**On Mechanistic Reasoning in Unexpected Places:**

**the case of population genetics**

LUCAS J. MATTHEWS

*Department of Psychology*

*University of Virginia*

*Gilmer Hall*

*Email: lucasjohnmatthews@virginia.edu*

*Phone: +1 (513) 582-3956*

ABSTRACT

A strong case has been made for the role and value of mechanistic reasoning in process-oriented sciences, such as molecular biology and neuroscience. This paper shifts focus to assess the role of mechanistic reasoning in an area where it is neither obvious or expected: population genetics. Population geneticists abstract away from the causal-mechanical details of individual organisms and, instead, use mathematics to describe population-level, statistical phenomena. This paper, first, develops a framework for the identification of mechanistic reasoning where it is not obvious: *mathematical* and *mechanistic styles of scientific reasoning*. Second, it applies this framework to demonstrate that both styles are integrated in modern investigations of evolutionary biology. Characteristic of the former, applied population genetic techniques provide statistical evidence for associations between genotype, phenotype, and fitness. Characteristic of the latter, experimental interventions provide causal-mechanical evidence for associations between the very same relationships, often in the same model organisms. The upshot is a richer perspective of how evolutionary biologists build evidence for hypotheses regarding adaptive evolution and general framework for assessing the scope of mechanistic reasoning across the sciences.

1. *Introduction*
2. *Population Genetics and Philosophy*
3. *In Search of Mechanistic Reasoning*
   1. *Mathematical and Mechanistic Styles*
4. *Reasoning about Adaptive Evolution*
   1. *Mathematical style confer statistical evidence*
   2. *Mechanistic style confer causal-mechanical evidence*
5. *Integration and Consilience*
6. *Conclusion*

**1. Introduction**

Eudoxus, a student of Plato, approached the challenge of modeling and explaining the heavenly bodies in a very specific style: he described motions of stars and planets in the night sky *mathematically,* through formal representations of the concentric spheres wrapped around earth at the center. Aristotle, on the other hand, drew on Eudoxus’ mathematical work to produce a different kind of model, characteristic of an alternative, *mechanistic* style of scientific reasoning: he sought to demonstrate *how* the heavenly bodies moved by creating a causal-mechanical, physical model, composed of organized and interacting parts.

Millennia later, the contrast between mathematical and mechanistic styles of scientific reasoning persists. On the one hand, we might treat the explanatory, investigative, and experimental practices described by the new philosophers of mechanisms as characteristic of the ‘mechanistic’style of scientific reasoning (Craver and Tabery 2016)*.* In that framework, to explain a phenomenon is to show *how* it works by identifying the mechanism – the set of organized and causally interacting parts – responsible for the phenomenon. This mechanistic approach does well to capture the manner in which sciences such as molecular biology and cognitive neuroscience are driven by mechanistic reasoning (Bechtel 2008; Bechtel and Richardson 2010; Craver 2007; Craver and Darden 2013; Darden 2006; Glennan 2002; Machamer et al. 2000).

Yet not all areas of scientific activity are so obviously mechanistic as molecular biology and neuroscience. Theoretical population genetics, for example, is a pattern-oriented field driven by mathematical modeling of population-level, probabilistic phenomena. Population geneticists do not create and intervene on physical models; rather, they construct formal models of theoretical populations, characteristic of Eudoxus’s *mathematical* style of scientific reasoning. What is the relation between these seemingly contrastive styles of mechanistic and mathematical reasoning? Are they incompatible? Are they competing approaches to explaining the same phenomena or do they offer avenues of consilience, for the integration of different kinds of evidence? In what follows I address these questions in light of how contemporary biologists investigate, explain, and build evidence for hypotheses regarding adaptive evolution.

I make my case in two primary steps. First, I develop a framework – *mathematical* and *mechanistic* – for identifying the role and value of mechanistic reasoning in the areas of science where it is not so obvious. Second, I apply this framework to contemporary case studies of adaptive evolution. The results evince an elaborate integration of both mathematical and mechanistic styles of evolutionary biology. On the one hand, applied population genetics, which is characteristic of the mathematical style, provides statistical evidence for associations between genotypes, phenotypes, and fitness. On the other hand, experimental interventions, which are characteristic of the mechanistic style, provide causal-mechanical evidence for associations between the same relationships, often in the same model organisms. Put another way, mathematical and mechanistic styles of reasoning drive consilience: practitioners use both styles to accrue different kinds of evidence for the same hypotheses regarding adaptive evolution.

**2 Population Genetics and Philosophy**

On Okasha’s (2015) view, population genetics is “a field of biology that studies the genetic composition of biological populations, and the changes in genetic composition that result from the operation of various factors, including natural selection.” According to Millstein and Skipper (2007) it is “a subfield of evolutionary biology that aims to represent mathematically the changes in the genetic variation of populations (specifically, sexually reproducing populations with Mendelian heredity) over time” (p. 1). Both construe population genetic approaches to investigating and understanding evolution as driven by mathematical modeling of population-level patterns.

Biologists and philosophers of biology have written extensively about conceptual and theoretical issues related to population genetics. There is, for example, disagreement regarding whether there are laws in population genetics (Beatty 1995; Ruse 1970; Waters 1998). There has been some discussion on the relation between population genetics and the semantic conception of scientific theories (Beatty 1980; Lloyd 1988). Considerable attention has been given to the value of population genetics to evolutionary theory. Critics question, for example, whether population genetic models are too abstract and idealized to confer knowledge of real biological populations (Craig 2010; Glymour 2006; Lewontin 1980, 2000; Pigliucci 2008). Others defend population genetics as providing a useful tool for understanding evolution (Lynch 2007; Millstein 2013; Morrison 2004).[[1]](#footnote-1) While each of these issues highlight important challenges for understanding evolution and evolutionary science, here I address a new philosophical question related to population genetics: what is its relation to the seemingly contrastive *mechanistic* way of investigating and explaining evolutionary patterns and processes?

The historical foundations of theoretical population genetics evince an approach to understanding evolution that is not obviously mechanistic. Before the modern synthesis, evolutionary investigations focused on the individual traits of organisms and their causal relations to environmental characteristics – recall Darwin’s careful attention to beak variation in finches and their relation to the size, shape, and rigidity of nuts and seeds. The development of population genetics through R. A. Fisher’s (1918, 1930) mathematical reconciliation of gradual Biometrician and discrete Mendellian models of evolution, however, captures a shift in focus from the physical characteristics of individuals to the statistical characteristics of population-level patterns. Other major contributors to the synthesis, such as S. G. Wright (1931) and J. B. S. Haldane (1932), were gifted mathematicians and statisticians. Thus, from a historical perspective, population genetics is an unlikely candidate for mechanistic reasoning because it represents an investigative shift of focus from physical traits of individual organisms to statistical characteristics of populations.

The statistical methodologies and formal theories of population genetics have given rise to philosophical conceptions of evolution and natural selection that are not obviously mechanistic. Reading metaphysics of natural selection from population genetic approaches to natural selection has given rise to the *causalist v. statisticalist* debate. The statisticalists – most notably Matthen and Ariew (2002) and Walsh et al. (2002) – present a view of natural selection contrary to a mechanistic style of evolutionary thinking:

“The statistics employed in thermodynamics explains something about the nature of heat and work, something we would not understand by having a history of molecular interactions in a pot of water, even assuming that our minds could comprehend that kind of detail. Similarly, the statistics of natural selection tells us something deep about the patterns instantiated in diverse biological histories. By appreciating these patterns, we come to understand something that we are not able to see when we are given the full biographical details of organisms in diverse populations” (Matthen and Ariew 2002, p. 81).

*Causalists,* on the other hand, argue that natural selection occurs at the level of individuals and is a causal process (Bouchard and Rosenberg 2004; Pence and Ramsey 2013; Ramsey 2013). Millstein (2006) carves out a middle ground, arguing that selection is a population-level, causal process.[[2]](#footnote-2) Thus, the historical shift from tracking concrete organismal traits to construction of abstract mathematical models of population variation, and the alternative philosophical conceptualizations of natural selection to which it gives rise, limn population genetics as a domain where mechanistic reasoning is neither obvious or expected.

