Genotype ≠ Phenotype: High-Dimensional Development, Plasticity, and the Limits of Allele Stories

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Abstract

The assumption that genotype algorithmically determines phenotype underlies much of evolutionary modeling, including recent work linking cooperative lifestyles to reduced cancer prevalence. We prove that this framing is incomplete in a specific, quantifiable sense: when phenotype emerges from low-dimensional genetic parameters passing through a high-dimensional developmental system that integrates environmental information, allele-based and plasticity-based models become *non-identifiable* from typical observational data. Using a minimal developmental network model, we demonstrate that (1) identical genotypes produce substantially different phenotypes—including different cancer mortality rates—under different environmental histories, (2) aggregate population patterns can arise equally well from either mechanism, and (3) these mechanisms diverge only in their predictions for environmental interventions. We formalize this via a "dimensional gap" Δ_D that quantifies when allele-centric models become uninformative. The allele story is not wrong but is a low-dimensional projection of a

high-dimensional developmental reality.

Keywords: genotype-phenotype map, developmental plasticity, non-identifiability, dimensional collapse, cancer evolution, phenotypic plasticity

1 Introduction

A common implicit assumption in evolutionary biology is that genotype determines phenotype in an approximately algorithmic sense: genetic variants have "effects" on traits, and phenotypic evolution proceeds via changes in allele frequency. This framing underlies genome-wide association studies, quantitative genetics, and many theoretical models of trait evolution. Yet GWAS have famously failed to account for the majority of heritable variation in complex traits—the "missing heritability" problem [8, 9]—suggesting that simple additive models omit something fundamental about how genotypes produce phenotypes.

Recent work has extended allele-centric modeling to cancer evolution. Sierra et al. (2025) demonstrated that cooperative mammalian species exhibit lower cancer prevalence than competitive, fast life-history species, and modeled this as selection on an "oncogenic variant" that increases late-life mortality [1]. Their finding that cooperative environments select against cancer-promoting alleles while competitive environments can favor them (via a demographic Hydra effect) is compelling.

However, we argue that such allele-centric models are incomplete in a specific, quantifiable way. As Pigliucci [3] emphasized, the "genes as blueprint" metaphor is "not only woefully inadequate but positively misleading." The genotype does not algorithmically encode the phenotype; rather, genotype provides low-dimensional parameters to a high-dimensional developmental system that integrates environmental information over time [4, 5]. The phenotype—including cancer-relevant traits like somatic repair allocation—emerges from this process.

This matters because the same aggregate pattern ("cooperative species have less cancer")

can arise from two mechanistically distinct processes:

- **Model A (allele-based):** Different alleles specify different late-life mortality rates μ_S; selection favors lower μ_S in cooperative lineages.
- **Model B (plasticity-based):** Organisms possess flexible developmental policies that allocate resources between somatic repair and reproduction based on perceived environmental cues; cooperative environments induce higher repair allocation, yielding lower emergent μ_S.

These models are *non-identifiable* from aggregate cross-species data but diverge sharply in their predictions for interventions: Model A predicts that changing an organism's environment should not change its cancer risk (determined by alleles), while Model B predicts substantial phenotypic shifts in response to environmental change.

This perspective aligns with recent theoretical shifts in this journal challenging the exclusivity of mutation-centric explanations for malignancy. Lissek [18] proposed "cancer memory"—a form of physiological learning—as an alternative to clonal evolution for establishing malignant phenotypes. Our work provides the information-theoretic dual to this biological argument: by defining the **Dimensional Gap** (Δ_D), we supply a formal bound on *why* such memory-based mechanisms are invisible to standard genetic tools. The high-dimensional "learned" state is lost when projected onto the low-dimensional genotype space.

In this paper, we:

1. Formalize a minimal developmental network model in which genotype parameterizes a dynamical system that maps environmental histories to phenotypes (Section 3).
2. Prove a non-identifiability proposition showing that any allele-based pattern can be matched by a plasticity-based mechanism (Section 4).
3. Demonstrate these results with simulations (Section 5).

4. Discuss the broader implications for evolutionary interpretation and prediction (Section 6).

2 Background

2.1 The Gene-as-Algorithm Assumption

Alberch [4] introduced the concept of genotype–phenotype (G→P) mapping to provide a framework for integrating genetics and developmental biology. The simplest such model treats the map $G \to P$ as approximately additive:

$$P = \sum_i \beta_i G_i + \epsilon \tag{1}$$

where G_i are allelic states, β_i are effect sizes, and ϵ is noise. This framing, while computationally tractable, obscures the developmental process that connects genotype to phenotype.

