Jurassic Park at 35: Reflections on evolutionary theory, genome engineering, and the science-society interface

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Abstract | 35 years after the release of Michael Crichton's *Jurassic Park*, I reflect on both technical and cultural themes of the novel that resonate in the current moment. Specifically, this perspective aims to highlight the various ways in which our genome engineering ambitions can be encumbered by scientific and ethical naïveté. First, I provide a technical review of three evolutionary genetics concepts—*plasticity*, *pleiotropy*, and *epistasis*—that complicate our efforts to engineer organisms with desirable phenotypes. I show how these ideas play out in the fictional narrative of *Jurassic Park* and in real-world genome engineering projects such as the "de-extinction" of the dire wolf. I then examine the technical challenges involved with broader aspirations to control complex living systems with the tools of bioengineering. Lastly, I survey the novel's cultural and social significance: its relevance for modern controversies in bioethics, its cautionary critique of techno-optimism, and its rich portrayal of scientists.

1 *"You create new life-forms, about which you know nothing at all."* (p. 342)

1.1 The continued relevance of *Jurassic Park*

2025 marked 35 years since the release of Michael Crichton's *Jurassic Park* (Knopf, 1990). It was an immediate commercial success, selling millions of copies within its first few years on the market. However, it is best known for inspiring the *Jurassic Park* films, which have grossed nearly USD 7 billion worldwide. The book's critical reception was largely positive (Lehmann-Haupt, 1990), and scholars across multiple disciplines have analyzed its narrative and cinematic adaptations, exploring topics such as ancient DNA (Jones, 2018), bioethics (Attwood, 2021) and beyond. Here, I use this anniversary to reflect on several themes from the novel in light of contemporary issues in evolutionary genetics and the interface between science and society. In addition to its scientific relevance, I propose that *Jurassic Park* provides a rich case study for understanding the interplay between science and the way that it is situated as a human activity.

The story of *Jurassic Park* focuses on the activities of a biotechnology company, InGen, founded by wealthy investor and philanthropist John Hammond, a dinosaur enthusiast who wants to build a theme park featuring resurrected dinosaurs. InGen scientists develop a method to extract DNA from extinct dinosaurs via mosquitoes that had once fed on them (fossilized in amber). Using cutting-edge molecular techniques, InGen scientists construct full-length genomes from extinct dinosaur DNA, with frog DNA used to fill in gaps introduced during fossilization. They then inject the engineered DNA into artificial eggs and grow embryos (all female by design) in the laboratory.

An evaluation of the feasibility of fictional methods in *Jurassic Park* would not be useful, as the impact of the story does not depend on the believability of the proposed science. One could argue that the aspirational nature of the technology in *Jurassic Park* was part of its appeal. Furthermore, Crichton wrote much of this in the 1980s, predating the Human Genome Project (National Human Genome Research Institute, 2025), well before sequencing and cloning tools became affordable and widely available. When we consider this, *Jurassic Park* was successful in the main endeavor of many speculative fiction works: building a world based on an imaginative extrapolation of technology, one believable enough to avoid distracting the reader from the story.

However, I propose that *Jurassic Park* achieved a goal more ambitious than world-building: it effectively articulated many technical and non-technical issues that are pertinent to genome engineering. To anchor this discussion, I will highlight a recent advance (in 2025) where *Jurassic Park* can be invoked for comparison: Colossal Biosciences' attempt to de-extinct *Aenocyon dirus*, better known as the dire wolf.

I provide scientific, cultural, and ethical perspectives on genome engineering generally, and de-extinction specifically, focusing on the many ways that naïveté can lead us astray. I begin with a brief introduction to the relevance of *Jurassic Park* as a model system, and summarize recent public conversations surrounding de-extinction. I then provide a review of three concepts from evolutionary biology that complicate genome engineering efforts, and propose a framework for considering our attempts to control biological systems using tools of bioengineering (Parts 2-5). Finally, I discuss several ethical and cultural issues that appear in the book and in other real-world settings (Part 6). This article is structured around quotations from the most resonant character in the book, Ian Malcolm, a fictional mathematician who serves as the vehicle for the story's ethical messages[1].

I have constructed this perspective to be read by both experts and non-experts with a basic to moderate understanding of evolutionary concepts[2]. For those interested in more technical descriptions, Boxes 1-3 provide additional detail, though their engagement is not necessary to follow the core arguments of this perspective article.

1.2 2025: Genome engineering and de-extinction science in the news

Several subfields of genetics have generated a large body of literature on ideas featured in *Jurassic Park*, many of which are similar to concepts central to modern de-extinction efforts. A 2013 article once asked, "What If Extinction Is Not Forever (Sherkow and Greely, 2013)?" In it, the authors highlight the potential of technologies to bring long-extinct species back, and the bevy of associated legal and ethical issues. And practitioners in the fields of ancient DNA and paleobiology have examined the science of resurrecting fossil species (Jones, 2018). Leaders have offered detailed summaries of the science of de-extinction, including the many challenges involved (Shapiro, 2017, 2015a).

The year 2025 brought unprecedented attention to the science of de-extinction. The April announcement from Colossal Biosciences involving the engineering of genetic information from the dire wolf (*Aenocyon dirus*)—which went extinct nearly 13,000 years ago (Gedman et al., 2025)—into the gray wolf (*Canis lupus*) was accompanied by widespread media coverage (Kluger, 2025;Zimmer, 2025;Jacobs, 2025;Max, 2025). In a press release, the Chief Executive Officer of Colossal Biosciences celebrated the event: "This massive milestone is the first of many coming examples demonstrating that our end-to-end de-extinction technology stack works (Colossal Biosciences (press release), 2025)." According to information provided by Colossal Biosciences, this required isolating the dire wolf genome from ancient DNA extracted from subfossil remains, then engineering mutations from this extinct species into cells of a modern surrogate species, the gray wolf. The effort reportedly involved several technical innovations, including the use of advanced paleogenomics techniques, the assembly of a high-quality dire wolf genome, and the application of CRISPR-based multiplex genome editing of dire wolf-specific loci in viable embryos.

Press coverage and company materials communicate that the team targeted 20 mutation edits across 14 gray wolf genes, all focusing on physical traits (morphology, bone structure, coat color, etc.). Reports say that of these 20 mutations, 15 were from the extinct dire wolf genome, and the other five mutations were derived from other gray wolves. The reason for this, Colossal Biosciences has explained, is that direct engineering of select dire wolf mutations has conferred unexpected defects in other canids (e.g., blindness, deafness) (Biosciences, 2025;Colossal Biosciences (press release), 2025). To avoid these defects, Colossal Biosciences engineered gray wolves in a manner that recapitulated some physical traits of dire wolves while avoiding the known deleterious effects. Photographs and videos of beautiful animals shared around the world highlighted the final result: an ostensibly successful genome engineering effort that generated an animal with certain physical attributes of two different species. That this event is a genome-editing excursion[3] rather than the successful de-extinction of

[1] Quotes are mostly co-opted for the article and are used outside of their context in the novel.

