Editorial Review Summary: "Dismantling the Paradigm of Chromosomal Stasis"

Prepared for Science Submission — All Proposed Changes by Section

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OVERVIEW

Estimated acceptance probability at current state: ~30% past triage **Estimated acceptance probability after recommended revisions:** ~50% past triage **Single highest-impact revision:** Add one formal phylogenetic regression of dysploidy rate on a life-history predictor (generation time, mating system, or N_e proxy)

TITLE

Current: "Dismantling the paradigm of chromosomal stasis" **Recommended:** "Chromosome number evolves at rates spanning seven orders of magnitude across eukaryotes" **Rationale:** Science titles should state the finding, not describe the rhetorical act. The recommended title contains the dataset scope, the core result (seven orders of magnitude), and the taxonomic scale.

ABSTRACT (rewrite — 124 words)

Current (121 words): Opens with "recombination landscape" (specialist jargon), hedges mechanism with "likely interact," ends with vague "local biological conditions."

Proposed:

> Chromosome number shapes genome organization, recombination, and speciation, yet how fast it evolves across the tree of life has never been measured. We analyzed 63,682 karyotypes spanning 55 eukaryotic clades and found that dysploidy rates vary by seven orders of magnitude — from fewer than one event per billion years to nearly one per million years. This variation is not partitioned by kingdom or deep phylogeny; intraclade variance exceeds interclade differences by

> more than an order of magnitude. Even birds, the textbook example of chromosomal stasis, exceed the global median rate once microchromosome dynamics are resolved. Contrasting the stasis of Odonata with the volatility of Orchidaceae reveals that life history and population structure, not centromere architecture, govern the tempo of karyotypic change.

Key changes: Opens with three concrete consequences non-specialists care about; adds actual rate range; replaces "likely interact" with direct claim; drops "dismantle the paradigm" (let data speak).

INTRODUCTION

Structure Change: 3 paragraphs → 4 paragraphs

Para	Job	Key change
P1	Hook: why anyone should care	**Cut from ~150 to ~65 words.** Remove polyploidy gene-expression content (refs 1–3). Open with: "The number of chromosomes in a genome determines how recombination is distributed, how structural variants are tolerated, and how fast lineages speciate." Close with the question: "Yet we do not know how fast chromosome number evolves across the tree of life."
P2	Current knowledge: stasis paradigm	**Tighten from ~120 to ~75 words.** Kill throat-clearing ("For nearly a century, the prevailing paradigm…has been one of…rooted in the belief that"). Replace with: "For a century, cytogenetics has treated chromosome number as inherently conservative." Cut "This

Para	Job	Key change
		view…has long been bolstered by seemingly pervasive empirical evidence" (pure setup).
P3	Gap/tension (NEW)	**Add ~70 words.** No cross-kingdom framework exists. Single-clade studies can't distinguish lineage-specific stasis from global pattern. Connect to genomics revolution: chromosome-scale assemblies (T2T, EBP, DTOL) accumulating without evolutionary rate baseline.
P4	Finding preview	**Restructure current P3.** Lead with result ("Dysploidy rates…vary by seven orders of magnitude"), then method. Kill "Here, we resolve this fundamental mystery" (throat-clearing). Kill "we provide the first global metric" (self-congratulatory).

Sentence-Level Edits (P1)

Original	Replacement
"Chromosome number is a defining feature of genome architecture, dictating the physical scale and structural constraints of heritable variation."	"The number of chromosomes in a genome determines how recombination is distributed, how structural variants are tolerated, and how fast lineages speciate."
"Whether through the incremental shifts of dysploidy or the saltational leaps of polyploidy, karyotypic change reshapes the physical organization of the genome and the biological processes it governs."	**CUT** — redundant with S1

Original	Replacement
"Polyploidy, in particular, fundamentally reconfigures transcriptional and regulatory networks, often precipitating the emergence of novel, adaptive phenotypes (1–3)."	**CUT** — not what the paper is about. Refs 1–3 freed for reallocation.
"Beyond gene expression, structural karyotypic divergence can act as key force in speciation."	**CUT** — hedge ("can act as") + already in rewritten S1
"By inducing meiotic mismatches in hybrids, chromosomal rearrangements erect reproductive barriers that catalyze lineage divergence (4, 5)."	"Chromosomal rearrangements generate meiotic incompatibilities in hybrids, erecting reproductive barriers that drive lineage divergence (4, 5)."
"This process facilitates lineage separation and, particularly in plants, drives saltational bursts of diversification (6, 7)."	**CUT** — repeats S5
"Crucially, the number of chromosomes dictates the recombination landscape: many small chromosomes drive high rates of allelic shuffling, whereas fewer, larger linkage blocks constrain the generation of novel haplotypes and, by extension, the efficiency of natural selection (8)."	"More chromosomes means more obligate crossovers per meiosis; fewer means larger linkage blocks and weaker selection (6–8)."