**3 In search of mechanistic reasoning**

The philosophers of mechanisms have built their case in light of scientific activity that is explicitly mechanistic. ‘Mechanism’ and related terminology (e.g., ‘parts’, ‘activities’, ‘interactions’) are unquestionably ubiquitous in molecular biology and neuroscience. In addition to mechanistic language, the textbooks and journal publications of these fields are teeming with visuo-spatial representations of mechanisms, through images and diagrams of putative mechanisms and mechanistic processes (e.g., protein synthesis and synaptic transmission). These cases evince not only the descriptive claim that molecular biology and neuroscience ‘explain mechanistically’, but the success of these approaches furnish a normative claim regarding the value of thinking about the world mechanistically.

Some question, however, whether the value of thinking mechanistically is limited to those sciences that are explicitly mechanistic, like molecular biology and neuroscience. There is evidence that reasoning mechanistically about a phenomenon positively influences scientific hypotheses that are in no obvious way mechanistic. I have shown elsewhere that the prima facie nonmechanistic field of statistical phylogenetics benefits from appeal to ‘embedded mechanisms’ (Matthews 2015). Embedded mechanisms are bits of causal-mechanical reasoning built in to mathematical models used to construct phylogenetic tree hypotheses. The case of embedded mechanisms in statistical phylogenetics demonstrates how that which is relevant about mechanisms to science and explanation is not always obvious and explicit – sometimes you’ve got to look under the hood.

Put another way, a well-informed philosophical perspective of science must take into consideration all the activity and phenomena that are relevant to the undoubtedly successful manner in which scientists investigate, explain, and predict the world. The explicit representation of mechanisms in journals is only part of the picture. From making observations and developing hypotheses to running experiments and publishing results, all the relevant things that scientists do should inform the ongoing efforts by philosophers to construct both (a) accurate descriptive accounts of scientific activity (e.g., explanation and methodology) as well as (b) useful normative accounts of how such activity could be done better (e.g., accurately, efficiently, ethically, etc.).

*3.1 Mathematical and Mechanistic Styles*

Capturing more of what is significant about the concept of mechanism to science requires that we look beyond the relatively narrow category of *mechanistic* *explanation* explicitly represented in journals and textbooks to the broader category of *mechanistic reasoning.* Capturing the role and value of mechanistic reasoning in unexpected places requires a diagnostic framework – a conceptual tool for making sense of the different styles of scientific reasoning that generate different kinds of activity, with special attention to those that are not obviously mechanistic.

To this end, I offer the following conceptual framework: the distinction between *mathematical and mechanistic styles of scientific reasoning*. I will show how this distinction makes sense of the relation between mechanistic thinking and the seemingly nonmechanistic area of population genetics, but note that this framework likely captures similar divisions broadly across the sciences. This framework rests on the shoulders of three important contributions to the philosophy of science. First, Hacking’s (1982, 1988, 1992, 1994, 2004, 2012) philosophical account of ‘styles of scientific reasoning’, which was developed in light of Crombie’s (1981, 1994) historical analysis of ‘styles of scientific thinking.’ Second is Winther’s (2006) distinction between two ways of doing biology: *formal* and *compositional.* Third is Tabery’s (2014) formulation of *variation-partitioning* and *mechanism-elucidation* approaches to human behavior genetics.

Hacking’s styles of reasoning are useful because attention to ‘reasoning’ captures more than what is obvious about scientific explanation and ‘styles’ capture the fuzzy, overlapping boundaries between seemingly contrastive methods and techniques used toward contemporary investigations of adaptive evolution. Tracking reasoning allows that we look under the hood of scientific explanations. Again, while there is nothing obviously mechanistic about phylogenetic tree hypotheses, their development is aided by mechanistic reasoning through the use of embedded mechanisms in mathematical models (Matthews 2015).

Attention to ‘styles’ is useful because, similar to styles of boxing, art, or tennis, styles of scientific reasoning lack necessary and sufficient conditions, and only loosely demarcate distinct techniques and methods. In the same way that there is no clean and distinct line between impressionist and surrealistic styles of art, there’s no satisfactorily categorical line between mathematical and mechanistic styles of scientific reasoning. Practitioners working in the impressionist style of painting tend to capture unususal visual angles, movement, and mood over detail with specific brush techniques, such as short, thick strokes of adjacent unmixed color contrasts. Practitioners working in the surrealist style, on the other hand, tend to capture illogical or nonsensical, dreamlike scenes with vivid detail and precision with specific techniques, such as frottage, decalcomania, grattage, and fumage.

While various painting techniques may be characteristic of one style of art over another, the use of one does not preclude the use of others. One could, for example, us surrealist techniques such as frottage and fumage to create impressionist art. Conversely, one could use impressionist techniques such as short, thick brush strokes, to create surrealist art. The boundaries between styles of art are at times vague and fuzzy. Similarly, there’s no clean and distinct manner in which we might delineate styles of scientific reasoning. While statistical analysis and formal modelling are techniques characteristic of the mathematical style of scientific reasoning, the same techniques are often used by practitioners whose work is typical of the contrasting, mechanistic style of scientific reasoning.

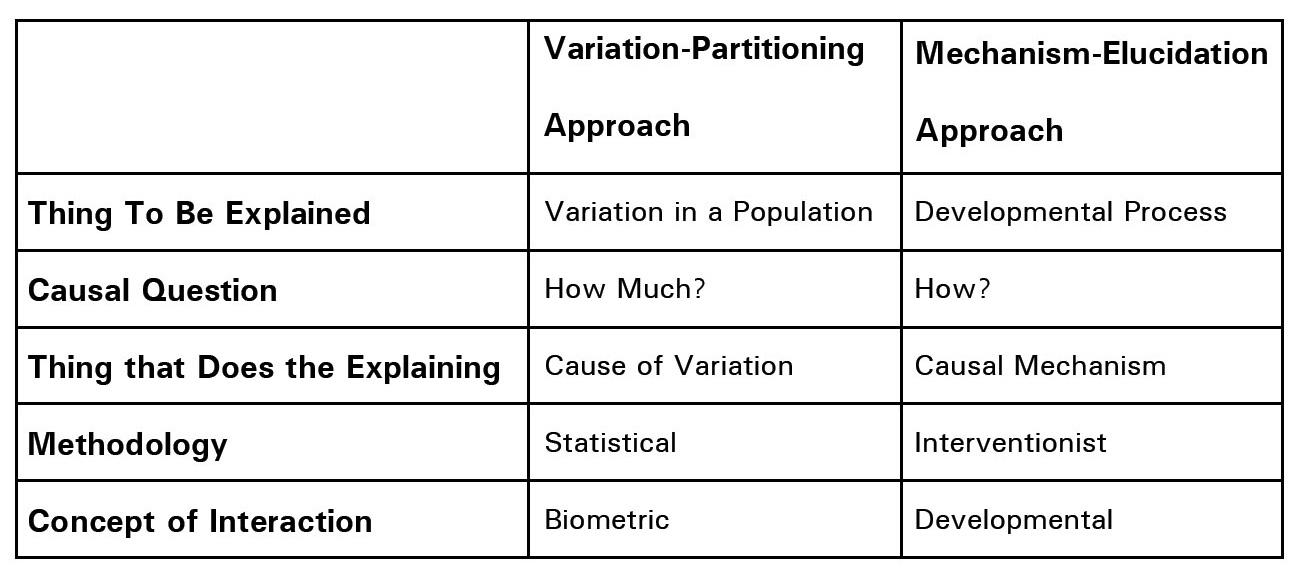
Winther’s distinction between formal and compositional biology is useful because it captures a similar division with respect to how biologists build evidence for hypotheses regarding adaptive evolution:

“In fact, I believe that there is a style of biological theorizing – compositional biology – that based on the notion of parts and wholes, as well as their respective functions and capacities. I contrast this style with formal biology, which focuses on mathematical laws and models that represent quantitative relations among terms (parameters and variables). The disciplines of comparative morphology, functional morphology, developmental biology, cellular biology, and molecular biology tend to employ the compositional style, while the disciplines of theoretical population genetics and theoretical ecology tend to adopt the formal style” (p. 471).