[2] For example, I do not explain concepts like *genotype*, *phenotype*, or *mutation*.

[3] If we accept the claims offered by Colossal Biosciences at face value, we can say that it was a successful genome engineering

anything was only obvious to those paying close attention.

1.3 From non-fiction to fiction and back

For illustrative purposes, one can compare the ambitions and activities of InGen (the fictional company in *Jurassic Park*) to those of Colossal Biosciences. Both aim to bring back extinct species using modern molecular techniques. Colossal Biosciences does not intend to build a theme park, and their genetically modified organisms are reared in controlled settings, sharing little in common with the world in which dinosaurs are engineered in *Jurassic Park*. But the technical errors from InGen in *Jurassic Park* reflect a lack of clarity around several important evolutionary concepts that may complicate our real-world genome engineering excursions, including de-extinction.

In the next several sections (2-4), I describe theoretical concepts that apply to the challenge of bioengineering a phenotype of interest through genomic modification: plasticity, pleiotropy, and epistasis. We will discuss the relevance of these topics through toy examples inspired by *Jurassic Park* and real-world settings, and follow up (Section 5) with discussions about the prospects for controlling biological systems using genomic modification approaches.

2 *"It isn't adapted to our world... Everything is different."* (p. 178)

2.1 Plasticity dictates the environmental robustness of engineered phenotypes

We begin our exploration of concepts that complicate genome engineering efforts with plasticity—a central idea in evolutionary biology that describes the ability of a genotype to produce different phenotypes across environmental contexts (Box 1). Its roots can be traced to Richard Woltereck's experiments in 1909 on water fleas, in which he coined the term "Reaktionsnorm (reaction norm)" to communicate how trait expression depended on the environment (Woltereck, 1909;Pigliucci, 2001).

The literature on plasticity is vast and several treatments have examined its great implications across the biosphere (West-Eberhard, 1989;Gomulkiewicz and Kirkpatrick, 1992;Scheiner, 1993;Schlichting and Smith, 2002;West-Eberhard, 2003;Forsman, 2015;Sommer, 2020). There are various types of plasticity, including discrete, categorical, developmental, and behavioral (Pigliucci, 2001;West-Eberhard, 1989, 2003;Sommer, 2020). *Phenotypic plasticity* often involves reversible changes in phenotype across environments, such as changes in leaf morphology in coffee trees depending on exposure to sun or shade (Matos et al., 2009). In contrast, *developmental plasticity* refers to traits that are plastic with respect to environmental conditions during development, which can lead to fixed phenotypes during adulthood, such as the architecture of plant roots that develop under heterogeneous nutrient availability (Yu et al., 2014).

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exercise.

Box 1: Plasticity

Plasticity is the ability of a genotype or organism to produce different phenotypes across environmental contexts (West-Eberhard, 1989;Gomulkiewicz and Kirkpatrick, 1992;Scheiner, 1993;Pigliucci, 2001;Schlichting and Smith, 2002;West-Eberhard, 2003;Sommer, 2020). It can be defined in several ways, two of which are presented below.

The first definition describes plasticity as the variance in phenotype across environmental contexts (Valladares et al., 2006):

$$\text{Plasticity} = \text{Var}(P_1, P_2, \ldots, P_n) \tag{1}$$

where $P_1, P_2, \ldots, P_n$ are phenotype values measured in n distinct environments.

The second definition expresses plasticity as a linear function relating phenotype to an environmental variable (Scheiner, 1993):

$$P(E) = a + bE \tag{2}$$

where $P(E)$ is the phenotype expressed in environment E, a is the intercept, and b is the slope representing the rate of phenotypic change per unit change in E. The linear function in Equation 2 applies only to the simplest, most circumscribed cases. Plasticity is more often the result of nonlinear relationships between the phenotype and the environment.

The *reaction norm* (sometimes referred to as the *norm of reaction*) is widely used in ecology and quantitative genetics to visualize how the trait values of genotypes vary across environments (Schlichting and Pigliucci, 1995, 1998;Pigliucci, 2001;Sultan and Stearns, 2005;Oomen and Hutchings, 2015, 2020). Not only does it highlight the environmental dependence of phenotypes, but also how genotypic performance interacts with the environment, a phenomenon called a *gene-by-environment interaction* (G×E) (Figure 1) (Sae-Lim et al., 2016;Kang, 2004). G×E interactions have been extensively studied and are now a part of the standard canon of evolutionary and population genetics. They complicate simple interpretations of performance and fitness, especially when comparing genotypes of a species, strain, or breed. For example: Which population of *Mimulus guttatus* (Seep Monkeyflower) grows the fastest? Which strain of *Escherichia coli* can break down sugar the most efficiently? Which variant of SARS-CoV-2 is the most transmissible? Plasticity proposes that the answer may depend on the environment, making our attempts to link genotype to phenotype more challenging.

The flexibility of phenotype is a property of many complex biological systems and has important implications for bioengineering. Robustness across a range of real-world environments is the goal of engineering a modified phenotype. For example, consider a hypothetical bioengineer interested in generating plants with a certain leaf morphology. Leaf shape is a well-known plastic trait that varies according to environmental factors such as temperature and light intensity (Nicotra et al., 2010, 2011). Consequently, anyone seeking to engineer a specific leaf shape must consider how environmental conditions influence its development.

Similarly, plasticity is evident both in the fictional ambitions of InGen and in the real aims of modern biotechnology companies. The scientists in *Jurassic Park* sought to create a *Tyrannosaurus rex* that would look and behave as it had in the late Cretaceous period: a large, intimidating, apex predator. But, as the Ian Malcolm quote that forms the title of this section suggests, the challenge is that the Jurassic ecosystem is vastly different from that of the early 1990s (or of 2025). Consequently, a scientist attempting to de-extinct *T. rex* must consider how phenotypes of interest, such as body mass or predator behavior, might be sensitive to the environment in which the organism exists.