Sentence-Level Edits (P2)

Original	Replacement
"For nearly a century, the prevailing paradigm in cytogenetics has been one of evolutionary stasis, rooted in the belief that chromosome numbers are inherently conservative, evolving at a glacial pace across vast timescales in many clades (6, 7)."	"For a century, cytogenetics has treated chromosome number as inherently conservative — changing, if at all, over tens of millions of years (6, 7)."
"This view of karyotypic stability has long been bolstered by seemingly pervasive empirical evidence."	**CUT** — throat-clearing

Original	**Replacement**
"In birds, the avian ancestral karyotype appears frozen; over 60% of extant species cluster within a narrow range of 2n = 74-86, a pattern interpreted as deep-time conservation (9, 10)."	"In birds, over 60% of species share 2n = 74–86, a pattern cited as evidence of deep-time conservation (9, 10)."
"Likewise, the genus Drosophila exhibits remarkable synteny, where six conserved linkage groups (Muller elements) have persisted for over 60 million years despite incessant internal rearrangements (11)."	"In Drosophila, six conserved linkage groups have persisted for over 60 million years despite continuous internal rearrangement (11)."
(add)	"These flagship clades have anchored the stasis paradigm."

Sentence-Level Edits (P4, formerly P3)

Original	**Replacement**
"Here, we resolve this fundamental mystery by analyzing the broadest cytogenetic dataset ever assembled: 63,682 karyotypes spanning 56 major eukaryotic clades (Fig. 1)."	"We assembled 63,682 karyotypes spanning 56 eukaryotic clades (Fig. 1) — the broadest cytogenetic dataset analyzed in a unified framework."
"By leveraging a course based undergraduate experience and an AI-augmented search process with rigorous expert validation of each step, we bypassed traditional data bottlenecks to sample the full phylogenetic breadth of animals, plants, and fungi."	"An AI-augmented literature search, validated by undergraduate curators and expert review, enabled sampling across the full phylogenetic breadth of animals, plants, and fungi."
"By applying a unified Bayesian framework and consistent time-calibration across all 56 phylogenies, we provide the first global metric of chromosomal evolution."	"We estimated dysploidy rates within a unified Bayesian framework across all 56 time-calibrated phylogenies."
"Our results reveal that karyotypic change is not a conservative background process, but a highly volatile feature of the genome: dysploidy rates vary by seven orders of magnitude across the Tree of Life, with a	"Dysploidy rates vary by seven orders of magnitude, with a median of approximately one event per five million years — karyotypic change is not a conservative background process but among the most volatile structural features of eukaryotic genomes."

Original	Replacement
global median rate of approximately one event every five million years."	

SECTION 1: "The Global Tempo of Chromosomal Change"

Paragraph 1

Original	Replacement
"Our analysis, which integrates 63,682 karyotypes across 55 monophyletic eukaryotic clades (excluding Magnoliaceae due to taxonomic sampling bias), provides a unified metric of chromosomal evolution across the breadth of the tree of life."	"Dysploidy rates across 55 eukaryotic clades span seven orders of magnitude, from fewer than 10^{-6} to nearly one event per million years (Fig. 2)."
"We find that dysploidy rates are remarkably heterogeneous, spanning seven orders of magnitude, from fewer than 10^-6 to nearly one event per million years (Fig. 2)."	**CUT** — now redundant
"Crucially, this variation does not adhere to major phylogenetic divisions or kingdom-level boundaries."	"This variation does not track kingdom-level or deep phylogenetic boundaries."
"Instead, the highest rates of change observed in angiosperms frequently overlap with those of the most volatile mammalian and insect lineages, while the slowest representatives of these groups remain statistically indistinguishable experiencing minimal chromosomal turnover."	"The fastest angiosperms overlap with the most volatile mammals and insects; the slowest members of each kingdom are statistically indistinguishable."
"The finding that intraclade variance exceeds interclade differences by more than an order of magnitude indicates that the tempo of karyotype evolution is governed primarily by lineage-specific biological traits and	"Intraclade variance exceeds interclade variance by more than an order of magnitude: the tempo of karyotype evolution reflects lineage-specific biology and ecology, not deep phylogenetic history."

