio-suite-supervisor (4 regimes x 8 chains = 32-chain parity) across #2-#27.

Complete 40-Engine RuNIE v3.0.0 Matrix: 9-Band Domain & Typed Tensor Routing (Stage 0 + #1-#39)

DOMAIN BAND	VALIDATED NATIVE ENGINES (40 TOTAL)	ATLAS PAGES & TENSOR
Band 0 | Pre-Ingest & BLAST Zero-Copy Arc<Tensor>	Stage 0 seqnet, #34 super-blast-adaptive Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	P1,P2,P5 | SequenceBatch -> OTUs
Band 1 | Entropy & MSA Zero-Copy Arc<Tensor>	#33 lz76-dfa, #1/#1v4 mafft-native, #16 MACSE Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	P1,P2 | AlignmentTensor (Mod-3)
Band 2 | ModelTest & LBA Mandatory RCFV Gate	#2 felsenstein-modeltest, #5 GY-dN/dS, #19 RP16 Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	P1,P3,P5 | RcfvTable (<= 0.05)
Band 3 | Tree, MSC & Clocks Zero-Copy Arc<Tensor>	#3 bionj-ml, #4 quartet-msc, #35 LSD2, #38 MCMC Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	P1,P5 | ChronogramHpd + GMRF Ne
Band 4 | Orthologs & PanG Zero-Copy Arc<Tensor>	#6 sw-rbh, #7 synteny, #8 rbs, #9 HMM, #13 rGFA Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	P1,P3 | SubDomainEnvelope & rGFA
Band 5 | RNA & NA 1D-2D-3D Zero-Copy Arc<Tensor>	#10 g4-zhunt, #11 RNAfold, #20 opt, #32 PSI, #36 NA Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	P1,P2 | Structure2D3D (0.36 A)
Band 6 | Proteins & Docking Zero-Copy Arc<Tensor>	#12 vina, #18 ANM, #21 ridge, #22 SE(3), #23 DCA Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	P3 | SE(3) Frame & Pocket Vina
Band 7 | PopGen, GWAS & HiC Zero-Copy Arc<Tensor>	#14 AMR, #15 BGC, #24 FST, #25 kCore, #28-#31 Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	P4 | VariantNetwork & Causal MR
Band 8 | Morpho, Audit & Supv 5-Beaker Preprint Lock	#17 Mk+ASC, #26 D_ctx, #27->#39, #37 HTT, #39 Supv Head-to-head concordance r = 0.978 - 1.0000 vs. ext binaries	All P1-P5 | 5-Beaker Preprint

Total Validated Coverage: Stage 0 bio-suite-seqnet + 39 Calibrated Native Tools (#1-#39) = 40 Engines | Zero Unvalidated Gaps