In Figure 1, we present a fictional scenario in which two traits are expressed in different environments. Relatedly, the success of de-extinction depends on the degree of plasticity in traits associated with fitness and the specific environment in which the animal lives. The book addresses this directly, noting that the engineered dinosaurs suffer from several defects, including susceptibility to disease, which are likely the result of attempting to survive in a foreign (modern, human-constructed) ecosystem. To quote Henry Loomis, a scientist in 2025's *Jurassic World Rebirth*: "*The fitness landscape of the Earth no longer suits them*[4] (Edwards, Gareth (director),

[4]The *fitness landscape* (often called the *adaptive landscape*) is a depiction of genotype-space that analogizes the process of evolution to a physical landscape, where evolution moves populations "towards fitness peaks" or "down fitness valleys." The concept was introduced

2025). ”

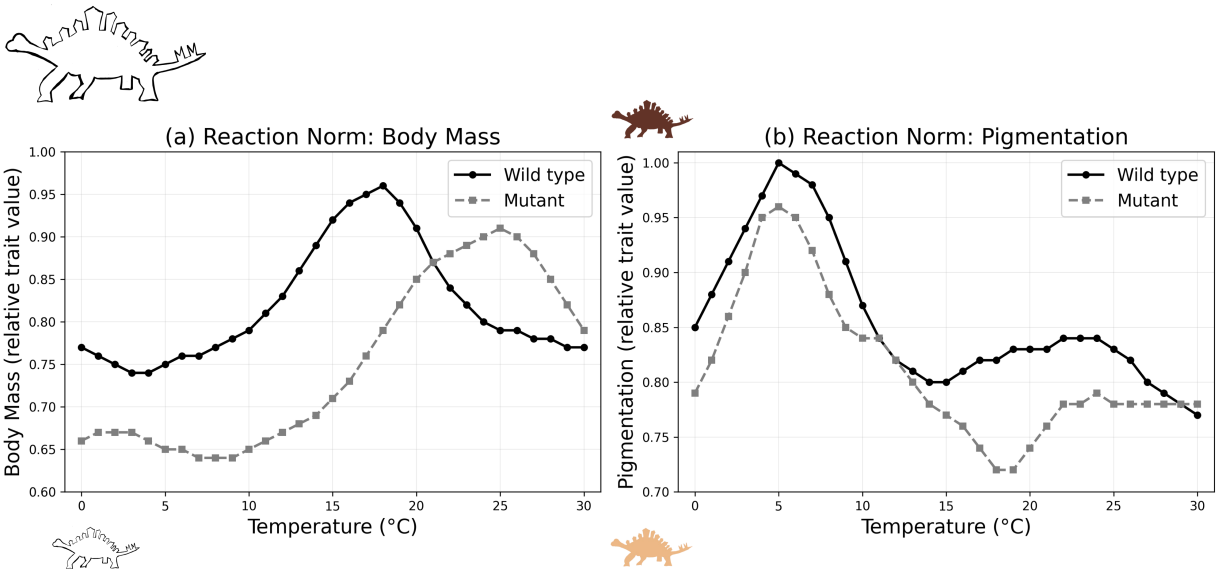

Fig. 1. Plasticity and pleiotropy. Fictional reaction norms illustrate how a single gene variant that affects multiple traits varies across environmental contexts (temperature). It depicts Wild type and mutant variants for two developmental traits in a genetically modified animal: (a) pigmentation and (b) body mass. The x-axis is temperature; the y-axis is trait value relative to a standard. Lines connect genotype mean values from measurements of individuals at selected developmental temperatures, with trait values fixed in adulthood (developmental plasticity). Plasticity is reflected in how genotypes differ across environments for a given trait (pigmentation, body mass). Crossing reaction norms indicate a *gene-by-environment* (G×E) interaction, where genotype performance depends on environment (Kang, 2004;Sae-Lim et al., 2016). Here, temperature is the environmental gradient, but environments may be continuous (e.g., pH) or categorical (e.g., location, resource presence/absence). Pleiotropy is observed when a single genotype differs across traits: the fictional gene affects both pigmentation and body mass, so changes in one trait accompany changes in the other. *Technical notes:* This example suggests that pigmentation and body size are significantly influenced by a single locus, though both traits are polygenic in most known animal species. Fictional animals in the figure are engineered homozygotes, avoiding dominance effects. Pigmentation peaks at cooler temperatures are inspired by literature on plasticity in thermal melanism (Clusella-Trullas et al., 2007, 2008). In the supplementary information, we have provided an alternative depiction of these data in the form of a trait space diagram (See S1).

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3 *“Such isolation is impossible. It simply cannot be done.”* (p. 101)

3.1 Pleiotropy underlies the complexity of genome engineering

Plasticity refers to the way measurable traits are expressed in different environmental contexts. Pleiotropy, on the other hand, is the propensity for a single gene to affect multiple (often unrelated) phenotypes (Stearns, 2010;Wagner and Zhang, 2011;Solovieff et al., 2013;Zhang, 2023) (Box 2). While the term pleiotropy was introduced by the German geneticist Ludwig Plate in 1910 (Stearns, 2010), the concept appeared in Gregor Mendel’s pea plant (*Pisum sativum*) experiments. In these experiments, Mendel discovered that the same genes that dictated the white and purple colors of flowers also influence the color of seed coats (Lobo, 2008;Hemani et al., 2018). Even Charles Darwin discussed phenomena related to pleiotropy under the guise of “correlated variation”

by Sewall Wright in 1932 (Wright, 1932) and has since become a foundation of modern population and evolutionary genetics (Svensson and Calsbeek, 2012;Hartl, 2014;Srivastava et al., 2026). I note that this quote from *Jurassic World Rebirth* is an unusual take on the fitness landscape, as it generally applies to populations of organisms or replicators, rather than a setting (like Earth).

between traits, offering that "Colour and constitutional peculiarities go together, of which many remarkable cases could be given amongst animals and plants" (Darwin, 1859). That pleiotropy appeared from the very beginnings of evolutionary biology and genetics is a testament to its fundamental status.

Many examples of pleiotropy also exist in complex organisms such as humans. A classical case involves Marfan syndrome, an autosomal dominant condition caused by mutations in the *FBN1* (fibrillin-1) gene. These mutations are associated with a variety of clinical symptoms, including an increased risk of aortic dissection, long limbs, myopia, hypermobile joints, and several others (Milewicz et al., 2021). This diversity of outcomes highlights the interconnectedness of genes and functions in humans. This becomes easier to understand when we learn that *FBN1* encodes a protein that contributes to the structure of connective tissue. Pleiotropy often appears when alterations occur in genes that contribute to basic components of the morphology or physiology of the organism.