Akin to ‘formal biology’*,* the use of mathematical models, statistical analyses, and proof from formalisms are all techniques characteristic of the mathematical style of scientific reasoning. Akin to ‘compositional biology’*,* emphasis on function and part-whole relationships are characteristic of the mechanistic style of scientific reasoning.

Tabery’s distinction between ‘variation-partitioning’ and ‘mechanism-elucidation’ approaches to human behavior genetics highlights a similar division regarding how biologists approach adaptive evolution today. Similar to variation-partitioners, practitioners working in the mathematical style use statistical methodologies in efforts to answer ‘how much?’ questions regarding population-level variance. Similar to mechanism-elucidators, ventures to answer ‘how?’ questions about developmental processes with interventionist methodologies are characteristic of the mechanistic style of scientific reasoning.

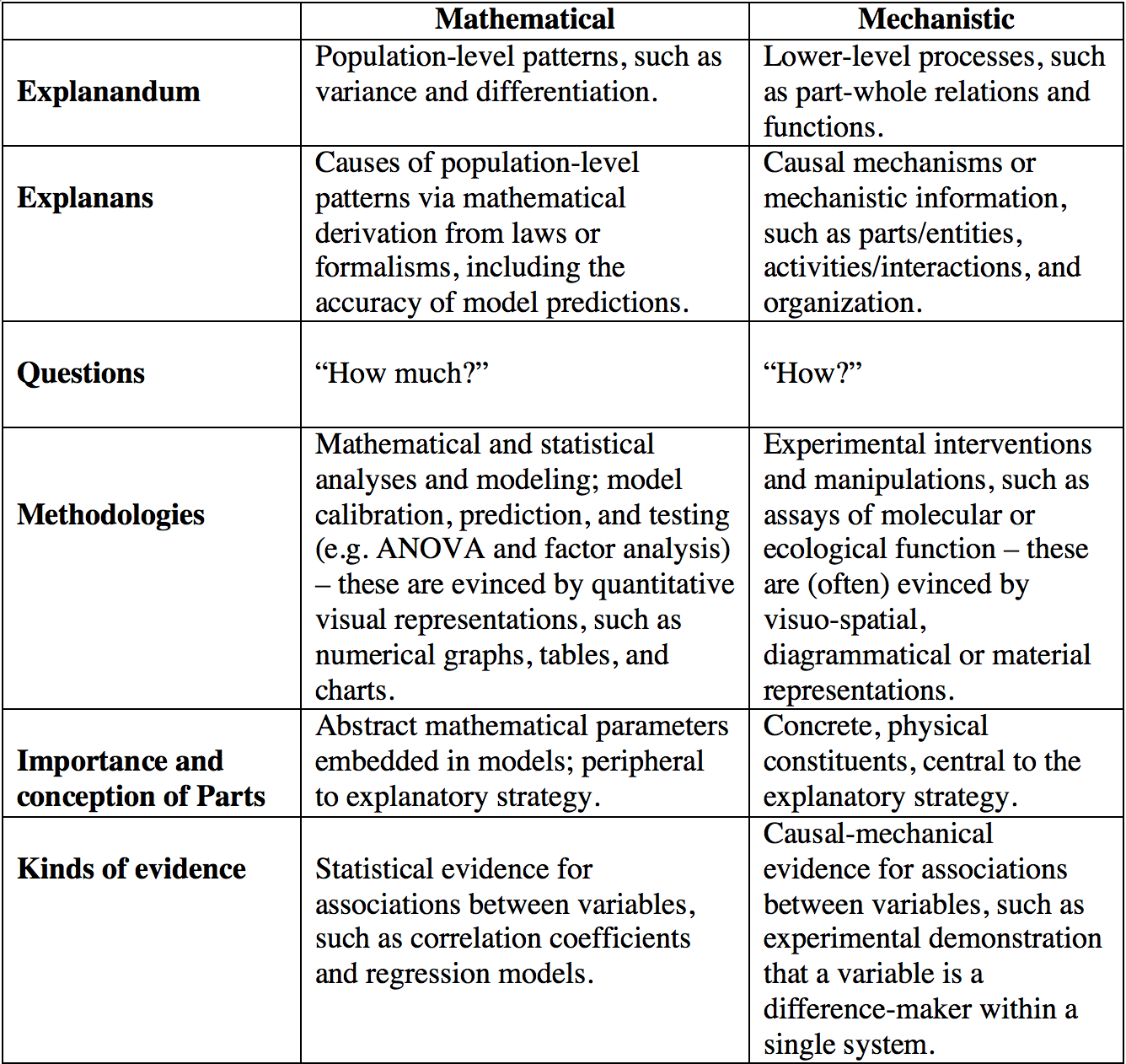
**Table 1**: Variation-partitioning v. mechanism-elucidation, adapted from Tabery (2014, p. 37)



The distinction between mathematical and mechanistic styles of scientific reasoning simplifies philosophical ontology by providing a broader framework that captures both Winther’s and Tabery’s conceptual divisions.The activities, theories, methodologies, kinds of evidence and explanations of practicing scientists across many disciplines provide evidence of these two styles of scientific reasoning. Theories that describe, track, and predict population-level patterns are characteristic of statistical reasoning. Those that explain or predict individual-level causal-mechanical interactions of entities or parts of systems are characteristic of mechanistic reasoning.

The use of mathematics, statistics, and probability theory to construct, calibrate, and apply models to either real or theoretical data is characteristic of a *statistical style of scientific reasoning.* The design, development, and application of material or diagrammatic models and experimental interventions on laboratory or field systems are characteristic of a *mechanistic style of scientific reasoning*. Efforts to answer questions about ‘how much?’ observed variance in a population is attributable to various causal sources is characteristic of the statistical style of reasoning. Efforts to answer ‘how?’ systems work, with respect to part-whole relationships and functions, are characteristic of mechanistic reasoning. Scientific practice driven by statistical reasoning provides *statistical evidence* for associations between variables*,* such as correlation-coefficients and regression models. Scientific practice driven by mechanistic reasoning provides *causal-mechanical evidence* for associations between variables in system*,* such as the experimental demonstration that intervention or manipulation on part of a system makes a difference elsewhere in the same system.

**Table 2**: *mathematical and mechanistic styles of scientific reasoning*



**4. Reasoning about Adaptive Evolution**

It would be difficult to deny that the discipline of population genetics is driven by the mathematical style of reasoning far more than it is driven by the mechanistic style. Population genetic curriculum emphasizes applied mathematics and statistics. Students in population genetic doctoral programs often work closely with departments of mathematics. In population genetic textbooks, one does not find ubiquitous diagrams of mechanisms; rather, one finds countless, quantitative tables and figures. There is no obvious way in which the field of population genetics is mechanistic.

That one might concede that the field of population genetics is not obviously mechanistic does not preclude, however, a positive assessment of its relation to mechanistic reasoning in general. Any well-informed philosophy of science does not only take into consideration the theoretical and academic categories of scientific fields, but also the activities of its practitioners. While there is no obvious manner in which mechanistic reasoning is prevalent in the field of population genetics, an analysis of practicing population geneticists– in the lab and in the field – generates a different perspective. Consider not the discipline of population genetics, but rather, the applicationof population genetic methodologies; the techniques, models, tests, and theories used toward the investigation of adaptive evolution by practicing biologists.

