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DISSOLVING DOMINANCE

I. INTRODUCTION

The time has come to dissolve the concept of dominance in genetics. The concept is a vestige of history, a frozen accident that may have aided Mendel's important discovery but is hardly essential as a basic principle of genetics (§II). Moreover, the concept of dominance is ill-framed and often misleading in terms of heredity, natural selection, and molecular and cellular processes (§III). More direct language is available to refer to the key relevant principles in inheritance and the phenotypic expression of genetic states (§IV).

At first, the concept of dominance seems simple enough: when two different traits are inherited, only one will be expressed—that trait is *dominant*, the other is recessive. But even this simple formulation hides a wealth of implicit assumptions about genotype-phenotype interaction, numbers of available alleles, the typical effects of combining two alleles in diploid organisms, interaction of allelic pairs, definitions of "similar" alleles, and more. This paper aims to tease apart these conceptual issues and clarify genetics by discussing how to proceed without the concept of dominance and the confusions it frequently generates.

II. WHENCE DOMINANCE?

Today's term 'dominance' originated, of course, in Gregor Mendel's now classic 1865 paper on "Experiments Concerning Plant Hybrids" (1866/1966). Those who read the original paper over a century later are often impressed with its clarity and modern style, accessible even to high school students. But the conceptual context has changed dramatically since Mendel's time, and contemporary readers often miss differences in meaning obscured by the use of familiar terms. These differences offer important clues, however, to understanding how the modern concept of dominance emerged, evolved and has continued to shape our thinking about genetics.

Mendel's "Discovery"

Mendel introduced the term *dominirende* (translated variously as 'dominating' or 'dominant') to refer to characters "which are transmitted entire, or almost unchanged in the hybridization" of two contrasting parental types (Mendel 1866, §4; see also §11). The other traits, of course, he termed *recessive*. While today's popular accounts tend to portray this as a significant and novel claim, Mendel and his contemporaries who conducted breeding experiments would have readily acknowledged that some parental forms are more likely to be found in offspring—a phenomenon

they called *prepotency*. Theories at the time, however, often attributed the prepotency to the sex of the parent (i.e., whether the trait was transmitted by the male or female gamete). By doing reciprocal crosses, Mendel was able to underscore the "interesting fact" that "it is immaterial whether the dominant character belongs to the seed plant or to the pollen plant" (§4). He was not wholly novel in this claim or approach. Mendel himself cites work by Gärtner, and there were others earlier in the century (Orel 1996). In this respect, Mendel's concept of dominant traits would have been important, but hardly revolutionary (and hence not especially noteworthy to his contemporaries). Dominance embodied a familiar notion—familiar even to non-scientists then as much as now—that some specific traits resemble one parent and not the other. By itself, it explained nothing new.

In discussing dominant traits as he did, Mendel thus addressed an existing misconception about parental influence in inheritance. At the same time, however, he provided a foundation for another misconception. That is, he primed a tradition of attributing the appearance of certain traits to the traits themselves. For later interpreters of Mendel, certain traits appeared *because* they were dominant, rather than because of, say, some feature of inheritance, development or the coupling of traits. The term "dominant," originally introduced as a mere descriptive label, became widely regarded as a causal property (precipitating some unexpected consequences and confusions, discussed more fully in §III below).

While noting that some traits are dominant, Mendel also noted that other, complementary traits—which he called “recessive”—“withdraw or entirely disappear in the hybrids, but nevertheless reappear unchanged in their progeny” (§4). The non-dominant traits were not lost by cross-breeding. Rather, they were "latent." Later, they reappeared wholly intact. In this case, too, Mendel’s results merely illustrated another familiar hereditary phenomenon: the reappearance of ancestral forms, known at the time as *reversion*. By calling such traits recessive, Mendel hardly did more than redescribe a widely known feature of inheritance in new terms.

Mendel's work was indeed exceptional—though not always in the ways or for reasons most frequently attributed to him. For example, among most biologists now, Mendel's legacy falls squarely in the abstract principles of inheritance, or genetics. Yet as much as people cite Mendel’s original paper, they often overlook the title that reveals Mendel's primary focus: "Experiments Concerning Plant Hybrids." Hybridization was an important field at the time—both for practical breeding purposes and for addressing questions about evolution and the origin of new species. Could hybrids ever breed true, for example? If so, under what conditions? Could they create new species or stable domestic varieties? For those studying hybridization, reversion had been relatively unpredictable and puzzling. Not so for Mendel.

Mendel highlighted the fact that recessive traits not only reappeared (or reverted) in a hybrid's offspring, but reappeared "unchanged," "fully developed," "without any essential alteration" and thus "remain constant in their offspring" (§§4, 5). As if pure, they could once again breed true, even if their hybrid parents did not. Indeed, a dominant trait, too, could also emerge from a hybrid in true-breeding form. The dominant character could have a "*double signification"* (§5), some plants being mixed (hybrids again) and others breeding true (like the original parents). For Mendel, this reappearance from hybrids of true-breeding forms—sometimes recessive, sometimes dominant—was as important as any “reversion” of the recessive trait. Something allowed both types of traits to be transmitted "unchanged"—and for them to reunite on occasions.

But only some offspring were true-breeding. Others behaved like the hybrid parents.