A more realistic view, dating to Waddington's "epigenetic landscape" [10], is that genotype provides parameters to a developmental dynamical system:

$$\frac{dh}{dt} = f(h, e(t); g) \tag{2}$$

where $h \in \mathbb{R}^m$ is a high-dimensional developmental state, $e(t)$ is environmental input, and g is the genotype [11, 12]. The phenotype x is then a readout of the final developmental state:

$$x = \phi(h_T) \tag{3}$$

In this view, the "effect" of a genetic variant is not a fixed quantity but depends on the environmental history the organism experiences—a phenomenon formalized in the reaction norm framework [13].

2.2 The Dimensional Gap

We define a quantity that captures the mismatch between genetic and phenotypic dimensionality:

Definition 1 (Dimensional Gap)**.** Let L be the dimension of the genotype space and k the dimension of measured traits. Let the developmental system evolve on a manifold $\mathcal{M}$ with **effective dimension** m_{eff}. The **dimensional gap** is:

$$\Delta_D = m_{\text{eff}} - (L + k) \tag{4}$$

Remark. While the physical state space of a biological system may be extremely high-dimensional, m_{eff} represents the degrees of freedom of the regulatory control network. When $\Delta_D \gg 0$, the mapping from genotype to phenotype is strictly non-invertible without full knowledge of the environmental history that constrained the path through $\mathcal{M}$.

When $\Delta_D \gg 0$, the developmental system has far more degrees of freedom than the genetic input or measured output. This creates a many-to-one mapping at both ends: many developmental trajectories are consistent with any given genotype, and many mechanisms collapse to the same observed phenotype. (In our toy model, Section 3, $\Delta_D \approx 24$; in real organisms it will be much larger.)

Projection from high-dimensional to low-dimensional spaces destroys information in systematic ways [6, 7]. Here we apply this insight to genotype-phenotype maps.

2.3 Cooperative Lifestyles and Cancer

Sierra et al. (2025) analyzed cancer prevalence across mammalian species and found a robust negative correlation between cooperative social structure and cancer mortality [1]; see also [16] for broader context on cancer across the tree of life. Species with group living, plural breeding, and helper contributions exhibited lower cancer rates than solitary, competitive species.

Their theoretical model posits two genotypes:

- G1: baseline late-life mortality μ_S
- G2: oncogenic variant with mortality $\mu_S + \delta$

In competitive environments with high fertility, the G2 variant can be favored via a Hydra effect: removing older individuals frees resources for younger breeders. In cooperative environments where older individuals contribute as helpers, this effect reverses.

This is a compelling result. Our point is not that it is wrong, but that the interpretation—that cancer prevalence differences reflect allelic differences—is not uniquely supported by the data.

2.4 Why Humans May Be a Special Case

Singh and Glowacki (2022) argued that Late Pleistocene humans did not inhabit a single "nomadic band" niche but occupied a wide range of social ecologies: hierarchical and egalitarian, sedentary and mobile, small-scale and large-scale [2]. This "diverse histories" model implies that human ancestors were exposed to systematically variable environments across generations.

Under such conditions, selection should favor *plastic developmental policies* over fixed allele-determined phenotypes [5]. An organism that can adjust its repair-vs-reproduction allocation based on local environmental cues will outperform one locked into a single strategy.

This provides a principled reason to expect Model B (plasticity-based) mechanisms to be particularly important in humans.

3 Model

We define a minimal developmental network that captures the key features: low-dimensional genetic input, high-dimensional developmental dynamics, environmental modulation, and

phenotypic readout.

3.1 Developmental Dynamics

Let $g \in \mathbb{R}^L$ be the genotype (with L small), $e_t \in \mathbb{R}^p$ be the environmental input at time t (with p environmental dimensions), and $h_t \in \mathbb{R}^m$ be the developmental state (with $m \gg L$).

The developmental dynamics follow:

$$h_{t+1} = \sigma\left(W_h h_t + W_e e_t + W_g g\right) \tag{5}$$

where W_h, W_e, W_g are weight matrices and σ is a nonlinear activation (we use tanh).