Research publication trends reveal that biologists use a variety of methods to investigate and understand the sophisticated relationships between genetic information, phenotypic traits, and fitness. Practitioners focus on three basic features of adaptive evolution – genotype (G), phenotype (P), and fitness (F) – and the statistical and causal associations between them: G—P, G—F, and P—F associations*.* First, methodologies and theories derived from population genetics are applied to evolutionary investigations characteristic of the mathematical style of reasoning and that they provide statistical evidence for G—P and G—F associations. Second, experimental biologists employ techniques in evolutionary investigations that are characteristic of the mechanistic style of reasoning, which provide causal-mechanical evidence for G—P, G—F, and F—P associations. The picture that emerges is one of an integration of mathematical and mechanistic methodologies that drive consilience of both statistical and causal-mechanical evidence for a triad of evolutionary relationships: G—P—F.

*4.1 Mathematical styles confer statistical evidence*

Biologists use a wide range of population genetic methodologies, techniques, and tests to elucidate statistical relations between genes, phenotypes, and fitness (Barrett and Hoekstra 2011; Okasha 2015; Pardo-Diaz et al. 2015). Initially, population genetic models were developed in light of theories regarding how theoretical populations of genes would be affected under evolutionary factors, notably drift and selection. Applied to real populations, these methods work toward two ends. First, they are used to associate broad or narrow regions of the genome with adaptive significance, namely by showing that a genotype is undergoing selection or, alternatively, that its patterns of variation provide evidence of selection elsewhere in the genome (i.e., G—F statistical association). Alternatively, population genetic techniques may be used to associate broad and narrow regions of the genome with prospective phenotypic traits of adaptive significance (i.e., G—P statistical association).

*G—F Statistical Association:* Population genetic techniques are most often used to assess whether population-level patterns are attributable to selection or drift.[[3]](#footnote-3) Population genetic models that accurately predict genotypic distributions provide statistical evidence for G—F associations. Models predict that different kinds of selection will impact genotypes in different ways, and constructing evidence for selection is a matter of detecting these ‘signatures’ of selection. Most notably, *positive selection* (of fitness-enhancing mutations) or *negative selection* (against deleterious mutations) may result in allelic variation, Linkage Disequilibrium (LD), population differentiation, frequency spectrum markers, and distinct dN/dS ratios. All of these genetic signals of selection are detected via mathematical modeling of population-level phenomena.[[4]](#footnote-4)

Population genetic models often provide ‘tests’ of neutral evolution. Each test makes specific assumptions regarding population-level patterns characteristic of selection. When applied to real populations, these tests attribute population genetic patterns to selection or null (i.e., neutral evolution). Each test is designed to track different population-level patterns that are observable given current technology. Some population genetic tests track the relation between single nucleotide polymorphisms (SNPs) and amino acid changes, as whether or not a nucleotide change results in an amino acid may be characteristic of different kinds of selection. The HKA test, for example, tracks the ratio polymorphisms to substitutions (Hudson et al. 1987). MacDonald-Kreitman-type tests track ratios of synonymous (‘silent’) and nonsynonymous polymorphisms (McDonald and Kreitman 1991). dN/dS tests track synonymous to nonsynonymous substitution ratios (Hughes and Nei 1988; Suzuki and Gojobori 1999).

Selection may affect population differentiation in statistically-detectable manners as well. FST based and related tests, for example, track patterns of population subdivision (Akey et al. 2002). Selection may also leave distinct patterns on the allele frequencies of various mutations in a population, summarized mathematically with ‘Frequency Spectrums’*.* Modeling of the spatial patterns left by selective sweeps, Tajima’s D, and related tests provide statistical evidence for G—F associations on frequency spectrums of sample populations (Tajima 1989).

Perhaps the most prominent signature of selection is tracked via the correlations between allelic variation at different sites: Linkage Disequilibrium (LD). For example, models predict that LD is *decreased* by balancing selection (i.e., any kind of selection that maintains variation) or *increased* by positive selection. Thus, population genetic techniques provide evidence for selection in genomic regions or SNPs by tracking either interspecific or intraspecific LD. The use of population genetic techniques to build evidence for G—F associations.

*G—P Statistical Association:* population geneticists use primarily two mathematical techniques that provide evidence for statistical associations between genotype and phenotype. First, one might seek to identify statistically significant, nonrandom covariation between some region of the genome – anything from a SNP to entire chromosomes – and a phenotype already believed to be adaptive (Pardo-Diaz et al. 2015). Conversely, one might work from a region of the genome already associated with phenotypes in some species, and to assess its significance in another. Both general approaches – often referred to as *forward* and *reverse* genetics, respectively – comprise a variety of specific population techniques that address statistical relationships between genotypic differences and phenotypic differences.

Quantitative Trait Loci (QTL) mapping, for example, is a key population genetic technique that tracks nonrandom variation between quantifiable phenotypes and narrow regions of the genome, such as specific loci. When variation in the trait is correlated with variation at one locus or more, then QTL mapping confers statistical evidence for a broad G—P association. Like the application of LD techniques for identifying G—F associations, QTL mapping techniques are often applied to the same model organisms as well. Genome Wide Association Studies (GWAS), another key population genetic technique, also provide statistical evidence for G—P mappings. Unlike QTL mapping, GWAS hold a single trait constant and track statistically significant SNP variation across entire genomes.

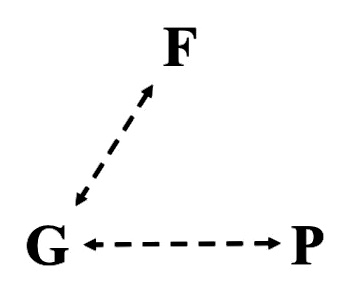
**Fig. 1**: G—F and G—P statistical associations conferred by mathematical methods of population genetics.

Fig. 1 summarizes the methodological implications of applied population genetic techniques. They are used both to link regions or loci of the genome to phenotypic traits of interest in building statistical evidence for G—P associations, and to assess whether population-level patterns are attributable to selection in building statistical evidence for G—F associations. These scientific practices are demonstrably characteristic of the *mathematical style of scientific reasoning*. They abstract away from the causal-mechanical features of lower-level phenomena and, instead, apply mathematical models and statistical tests to population-level patterns. They seek to address *how much* genetic variation is attributable to selection (in G—F studies) or the presence of a quantifiable trait (in G—P studies).

Note as well that LD studies, QTL mapping, GWAS, and other population genetic techniques are all used in the same model organisms, such as the threespine stickleback, *Gasterosteus aculeatus.* Hohenlohe et al. (2012), for example, used LD analyses to build statistical evidence for divergent selection in oceanic and freshwater stickleback populations. Peichel et al. (2001) used QTL mapping to identify associations between specific loci (*Spine2-b*) and specific traits in the size and shape of armor plating ofin stickleback populations. Finally, Jones at al. (2012) scanned entire stickleback genomes to provide evidence for G—P statistical associations related to marine-freshwater evolutionary divergence. In the following subsection, however, it will become evident that these practices only account for part of the story regarding how one investigates adaptive evolution.

*4.2 Mechanistic styles confer causal-mechanical evidence*

While LD, QTL mapping, GWAS, and related techniques confer evidence for statistical associations between genotype, phenotype, and fitness. Unfortunately, statistical associations leave open the possibility of false positives. Thus, many practitioners seek to bolster statistical evidence for G—P—F associations derived from applied population genetics with causal-mechanical evidence from experimental interventions.[[5]](#footnote-5) Pardo-Diaz et al. (2015), for example, describe a multistep methodology that integrates both population genetics with experimental interventions:

First, it is necessary to corroborate that a trait affects fitness in the field and is in fact adaptive. Then, the region(s) of the genome in which genotypes are correlated with adaptive phenotypes should be defined either with classical genetic tools or applying new genomic approaches. . . Ultimately, functional experiments are required to prove that a gene or mutation is actually responsible for the phenotype observed. Once individual genes or SNPs have been identified, it is important to quantify their effect in the ‘trait value’ (i.e. how much variation in the phenotype is explained by the candidate SNPs/genes). Finally, the genetic variation in the genes shaping those adaptive traits should be evaluated in field selection experiments in order to establish a definite connection between genotype, phenotype and fitness. (pp. 457—458)