Mendel quantified this pattern in the now familiar 1:2:1 (or 2:1:1) ratio, and showed that the pattern repeated itself in successive generations of hybrids (§§5-7). He thereby revealed an unexpected regularity to or "law" in the development of hybrids (also see Olby 1997, §III). Several times during his original paper, Mendel repeated his thematic claim in virtually identical phrasing (see Hartl and Orel 1992):

> *. . . it is now clear that the hybrids form seeds having one or the other of the two differentiating characters, and of these one-half develop again the hybird form, while the other half yield plants which remain constant and receive the dominant or the recessive characters in equal numbers*. (Mendel 1866, §6, original italicized; also see §§7, 8, 9)

That is, hybrids produced equal numbers of hybrid and true-breeding offspring; of the true-breeding forms, half showed the dominant trait and half the recessive. Mendel further elaborated the ratios mathematically in terms of a "developmental series" (based on the binomial expansion). Most important, the "foundation and explanation" of this pattern was the formation of *different* gametes, each representing one of the two "pure" characters originally brought together in the hybrid (hence, Aa x Aa ==> A + 2Aa + a). Genes, we say now, segregate and recombine without losing their integrity. That was Mendel's significant insight, not dominance.

Mendel's conception of the "laws" or mathematical rules of the development of hybrids relied very much on thinking about pairs of different gametes (egg and pollen) and pairs of distinct traits. He thought "in twos" and in combinations of twos. Mendel's insight was thus intimately linked to his choice of dichotomous traits—those that can be designated as either dominant or recessive. Mendel was aware of another common conception of the era: *blending inheritance.* According to this notion, traits mixed (or "blended"), producing intermediate forms while becoming inseparable in later generations. For Mendel to explain his results, traits could not blend or become impure or lose their discrete integrity in hybrids. After all, they were able to reappear in true-breeding forms (again, recessive as well as dominant traits). Hence, Mendel emphasized that no intermediate forms (which might indicate blending) occurred. The dominant characters "in themselves constitute the characters of the hybrids," he said, with no ostensible contribution from the recessive characters which, though present, are "latent" or "withdraw." The recessive characters do not just partially disappear; they "entirely disappear" (§4). For Mendel, as for others to follow, dominant characters wholly eclipse the corresponding recessive characters. "*Transitional forms were not observed in any experiment*," he stressed (§5). For Mendel, the discrete distinction between dominant and recessive traits corresponded to the purity of each trait through the various processes of hybridization, gamete formation, fertilization and development.[1]

In retrospect, we can easily see that Mendel confused genotype and phenotype (a distinction that emerged only much later). Here, he seems to have assumed that any phenotypic combination of traits in intermediates also reflected an irreversible mixture of "traits" genotypically. Mendel's conclusions about the segregation and recombination of genetic material or genes (in today's terms) still hold, however, even if there is no sharp dichotomy of dominant and recessive traits phenotypically (for example, in cases of "incomplete dominance" and "codominance," reviewed further below). Still, one can appreciate how Mendel's own reasoning and original conclusions were likely facilitated by (if not wholly dependent upon) the concept of dominance, with strictly dichotomous traits. In this case, a false model may have been integral to, or even essential for, Mendel's discovery (see Wimsatt 1987). For us, over a century later, the principles of dominance and segregation are clearly independent. Understanding how they were once closely coupled historically, however, allows us to perceive more clearly how we might

abandon the former without disturbing the later. We need not embrace a mere contingency of history.

Mendel himself certainly recognized that not all traits are expressed in dominant and recessive pairs. Indeed, Mendel essentially admitted that dominance was not the exclusive norm. Even before introducing dominant traits he noted, for example: "with some of the more striking characters, those, for instance, which relate to the form and size of the leaves, the pubescence of the several parts, etc., the intermediate, indeed, is nearly always to be seen" (§4). Later he commented: "as regards flowering time of the hybrids, . . . the time stands almost exactly between those of the seed and pollen parents" (§8). Mendel certainly saw in the years immediately following his work on peas that his results on dominance in *Pisum* did not generalize to *Hieracium*, or hawkweed (Mendel 1869). For Mendel this merely meant that his law of hybrid development applied only to "those differentiating characters, which admit of easy and certain recognition" (§8). Other characters followed another, different rule or law. Dominance, even for Mendel, had a limited domain.

Mendel's Legacy

Mendel's work became a guide, of course—almost a touchstone—for the pioneers of the new science of genetics at the turn of the century. However, the particular concept of dominance was not uniformly endorsed. Indeed, the scientific reception of this element of Mendel's work in the early 1900s illustrates that its status was never secure. William Bateson, for example, was perhaps the strongest advocate of the new Mendelism among English-speaking researchers. He found Mendel's quantitative style consonant with his own, hailed the recombination of pure Mendelian units as an explanation for both heredity and the source of variation in evolution, and thus boasted that genetics had discovered the fundamental biological units and rules of combination akin to chemical stoichiometry (see Olby 1997, §VI). At the same time, Bateson demurred, even at the outset, from accepting any principle or law of dominance:

> In the *Pisum* cases the heterozygote normally exhibits only one of the allelomorphs [alternative phenotypic forms] clearly, which is therefore called the dominant. It is, however, clear from what we know of cross-breeding that such exclusive exhibition of one allelomorph in its totality is by no means a universal phenomenon. Even in the pea it is not the case that the heterozygote always shows the dominant allelomorph as clearly and in the same intensity as the pure dominant . . . (Bateson 1902, p. 129)

Bateson's own work on inheritance in poultry showed that traits "mixed" in hybrids, though the traits still segregated neatly in offspring according to Mendel's model. "The degree of blending in the heterozygotes," Bateson declared, "has nothing to do with the purity of the gametes" (p. 152). (Again, intermediate forms were possible, denoted here by Bateson—erroneously—as a form of "blending inheritance"). Bateson's example of Andalusian fowl—blue-grey hybrids of black and white parents that formed a 1:2:1 ratio in the F_2 generation—soon became a classic case, cited in textbooks throughout the century (see, e.g., Russell 1992, p. 98, and below).