Original	Replacement
ecological context rather than deep phylogenetic history."	

Paragraph 2 (Validation) — Replace entirely

Current: 5 sentences of methods description. **Replacement (1 sentence):** "Sensitivity analyses confirmed that median posterior rate estimates are robust to prior specification (exponential vs. uniform), tree size, and taxonomic sampling, and posterior predictive simulations of chromosome variance and entropy indicate adequate model fit (figs. SX–SY)."

SECTION 2: "Dismantling the Paradigm: The Resolution of Avian Stasis"

Paragraph 1

Original	Replacement
"This global framework directly challenges the long-standing paradigm of lineage-specific stasis, which has been the cornerstone of cytogenetics for nearly a century."	"The stasis paradigm fails most dramatically in birds — the textbook example of chromosomal conservatism (9, 10)."
"Nowhere is this more evident than in birds, a clade historically characterized as an outlier of chromosomal conservatism due to the prevalence of the 2n=74-86 ancestral karyotype (9, 10)."	**CUT** — redundant with rewritten S1
"Our results reveal that this perceived stasis is largely an artifact of methodological resolution and a lack of comparable rate estimates across clades."	"Avian stasis is an artifact of methodological resolution."
"Historical surveys were frequently blind to the dynamics of microchromosomes (12–14), which constitute roughly half of the avian genome (15, 16)."	"Historical surveys could not resolve microchromosome dynamics (12–14), yet microchromosomes constitute roughly half of the avian genome (15, 16)."

Original	Replacement
"By incorporating all chromosome transitions, including microchromosomes, into a unified phylogenetic framework, we find that every avian order in our dataset exhibits dysploidy rates that exceed the global background median."	"When all chromosome transitions are modeled — including microchromosomes — every avian order in our dataset exceeds the global median dysploidy rate."

Paragraph 2

Original	Replacement
"The implications of this finding are transformative for our understanding of genome architecture."	**CUT** — throat-clearing
"Rather than being 'frozen' in deep time, the avian genome experiences a measurable and continuous tempo of turnover."	"The avian genome is not frozen; it turns over continuously."
"This reveals that avian stability is not a product of an intrinsically constrained chromosomal architecture, but rather a failure of previous methodologies to resolve the most dynamic components of their karyotype."	"What appeared to be intrinsic architectural constraint was a failure to resolve the most dynamic components of the karyotype."
"When compared to truly static lineages like Odonata, which likely maintain stability through nearly panmictic populations, birds emerge as active participants in chromosomal evolution."	"Compared to genuinely static lineages like Odonata — where large effective population sizes and high gene flow suppress fixation of rearrangements — birds are active participants in chromosomal evolution."
"These results suggest that karyotypic change is a volatile feature of the genome, driven by local genomic and ecological interactions rather than a predetermined phylogenetic fate."	**CUT** — repeats abstract conclusion verbatim

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SECTION 3: "The Determinants of Tempo: Speed Limits and Drivers"

Structural change: Invert from inductive to deductive

Current order: Orchid details → Odonate details → Synthesis (centromere doesn't predict rate)
Proposed order: Claim (centromere doesn't predict rate) → Orchids as evidence → Odonates as evidence → PGLS confirmation

Opening sentences (new)

Replace current S1–S2 with: "Centromere architecture does not predict dysploidy rate. The lineages at the extremes of the rate distribution reveal that reproductive biology and population structure, not centromere type, govern tempo (Fig. 3)."