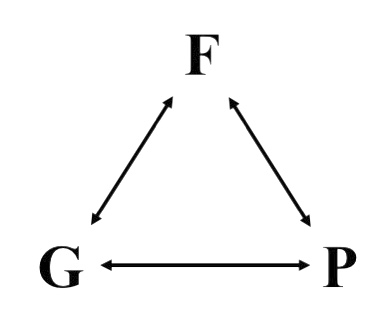
*G—P Causal-Mechanical Association:* Experimental techniques come in a variety of flavors in evolutionary biology. A key method is the development of *transgenic organisms*, in which an exogenous gene is inserted into the genome of an embryo and subsequent phenotypic effects are tracked. In other words, biologists intervene at G and track differences at P, which may provide causal-mechanical evidence for a given G—P associations. In many cases, this kind of mechanistic experimental intervention is driven by previous research that has already provided statistical evidence for a specific G—P mapping. Investigation of the genetic underpinnings of abdominal pigmentation in *Drosophila melanogaster* provides an excellent example of the sequential application of both mathematical and mechanistic styles of reasoning to the same phenomenon. First, Pool and Acquadro (2007) developed statistical evidence for an association between light and dark abdominal pigmentation and the *ebony* gene of *Drosophila melanogaster.* Later, Rebeiz et al. (2009) investigated the same G—P relationship mechanistically by conducting transgenic complementation experiments on *ebony* genes U62 and U76.

Another key interventionist strategy that is characteristic of mechanistic reasoning is the *candidate gene* approach. In this approach, one uses a variety of techniques to experimentally manipulate specific regions of the genome that have already been shown significant in other species. Using *gene knockouts,* for example, practitioners use experimental intervention to assess how the removal of a candidate gene affects the phenotype of a given model organism. By removing a gene of interest and tracking developmental and phenotypic changes, gene knockouts provide causal-mechanical evidence for prospective G—P relationships. Gene knockout techniques have been applied to the threespine stickleback fish as well. Chan et al. (2010), for example, associated pelvic reduction in *Gasterosteus aculeatus* with the *Pitx1* via gene knockout experimental interventions.

Instead of removing it entirely, one might intentionally reduce (*gene knockdown*) or amplify (*gene rescue*) gene expression to further understand causal-mechanical G—P associations. These *gene knockdown* experiments provide evidence for causal-mechanical G—P associations as well. Shu et al. (2011), for example, use knockdown techniques to associate the Retinitis Pigmentosa 2 (RP2) gene with retinal pigmentation in the zebrafish. Practitioners may as well use *gene replacement* techniques in which candidate genes are swapped in further mechanistic assays of molecular function of specific genes (Gong and Golic 2003).

*G—F and P—F Causal-mechanical Association:* while the experimental interventions described above may provide evidence that a given gene is associated with a trait of interest (i.e., causal-mechanical G—P association), they do not speak to the *adaptive* significance of these variables. Thus, practitioners must use a different set of techniques characteristic of the mechanistic style of reasoning to assess the causal-mechanical associations between genes, traits, and fitness.

*Field selection experiments* are the most common way to investigate G—F and P—F relationships (Barrett and Hoekstra 2011; Irschick and Reznick 2009; Pardo-Diaz et al. 2015). Current methods of ecological intervention involve two basic approaches: either hold the environment constant and manipulate the organism (or specific traits of the organisms) or hold the organism constant and manipulate the environment. Both approaches are achieved through the displacement of organisms from their natural environments. One might, for example, introduce organisms exhibiting adaptively significant phenotype variation into the same environment in order to track fitness effects, such as predation. Alternatively, one might introduce the same organism into a variety of different environments for the same purpose. Again, the threespine stickleback has been subject to G—F causal-mechanical association via assays of ecological function. Rundle et al. (2003), for example, created nine artificial, experimental ponds and hybridized *Gasterosteus aculeatus* to build evidence for effects of competition on traits associated with divergent selection, such as mean growth rates.

**Fig. 2**: G—P, G—F, and P—F causal-mechanical associations conferred by mechanistic methods of experimental biology.

Introduction of organisms into novel environments involves manipulating not individual traits of adaptive significance, but *entire* organisms. In order to narrow in on P—F associations, practitioners seek to manipulate specific traits of interest through the creation, manipulation, and introduction of *artificial organisms.* Linnen et al. (2013), for example, created and introduced artificial mice of varying coat color into environments in order to track predation effects, which confer evidence for the adaptive significance of variation in coat color. Merrill et al. (2012) created artificial butterflies (*Heliconius*), altered wing patterns, introduced them to natural environments, and then tracked frequency of attacks from birds. Both experiments provide causal-mechanical evidence for P—F associations in that they demonstrate that interventions at the level of phenotype affect fitness.

**5. Integration and Consilience**

Scientific investigation toward the identification of loci of adaptive evolution demonstrates the integration of mathematical and mechanistic styles of reasoning. This sense of integration is compatible with Mitchell’s (2003) account of *integrative pluralism*, but slightly different. While Mitchell focuses on representation, what is relevant here is the notion that mathematical and mechanistic styles of reasoning offer alternative perspectives of the same phenomenon, and there is an increasing trend to apply *both* perspectives to the very same species. Yet it is not just that the activities of contemporary evolutionary biologists evince alternative styles of reasoning about the same phenomena, but that these alternative styles beget different kinds of methods and techniques, which in turn beget different kinds of evidence.

The point is that whether building evidence using methods of either style, both are applied to building a triad of statistical *and* causal-mechanical associations between G, P, and F. A variety of methods and models of population genetics, driven by mathematical reasoning, are used in two basic ways. First, they help identify regions or loci of the genome that might be linked to traits of adaptive significance. In other words, much of applied population genetics involves the development of evidence for statistical G—P associations, such as QTL mapping and GWAS. Yet demonstration of a statistical association between genotype and phenotype does not confer evidence of adaptive significance. Rather, that requires a second major application of population genetic methods: the use of mathematical models (of both real and theoretical populations) for the development of statistical evidence that a genotype of interest exhibits adaptive significance – i.e., G—F statistical association (e.g., MacDonald-Kreitman tests, HKA tests, frequency spectrum analyses, LD studies, etc.).

Statistical associations conferred by population genetics should be bolstered by causal-mechanical associations conferred by experimental biology. In conjunction with mathematical studies of genotypes, phenotypes, and fitness, practitioners either intervene on each of these components of adaptive evolution for the purpose of tracking differences elsewhere in the triad. That is, practitioners intervene on genotypes in development of causal-mechanical evidence for G—P associations via assays of molecular function (e.g., gene knockouts, knockdowns, candidate gene approaches, etc.). In other cases, practitioners intervene on phenotypes in order to elucidate their causal-mechanical P—F associations, such as field selection experiments. In both cases, research often proceeds from or in conjunction with the mathematical efforts of population geneticists who investigate the very same G—P—F associations of the very same organisms.

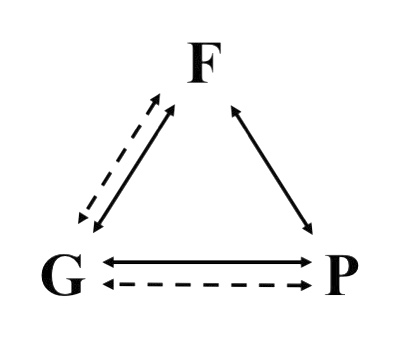
A philosophical case for the integration of mathematical and mechanistic reasoning in evolutionary biology is supported elsewhere in the literature, albeit indirectly. In making a case for natural selection as a population-level causal process, Millstein (2006) describes evolutionary investigations of *Chrysomelidae,* the elegant montane willow leaf beetle (Dahlhoff and Rank 2000; Rank 1992; Rank and Dahlhoff 2002). Her account of Rank and Dahlhoff’s investigations of the Phosphoglucose Isomerase (PGI) locus further evince the view that, in modern biology, satisfactory evidence of hypotheses regarding adaptive evolution involves the integration of both population genetic, statistical methods as well as mechanistic methods:

We need either to perform a laboratory experiment to demonstrate that the selective agent indeed acts on the phenotype in the way we think it does, or we need to provide the underlying mechanism to show that the genotypes have the abilities that we say that they do, or both. Rank and Dahlhoff do both; the laboratory experiment is described above, and they explain that the different PGI genotypes’ differing abilities to withstand heat and cold are the result of the production of differing amounts of heat shock protein at different temperatures. This causal and mechanistic information, together with the other information presented, provides strong evidence for Rank and Dahlhoff’s conclusions. (p. 640)

On this reading, researchers first developed statistical evidence from population genetic modeling that the PGI locus was undergoing selection (i.e., G—F statistical association). That statistical evidence, however, was later bolstered with causal-mechanical evidence through the identification of a causal pathway from the PGI locus to heat shock protein production in *Chrysomelidae,* which confers a fitness advantage for populations at lower elevation (i.e., G—P—F causal-mechanical association).