Others objected to dominance as a universal feature of inheritance. Case after case of intermediate form was cited. In contrast to Mendel's work on color in seed pods, seed endosperm and unripe pods, for instance, hybirds of red and white four o'clock flowers were neither red nor white, as predicted by dominance, but pink. For most informed breeders and geneticists, characters that differentiated into only two forms, such as Mendel's tall/dwarf or

green/yellow, were relatively rare. Thus they did *not* form a secure model for interpreting heredity generally. Indeed, the lack of the universality of dominance was perhaps the single most cited reason for rejecting Mendelism outright (see also note 1). Thomas Hunt Morgan and his students summarized the prevailing view by 1915:

> Whether a character is completely dominant or not appears to be a matter of no special significance. In fact, the failure of many characters to show complete dominance raises a doubt as to whether there is such a condition as complete dominance. (Morgan et al 1915, p. 31)

By 1926 Morgan had abandoned any special reference to dominance. In his landmark and synoptic *Theory of the Gene*, which summarized over two decades of findings in classical genetics, dominance failed to appear in the table of contents, in the index, or even as part of Morgan's formal statement of the theory of the gene (Darden 1991, p. 72).

In carrying forward the legacy of Mendelism, textbooks in the ensuing decades and throughout the century have continued to reflect the ambivalence towards dominance as a universal "law" or basic model. For example, an early 1906 text by Lock states that dominance is not universal (Darden 1991, p. 72). Likewise, a 1921 text lauds Mendel's landmark discovery of dominance, then adds ironically, "of course breeding is not so simple as this, and some characteristics do blend or average in the hybrids" (Moon 1921, p. 543). A 1933 zoology text, too, follows its description of dominance with a cautionary note: "dominance and recessiveness do not, however, characterize all cases of inheritance" (Curtis and Gurthrie 1933, p. 184), and then introduces the examples of Andalusian fowl and pink four o'clock flowers. In 1969, we find another text carefully detailing "Mendel's law of dominance," then citing the very same two examples, noting that:

> Since Mendel's time, we have found that the law of dominance does not always hold. . . . It is clear that we cannot speak of a "law" of dominance even though dominance occurs frequently. (Kroeber, Wolff and Weaver, 1969, pp. 412-412)

Could more equivocation be found?: dominance is both a law and not a law. By the 1990s dominance and recessiveness had retreated to the status of a "feature" in one standard genetics text (Russell 1992, p. 41).

Despite the ambivalence, dominance continues to be preserved as an essential or core feature of genetics, consistently introduced before it is dismissed or qualified by any exceptions. Why? Why has dominance persisted as a standard or model, even if in disrepute? Whereas Mendel associated dominance with segregation, we now associate dominance with Mendel himself, as a scientist of mythic proportion (see, e.g., Brannigan 1981; Sapp 1990). Nearly every introductory biology textbook introduces Gregor Mendel with a picture and supplemental comments. They implicitly portray him as an exemplary scientist. He worked alone in an Austrian monastery: scientists modestly seek the truth; they do not ambitiously pursue fame or wealth. Mendel used peas; scientists choose "the right organism for the job." He counted his peas: scientists are quantitative. He counted his peas for many generations over many years: scientists are patient. He counted thousands and thousands of peas: scientists are hard-working. After all this, Mendel was unfairly neglected by his peers, who failed to appreciate the significance of his work, but was later and justly "rediscovered": ultimately, scientific truth triumphs over social prejudice. Above all, Mendel was right. By all these measures, Mendel is a model scientist, a biological hero to parade before students. How could we admit that Mendel erred (good scientists don't make mistakes)? Because dominance was part of Mendel's original scheme and, at

the same time, we honor Mendel almost religiously, we do not exclude dominance from basic genetics. Dominance has become entrenched in the romantic lore of Mendel.

The acceptance of dominance as a model has not been without consequences, however. Most notably, the many “exceptions” that emerge by regarding dominance as a norm have led to a proliferation of otherwise needless concepts. That is, textbooks typically begin genetics with the eponymous "Mendelian" genetics. But then they proceed to note several "exceptions" or qualifications. For example, Bateson’s Andalusian fowl and pink four o’clocks exemplify *incomplete dominance*. As noted above, the basic Mendelian pattern of segregation and recombination still occurs, but with no eclipsing "dominance"; rather, the hybrid phenotype is intermediate. Texts also commonly distinguish *codominance*, exemplified by blood type, where both alleles contribute concretely to a "compound" phenotype. The dominance model further implies antagonistic or complementary pairs, so *multiple alleles* must also be mentioned (also illustrated by blood type). And because dominance is presented as absolute (and sufficient cause), any occasion when the "dominant" trait does not appear in all individuals with the allele, or does not appear to the full extent, also requires special note—hence, *penetrance* and *expressivity* (e.g., Russell 1992, pp. 54, 112-114). When one refrains from recognizing dominance as a prior model, however, all these concepts—incomplete dominance, codominance, multiple alleles, expressivity and penetrance—become superfluous. Because these concepts have populated the standard repertoire and vocabulary for so long, though, we can easily fail to notice the alternatives. Yet the "exceptions" dissolve conveniently when one removes dominance as a faulty standard.

It seems that dominance must be "basic" by some standard. But is it? It is certainly not foundational, in the sense of being simplest or making the fewest assumptions. The most basic assumption would be that each allele is expressed; hence, if two alleles are present, both are expressed. Dominance requires an *additional* assumption about the relationship between two alleles. By contrast, one can describe all the "exceptions" more simply and uniformly by: (a) knowing that diploid organisms have *two* alleles, and (b) noting the characteristic expression of each allele, even if it is a "truncated" version of another trait (see §IV below). Dominance is not a model by virtue of simplicity.