Box 2: Pleiotropy

Pleiotropy refers to the tendency of a single gene or locus to influence multiple, often distinct, phenotypic traits (Stearns, 2010;Solovieff et al., 2013;Paaby and Rockman, 2013;Zhang, 2023). A simplified way to represent this is as a property of the genotype–phenotype map, where a genotype contributes to more than one trait. In quantitative genetics, this can be illustrated with a linear model (Lynch and Walsh, 1998):

$$P = \mu + BG + \epsilon \tag{3}$$

where P is a vector of phenotypic trait values, μ is the baseline (population) mean, G is the genotype, B is a vector or matrix of regression coefficients describing pleiotropic effects, and ϵ captures residual variation due to environment, noise, or unmeasured loci. While this form highlights the basic idea, the genetic architecture of pleiotropy is often more complex, involving nonlinear and context-dependent effects.

Pleiotropy arises from a feature of many complex systems in which the number of possible functions exceeds the number of elements that construct them. In biology, this means that there are far fewer genes (in *Homo sapiens*, roughly 20,000 protein-coding genes) than discrete phenotypes (an unknown but larger number, depending on how we define a phenotype). This disparity is reconciled through combinatorial recombination and reorganization of genetic information through many mechanisms (e.g. variable gene expression, alternative splicing), allowing each genetic element to contribute to multiple phenotypes (Zhang and Xu, 2022;Zhang, 2023). This represents an important feature of genome evolution: biological information is engineered to be wired and re-wired, and this feature underlies the evolutionary potential of new functions (Wagner and Zhang, 2011).

This is related to an idea in evolution called the *cost of complexity* in evolutionary biology, where widespread pleiotropy in complex organisms constrains evolution, because it is challenging to modify genes (through mutation, as occurs during molecular evolution) without affecting other functions (Orr, 2000;Wagner et al., 2008). For example, in a hypothetical case that all genes in a mouse play a role in all mouse phenotypes (related to a concept called *universal pleiotropy*)[5], mutations in any given mouse gene are likely to have widespread, potentially negative fitness consequences, thereby decreasing evolutionary potential. However, evidence suggests[6] that the cost of complexity can be mitigated by *modularity*, the tendency for biological information to be organized into functional units (Welch and Waxman, 2003;Wagner et al., 2007, 2008). This means that tweaking certain genes will not always perturb functions across an organism, but mainly those within a module. This can limit the negative pleiotropic consequences of altering genes, which can facilitate (or promote) adaptive evolution (Wagner et al., 2007;Wagner and Zhang, 2011).

How does pleiotropy appear in genome engineering efforts such as those depicted in *Jurassic Park* and in the dire wolf project? The genetic contribution to multiple phenotypes presents a significant complication because it implies (often unpredictable) "off-target" effects of modifying genes, where altering one part of a system can

[5]Universal pleiotropy can be interpreted to follow from Fisher's Geometric Model (Fisher, 1930;Tenaillon, 2014), a foundational concept in evolutionary genetics. A full description is beyond the scope of this article, but I refer readers to the cited references for more information.

[6]There have been discussions about whether universal pleiotropy is a reasonable null hypothesis in evolutionary genetics or simply a useful abstraction (Wagner and Zhang, 2012).

influence others (Zhang et al., 2015). As in Marfan syndrome, changes in a gene can have multiple phenotypic consequences, many of which are difficult to predict. This uncertainty is magnified when we engineer genomes in organisms with which we are unfamiliar, as was the case in *Jurassic Park*, and in modern de-extinction efforts. Like the *FBN1* gene in *Homo sapiens*, dire wolf mutations can affect more phenotypes than the intended physical traits when expressed in the genomic background of another animal.

Figure 1 demonstrates a fictional scenario using a gene that plays a role in two phenotypes and a range of environments (temperature). Even if we have a rigorous understanding of how environmental context shapes our phenotype of interest (e.g., coat color in an animal and temperature), the gene of interest can influence multiple phenotypes.

4 *"It is inherently unpredictable, just as the weather is."* (p. 178)

4.1 Epistasis facilitates surprising interactions between engineered mutations

The source of unpredictability in pleiotropy is the fact that genes can participate in more than one function. But what are other major sources of unpredictability? One involves questions about the very nature of mutation effects. In theoretical population genetics, this has been studied with regard to the distribution of fitness effects, a statistical picture of mutations in terms of being neutral, beneficial, or deleterious (Eyre-Walker and Keightley, 2007;Keightley and Eyre-Walker, 2010). But another concept illustrates how the phenotypic effects of mutations depend on genomic context, a phenomenon known as *epistasis*.

There is a colloquial characterization of epistasis that I have found useful: "our surprise at the phenotype when mutations are combined, given the constituent mutations' individual effects" (Weinreich et al., 2013). Or, I know what mutation [A] does to a phenotype and I know what mutation [B] does to a phenotype. But when I combine them, I get a phenotype that I could not have predicted from their individual contributions. More formally, epistasis refers to non-additive interactions between genes or mutations (Phillips, 2008;Sackton and Hartl, 2016;Bank, 2022;Ogbunugafor and Scarpino, 2022) (Box 3). It was conceptualized by William Bateson in 1909 to describe how the effects of some genes can mask those of others (Bateson, 1909;Miko, 2008).

As in pleiotropy, one can invoke examples from human disease. Cystic fibrosis is a well-characterized Mendelian[7] disease that follows an autosomal recessive pattern (Riordan et al., 1989;Elborn, 2016). Symptoms present in multiple systems (e.g., respiratory, digestive), which also reflects the pleiotropic effects of the affected gene (not unlike the mutations in *FBN1* responsible for Marfan syndrome). Affected individuals generally carry two copies (one from each biological parent) of a mutated cystic fibrosis transmembrane conductance regulator (*CFTR*) gene (often ΔF508), which encodes a protein that regulates chloride and other electrolytes. Despite the purported simplicity of the cystic fibrosis disease phenotype[8], studies have shown that its severity is influenced by mutations in other genes, such as *TGFB1*, which encodes transforming growth factor β-1 (TGFβ-1). *TGFB1*-specific mutations can worsen the severity of cystic fibrosis (Cutting, 2010;Bremer et al., 2008), suggesting that the genetic effects of *CFTR* mutations are modified—through epistasis—by mutations in the *TGFB1* gene.

[7] By "Mendelian," I mean that it follows a pattern of inheritance where the phenotype—disease in this case—can be understood as the direct consequence of an allele passed down from each parent

[8] We commonly describe Mendelian traits as being "simple," as opposed to phenotypes that are "complex," as in, they are the product of multiple genes that contribute to a phenotype in a complicated manner (Nature Education, 2014).