Integration of mathematical and mechanistic styles of reasoning about adaptive evolution is not limited to select cases, such as Rank and Dahlhoff’s analyses of the *Chrysomelidae.* There may have been a time when a majority of biology labs were driven *either* by mathematical or mechanistic reasoning – a time that has been tracked closely by philosophers of science and biology – but today this is the exception rather than the norm. Investigations of *Drosophila* *melanogaster*, *Caenorhabditis elegans*, *Gasterosteus aculeatus*, and others all evince publication patterns of both statistical population genetic analyses driven by mathematical reasoning as well as causal-mechanical field selection experiments driven by mechanistic reasoning. Good scientists recognize the difficulty in making a strong case for adaptive evolution and consequently pool their resources by using different kinds of evidence from different perspectives.

The picture that emerges is one about both integration of different styles of reasoning and consilience of different kinds of evidence. That practitioners both (a) model stickleback nucleotide patterns mathematically and (b) assess how interventions on specific nucleotide patterns affect stickleback fitness evince integration of two styles of reasoning about the same phenomenon. Moreover, that practitioners publish peer-reviewed scientific papers that appeal to both (a) the statistical evidence for genotype-fitness associations conferred by applied population genetics and (b) the causal-mechanical evidence for the same genotype-fitness associations conferred by field selection experiments evinces the consilience of different kinds of evidence for the same phenomenon.

**Fig. 3:** Integration of mathematical methods of population genetics and mechanistic methods of experimental biology.

Readers may worry that attention to *styles* of mechanistic reasoning instead of mechanistic explanation,proper, incites at least a few objections. First, one may object that attention to styles of reasoning renders evidence in favor of the philosophy of mechanisms too easy. If experimental intervention is all that is required to build the case for the philosophy of mechanisms, then attention to mechanistic reasoning explains nothing by explaining too much. Similarly, one may worry that this project talks past the philosophers of mechanism and their critics by focusing on styles of mechanistic reasoning instead of mechanistic explanation.

Both worries should be assuaged by the fact that the thesis of this paper – that the practices of contemporary evolutionary biologists evinces an integration both mathematical and mechanistic styles of reasoning – stands independent of the philosophy of mechanisms and its critics. It is true that mechanistic reasoning is not mechanistic explanation, but the two are indeed related and understanding the former is absolutely important to a well-informed philosophy of science. Put another way, it should be a boon of this analysis that it looks past the new mechanists as it demonstrates that what is explicitly represented in the language and diagrams of the explicitly mechanistic sciences of molecular biology and neuroscience do not capture everything that is informative and relevant about the manner in which scientists think about, investigate, explain, and build evidence for hypotheses about the world.

**6. Conclusion**

The things evolutionary biologists say and do has stood to inform philosophers of biology tackling epistemological questions, such as interest in evidence for evolution, as well as metaphysical issues, such as the ‘nature’ of selection. Because Darwin tracked the causal relationship between individual organismal traits (e.g., the size and shape of finch beaks) and environmental variation (the size and shape of seeds and nuts), philosophers have conceived of selection as a *causal* phenomenon. Yet because Fisher, Wright, Haldane, and others tracked population-level genetic patterns, other have conceived of selection as a *statistical* phenomenon. The disagreement between *causalists* and *statisticalists* is an excellent example of how scientific theorizing informs philosophical metaphysics regarding the nature of selection, reifying the importance of getting the science right.

To that end, this paper seeks to get the science right. It shows that – metaphysical questions aside – contemporary investigations of adaptive evolutionary biology demonstrate an integration of different kinds of evidence, derived from distinct styles of scientific reasoning. Any hypothesis regarding adaptive evolution requires that one elucidates the tripartite relationship between genotype (G), phenotypic (P), and fitness (F). On the one hand, experimental interventions in the field or laboratory provide causal-mechanical evidencefor G—P, P—F, and F—G associations, which is characteristic of a mechanistic style of scientific reasoning*.* On the other hand, mathematical models and statistical tests in theoretical and applied population genetics provide statistical evidencefor G—F and G—P associations, which is characteristic of a *statistical style of scientific reasoning.* Importantly, both styles are used toward investigations of the same G—P—F relations, often in the same model organisms, such as the threespine stickleback.

At the heart of the issue is the curious distinction between two seemingly contrastive styles of scientific reasoning. Like alternative styles of painting or art, the distinction between mathematical and mechanistic styles are neither in opposition or neatly delineated. It is not just that those who practice in the mathematical style use statistics and math, and those who practice in the mechanistic style only conduct experimental interventions. The boundaries between styles are fuzzy and overlapping. Statistics and mathematics are par for the course across the sciences – all the empirical evidence accrued through mechanistic styles of reasoning must be filtered and tested for statistical significance with mathematics. It would be a mistake as well to think that mathematical practitioners do not think about or appeal to causal-mechanical evidence characteristic of mechanistic reasoning. In the same way that biologists manipulate genotype-phenotype associations by intervening on nucleotide sequences and tracking differences in traits, population geneticists experiment on mathematical models by manipulating variables and parameters to assess effects elsewhere in the system. I anticipate that this distinction will apply across the sciences.

And while it may be the case that those who favor the mechanistic style lament the insufficiency of statistical evidence conferred by mathematical styles, and that mathematical modelers highlight the limitations of what may be manipulated experimentally, these alternative styles need not stand in opposition. At the end of the day, effectively investigating and explaining our world in its astonishing complexity is one unquestionably arduous and gran endeavor – so we pool our resources. A strong case for any hypothesis regarding adaptive evolution calls for both the statistical evidence driven by mathematical styles of reasoning as well as the causal-mechanical evidence driven by mechanistic styles of reasoning.

The division between mathematical and mechanistic styles in evolutionary biology echoes back to Eudoxus’ and Aristotle’s mathematical and mechanistic models of the heavens. Indeed, the division persists, millennia later. But perhaps the lesson we learn from contemporary investigations of adaptive evolution is that the two styles are not in opposition or competition, they’re simply two different perspectives of the same thing, both of which may be indispensable to a better understanding of the wonderfully sophisticated world in which we live.

**Acknowledgements**

Many thanks to Steve Downes, Matt Haber, Roberta Millstein, Anya Plutynski, Jon Seger, Mike Shaw, Jim Tabery, Eric Turkheimer, and anonymous reviewers.

**References**

Akey, Joshua M., Ge Zhang, Kun Zhang, Li Jin, and Mark D. Shriver. 2002. “Interrogating a High-Density SNP Map for Signatures of Natural Selection.” *Genome Research* 12 (12): 1805–14.

Barrett, Rowan D. H., and Hopi E. Hoekstra. 2011. “Molecular Spandrels: Tests of Adaptation at the Genetic Level.” *Nature Reviews Genetics* 12 (11): 767–80.

Beatty, John. 1980. “What’s Wrong with the Received View of Evolutionary Theory?” *PSA: Proceedings of the Biennial Meeting of the Philosophy of Science Association* Two: Symposia and invited papers: 397–426.

———. 1995. “The Evolutionary Contingency Thesis.” In *Concepts, Theories, and Rationality in the Biological Sciences: The Second Pittsburgh-Konstanz Colloquium in the Philosophy of Science*, edited by G. Wolters and Lennox, J., 45–81. Pittsburgh, PA: University of Pittsburgh Press.