Is dominance "basic," then, in the sense of being most prevalent? —Or might the "exceptions" even outnumber the "model"? As early as 1907 Morgan quoted Hurst as saying that incomplete dominance is twice as frequent as complete dominance (Darden 1991, p. 68). A more recent estimate also suggests that fewer than one-third of human clinical genetic conditions follow the dominant-recessive rule (Rodgers 1991, p. 3). Has there ever been a systematic study documenting this other "Mendelian" ratio? An indirect measure might be the scarcity of good "textbook examples" of complete dominance in humans. To illustrate Mendelian traits, we often appeal to "attached earlobe," "hitchhiker's thumb," "short little finger," "widow's peak," "woolly hair," "crumbly earwax," "tongue-curling," "PTC-tasting." These are trivial. They hardly reflect important dimensions of human genetics. Nearly all interesting or significant cases have more complex stories (see §IV, for example). Dominance is not a model by virtue of frequency, either.

Viewed retrospectively, then, the concept of dominance is not essential. It was first coupled with other basic patterns of inheritance by Mendel, who likely found it integral to inferring segregation. Since Mendel, authors seem to have been unwilling to challenge Mendel's conceptual precedent, though all cite problems or exceptions. Curtis and Guthrie summarized a prospective view well in their 1933 text:

The course of inheritance for characteristics that do not exhibit dominance, therefore, is in

no way different from that for characteristics in which dominance occurs. (p. 185)
Dominance can be abandoned without loss. Though historically dominance has been intimately linked with Mendelism and the rules of heredity, and perpetuated for this reason, it is not essential to understanding basic genetics.

III. MISCONCEIVING AND MISFRAMING DOMINANCE

What, indeed, does dominance mean? Is it fundamentally a noun, an adjective, or a verb? Is it descriptive or explanatory? Does it refer to the phenotype or the genotype, inheritance patterns or mechanisms of genetic expression? Is it a "law," a "principle," a "feature" or something else?

On such questions the tendency is to refer to Mendel himself as an authority although, as noted above, others have shaped and reshaped our concepts of "Mendelian" genetics. Unfortunately, Mendel never clearly characterized "dominant" and "recessive" as concepts. Rather, he used them as *labels*, identifying certain sets of heritable characters in contrast to one another. Even modern textbooks find themselves in similar situations and typically introduce the terms, not in clear statements, but by ostension or exemplification (using such conditional phrases as "when traits combine in hybrids . . ."; e.g., see §I above). Moreover, Mendel defined these terms from observable behavior. Since then, we have inverted the meaning, such that we now attribute the observed phenotype to dominance: a trait is dominant when we observe it in the hybrid, and the hybrid exhibits this trait because it is dominant. The characterization of dominance is circumspect in its current circularity.

Curiously, perhaps, Mendel only used the adjectival form, *dominirende*. He never used a noun or verb equivalent. That is, he never described a general principle or relationship between two characters as "dominance," nor referred to one trait as "dominating" another. Rather, he merely sorted characters into two categories based on the visible traits of hybrid offspring. This descriptive modesty contrasts with later usage, which commonly characterizes dominance as a principle or even a law (a "Mendelian" law, no less!)—that is, as something more than a convention of nomenclature. The linguistic change marks an important conceptual shift. Dominance has been subtly *reified* into a concrete property that can be causal and explanatory, not merely descriptive.

In addition, it is rarely clear whether dominance refers to the phenotypic trait or the genetic allele associated with it—or both. Mendel labeled only the trait, or visible character. Whether he intended dominance to refer to any abstract underlying gene or "element" is unclear—his language and notation are certainly ambiguous (and inspire contentious debate among historians!). Nowadays, over a century after Mendel, the referents for dominance are slippery. Sometimes, one *trait* is dominant. At other times, it is the dominant *allele*, or *gene*. The second type of reference reinforces the notion that dominance is a property of the individual allele, not a larger context (see below). No one considers a phenotype to be causally important genetically, for example; it is the product or effect, not the cause. By contrast, we view genes as causal. Hence, referring to an allele rather than a trait as dominant carries substantially more content semantically.

Mendel also set a precedent with his choice of words. The term *dominirende* is now largely obsolete (in German), but in Mendel's time it carried the meaning or connotation (in a modern translation) of "coming to the fore," though it was based on the Latin root for "master" (Charles and Barbara Elerick, personal communication). Similarly, after Mendel first described

recessive traits as “latent,” he noted that he chose the expression “recessive” because “the characters thereby designated withdraw or entirely disappear” (§4). Between the paired elements that guide development in their "enforced union" in hybrids, "some sort of compromise is effected" (§11). Whether deliberately or not, Mendel cast the relationship between dominant and recessive characters in terms that could easily be interpreted in terms of power and forces.

All the initial translations of Mendel early in the next century preserved Mendel's original root: *dominant* in Bateson’s English; *dominirt* in Correns’ German; although there was pointed disagreement between de Vries, who preferred the French *dominant*, and Cuénot, who considered *dominé* more appropriate. They carried forward Mendel's pregnant images, while at the same time changes in the vernacular meaning of "dominant" only amplified the connotations of power. The interpreted meaning became explicit as Mendelism entered textbooks. A popular 1921 text, for example, calls the dominant traits “stronger,” though the recessive traits eventually “overcome” this (Moon 1921, p. 543). A 1933 text likewise calls the recessive trait “obscured or suppressed” (Curtis and Guthrie 1933, p. 183). Still, in 1969, the dominant trait “dominates or hides” the recessive (Kroeber, Wolff and Weaver 1969, p. 412). Even a late 20th-century genetics text follows the pattern, describing the “missing” recessive trait as “masked by the visible trait” (Russell 1992, p. 41). Throughout its history, the meaning of the term dominant (or dominance) in genetics has resonated with the term’s vernacular meaning.