3.2 Phenotype and Cancer Risk

The phenotype $x \in \mathbb{R}^n$ is a linear readout of the final developmental state:

$$x = W_{out} h_T \tag{6}$$

We extract a "repair allocation" variable $r \in [0, 1]$ from the phenotype, representing the organism's investment in somatic maintenance versus reproduction/competition—a classic life-history tradeoff [14, 15]. The emergent cancer mortality is:

$$\mu_S(x) = \mu_0(1 - \alpha \cdot r(x)) \tag{7}$$

where μ_0 is baseline mortality and $\alpha \in (0, 1)$ is the efficacy of repair.

3.3 Environmental Regimes

We define two environmental regimes:

- **Cooperative:** Low variance in resources, high social support, low conflict.

- **Competitive:** High variance in resources, low social support, high conflict.

Parameter values: Throughout, we use $L = 5$ (genotype dimension), $m = 20$ (developmental state dimension), $n = 10$ (phenotype dimension), and $p = 3$ (environmental input dimension). Cancer mortality parameters are $\mu_0 = 0.1$ (baseline) and $\alpha = 0.8$ (repair efficacy). In simulations, cooperative environments are implemented as low-variance, slowly varying resource and support signals, whereas competitive environments are higher-variance and more volatile (see code for exact form).

3.4 Causal Structure

Figure 3 illustrates the causal difference between the two models:

- **Model A:** $G \to \mu_S \to$ Cancer, with environment only modulating selection on G.
- **Model B:** $G \to$ Dev $\to \pi(E) \to r_t \to \mu_S \to$ Cancer, with environment entering directly into development and policy.

Crucially, both graphs collapse to the same two-node summary (Environment $\to \mu_S$) when projected onto low-dimensional observables—this is precisely the Δ_D problem.

4 Non-Identifiability Result

Proposition 2 (Non-identifiability of allele vs. policy mechanisms)**.** *Let Model A be any allele-based system where late-life mortality takes values* $\{\mu, \mu + \delta\}$ *across two ecological regimes, with* $0 \leq \mu < \mu + \delta \leq \mu_0$*. Let Model B be any plasticity-based developmental system* ***capable of realizing any repair allocation*** $r \in [0, 1]$ ***via some environmental history****, and where* $\mu_S = \mu_0(1-\alpha r)$ *as in Equation 7. Then for any pair* $(\mu, \mu+\delta)$ *satisfying these constraints, there exists an environment pair* (E_{coop}, E_{comp}) *such that the induced* μ_S *distributions in Model B match those in Model A for all species-level summary statistics.*

Proof. Take any $(\mu, \mu + \delta)$ from Model A. We construct environments that induce matching μ_S distributions in Model B.

Choose r_{coop} and r_{comp} such that:

$$\mu_0(1 - \alpha r_{\text{coop}}) = \mu \tag{8}$$

$$\mu_0(1 - \alpha r_{\text{comp}}) = \mu + \delta \tag{9}$$

Solving: $r_{\text{coop}} = (1 - \mu/\mu_0)/\alpha$ and $r_{\text{comp}} = (1 - (\mu + \delta)/\mu_0)/\alpha$.

For sufficiently expressive dynamics (e.g., the recurrent network of Equation 5), there exists a mapping from environmental histories to any desired r; this is empirically illustrated in Figure 1D. Thus there exist environments E_{coop} and E_{comp} that induce these repair levels.

Therefore, any species-level summary (mean μ_S, variance, etc.) that Model A produces can be exactly matched by Model B with appropriate environment choice. The models are observationally equivalent at this level. □

Remark 3. This result formalizes the sense in which allele models are "incomplete": they are not wrong, but they are *non-identifiable* from aggregate data. The models become distinguishable only through interventions that change environment while holding genotype fixed.

5 Results

All figures (1–6) show simulated outputs from the developmental network model in Section 3; no empirical data are used.

5.1 Same Genotype, Different Phenotypes

Figure 1 demonstrates that a single genotype produces substantially different phenotypes depending on environmental history.