Box 3: Epistasis

Epistasis occurs when the combined phenotypic effect of two (or more) mutations is not equal to the sum of their individual effects, relative to a defined baseline (e.g., wild type) (Phillips, 2008;Weinreich et al., 2013).

$$\Delta P_{AB} \neq \Delta P_A + \Delta P_B \tag{4}$$

where ΔP_A and ΔP_B are the phenotypic effects of single mutations A and B relative to the wild type, and ΔP_{AB} is the effect of the double mutant. An alternative definition expresses epistasis in a statistical genetics framework, where the phenotype is modeled as the sum of additive and interaction effects (Hansen, 2006):

$$P = \mu + \sum_i a_i x_i + \sum_{i<j} \epsilon_{ij} x_i x_j \tag{5}$$

where P is the phenotypic value, μ is the baseline phenotype, a_i are additive effects, x_i encodes the genotype at locus i, and ϵ_{ij} captures the epistatic interaction between loci i and j. Although epistasis can be described with simple forms such as Equations 4 and 5, it often involves complex, higher-order interactions, where more than two mutations or genes are interacting.

In broader discussions, epistasis encompasses different definitions and use cases (Cordell, 2002;Phillips, 2008;Sackton and Hartl, 2016;Ogbunugafor and Scarpino, 2022). It can be classified by the quantitative consequences of interactions between gene variants or mutations: *positive epistasis* occurs when two mutations produce a non-additive positive effect; *negative epistasis* when the effect is less than the additive combination; and *sign epistasis* when the direction of the effect (positive or negative) differs from that of the component mutations or genes—often the 'biggest surprise.' Figure 2 is a fictional depiction of how epistasis emerges between mutations in a gene that plays a role in pigmentation. When epistasis is present, we cannot predict the phenotypic consequences of combinations of mutations based on their individual contributions.

The notion that mutations can interact in a non-additive fashion complicates the relationship between genotype and phenotype and makes it difficult to predict the consequences of mutations, especially in complex organisms where many gene products and pathways interact. In the setting of *Jurassic Park*, epistasis helps explain why inserting foreign DNA into a dinosaur genome could produce unexpected results. InGen scientists filled gaps in dinosaur DNA with amphibian DNA[9] (due to breaks during fossilization). This inserted amphibian DNA had unexpected consequences, most notably the birth of males when all dinosaurs were designed to be female[10]. Whatever the mechanism, this genetic 'surprise' can be attributed to epistasis between amphibian genes and the genomic background of dinosaurs (note that pleiotropy may also be at work here; perhaps the frog genes that InGen scientists thought participated in one function played an unforeseen role in sex determination, or some other trait).

The importance of epistasis is also evident in the dire wolf genome engineering exercise. As noted above, 20 mutations were engineered into 14 genes in the gray wolf. Fifteen of these mutations came from the reconstructed ancient genome of the extinct dire wolf. The other five were from extant genetic variants in gray wolves. These were engineered at two gray wolf loci—*MC1R* and *MFSD12*, both of which are associated with pigmentation (Hubbard et al., 2010;Crawford et al., 2017). Recall that gray wolf mutations were used because several dire wolf mutations had deleterious effects in other canids, including blindness and deafness (Zimmer, 2025;Kluger, 2025). Why is this so? Given the evolutionary history of the dire wolf (Gedman et al., 2025), its genome differs sufficiently from that of existing canids to qualify as a meaningfully different genotypic background. Because of this, donor mutations from the dire wolf are engineered into the genome of another species. These mutations operate outside their evolved context, a substrate for epistatic surprise.

[9] No detailed explanation for this was offered in the book.

[10] The bigger point in the story is that this allowed breeding on the island, which the InGen scientists did not want.

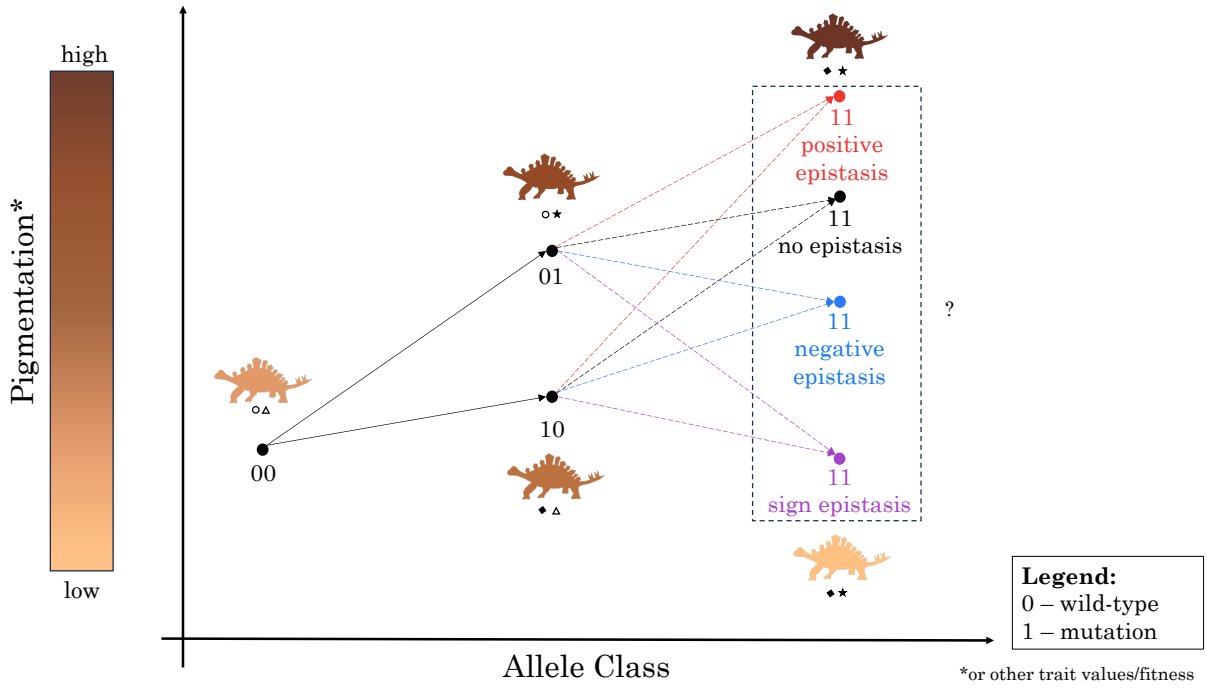

Fig. 2. Epistasis. In this fictional schematic, two engineered mutations in an extinct animal gene affect pigmentation at 25 ℃. Binary notation denotes genotypes: [0] is the wild type locus, [1] is a mutation. The x-axis shows pigmentation relative to a standard estimate. Combining mutations ([11]) produces a synergistic effect greater than the sum of their individual effects ([01], [10]). In evolutionary genetics, this reflects a G×G interaction, where a mutation's effect depends on genetic and genomic context. *Technical notes:* As in Figure 1, this example treats pigmentation as being influenced by a single locus. Studies have shown that pigmentation is polygenic (Jablonski, 2004) and we have no information about its genetic architecture in dinosaurs. Fictional animals are engineered homozygotes, avoiding dominance effects. Values are for schematic purposes only. This figure is adapted from a study on epistasis in viral pathogens (Manivannan et al., 2025).