As a result of the continued use of the term dominance, misconceptions about inheritance abound. They are more typically found among students and non-professionals. Still, the confusions can confound efforts in genetic counseling and social policy decisions, now made more urgent by the Human Genome Initiative. Some conceptions that teachers confront regularly include (these appeared widely, for example, on the national college-level AP Biology essay exam recently; also see Donovan 1997):

- Dominant traits are “stronger” and “overpower” the recessive trait.
- Dominant traits are more likely to be inherited.
- Dominant traits are more “fit,” or more adaptive in terms of natural selection. (Also, any recessive adaptive mutant trait will eventually evolve to become dominant.)
- Dominant traits are more prevalent in the population.
- Dominant traits are “better.”
- “Wild-type” or “natural” traits are dominant, whereas mutants are recessive.
- Male or masculine traits are “dominant.”

None of these claims is necessarily true. Some are false. All are misleading. One might wonder, therefore, why students of genetics (and, in some cases, prominent biologists historically) so readily and commonly assume(d) their validity. Moreover, these preconceptions and images are notoriously resilient—difficult for instructors to rectify even when they note and address them explicitly. Notice, though, how the vernacular meaning of dominance, where one thing “dominates” another, percolates through every misconception.

Clarifying the meaning of dominance in genetics is further frustrated by other uses of the same term within biology. For example, in ethology, dominance describes political hierarchies among social organisms, just as the vernacular sense of the term suggests. The untutored person imagines “dominant” genes to “behave” the same way: they “dominate” over other alleles or traits through competitive interactions, etc. In ecology, dominance refers instead to the relative biomass of one species in a particular ecosystem: the “dominant” species is typically viewed as the most influential or important because of its sheer bulk (a combination of size and frequency).

Biologically, dominance seems to be a technical measure of influence or power, as one might expect from the term's common usage.

In *Metaphors We Live By*, Lakoff and Johnson (1980) describe how our thinking is shaped by the words we choose and their meanings in other contexts. "Dominance," though it may be well *defined* as a term strictly within the field of genetics, unavoidably carries with it the meanings or connotations from other biological as well as non-biological contexts. Hence, a dominant trait is expressed, not "in lieu of," but "*over*" the recessive. Likewise, the concept of *predominant* can easily shape expectations about the frequency of *dominant* alleles (or traits) in a population or subsequent generation, for instance. No wonder people can mislead themselves. They reason about the prevalence of alleles, the interaction of genes, heritability, reproductive fitness, normality and gender using the language available. In this case, using the single term "dominance" primes the multiple misconceptions enumerated above.

The resonant meanings of dominance are significant in part because the conceptual "space" is open for them to fill. Who *explains* dominance? No clear single molecular or cellular mechanism describes why or how one trait is dominant while another is recessive. No proper explanatory concept can eclipse misconceptions before they develop or replace them afterwards.

Many conceive or explain dominance as a form of gene regulation. They suppose that the dominant allele somehow *inhibits* the expression of the recessive allele (see, e.g., the popular textbook by Lewin, 1997, p. 62). It must produce or induce a repressor protein, say, that *actively prevents* the transcription of the recessive allele's DNA on the homologous chromosome. At the same time, the recessive trait "withdraws" or is "latent"—virtually powerless to express itself. Here, the "dominance" metaphor appears with a vengeance, though filtered through standard biological concepts. One presumes that the dominant allele has some ability to "shut off" or "dominate" the recessive allele. While such genetic regulation is conceivable, however, no such direct interaction or suppression is yet known to occur. The common conception of dominance as gene regulation is false, though obviously fueled by the term "dominance."

Others conceive or explain dominance as the presence or absence of a trait. That is, the recessive trait is not due to the presence of a specific recessive allele or protein but is due instead to the absence of a functional dominant allele. This interpretation has a rich history, with roots extending back to a popular 1905 proposal by Bateson and Punnett (Darden 1991, pp. 69-71). Variations persist today (e.g., Lewin 1997, p. 62). At the level of alleles, this concept is patently absurd. Both alleles are inherited; both are present. The deficit must therefore appear in gene expression: recessives fail to produce a functional protein—or to produce any polypeptide whatsoever (for example, as illustrated in Lewin's text). In severe cases, the absence might even be lethal (e.g., Russell, pp. 110-112). But how the absence occurs is typically unexplained. While a change in the function of protein is important, the presence-absence interpretation implies, again, that the recessive allele or gene produces no protein and hence contributes nothing to the character of the individual—and thus can be safely dismissed (again, echoing Mendel's notion of eclipsing traits). Again, this is overstated. For example, in cases of Tay Sachs, cystic fibrosis and other "recessive" disorders, geneticists can detect heterozygote carriers specifically because their "recessive" allele produces a detectable alternative protein. A recessive protein is present. In an evolutionary context, the presence-absence conception is flawed because it implies that all changes in genes are losses of function; hence, adaptation and evolution itself would seem impossible. The presence-absence assumption is further challenged by contrary cases where the "presence" of a specific protein can be dysfunctional, making the normal function oddly due to an

"absence." Sickle cell anemia, for example, is not merely the absence of hemoglobin. Rather, there is a variant hemoglobin with its own distinctive phenotype, including the transport of oxygen but also the characteristic "sickling" of cells that blocks capillary circulation. In other cases, such as "dominant negative mutants," an ostensibly functional protein is "present" in the heterozygote, but the variant allele subverts its normal function (see, e.g., discussion of osteogenesis imperfecta, §IV below; many similar cases were debated early in the century, as well; see Darden, 1991, p. 70.) In these instances, the *absence* of a particular trait is functional. Ultimately, the presence-absence hypothesis cannot explain dominance fully because it does not address the very details of why or how function is lost or changes. A robust interpretation of dominance must explain generally: (1) why traits (or alleles) differ in expression, and (2) how those traits overlap when coupled in diploid organisms.