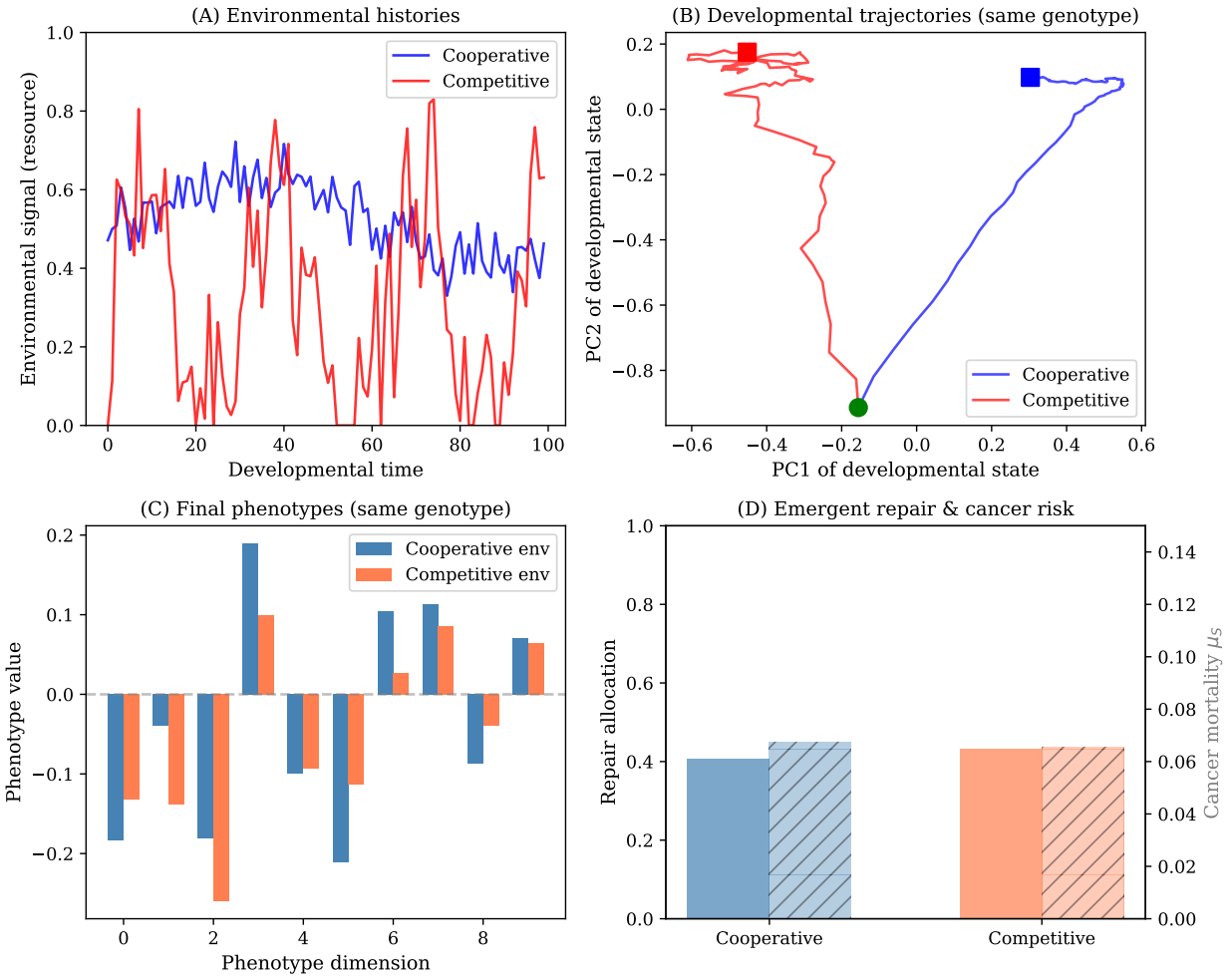

Figure 1: **Simulated developmental trajectories.** Same genotype, different environments → different phenotypes. (A) Environmental histories for cooperative (blue) and competitive (red) regimes. (B) Developmental trajectories in state space (PCA projection); green circle marks start, squares mark end states. (C) Final phenotype vectors differ substantially. (D) Emergent repair allocation and cancer mortality: cooperative environments induce higher repair and lower μ_S.

The key observation is panel (D): the same genotype produces different cancer mortality rates depending on developmental environment. This is the empirical foundation for Proposition 2.

5.2 Population-Level Patterns

Figure 2 shows that aggregate population patterns can arise from either allele-based or plasticity-based mechanisms.