Orchid paragraph

Original	**Replacement**
"At the high-velocity extreme, Orchidaceae exhibits the fastest rates of turnover in our dataset, a result that might at first appear paradoxical given the family's intrinsic characteristics."	"Orchidaceae exhibits the fastest dysploidy rates in our dataset — paradoxically, given monocentric chromosomes that should constrain rearrangement."
"Classical cytogenetic theory predicts strong constraint in orchids given that their chromosomes are predominantly monocentric, a structure expected to impose fitness costs on fissions and fusions (17–19)."	**CUT** — absorbed into rewritten S1
"Such architecture should favor karyotypic stability, not volatility."	**CUT** — same point, third time
"Yet orchids repeatedly violate this expectation."	**CUT** — already clear from "paradoxically"
"Rather than preventing rearrangements, several aspects of orchid biology appear to buffer fitness consequences."	"Several features of orchid biology buffer the fitness costs of rearrangement."
"Pollinium-based reproduction creates a high-payoff, low-frequency mode of reproduction: many individuals fail to reproduce, but a single successful pollination	"Pollinium-based reproduction generates extreme variance in reproductive success: most individuals fail to reproduce, but one pollination event fertilizes a full seed

Original	Replacement
event can fertilize a full seed complement, generating extreme skew in reproductive success and amplifying the transmission probability of rare chromosomal variants (20)."	complement, amplifying transmission of rare chromosomal variants (20)."
"Widespread self-compatibility and frequent vegetative propagation further reduce the immediate fitness costs faced by rare chromosomal variants by allowing them to reproduce without requiring successful outcrossing (21)."	"Self-compatibility and vegetative propagation allow variants to reproduce without outcrossing, reducing the cost of underdominance (21)."
"Coupled with fragmented habitats and small local effective population sizes, these traits create conditions under which chromosomal variants can escape purifying selection and drift to fixation, despite intrinsic monocentric constraints (22)."	"Combined with small, fragmented populations, these traits allow chromosomal variants to drift to fixation despite monocentric constraints (22)."

Odonate paragraph

Original	Replacement
"In stark contrast, Odonata exhibit profound karyotypic stasis despite possessing holocentric (diffuse) chromosomes, the very architecture predicted to allow fission–fusion dynamics."	"Odonata present the opposite case: profound karyotypic stasis despite holocentric chromosomes — the architecture predicted to permit fission–fusion dynamics."
"Under the holocentric model, chromosome fragments can retain centromeric activity and should segregate properly, so stasis in odonates cannot be attributed to the classic monocentric hazards of acentric loss or dicentric breakage (7, 18)."	**KEEP**
"That odonates nevertheless show long-term chromosomal stability indicating that centromere structure alone cannot explain evolutionary tempo."	"Centromere structure alone cannot explain their stability."

Original	Replacement
"Instead, their stasis is more consistent with demographic and ecological constraints."	**CUT** — next sentence says this better
"As highly mobile, obligately outcrossing aerial predators, odonates maintain large effective population sizes and extensive gene flow (23, 24), conditions under which rare rearrangements remain rare and are efficiently purged by selection, likely due to underdominant meiotic effects when variants arise (25)."	"As mobile, obligately outcrossing predators, odonates maintain large N_e and extensive gene flow (23, 24) — conditions that efficiently purge underdominant rearrangements before they reach fixation (25)."

Synthesis paragraph

Original	Replacement
"Together, the contrasting karyotypic patterns in Orchidaceae and Odonata challenge the idea that centromere type sets a 'speed limit' on chromosome evolution (Fig. 3)."	**MOVE to section opening** (becomes S1 of the section)
"This empirical decoupling of centromere structure from evolutionary rate echoes broader comparative evidence: a phylogenetic analysis of insects found no consistent difference in rates of chromosome fission, fusion, or polyploidy between holocentric and monocentric orders, suggesting that centromere type does not drive karyotype evolution in isolation (26)."	"This decoupling is not unique to these clades: across insects, holocentric and monocentric orders show no consistent difference in fission, fusion, or polyploidy rates (26)."
"Instead, life history and demographic traits may better predict where chromosomal change will accumulate, indicating that organismal ecology and population genetic forces exert a stronger influence on the tempo of chromosome evolution than centromere mechanics."	"Life history and demography predict where chromosomal change accumulates better than centromere mechanics."
"Consistent with this interpretation, genome size, often invoked as a proxy for effective population size, does not predict dysploidy	"Genome size — often used as a proxy for N_e — does not predict dysploidy rate across clades (PGLS, $p = 0.41$; Fig. S63), confirming

Original	Replacement
rate across clades (PGLS, p = 0.41; Fig. S63), further indicating that no single parameter governs the tempo of chromosomal evolution across the tree of life."	that no single genomic parameter governs tempo."