Ideally (as suggested by these two prevalent misconceptions), we might want to explain dominance at the molecular level through some single, well defined mechanism. We want all dominant traits to be dominant for the same reason. However, genotype is linked to phenotype at several stages or layers of expression, from the levels of biochemistry and the cell to the levels of physiology and social behavior. The familiar textbook notion of "one gene, one protein" and the processes of transcription and translation only begin to characterize the multi-layered process of gene expression. In a sense, we must rethink our notion of phenotype to include "traits" from all levels, from biochemistry and the cell to the organism.

Consider, for example, two renowned traits from classical genetics: Mendel's wrinkled peas and Morgan's white-eyed fruit flies (Guilfoile 1997). The wrinkled (versus smooth) trait in pea seeds has now been isolated to a transposon in the exon of a gene for a starch-branching enzyme (SBE1). In one form ("smooth") the protein acts enzymatically to convert amylose to amylopectin. As a result, starch accumulates in the developing seed. In another genetic form ("wrinkled") the gene is presumably transcribed, but it is either not translated (due to the sizable DNA insertion) or the resultant protein does not fold into a similar shape. Consequently, the same reaction is not catalyzed. Instead, unpolymerized amylose and sucrose molecules accumulate in the developing seed, which osmotically imbibes considerably more water, producing a temporarily larger seed. When the seed matures and dries, however, the endosperm contracts and the now-enlarged seed coat wrinkles. The appearance of wrinkled seed is thus due to the cascading downstream developmental effects of a protein without specific catalytic activity. It is a trait with many components, including relative sugar and starch composition as much as visual appearance. But, of course, this is only half the story. What happens when the two allelic variants appear together in a hybrid? Apparently, one gene of the first ("smooth") type alone can produce enough of the enzyme to convert the sugars fully into starch. Hence, "smooth-seed" appears dominant, while "wrinkled-seed" appears recessive. However, there is no "dominating" influence between alleles, which are each expressed independently. We can expect hybrids to express the "wrinkled-seed" allele and to contain the "wrinkled-seed" protein even though they appear smooth. The key information is that one allele alone in this pair is sufficient physiologically for promoting the reactions associated with smooth starchy seeds. The dominant/recessive label adds nothing to this simplified explanation, here. "Dominance" as a distinct property is an artifact.

The case of eye color pigments in fruit flies reveals similar complexities and redundancies (again, Guilfoile 1997, pp. 93-94). Pigment development relies on precursors that are transported into the eye cells by various membrane proteins. The gene variant associated with white-eye,

	"Level" of Genetic Expression (Phenotype)	Examples
1	DNA TRANSCRIPTION	elongated mRNA / blood type A2 [110300.0003] multiple repeats / Huntingdon chorea
2	mRNA EDITING & TRANSLATION	new exon arrangements of mRNA / alcaptonuria #4 premature translational stop / phenylketonuria #1
3	PROTEIN STRUCTURE	keratin / skin conditions collagen / osteogenesis imperfecta dystrophin / Duchenne's muscular dystrophy
4	PROTEIN FUNCTION	hemoglobin / sickle cell anemia, thalassemia blood clotting Factor VIII / hemophilia insulin or insulin receptor / diabetes
5	ENZYMATIC REACTIONS	lactase / lactose intolerance fructose-1,6-diphosphatase / hypoglycemia
6	PRODUCTS OF ENZYMATIC REACTIONS	tyrosinase / albinism (melanin) glycosyl transferases / AB blood type (red blood cell antigens)
7	PHYSIOLOGICAL AND DEVELOPMENTAL EFFECTS	GM2-hexoaminidase / Tay Sachs cystic fibrosis transmembrane conductance factor / cystic fibrosis
8	BEHAVIOR: proteins in nerve cells	dopamine receptor D2 / schizophrenia? —?— / handedness? serotonin receptors / depression, anxiety

TABLE 1. LEVELS OF FUNCTION IN THE GENETIC EXPRESSION OF A TRAIT. "Dominance" appears due to the differential expression of coupled alleles, often with observable differences traceable to certain levels of expression. Here, various human genetic traits are identified with the level, or type, of expression where function diverges.

located on the fruit fly's X chromosome, seems central to all such transport systems. The specific variation in DNA sequence has not yet been isolated. Still, one can see that even if the protein is synthesized and becomes embedded in the membrane, it need not be shaped like its counterpart in red-eyed individuals. It does not transport pigment precursors into the cell. (Moreover, in an apparent pleiotropic effect, it may also affect courtship behavior in males when expressed in all cells: we might suspect that the transported elements have adopted more than one role in the cell.) In this case, by following inheritance patterns, one can infer that a single copy of the gene can generate sufficient protein for membrane transport. Again, in hybrids, both alleles are expressed. What matters is what each allele leads to independently. How does labeling "red-eye" as dominant and "white-eye" as recessive contribute further to this explanation?

The two cases of wrinkled-seed in peas and red-eye in fruit flies illustrate that dominance is not a property of the "dominant" allele. Nor is it a special interaction between two alleles. Rather, what we call dominance is a contingent emergent feature based on the particular pair of alleles and the expression of each. To understand inheritance patterns fully, then, one must appreciate how the expression of genetic variants can diverge. The two classic cases above begin to exemplify how to conceive genetic expression at many levels. Additional cases from human genetics can help further articluate, at least broadly, the many levels (Table 1). A phenotypic "trait" will depend on the nature of the DNA sequence and the role of the protein physiologically or developmentally. Thus, genetic variants may and may not both be transcribed, may or may not both produce proteins. They may or may not have the same three-dimensional configuration—and may or may not fit with other protein units in multimers. They may or may not have similar catalytic activity (enzymes), signaling properties (hormones) or activation potential (neurotransmitters, membrane receptors, etc.). Even subtle variations in enzyme activity may lead to different reaction rates or the amount of an enzymatic product. These variations, in turn, may have further physiological effects, developmental responses or behavioral differences (for example, if they are affecting certain types of cells within the nervous system). The expression of variant alleles may potentially vary or diverge at any of these levels. In a sense, every allele is expressed phenotypically. The question is: how, and what are the various downstream consequences? Dominance implies that one of the two chains of expression is completely suppressed, with no consequences for the organism. But there is no single property that leads to one gene being expressed in contrast to its homolog. All hybrid phenotypes are compound traits. The key is interpreting the dual contributions simultaneously at the many levels of genetic expression. Hence, it should surprise no one that cases coded as "complete" dominance are neither in the majority, nor representative, nor fundamental.