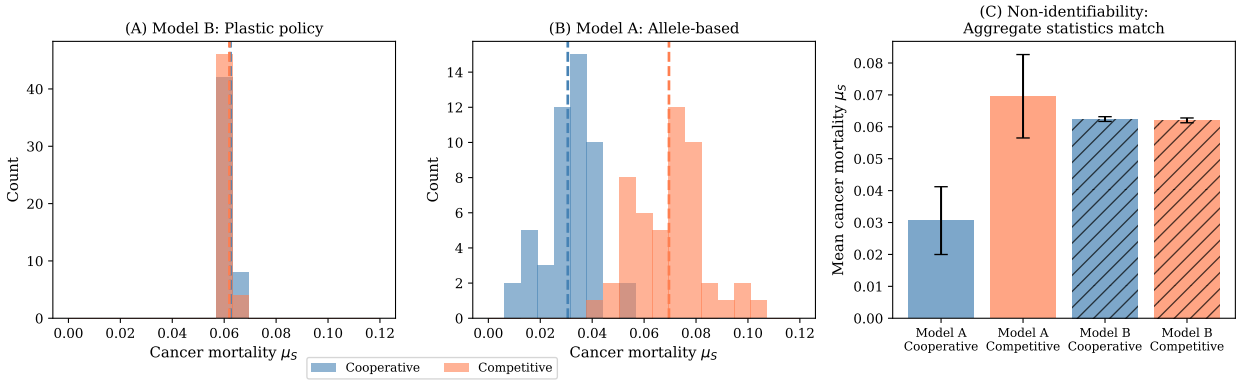

Figure 2: Non-identifiability at the population level. (A) Model B (plastic policy): same genetic distribution in different environments produces different μ_S distributions. (B) Model A (allele-based): different genetic distributions can produce similar patterns. (C) Aggregate statistics (mean $\pm$ SD of μ_S) are indistinguishable between models.

5.3 Causal Structure

Figure 3 shows the causal graphs for both models. The key difference is that environment is purely a selection context in Model A but a direct developmental input in Model B; this distinction underlies the non-identifiability result. Critically, both causal structures collapse to the same two-node summary (Environment $\rightarrow \mu_S$) when projected onto low-dimensional observables—this is precisely where $\Delta_D > 0$ creates ambiguity.

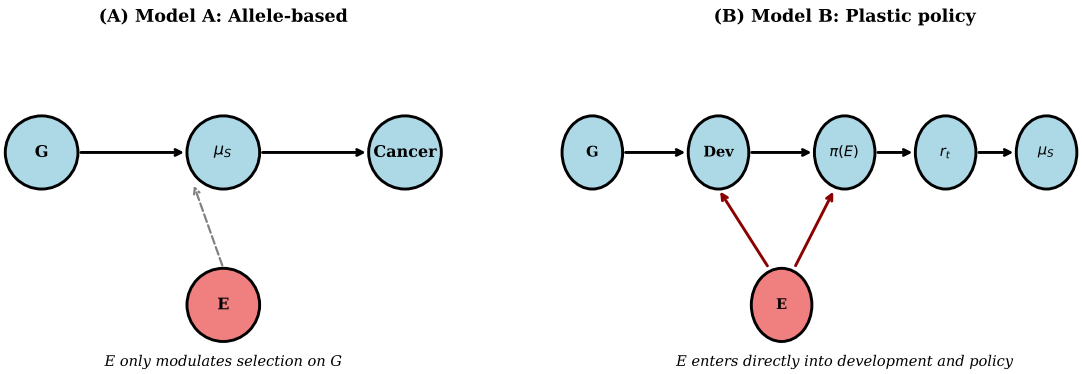

Figure 3: Causal structure of the two models. (A) Model A: genotype directly determines μ_S; environment only modulates selection. (B) Model B: genotype parameterizes a developmental system; environment enters directly into development and policy, producing emergent μ_S.

5.4 Information Loss Under Projection

Figure 4 illustrates the information loss that results from dimensional projection. Panel C quantifies this: in the full model, environment explains most of the variance in μ_S, but an allele-only regression would misattribute much of this variance to "genetic effects."