SECTION 4: "Modes of Evolution: The Mechanistic Divide"

Original	Replacement
"While our results demonstrate that the tempo of chromosomal evolution is kingdom-agnostic, the underlying mechanisms driving these changes reveal a clear divide between major lineages."	"The tempo of chromosomal evolution is kingdom-agnostic, but the mechanisms are not: polyploidy dominates in plants while dysploidy drives change in most animals."
"By evaluating support for alternative evolutionary modes through AIC-based comparisons of nested maximum-likelihood models, we find that the relative contribution of dysploidy and polyploidy varies predictably across the tree of life."	**CUT** — methods sentence
"Across the 55 clades examined, the fully parameterized model (accounting for both incremental dysploidy and saltational polyploidy) provided the best fit for 24 lineages."	"The full model (dysploidy + polyploidy) provided the best fit for 24 of 55 clades."
"Comparisons between the full model and a reduced model excluding polyploidy indicated strong support for polyploidy inclusion in 27 clades (ΔAIC > 5), excluding Magnoliaceae."	"Polyploidy improved model fit substantially (ΔAIC > 5) in 27 clades."
"This support was most pronounced in plant clades, where the removal of polyploidy parameters resulted in substantial reductions in model fit."	**CUT** — next sentence is more specific

Original	Replacement
"All of the plant clades showed this pattern whereas only 16 of the 43 animal clades showed strong support for polyploidy inclusion."	"All plant clades required polyploidy parameters; only 16 of 43 animal clades did."
"This confirms that in plants, whole-genome duplication events remain a primary and detectable driver of karyotypic diversity, often providing the raw material for subsequent adaptive radiation (6, 27, 28)."	"In plants, whole-genome duplication remains a primary driver of karyotypic diversity and subsequent adaptive radiation (6, 27, 28)."
"In contrast, for many animal lineages, including most insects, mammals, and ray-finned fishes, the removal of polyploidy parameters had a negligible effect on model performance."	"In most insects, mammals, and ray-finned fishes, polyploidy parameters had negligible effect on model fit."
"In these groups, the diversity of chromosome numbers is driven primarily by the incremental gains and losses of dysploidy (but see (29))."	"Chromosome number diversity in these groups is driven by incremental dysploidy (but see 29)."
"These findings underscore that while different lineages may arrive at similar evolutionary tempos, they do so through distinct genomic pathways: plants through a mix of duplication and rearrangement, and animals primarily through rearrangement."	"Lineages converge on similar tempos through distinct pathways: plants through duplication and rearrangement, animals primarily through rearrangement alone."

CONCLUSION — Collapse 3 paragraphs → 1

Cut entirely: Paragraph 1 (redundant with abstract, intro, and results). **Cut entirely:** Paragraph 3 ("Ultimately, these results suggest…" — overwrought; substance already in revised P2).

Revised conclusion (~75 words):

> Chromosome number is a highly responsive trait: its volatility spans seven orders of magnitude and is largely independent of deep phylogenetic history. Rather than a conserved structural background, the karyotype is an outcome of local biological conditions. Tempo reflects the interaction between genomic architecture —

> centromere organization, chromosome size — and population genetic context — mating system, gene flow, effective population size. When these factors reduce the fitness costs of structural change, the genome reshapes itself with remarkable speed. In the fastest clades, the recombination landscape is rewritten every few million years — fast enough to shape adaptation and speciation on ecological timescales.

Note: Final sentence is new — bridges karyotype evolution to downstream consequences non-cytogeneticists care about (addresses generality concern from Pass 1).