The second major aspect of interpreting traits labeled as dominant and recessive is to understand the *coupled* expression of *pairs* of alleles in *diploid* organisms. Genes are not just expressed. They are expressed in pairs. According to the conventional view of dominance, the number of copies of a gene should not really matter: "dominant" homozygotes and heterozygotes should be identical phenotypically. However, some "dominant" traits express themselves differently when in single versus double copies (work by Bruce Cattantach and M. Kirk, cited in Rodgers 1991, p. 5). More familiar may be the dramatic phenotypic effects of a third copy of a chromosome, most notably trisomy 21, or Down's syndrome. Less well known may be the fact that the sex of the parent contributing the third chromosome in these cases can affect the phenotype (Rodgers 1991, p. 5). There are other cases of aneuploidy, as well, including, of course, the sex chromosomes (XO, XXY, XYY, etc.). All autosomal monosomics are apparently

lethal (Russell 1992, p. 598) though, again, according to Mendelian frameworks, the number of alleles should not matter. In fact, a dominant allele is not uniformly expressed; it is not predictably the same in single, double or triple copies. Dominance does not inhere in an individual allele. And phenotypes are not either-or, based on simple dichotomous features. Rather, traits are based more fundamentally on the alleles that are present (whether one, two or more) and how each is expressed.

The phenotype of hybrids is compound. Two alleles are expressed. The challenge is to interpret the many possible patterns of double expression—as illustrated below (§IV). "Dominance" is one possible pattern, seen at a large (organismal) scale. But it is still not caused by any relationship between the alleles. Each allele is independent. Once again, there is a tendency to *reify* dominance as a causal property or process, when it is nothing more than an observable pattern. "Dominance"—or anti-recessiveness—means, modestly, almost just as Mendel stated, that one trait is manifest in a hybrid and, simultanesouly, its allele is coupled with another allele whose phenotypic expression is minimal or not visibly significant at the macroscopic level. There are no corresponding molecular overtones. When one properly narrows the definition thus, the concept loses its current scope—and much of its intended significance.

Misconceptions about dominance persist largely because it is so rarely explained and its domain is not explicitly limited. Explaining the molecular or developmental basis for each trait would contribute to alleviating current misconceptions, yet dissolving the concept of dominance in genetics would help prevent such misconceptions at the outset. Indeed, many professional geneticists are already purging the term from their discourse or simply abandoning it as uninformative. Online Mendelian Inheritance in Man (OMIM), the major reference for human genetics, for example, discontinued classifying traits as dominant and recessive in 1994. The concept of dominance is obsolete.

IV. RECASTING DOMINANCE

Ultimately, dissolving dominance can clarify discussion and interpretations of genetics. For example, our concepts and language should describe both the levels of intergenerational transmission and molecular expression, while facilitating understanding of the relationship between them. In place of the confusions and complexities of dominance and all its exceptions and qualifications, along with the now separate and often inconsistent discussions of its molecular mechanism(s) (§III), only two basic elements are needed, as noted above. First, what is the expression or developmental meaning of each trait? Second, how do any pair of traits establish a "joint" phenotype in concert? The remainder is explained by the segregation and recombination of alleles and by the background knowledge of the layers of genetic expression (Table 1).

Indeed, one can find the prospective model already deployed in the standard conception and discussion of ABO blood types (OMIM #110300). First, many possible alleles are acknowledged: A, B and O, commonly, and others (including a remarkable form, cis-AB, that shows dual enzymatic function). However, due to the sexual nature of human reproduction, each individual carries just two alleles, one from each parent. The relevant blood-type phenotypes originally became evident from agglutination of blood mixtures, indicating that red blood cells can have specific antigenic properties. The now well-known safe transfusions between blood types indicate that the O allele does not generate specific antigens, while A and B produce distinct antigens. Hence, an O allele in combination with A or B becomes functionally "invisible" when

considering transfusions, by virtue of producing no antigen. (Note, here, that no one sees the need to call A or B "dominant" to O.) Nor is there any confusion when, by contrast, A and B alleles combine: each contributes an antigen to the red blood cells. The hybrid is a hybrid. Furthermore, one can predict possible allelic make-ups from observed blood type, as well as possible phenotypes of the prospective offspring from two parental genotypes. How simple. How clear. (And how free of dominance.)

The discourse of blood types illustrates a model that can be applied uniformly and consistently across all cases. One set of concepts and language can embrace both the limited domain of dominance and its "exceptions." The relevant information is always knowing which of many alleles are present and what each means for the individual's physiology or development. Thus, though blood types are typically labeled as a case of "co-dominance," the concept of dominance itself is wholly peripheral. Co-dominance dissolves. All phenotypes are dual phenotypes, with each of two genes contributing. Hence, pink flowers and Andalusian fowl, for example, are neither heritable traits on their own (distinct alleles), nor "half-traits" based on one allele being "incompletely" expressed. Rather, they result when full saturation of a particular color requires a "double dose" of a pigment. A single dose (in a hybrid) appears "diluted" by contrast, but only in relation to the double, more fully saturated color. Incomplete dominance likewise dissolves.