Bechtel, William. 2006. *Discovering Cell Mechanisms: The Creation of Modern Cell Biology*. 1 edition. Cambridge: Cambridge University Press.

———. 2008. *Mental Mechanisms: Philosophical Perspectives on Cognitive Neuroscience*. New York, NY: Taylor & Francis Group, LCC.

Bouchard, Frédéric, and Alex Rosenberg. 2004. “Fitness, Probability and the Principles of Natural Selection.” *The British Journal for the Philosophy of Science* 55 (4): 693–712.

Chan, Yingguang Frank, Melissa E. Marks, Felicity C. Jones, Guadalupe Villarreal, Michael D. Shapiro, Shannon D. Brady, Audrey M. Southwick, et al. 2010. “Adaptive Evolution of Pelvic Reduction in Sticklebacks by Recurrent Deletion of a Pitx1 Enhancer.” *Science* 327 (5963): 302–5.

Craig, Lindsay. 2010. “The so-Called Evolutionary Synthesis.” *Biological Theory* 5 (2): 117–23.

Craver, Carl F. 2007. *Explaining the Brain: Mechanisms and the Mosaic Unity of Neuroscience*. 1 edition. Oxford: Oxford University Press.

Craver, Carl F., and Lindley Darden. 2013. *In Search of Mechanisms: Discoveries across the Life Sciences*. Chicago; London: University of Chicago Press.

Craver, Carl, and James G. Tabery. 2016. “Mechanisms in Science.” Edited by Edward N. Zalta. *The Stanford Encyclopedia of Philosophy*. URL = <http://plato.stanford.edu/archives/fall2016/entries/science-mechanisms/>.

Dahlhoff, Elizabeth P., and Nathan E. Rank. 2000. “Functional and Physiological Consequences of Genetic Variation at Phosphoglucose Isomerase: Heat Shock Protein Expression Is Related to Enzyme Genotype in a Montane Beetle.” *Proceedings of the National Academy of Sciences* 97 (18): 10056–61.

Darden, Lindley. 2006. *Reasoning in Biological Discoveries: Essays on Mechanisms, Interfield Relations, and Anomaly Resolution*. 1st edition. Boca Raton, Fl.: Cambridge University Press.

Fisher, Ronald Aylmer. 1918. “The Correlation Between Relatives on the Supposition of Mendelian Inheritance.” *Transactions of the Royal Society of Edinburgh* 52: 399–433.

———. 1930. *The Genetical Theory of Natural Selection*. New York, NY: Dover.

Gannett, Lisa. 2013. “Projectibility and Group Concepts in Population Genetics and Genomics.” *Biological Theory* 7 (2): 130–43.

Glennan, Stuart. 2002. “Rethinking Mechanistic Explanation.” *Philosophy of Science* 69 (S3): S342–53.

Glymour, Bruce. 2006. “Wayward Modeling: Population Genetics and Natural Selection\*.” *Philosophy of Science* 73 (4): 369–89.

Gong, Wei J., and Kent G. Golic. 2003. “Ends-Out, or Replacement, Gene Targeting in Drosophila.” *Proceedings of the National Academy of Sciences* 100 (5): 2556–61.

Hacking, Ian. 1982. “Language, Truth and Reason.” In *Rationality and Relativism*, edited by Hollis and Lukes, 48–66. Oxford: Blackwell Publishers Ltd.

Hacking, Ian. 1988. “On the Stability of the Laboratory Sciences.” *The Journal of Philosophy* 85 (10): 507–14.

Hacking, Ian. 1992. “‘Style’ for Historians and Philosophers.” *Studies in History and Philosophy of Science Part A* 23 (1): 1–20.

Hacking, Ian. 1994. “Styles of Scientific Thinking or Reasoning: A New Analytical Tool for Historians and Philosophers of the Sciences.” In *Trends in the Historiography of Science*, 1994th ed., 151:31–48. Boston Studies in the Philosophy and History of Science. Springer.

Hacking, Ian. 2004. *Historical Ontology*. Cambridge: Harvard University Press.

Hacking, Ian. 2012. “‘Language, Truth and Reason’ 30 Years Later.” *Studies in History and Philosophy of Science Part A*, Part Special Issue: Styles of Thinking, 43 (4): 599–609.

Haldane, John Burdon Sanderson. 1932. *The Causes of Evolution*. Princeton, NJ: Princeton University Press.

Hohenlohe, Paul A., Susan Bassham, Mark Currey, and William A. Cresko. 2012. “Extensive Linkage Disequilibrium and Parallel Adaptive Divergence across Threespine Stickleback Genomes.” *Phil. Trans. R. Soc. B* 367 (1587): 395–408.

Hudson, Richard R., Martin Kreitman, and Montserrat Aguadé. 1987. “A Test of Neutral Molecular Evolution Based on Nucleotide Data.” *Genetics* 116 (1): 153–59.

Hughes, A. L., and M. Nei. 1988. “Pattern of Nucleotide Substitution at Major Histocompatibility Complex Class I Loci Reveals Overdominant Selection.” *Nature* 335 (6186): 167–70.

Huxley, Julian S., and Lancelot T. Hogben. 1922. “Experiments on Amphibian Metamorphosis and Pigment Responses in Relation to Internal Secretions - University of Virginia - Virgo.” *Proceedings of the Royal Society of London*, series B, containing papers of a biological character, 93: 36–53.

Irschick, D., and D. N. Reznick. 2009. “Field Experiments, Introductions, and Experimental Evolution.” In *Experimental Evolution: Concepts, Methods, and Applications of Selection Experiments*, edited by T. Garland and M. R. Rose, 173–93. Oxford: Oxford University Press.

Jones, Felicity C., Manfred G. Grabherr, Yingguang Frank Chan, Pamela Russell, Evan Mauceli, Jeremy Johnson, Ross Swofford, et al. 2012. “The Genomic Basis of Adaptive Evolution in Threespine Sticklebacks.” *Nature* 484 (7392): 55–61.

Lewontin, Richard C. 1980. “Theoretical Population Genetics in the Evolutionary Synthesis.” In *The Evolutionary Synthesis: Perspectives on the Unification of Biology*, edited by Ernst Mayr and William B. Provine, 58–68. Cambridge, MA: Harvard University Press.

———. 2000. “What Do Population Geneticists Know and How Do They Know It?” In *Biology and Epistemology*, edited by Richard Creath and Jane Maienschein, 191–214. Cambridge Studies in Philosophy and Biology. Cambridge, MA: Cambridge University Press.

Linnen, Catherine R., Yu-Ping Poh, Brant K. Peterson, Rowan D. H. Barrett, Joanna G. Larson, Jeffrey D. Jensen, and Hopi E. Hoekstra. 2013. “Adaptive Evolution of Multiple Traits Through Multiple Mutations at a Single Gene.” *Science* 339 (6125): 1312–16.

Lloyd, Elisabeth Anne. 1988. *The Structure and Confirmation of Evolutionary Theory*. 37. Princeton, NJ: Princeton University Press.

Lynch, Michael. 2007. *The Origins of Genome Architecture*. 1 Edition. Sunderland, MA: Sinauer Associates Inc.

Machamer, Peter, Lindley Darden, and Carl F. Craver. 2000. “Thinking about Mechanisms.” *Philosophy of Science* 67 (1): 1–25.

Matthen, Mohan, and André Ariew. 2002. “Two Ways of Thinking about Fitness and Natural Selection.” *The Journal of Philosophy* 99 (2): 55–83.

Matthews, Lucas J. 2015. “Embedded Mechanisms and Phylogenetics.” Philosophy of Science 82 (5): 1116–26.

Matthews, Lucas J. 2016. “On Closing the Gap between Philosophical Concepts and Their Usage in Scientific Practice: A Lesson from the Debate about Natural Selection as Mechanism.” *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 55 (February): 21–28.

Matthews, Lucas J., and James G. Tabery. 2018. “Mechanisms and the Metaphysics of Causation.” In *Routledge Handbook of Mechanisms and Mechanical Philosophy*, edited by Stuart Glennan and Phyllis McKay Illari. Routledge.