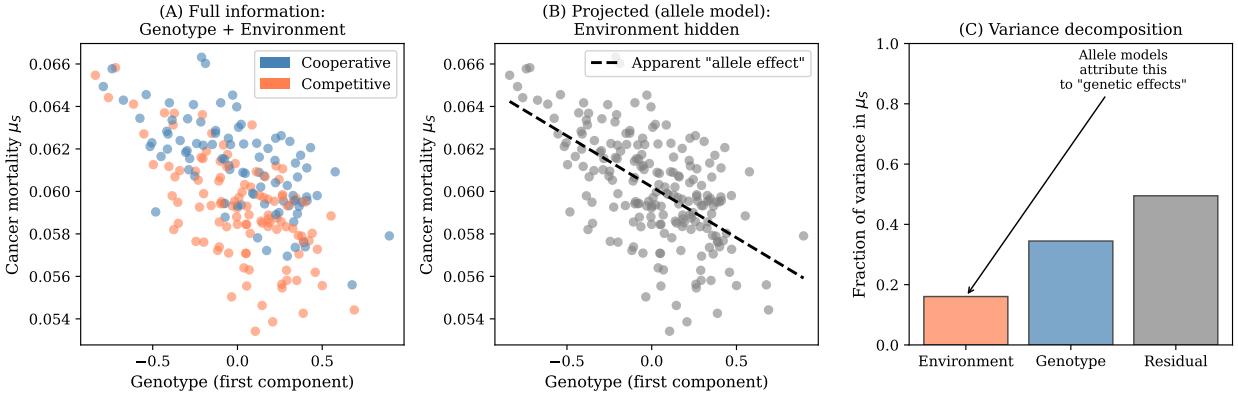

Figure 4: Information loss under projection. (A) In full genotype × environment space, cooperative and competitive regimes are clearly separated. (B) In projected (allele-only) space, environment is hidden. (C) Variance decomposition: environment explains most variance in μ_S, but allele models attribute this to genetic effects.

5.5 Twin Worlds Experiment

Figure 5 provides a decisive demonstration: identical genotype distributions in different worlds produce patterns that naive allele models would interpret as genetic differences. A naive comparative study could infer different "oncogenic allele frequencies" between worlds that in fact share identical genotype distributions.

Crucially, an observer calculating the genetic distance between the World 1 and World 2 populations would find a Fixation Index of $F_{ST} \approx 0$, yet would observe significantly different phenotype distributions ($P_{ST} \gg 0$). A standard GWAS trained on this combined data would fail to find significant SNPs, leading to the conclusion of "missing heritability," when in fact the heritability is entirely environmental.

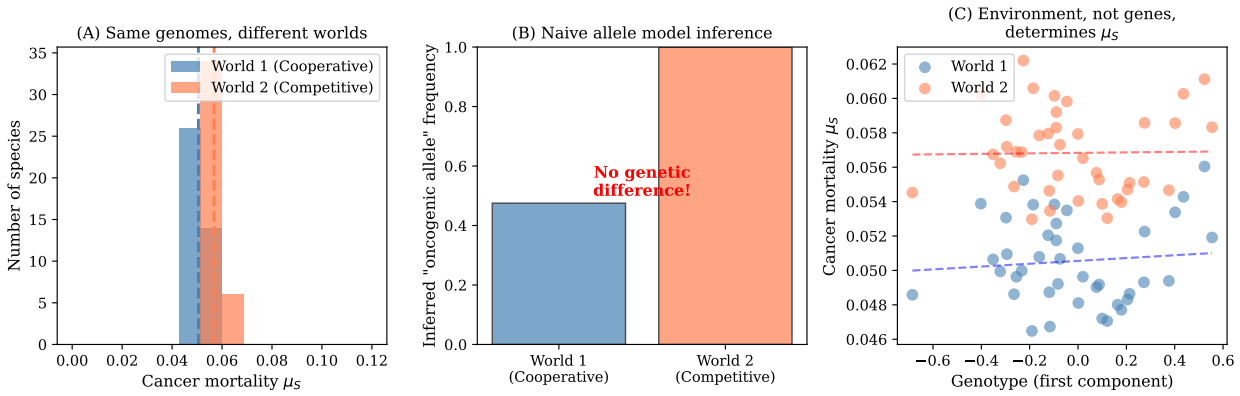

Figure 5: Twin worlds experiment. (A) Same genotype distribution developed in cooperative vs. competitive worlds produces dramatically different μ_S distributions. (B) A naive allele model would infer different "oncogenic allele frequencies" despite no genetic difference. (C) Genotype has minimal correlation with μ_S; environment determines the outcome.

5.6 Divergent Predictions

Figure 6 shows where the models make different predictions. This makes environmental interventions the critical empirical test for discriminating allele- vs. policy-based mechanisms.