5 *"What we call 'nature' is in fact a complex system of far greater subtlety than we are willing to accept."* (p. 102)

5.1 Integrations between plasticity, pleiotropy, and epistasis

In the previous three sections, we highlighted how plasticity, pleiotropy, and epistasis underlie many challenges with genome modification (Summarized in Box 4) and should be considered in our broader applications. I should also emphasize that these concepts do not have strict boundaries and are not mutually exclusive. As shown in Figure 1, plasticity and pleiotropy can occur for the same gene variant. And there is a growing literature that asks questions about whether trait correlations can constrain plasticity (Matesanz et al., 2021;Walworth et al., 2021). Epistatic interactions can also appear in multiple phenotypes through pleiotropy (Remold and Lenski, 2004;Lunzer et al., 2005;Ogbunugafor et al., 2023), a phenomenon that has been referred to as *epistatic pleiotropy* (Wolf et al., 2005) or *pleiotropic epistasis* (Zhang et al., 2016), although a single term is not consistently used in the literature. In addition, there is overlap between plasticity and epistasis, when epistatic effects manifest differently across environments (Flynn et al., 2013;Lindsey et al., 2013;Ogbunugafor, 2022;Diaz-Colunga et al., 2023). This is called *environmental epistasis* (Lindsey et al., 2013), and can be depicted by the *mutation effect reaction norm*, which tracks mutation effects and epistasis across environments (Ogbunugafor, 2022). There are even examples in which plasticity, pleiotropy, and epistasis can be examined within a single data set, when mutation effects differ for traits across environmental contexts[11]. And finally, very recent work has demonstrated how interactions between environments can manifest in a manner not unlike interactions between mutations in epistasis, in the form of an *environment-by-environment* (E×E) interaction (Schmidlin et al., 2025).

[11] In one example, we observed how different mutations affect growth and resistance to an antimicrobial drug across cellular environments (Guerrero et al., 2019;Ogbunugafor and Scarpino, 2022).

In sum, I believe that concepts at the margins between the many forces of evolutionary genetics constitute an exciting future research direction, one with both theoretical value and applied utility.

Box 4: Evolutionary concepts relevant for genome modification and de-extinction

Here we summarize three concepts that complicate de-extinction and genome engineering.

- *Plasticity*: The ability of a genotype to produce different phenotypes across environmental contexts (e.g., the fictional velociraptor, *Velociraptor mongoliensis*, of *Jurassic Park* evolved in an ecosystem vastly different from that of the proposed 1990s theme park. Such contextual differences would likely have phenotypic consequences).
- *Pleiotropy*: The propensity for a single gene or locus to influence multiple, often unrelated, phenotypes (e.g., in an animal de-extinction effort, modifying a gene for a desired trait could have unintended effects on other traits due to pleiotropy).
- *Epistasis*: The non-additive interaction between genes or mutations, where the effect of one depends on the presence of others (e.g., donor mutations from one species can interact with mutations and gene variants on a recipient species' genome, and have surprising, unforeseen phenotypic effects).

Though these concepts are relevant to today's biotechnological pursuits, they were all mentioned (not invented) by Sewall Wright, an eminent evolutionary theorist. For plasticity, he wrote about "Lability as the condition for evolution[a]," referring to the need for plastic responses to environmental conditions (Wright, 1931). With regard to pleiotropy, he mentioned "In general, each gene replacement has effects on many characters (the principle of universal pleiotropy)[b] (Wright, 1968)." And he appealed to epistasis, stating that "...interaction effects are universal in the more complex characters that trace such processes (Wright, 1968) [c]." I mention this to emphasize that these are not novel concepts, but are part of the standard canon of evolutionary and population genetics.

[a] pg. 147 in his famed 1931 manuscript, "Evolution in mendelian populations."
[b] pg. 59-60 in the volume "Evolution and the Genetics of Populations."
[c] pg. 71 in the volume "Evolution and the Genetics of Populations."

5.2 Notes on control in genome engineering and de-extinction

What makes de-extinction efforts, such as the one depicted in *Jurassic Park*, so provocative? The risk and reward (discovery) reside in the fact that we have never interacted with the target organisms and have limited knowledge of their genotype-phenotype maps and physiology.

Another distinguishing feature of bioengineering is that it does not rely on the typical tempo of adaptive evolution, which can take hundreds of generations (or more). Using modern molecular tools, we can introduce genetic novelties in minutes or hours, depending on the method and setting. But this is also a drawback. Pleiotropy and epistasis teach us that genomes do not always work like Lego bricks, where individual loci can be swapped in and out without consequences. Natural selection often works on entire genomes that function through the coordinated interaction between their component genes and gene products. For example, forces such as viral infection (Enard et al., 2016) and horizontal gene transfer (Soucy et al., 2015;Crisp et al., 2015) can introduce new parcels of genetic information into genomes, but they only persist in a population if they contribute to a fit and functional organism. But as we observe in *Jurassic Park*, biotechnologists rarely work with the patience of natural selection. Instead, they focus on a phenotypic outcome without full knowledge of (or regard for) the often gradual nature of the evolutionary processes that generate functional organisms.

Challenges notwithstanding, de-extinction, genome engineering, and synthetic biology constitute some of the most exciting technologies in all of the life sciences. They offer hope that we can translate our theoretical ideas into a means of controlling biological systems. Next, I propose a conceptual framework for our present and

future attempts to control living systems.

$$Control = Prediction + Engineering \tag{6}$$

The desire to control complex biological systems predates modern science. For thousands of years, humans have controlled the genotype-phenotype maps of animals and crops through selective breeding (Hill and Kirkpatrick, 2010;Reeves and Cassaday, 2002). And controlling human populations was the goal of the eugenics movement[12] (Rutherford, 2022;Kevles, 1995).

In recent times, scientists have taken steps to control how evolution works (Ogbunu, 2023). Examples include steering cancer cell populations for more effective therapy (Acar et al., 2020), and the use of directed evolution to build new biomolecules (Arnold, 2019)[13]. Other modern technologies have a similar ambition, first popularized in the "genetically-modified (GM)" crop debates, where agriculturalists aimed to improve crop quality and yields using tools to directly tweak specific genes (Sreevathsa, 2025;Connor, 2018). And even more contentiously, recent efforts include human embryo selection—where embryos are chosen for fertilization based on polygenic risk metrics for certain phenotypes (e.g., disease, physical traits) (Smart, 2023)—and the creation of "CRISPR babies," in which embryos are directly edited to confer specific phenotypic outcomes (Reza, 2018)[14]. These modern efforts, even if framed with the positive aim of improving the human condition, have been compared to Eugenics (Sufian and Garland-Thomson, 2021;Merchant, 2025).