McDonald, J. H., and M. Kreitman. 1991. “Adaptive Protein Evolution at the Adh Locus in Drosophila.” *Nature* 351 (6328): 652–54.

Merrill, Richard M., Richard W. R. Wallbank, Vanessa Bull, Patricio C. A. Salazar, James Mallet, Martin Stevens, and Chris D. Jiggins. 2012. “Disruptive Ecological Selection on a Mating Cue.” *Proceedings of the Royal Society of London B: Biological Sciences* 279 (1749): 4907–13.

Millstein, Roberta L. 2006. “Natural Selection as a Population-Level Causal Process.” *The British Journal for the Philosophy of Science* 57 (4): 627–53.

———. 2013. “Exploring the Status of Population Genetics: The Role of Ecology.” *Biological Theory* 7 (4): 346–57. doi:10.1007/s13752-012-0056-0.

———. 2016. “Genetic Drift.” Edited by Edward N. Zalta. *The Stanford Encyclopedia of Philosophy*, Fall 2016 Edition. URL = <http://plato.stanford.edu/archives/fall2016/entries/genetic-drift/>.

Millstein, Roberta L., and Robert A. Skipper. 2007. “Population Genetics.” In *The Cambridge Companion to the Philosophy of Biology*, edited by David L. Hull and Michael Ruse, 22–43. New York, NY: Cambridge University Press.

Mitchell, Sandra D. 2003. *Biological Complexity and Integrative Pluralism*. New York, NY: Cambridge University Press.

Morrison, Margaret. 2004. “Population Genetics and Population Thinking: Mathematics and the Role of the Individual.” *Philosophy of Science* 71 (5): 1189–1200.

Nielsen, Rasmus. 2005. “Molecular Signatures of Natural Selection.” *Annual Review of Genetics* 39: 197–218.

Okasha, Samir. 2015. “Population Genetics.” Edited by Edward N. Zalta. *The Stanford Encyclopedia of Philosophy*, Fall 2015 Edition. <http://plato.stanford.edu/archives/fall2015/entries/population-genetics/>.

Pardo-Diaz, Carolina, Camilo Salazar, and Chris D. Jiggins. 2015. “Towards the Identification of the Loci of Adaptive Evolution.” *Methods in Ecology and Evolution* 6 (4): 445–64.

Peichel, Catherine L., Kirsten S. Nereng, Kenneth A. Ohgi, Bonnie L. E. Cole, Pamela F. Colosimo, C. Alex Buerkle, Dolph Schluter, and David M. Kingsley. 2001. “The Genetic Architecture of Divergence between Threespine Stickleback Species.” *Nature* 414 (6866): 901–5.

Pence, Charles H., and Grant Ramsey. 2013. “A New Foundation for the Propensity Interpretation of Fitness.” *The British Journal for the Philosophy of Science* 64 (4): 851–81.

Pigliucci, Massimo. 2008. “The Proper Role of Population Genetics in Modern Evolutionary Theory.” *Biological Theory* 3 (4): 316–24.

Pool, John E., and Charles F. Aquadro. 2007. “The Genetic Basis of Adaptive Pigmentation Variation in Drosophila Melanogaster.” *Molecular Ecology* 16 (14): 2844–51.

Ramsey, Jeffry L. 2008. “Mechanisms and Their Explanatory Challenges in Organic Chemistry.” *Philosophy of Science* 75 (5): 970–82.

Ramsey, Grant. 2013. “Organisms, Traits, and Population Subdivisions: Two Arguments against the Causal Conception of Fitness?” *The British Journal for the Philosophy of Science* 64 (3): 589–608.

Rank, Nathan E., and Elizabeth P. Dahlhoff. 2002. “Allele Frequency Shifts in Response to Climate Change and Physiological Consequences of Allozyme Variation in a Montane Insect.” *Evolution* 56 (11): 2278–89.

Rank, Nathan Egan. 1992. “A Hierarchical Analysis of Genetic Differentiation in a Montane Leaf Beetle Chrysomela Aeneicollis (Coleoptera: Chrysomelidae).” *Evolution* 46 (4): 1097–1111.

Rebeiz, Mark, John E. Pool, Victoria A. Kassner, Charles F. Aquadro, and Sean B. Carroll. 2009. “Stepwise Modification of a Modular Enhancer Underlies Adaptation in a Drosophila Population.” *Science* 326 (5960): 1663–67.

Rundle, Howard D., Steven M. Vamosi, and Dolph Schluter. 2003. “Experimental Test of Predation’s Effect on Divergent Selection during Character Displacement in Sticklebacks.” *Proceedings of the National Academy of Sciences* 100 (25): 14943–48.

Ruse, Michael E. 1970. “Are There Laws in Biology?” *Australasian Journal of Philosophy* 48 (2): 234–246.

Shu, Xinhua, Zhiqiang Zeng, Philippe Gautier, Alan Lennon, Milica Gakovic, Michael E. Cheetham, E. Elizabeth Patton, and Alan F. Wright. 2011. “Knockdown of the Zebrafish Ortholog of the Retinitis Pigmentosa 2 ( *RP2* ) Gene Results in Retinal Degeneration.” *Investigative Opthalmology & Visual Science* 52 (6): 2960.

Suzuki, Y., and T. Gojobori. 1999. “A Method for Detecting Positive Selection at Single Amino Acid Sites.” *Molecular Biology and Evolution* 16 (10): 1315–28.

Tabery, James G. 2014. *Beyond Versus: The Struggle to Understand the Interaction of Nature and Nurture*. Life and Mind: Philosophical Issues in Biology and Psychology. Cambridge, MA: MIT Press.

Tajima, F. 1989. “Statistical Method for Testing the Neutral Mutation Hypothesis by DNA Polymorphism.” *Genetics* 123 (3): 585–95.

Walsh, Denis M., Tim Lewens, and André Ariew. 2002. “The Trials of Life: Natural Selection and Random Drift\*.” *Philosophy of Science* 69 (3): 429–46.

Waters, C. Kenneth. 2007. “Causes That Make a Difference.” *The Journal of Philosophy* 104 (11): 551–79.

Waters, Kenneth C. 1998. “Causal Regularities in the Biological World of Contingent Distributions.” *Biology and Philosophy* 13 (1): 5–36.

Winther, Rasmus Grønfeldt. 2006. “Parts and Theories in Compositional Biology.” *Biology & Philosophy* 21 (4): 471–99.

Woodward, James. 2003. *Making Things Happen: A Theory of Causal Explanation*. Oxford Studies in the Philosophy of Science. New York, NY: Oxford University Press.

Wright, Sewall. 1931. “Evolution in Mendelian Populations.” *Genetics* 16 (2): 97–159.

1. Less relevant to this analysis is the relation of population genetics to philosophy of race. Gannett (2015), for example, considers the projectability of group concepts from population genetics to natural kinds, such as race. [↑](#footnote-ref-1)
2. Note that the disagreement between Causalists and Statisticalists parallels a similar and related debate regarding whether or not natural selection is a mechanism. Although the two lines of disagreement are distinct, causal interpretations of selection are more compatible with the view that selection is a mechanism (Matthews 2016). [↑](#footnote-ref-2)
3. Population geneticists theorize that many different factors may be the source of population-level genetic patterns. Here I focus on efforts to distinguish patterns of selection from patterns from drift. Drift is an important and challenging concept for both biologists and philosophers of biology. See Millstein (2016) for an excellent review of drift. [↑](#footnote-ref-3)
4. See Nielsen (2005) for a thorough review of molecular evidence for selection. [↑](#footnote-ref-4)
5. Note the four distinct views regarding causation and mechanisms, some of which out to capture the notion of causal-mechanical evidence (Matthews and Tabery 2018). At face value, the manner in which experimental biologists intervene on development systems appears most compatible with the counterfactual difference-making account associated with Woodard (2003) and Waters (2007). [↑](#footnote-ref-5)