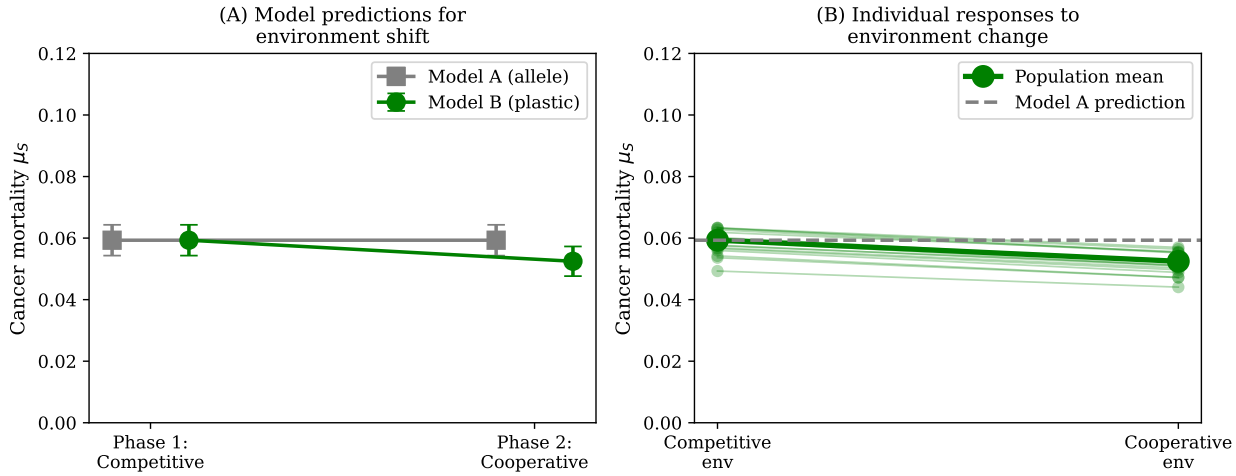

Figure 6: Divergent predictions for environmental change. (A) Model A predicts no change in μ_S when environment shifts; Model B predicts substantial reduction. (B) Individual trajectories show systematic phenotypic change without genetic change.

6 Discussion

6.1 Steelmanning the Allele View

We emphasize that allele-based models are not wrong. Sierra et al.'s finding that cooperative species have lower cancer prevalence is real and important. Selection does act on heritable variation, and over evolutionary time, lineages in cooperative environments likely do accumulate genetic changes that support higher somatic investment [17].

Our point is narrower: the aggregate pattern "cooperative = less cancer" is equally consistent with:

1. Selection having already fixed cancer-suppressing alleles in cooperative lineages (Model A).

2. Selection having favored plastic developmental policies that respond to cooperative cues (Model B).

3. **Genetic assimilation:** A process where an initially plastic response (Model B) becomes canalized into a fixed genetic trait (Model A) over evolutionary time due to the

consistent adaptive value of the phenotype in stable environments.

The models are non-identifiable from cross-species comparative data. Distinguishing them requires environmental manipulation experiments.

6.2 When Allele Stories Work vs. Fail

Taxonomy: When Allele Stories Become Non-Identifiable

Allele stories work when:

- Traits are low-dimensional
- Plasticity is weak
- Environments are stable
- Δ_D is small

Allele stories become non-identifiable when:

- $\Delta_D \gg 0$ (high-dimensional development)
- Environments vary across generations
- Phenotype is policy-based rather than algorithm-generated
- Identical genotypes produce divergent phenotypes depending on $E(t)$
- Low-dimensional measurement destroys mechanistic information

Cancer risk in cooperative vs. competitive mammals, facial morphology, and human life-history traits sit squarely in the second category.

6.3 Specific Empirical Predictions

While the models often produce indistinguishable aggregate statistics, they diverge structurally. Table 1 contrasts the mechanistic assumptions and specific predictions of each framework.

Table 1: **Contrasting Allele-Centric vs. Plasticity-Centric Models.** Model A and Model B are indistinguishable from static data but diverge under environmental intervention.

Feature	**Model A (Allele-Based)**	**Model B (Plasticity-Based)**
Core Mechanism	Genotype algorithmically determines phenotype (additive effects).	Genotype parameterizes a high-D developmental system; phenotype is emergent.
Role of Environment	*Filter:* Modulates selection pressures on alleles over generations.	*Input:* Enters directly into developmental dynamics to shape phenotype in real-time.
Interpretation of "Cooperative Safety"	Selection favored "low cancer" alleles in cooperative lineages.	Cooperative cues induce plastic policies allocating more resources to repair.
Divergent Predictions (Testable)		
Environmental Shift	**No immediate change.** Phenotype is locked by genotype.	**Immediate shift.** Phenotype adjusts to new environmental cues.
Twin Worlds Result	Identical genomes $\rightarrow$ identical cancer rates ($F_{ST} \approx P_{ST}$).	Identical genomes $\rightarrow$ divergent cancer rates ($F_{ST} \approx 0$, $P_{ST} \gg 0$).
GWAS Implication	"Missing heritability" due to many small-effect variants.	"Missing heritability" is a projection artifact ($\Delta_D \gg 0$).