Breakthroughs in gene editing (as with the dire wolf project) are central in our quest to engineer genotype-phenotype maps. Similarly, InGen scientists in *Jurassic Park* should be recognized for their triumphs: finding a way to isolate the DNA of an extinct animal and build a functional genome and organism. However, their predictive capacities were lacking[15]. This led to the myriad problems experienced on Isla Nublar, the fictional island near Costa Rica where the dinosaur park was built.

There is a subtle point to highlight in our efforts to engineer biological systems: As described in Equation 6, we must not mistake engineering achievements for effective control. It does not matter how well the engineer can tinker with the pieces of a complex system; if the target system's behavior cannot be reliably predicted, then whatever contraption is being built cannot be said to be effectively controlled. In 2025, I believe that we are much further along in the tinkering aspects than we are in predicting biological outcomes[16].

6 *"Scientists. . . are focused on whether they can do something. They never stop to ask if they should do something."* (p. 318)

6.1 Dubious dinosaurs and dire wolf de-extinction

In the preceding sections, we examined technical ideas in evolutionary genetics relevant to genome engineering efforts not unlike those portrayed in *Jurassic Park*. Here, we explore the social, cultural, and ethical issues that emerge from a close reading of the text[17].

Unlike most well-known works of fiction, *Jurassic Park* lacks a single standard protagonist or antagonist[18]. Its characters are vehicles for a story about chaos, arrogance, greed, ethics, and unpredictability. Among its themes

[12] I am referring to the eugenics movement of the 20th century.

[13] The 2018 Nobel Prize in Chemistry was awarded to Frances Arnold for pioneering work on directed evolution (Arnold, 2019;Rennie, 2018).

[14] The ethical and technical dimensions to human genomic prediction and genome modification efforts were explored in a perspective article based on the film *Gattaca* (Niccol, 1997) (Ogbunugafor and Edge, 2022).

[15] Perhaps due to plasticity, pleiotropy, epistasis, and other forces.

[16] There are certain biological systems that we can control by many definitions, but the quest continues on the molecular or cellular scale.

[17] *Jurassic Park* is part of a long history of science-fiction works that bring social issues to light. Ethical issues are the subject of many classics. And several, including Mary Shelley's *Frankenstein* (Lackington, Hughes, Harding, Mavor, and Jones, 1818) and Aldous Huxley's *Brave New World* (Chatto and Windus, 1932) openly discussed issues related to bioengineering. And even the term de-extinction has been traced to the science fiction writer Piers Anthony (Shapiro, 2015b,a).

[18] Alan Grant, a paleontologist in the book, could qualify as a protagonist by many standards. This point has been debated among fans.

is an indictment of the tunnel vision of ambitious and powerful people. John Hammond, the wealthy benefactor most responsible for the Jurassic Park project, is not guilty of having bad intentions; but of toxic naïveté.

These topics may be relevant in discourse surrounding today's de-extinction efforts. The 2025 dire wolf project generated an initial wave of enthusiasm, followed by criticism and debate (Lynch, 2025b,a;Höglund, 2025). One important question asks whether the products of Colossal Biosciences' endeavor are truly dire wolves. Their Chief Scientific Officer once remarked, "People are yelling at us that these aren't real dire wolves. But no one has ever questioned whether the dinosaurs in *Jurassic Park* are real dinosaurs (Phys.org, 2025)." The comment suggests that critics were inconsistent in their takes of the dire wolf project. Yet, this exact sentiment arose in the *Jurassic Park* universe. During the third film, fictional paleontologist Alan Grant exclaims: "What John Hammond and InGen did at Jurassic Park is create genetically engineered theme park monsters. Nothing more and nothing less (Johnston, Joe (director), 2001)." Indeed, Colossal Biosciences recently acknowledged that their engineered animals are modified gray wolves, not dire wolves (Le Page, 2025).

The disagreement surrounding whether an engineered animal is real or not could be charged to semantics. And a debate about whether the fictionally engineered *T. rex* in *Jurassic Park* was truly a *T. rex* feels less important than other technical and ethical concerns. But the question of what constitutes essential differences between individuals and populations is an old one in evolutionary biology, and has social implications. For example, suggesting that two humans of different geographical ancestry who differ by more than 20 mutations (far fewer than biological siblings) are truly different animals would be absurd[19]. No, we cannot compare the marketing campaign of a de-extinction company to debates around the genetics of human differences, or imply that the former carries any of the historical (and contemporary) baggage of the latter. But anyone who talks about essential genetic differences between two animals should consult a large body of literature and lessons learned from over a century of broken thinking in this realm. As Colossal Biosciences' scientific leadership includes many respected geneticists, care in navigating this topic is a reasonable expectation, as it is for anyone working in this area.

6.2 Lessons on technological ambition for today and tomorrow

There is an old idiom for situations where our ambitions outweigh our capacities: "Your eyes are bigger than your belly." It describes the goals of InGen in *Jurassic Park* and should be considered in our modern genome engineering efforts. The eyes-belly analogy also applies to the tech "overlords" of our era, who aim to improve society through artificial general intelligence, bioengineering to prolong life, and technology to terraform other planets (Becker, 2025). These perspectives highlight the true villains of *Jurassic Park*: (i) unbridled techno-optimism and (ii) the use of abundant resources as a shield from having to justify our scientific ambition. The story teaches us the dangers of naïveté and the need for transparency and ethical care in our biotechnological pursuits.

These ideas are especially worth reflecting on in light of perilous attacks on science infrastructure in the USA in recent times. The changes compel us to rethink how science will be conducted in the present and future. One prediction is that there will be an increase in privately funded research, for better or worse. The biotechnology sector has played a central role in some of the most important social good discoveries in recent years, such as the COVID-19 mRNA vaccine. In addition, the private sector was central in the development of AlphaFold, which has already revolutionized the study of protein folding[20]. But the private model comes with its own limitations, some of which were evident in *Jurassic Park*. Profit-driven research funded by investors can oversell achievements and ignore relevant technical and ethical shortcomings[21]. Whatever the future holds for how science functions, it should adhere to the advice from the fictional Ian Malcolm and generations of real-life scholars: we must be mindful of what we are doing and ask difficult questions about why we are doing it.