Consider, too, the cases that resonate most closely with the presence-absence hypothesis proposed early in the century. These are perhaps the best candidates for imagining any residual relevance for dominance (or "complete dominance"). Alcaptonuria (OMIM #203500) is a dramatic example and noteworthy as one of the earliest recognized "inborn errors of metabolism" (described as Mendelian by Archibald Garrod in 1902). Alcaptonuria patients pass black urine. They lack a functional enzyme (homogentisate 1,2 dioxygenase, or HGD), one of a series that breaks down phenylalanine into excreted waste. As a result, the compound "upstream" of the enzyme accumulates, turning black when alkalinized in the urine. Here, one might imagine calling the black-urine alleles "recessive" and their yellow-urine counterparts "dominant." But it is far simpler and more direct to state that any individual has two alleles: when at least one of them produces the enzyme, the urine is yellow; when neither does, the urine is black. Indeed, one need not even to refer to the cellular processes at all: one copy of the "yellow-urine" gene is sufficient to ensure yellow urine. This adequately describes the particular pattern of expression when two alleles combine—and dominance dissolves. All genetic expression—dominant or not—is thereby unified conceptually.

The same simple concepts and direct discourse can apply to cases that otherwise appear awkward or convoluted on the dominance model. Take, for example, osteogenesis imperfecta (OMIM #120160), a condition of extremely fragile bones. Collagen is a triple helix protein, assembled from two procα1(I) chains and one procα2(I) chain. One allele forms an altered procα2(I) chain that does not self-assemble into the helix. In this case, the altered protein chain can bind partially to procα1(I) but subverts the overall structure, even if some functional procα2(I) is present. With insufficient collagen fibers, then, individuals are especially susceptible to bone injury. Here, one copy of the allele can precipitate the condition. In the language of dominance, osteogenesis imperfecta is "dominant," by virtue of the trait's expression in hybrids. At the same time, it seems awkward to say that the "recessive" trait—in this case, the functional trait—has "withdrawn," is "latent," or is not expressed. After all, the allele is expressed and the protein appears in precisely the same form as when fully functional. Here, it is clearer to state that

one copy of the variant gene is sufficient to *interfere* with the otherwise standard function (in contrast to other cases where one copy is sufficient to maintain the function). One does not have to invert the meanings implied by first referring to dominance.

Finally, consider the classic case of sickle cell anemia (OMIM #141900.0243). The disease appears in severe form when individuals have no regular hemoglobin (i.e., are homozygous for the “sickle-cell” allele). Thus the disease has conventionally been construed as recessive. However, individuals with one of each allele have both forms of hemoglobin and do exhibit distinct physiological symptoms. The hybrid has a third phenotype, mild hemolytic anemia. The condition is also noted for a pleiotropic effect, resistance to malaria, associated with the “sickle-cell” allele. Even one copy of this gene can provide benefit. These complexities wreak havoc with assignments of dominance. Hence, if the trait is a life-threatening disease, the “non-sickle hemoglobin” allele is dominant. If the trait is physiology, then perhaps it is incompletely dominant. If the trait is malaria resistance, then the same gene is recessive. The same allele can exhibit three forms of dominance, depending on how one delineates the character. How paradoxical. But, of course, nothing important hangs on the label. All the essential information can be conveyed by noting: (a) the properties of expressing each allele and (b) which alleles are paired. In this case, there are three distinct phenotypes based on combining two specific hemoglobins, with each allele contributing something significant. Once again, the current discourse on blood types provides a fully functional and unifying model.

Ultimately, once one understands molecular genetics, the whole concept and language of dominance unravels, even at the level of transmission (or classical) genetics. The dominant-recessive concept depends on being able to sort traits neatly as expressed or unexpressed. Phenotypes must be essentially dichotomous—at least at the macroscopic, or observable, level. Fuller familiarity with molecular biology, however, reveals that phenotype exists at all levels simultaneously (Table 1). Traits that seem unexpressed at one level may certainly be expressed at another. Indeed, as noted above, focusing on "traits" only at the organismal level can hide or obscure important phenotypic differences at the molecular or cellular level. Any distinction that privileges one level of expression as "the" phenotype is arbitrary and potentially misleading. The Mendelian who hopes to characterize a trait as "dominant" because of observed differences in the organism thereby risks mischaracterizing the trait. Hence, even without detailing the molecular story of each gene, one needs to ensure that the multiple levels of intepretation will at least be commensurable. Dominance fails, even for classical genetics, because it draws an artificial or overstated boundary between the expressed and the unexpressed. Inferences about suppression or latency of traits (dominance or recessiveness), in view of molecular understanding, are false. Dominance is an artifact of interpreting phenotype only macroscopically. Coupled alleles are each expressed independently. Our language can—and should—reflect that.

Dominance does not mark any important property beyond the trait itself and how it is expressed. We can abandon the concept without loss, while preserving the other basic principles of inheritance that Mendel noted. Again, one can echo Curtis and Guthrie in their 1933 text:

> The course of inheritance for characteristics that do not exhibit dominance, therefore, is in no way different from that for characteristics in which dominance occurs. (p. 185)

One merely needs to keep in mind the coupled alleles and the dual phenotype. Dominance is superfluous. It fosters misconceptions. Simple alternative language is available. We are ready to dissolve dominance.

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NOTES

[1]Distinguished English geneticist William Bateson echoed Mendel's misconceptions in his own conceptual development in 1902. At first Bateson praised Mendelism as an explanation only for discontinuous, or non-blending, variation. He, too, interpreted the purity of the genes as requiring the dominant-recessive relationship. Later, he was able to conceive intermediate forms (expressed in the heterozygotes) as contributing to continuous variation, especially where there might be many alleles that could form a series of phenotypic forms (Olby 1987, pp. 414-415, 417).

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