As shown in Figure 6, environmental interventions provide the critical test. Model A predicts that moving a "competitive" genotype to a cooperative environment will not change its baseline mortality μ_S. Model B predicts a significant reduction in μ_S as the developmental system integrates the new safety cues.

6.4 Dimensional Constraints on Interpretation

The key insight is that genotype-phenotype maps involve multiple projections:

$$\begin{array}{ccc} \text{High-D developmental state} & \xrightarrow{\text{projection}} & \text{Low-D observed phenotype} \\ (g, E, h_T) \in \mathbb{R}^{L+pT+m} & & x \in \mathbb{R}^n \end{array}$$

Allele-based models further project by marginalizing over environment:

$$P(x \mid g) = \int P(x \mid g, E) P(E)\, dE \tag{10}$$

This marginalization loses information about the environment-dependent structure [6, 7]. The "genetic effect" β that emerges is not a property of the allele alone but of the allele-environment interaction averaged over some implicit environmental distribution.

Even in our minimal toy model, with $L = 5$ genetic dimensions, $m = 20$ developmental state dimensions, $n = 10$ phenotype dimensions, and $k = 1$ measured trait (μ_S), we have $\Delta_D = (20 + 10) - (5 + 1) = 24$. In real organisms, Δ_D will be vastly larger, making non-identifiability correspondingly worse.

6.5 Theoretical Context: Memory vs. Mutation

Our results offer a mathematical formalization for the "cancer memory" hypothesis recently debated in this journal [18]. While Lissek argued biologically that malignancy can arise from epigenetic or physiological memory rather than random mutation, our "Twin Worlds" experiment (Figure 5) demonstrates the statistical consequences of this mechanism.

When $\Delta_D \gg 0$, the developmental system acts as a high-capacity memory buffer that integrates environmental inputs [19, 20]. The "missing heritability" in cancer studies is thus not missing genetic data, but rather the "forgotten" information of environmental history—information that is causally active in the phenotype but mathematically marginalized in the allele model.

This connects to broader systems-theoretic perspectives on evolution. Corning [21] argued that evolution is primarily about functional organization rather than individual genes; Fontana [22] proposed unified developmental models linking ageing and cancer. Our frame-

work provides the formal information-theoretic machinery: the distinction between "evolved" (Model A) and "learned" (Model B) cancer traits is not merely semantic but represents a fundamental topological gap—the Dimensional Gap Δ_D—in how we map genotype to phenotype.

In the tradition of critiques of algorithmic biology [23], we demonstrate that the gene-as-algorithm assumption is not merely an approximation but a projection that actively discards the causal structure of the developmental system.

7 Conclusion

The allele-centric view is a special case of a broader, dimensionality-constrained developmental mapping. When Δ_D is large—when development is high-dimensional and plastic—allele effects become non-identifiable from observational data, and plastic policies dominate phenotype formation.

Cancer prevalence in cooperative vs. competitive species is an instance of this general phenomenon. The pattern Sierra et al. documented is real; our contribution is to show that it admits multiple mechanistic interpretations that are indistinguishable from aggregate data but make different predictions for intervention.

Genotype does not algorithmically determine phenotype. Genotype provides parameters to a high-dimensional developmental system that integrates environmental information to produce phenotypic outcomes. Recognizing this is essential for prediction, intervention, and understanding rapid phenotypic change.

Data and Code Availability

Simulation code is available at `https://github.com/todd866/genotype-vs-phenotype`. The repository includes `developmental_network.py`, which implements the developmental network (Equations 2–3, 5–7), generates all figures, and demonstrates the Twin Worlds

experiment (Figure 5).

Declaration of competing interest

The author declares that there are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author used Claude Code (Claude 4.5 Opus) for primary drafting and model development, with feedback from Gemini 3 Pro and GPT 5.1 Pro. After using these tools, the author reviewed and edited the content as needed and takes full responsibility for the content of the published article.

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