[19]There is a large literature surrounding the issue of biological essentialism and genetic determinism, from scholars and scientists of many kinds. In terms of race specifically, I point the reader to *Backdoor to Eugenics* (Routledge, 2004) and *The Nature of Difference* (MIT Press, 2009).

[20]The science behind the mRNA vaccine and Alphafold were awarded the Nobel Prizes in Physiology, Medicine and Chemistry, respectively (Nobel Prize Outreach, 2023, 2024)

[21]Surely other research models can be guilty of the same.

I am not implying that de-extinction or other biotechnological exploits are incorrigibly fraught and doomed to fail. Ambitious bioengineering delivers discovery on a daily basis and produces impressive molecular gadgets of various kinds. And I believe that these approaches will be important in our present and future conquest against disease, climate change, and other threats to our existence and well-being. Even in the case of de-extinction science, there are arguments that a version of it could be a powerful tool for conservation (Shapiro, 2015a;Sherkow and Greely, 2013). But most would agree that the possibility of discovery in the future is not a universal pass to do whatever one wants today.

When we combine the messages of *Jurassic Park* with knowledge of potential barriers to effective real-world genome engineering, we must consider how naïveté can be akin to playing with genotype-phenotype fire. And should we cause harm, who can we blame? Only our lack of appreciation for the sometimes inconspicuous, often capricious, and always powerful forces that define living systems. We should be careful. As Ian Malcolm famously said in the 1993 film adaptation: "*Genetic power is the most awesome force the planet's ever seen, but you wield it like a kid that's found his dad's gun* (Spielberg, Steven (director), 1993)."

6.3 On the portrayal and image of scientists

I end with a short discussion of Ian Malcolm[22], who has emerged as a cult figure in science fiction lore. There are several reasons why he serves as an effective vehicle for the core messages of *Jurassic Park*. Malcolm is a mathematician brought to the island by John Hammond because of his work on chaos theory and his views on nonlinearity and unpredictability. More importantly, he is there to offer an informed, dissenting view. Hammond's hope of persuading Malcolm fails, but the inclusion of an alternative voice was a commendable aspect of the project, one we can all learn from.

Malcolm is employed at the University of Texas at Austin and in the sequel, *Jurassic Park: The Lost World* (Knopf, 1995), is a professor at the Santa Fe Institute, an institution known for research in chaos theory (Malcolm's research focus) and other areas of complexity science[23]. His lasting appeal stems from his iconoclastic nature. He is a theoretician unafraid to apply his expertise to real-world problems, and his fears about the inevitable failure of the park are realized. Malcolm offers a memorable example of someone with a strong ethical foundation who communicates ideas with clarity. This depiction of a scientist is of cultural importance, as it may encourage aspiring mathematicians to see themselves in science, dispelling the notion that there is an archetype to which they must adhere.

These may be unusual lessons to emphasize in a technical perspective, but they underscore a crucial need for science in an age of significant threats to its infrastructure. We need better front-facing images of scientists to build trust in a world where public perception can change rapidly (Tyson and Kennedy, 2024). This is especially true for fields like theoretical and population biology, where visible truth-telling can help counter the negative consequences of misinterpretations of knowledge in fields like evolutionary biology, genetics, ecology, and public health.

[22] I note that I am discussing his depiction in the novel and not the 1993 film.

[23] I am currently a resident professor at the Santa Fe Institute. I mention this because the institute, once described as a "Justice League of renegade geeks" by *Rolling Stone Magazine* (Kushner, 2007), fashions itself as a space for intrepid scientists, not unlike the fictional Ian Malcolm.

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Abbreviations

CFTR: Cystic fibrosis transmembrane conductance regulator
CRISPR: Clustered regularly interspaced short palindromic repeats
DNA: Deoxyribonucleic acid
G×E: Gene-by-environment interaction
GM: Genetically modified
InGen: International Genetic Technologies (fictional company in *Jurassic Park*)

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Competing Interests

The author declares no competing interests.

Author Contribution Statement

CBO conceived the project, generated and analyzed the fictional data, and wrote the original and revised versions of the manuscript.

Data/Code Availability Statement

There are no biological data in this manuscript. All of the figures are built using fully simulated data and are intended to be fictional. Tables of the simulated data used to generate Figure 1 are available on GitHub: https://github.com/OgPlexus/JP1.

Ethics Statement

Not applicable. This study did not involve human participants, human tissue, or animal experiments.

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Supplementary Material

Figure S1: A trait-space depiction of the pleiotropic relationship between body mass and pigmentation. This offers an alternative to the reaction norm depiction in Figure 1.

Keywords

de-extinction; epistasis; evolutionary genetics; genome engineering; *Jurassic Park*; pleiotropy; phenotypic plasticity; science and society; science fiction

Supplementary Information

Jurassic Park at 35: Reflections on evolutionary theory, genome engineering, and the science-society interface

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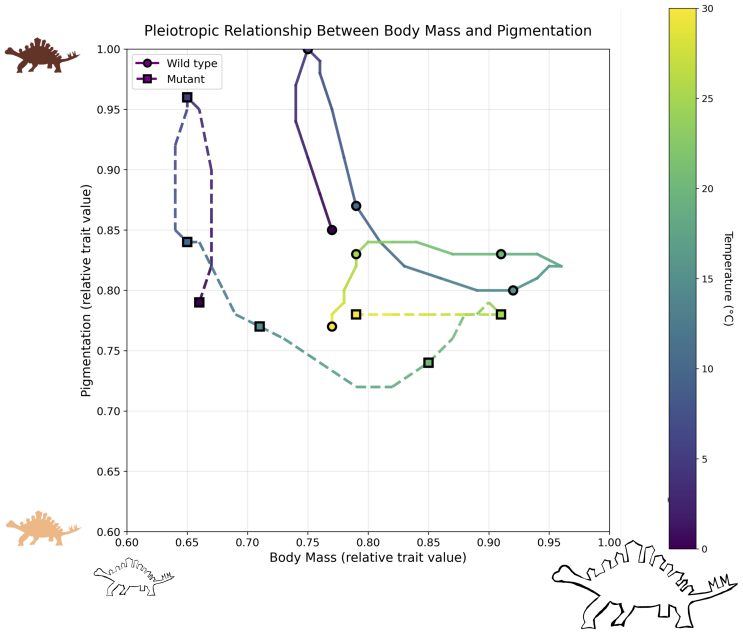

Fig. S1. A trait-space depiction of the pleiotropic relationship between body mass and pigmentation. This offers an alternative to the reaction norm depiction in the main text Fig. 1. Here we see the relationship between the two fictional dinosaur traits of interest across a breadth of temperatures. Colors correspond to a temperature gradient.