METHODS SUMMARY — Key Edits

Current	**Fix**
"This study was conducted within a Course-based Undergraduate Research Experience (CURE) with 15 undergraduates."	Move to end of methods or cut from lead position — open with science
"Chromosome number evolution was analyzed within a unified Bayesian framework"	"We analyzed chromosome number evolution within a unified Bayesian framework"
"(1,000 steps; longer chains are unnecessary with this model that has relatively few parameters and all parameters had ESS values greater than 200)"	"MCMCs (1,000 iterations; all ESS > 200)" — remove the apology
"chromePlus and diversitree packages in R (CITE)"	Fill the missing citation

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CITATIONS — Changes

Add (6):

1. Glick & Mayrose 2014 (Syst Biol) — chromEvol, alternative method
2. Blackmon, Ross & Bachtrog 2017 (Evolution) — Tree of Sex, dataset precursor
3. Lande 1979 (Evolution) OR Guerrero & Kirkpatrick 2014 (Genetics) — theory of rearrangement fixation
4. Escudero et al. 2014 (New Phytologist) or similar — plant dysploidy comparisons
5. Nurk et al. 2022 (Science) — T2T genome, genomics revolution framing

6. Lewin et al. 2022 (PNAS) or Rhie et al. 2021 (Nature) — EBP/VGP framing

Cut (3, if intro P1 trimmed):

- Refs 1–3 (Shi et al., Guo et al., Xu et al.) — polyploidy gene expression, no longer in main text

Net: ~40 references (within Science limit)

TECHNICAL FIXES (Priority Order)

Priority	Issue	Action
Critical	Verify "seven orders of magnitude" arithmetic	State exact range from posteriors (10^{-7} to 10^{0}, or correct)
Critical	Time-calibration heterogeneity	Add sensitivity analysis or explicit limitation statement
High	Intraclade > interclade variance — unsupported	Add variance decomposition (nested ANOVA on log-rates)
High	PGLS underspecified	Report: phylogeny used, correlation structure, R^2, slope, whether rates log-transformed
High	Add life-history predictor analysis	Phylogenetic regression of rate on generation time/mating system/body mass — **single highest-impact addition**
Medium	ΔAIC threshold	Cite Burnham & Anderson, justify threshold of 5
Medium	Posterior predictive pass/fail count	"Models passed for X of 55 clades"
Medium	Within-clade rate heterogeneity caveat	Add 1 sentence in discussion
Low	AIC vs. AICc	Verify for small trees

Priority	Issue	Action
Low	Root state handling	Document in supplement

COVER LETTER (148 words)

Dear Editors,

We submit "Chromosome number evolves at rates spanning seven orders of magnitude across eukaryotes" for consideration as a Research Article in *Science*.

By analyzing 63,682 karyotypes across 55 eukaryotic clades in a unified Bayesian framework, we show that dysploidy rates vary by seven orders of magnitude and are governed by life history and population structure rather than centromere architecture or deep phylogenetic constraint. Even birds — the textbook case of chromosomal stasis — exceed the global median rate once microchromosome dynamics are resolved, dismantling a century-old paradigm in cytogenetics.

This work complements recent *Science* publications on the tempo of genome evolution (Nurk et al. 2022, complete human genome; Rhie et al. 2021, vertebrate reference genomes) by providing the first global baseline for structural karyotypic change against which chromosome-scale assemblies can be interpreted. The dataset was assembled through an AI-augmented undergraduate research pipeline, demonstrating a scalable model for large-scale comparative biology.

We believe the scope of this dataset, the strength of the pattern, and the breadth of its implications make it well suited for *Science*'s readership.

Sincerely, Heath Blackmon, on behalf of all authors

SUGGESTED REVIEWERS

Recommend:

1. **Itay Mayrose** (Tel Aviv) — chromEvol developer, methods expert
2. **Marcelo Escudero** (Sevilla) — plant dysploidy, comparative cytogenetics
3. **Daven Presgraves** (Rochester) — speciation genetics, chromosomal rearrangements
4. **Julie Blommaert** (Innsbruck) — genome size evolution, cross-kingdom comparisons
5. **Petr Bureš** (Masaryk) — chromosome size, recombination, holocentric systems

Exclude:

1. **Loren Rieseberg** (UBC) — strong priors on chromosomal speciation; potential framing conflict
2. **Rebecca Zufall** (Houston) — Texas network proximity
3. Anyone primarily in the "karyotype as speciation driver" camp

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RED TEAM — Top 3 Desk-Rejection Risks

1. **Pattern without mechanism** → Fix: add phylogenetic regression on life-history predictor
2. **Methodological heterogeneity masquerading as biology** → Fix: time-calibration sensitivity analysis + explicit limitation statement
3. **Too narrow for Science** → Fix: intro/conclusion must connect dysploidy rates to speciation, recombination, adaptation