EPIGENETIC LANDSCAPES

DRAWINGS AS METAPHOR

SUSAN MERRILL SQUIER

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Mumbai in an Estuary, from their *SOAK* exhibition
and book, 2009. Courtesy of the artists.

To Gowen Roper, always

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INTRODUCTION

Figuring Development beyond the Gene

> Figuring is a way of thinking or cogitating or meditating or hanging out with ideas. I'm interested in how figures help us avoid the deadly fantasy of the literal. Of course, the literal is another trope but we're going to hold the literal still for a minute, as the trope of no trope. Figures help us avoid the fantasy of "the one true meaning." They are simultaneously visual and narrative as well as mathematical. They are very sensual.
>
> —DONNA HARAWAY, "Anthropocene, Capitalocene, Chthulhocene"

Epigenetics, "the study of changes in organisms caused by modification of gene expression rather than alteration of the genetic code itself," has been hailed in the popular press as a breakthrough field that can liberate us from the idea that we are controlled by our DNA.[1] Although the term "epigenetics" has been around in its current form since geneticist Conrad Hal Waddington introduced it in 1940, interest in this scientific field has spiked dramatically in the past several decades. Scholarly books on the topic proliferate.[2] The field appeals to so many because it seems to have a wide range of potential applications. To researchers interested in social, racial, and gender justice, the epigenetic dimension seems to hold exciting promise to free us from the idea that we are what our genes make us and enable us instead to identify those factors beyond genetics that shape us to become who we are. Could maternal diet, parenting style, or environment explain "the developmental origins of health and disease" (Loi et al. 2013, 142)? Did our grandmothers face starvation during pregnancy, leaving us a legacy of weight problems or undernourishment? Did a toxic physical or social environment limit our lung capacity or stress us so that we became vulnerable to depression? Epigenetics seems to reach from the body to society, holding out hope to illuminate issues as diverse as the development of gender identity; the intergenerational impact of slavery, war, or starvation; the range of factors that make us more vulnerable to depression or psychosis; or even the many variables that shape the health or illness of an ecosystem and the human beings dwelling within it (Fausto-Sterling 2012; Jablonka et al. 2014; Landecker 2011; Loi et al. 2013; Sullivan 2013).

These hyperbolic hopes may obscure the reality: there is significant uncertainty about the field of epigenetics. As this book was going to press, a widely cited study in *PloS Genetics* argued that epigenome-wide associations studies (EWAS) that claimed to document environmental contributions to heritable changes in disease risk were impossible to evaluate because of flaws in both their design and their execution. It was impossible, the researchers argued, to confirm "that epigenetics is responsible for the effects" the studies purport to show, and they concluded that "no EWAS to date can be said to be fully interpretable" (Birney et al. 2016). John M. Greally, an epigenetics researcher at Albert Einstein College of Medicine in New York City and one of the study's co-authors, explained to a *New York Times* reporter that a serious reexamination of the field was needed—*after* the team applied the classic remedy for research disappointment: "We need to get drunk, go home, have a bit of a cry, and then do something about it tomorrow" (quoted in Zimmer 2016).

In this study, I move away from the contemporary debates about epigenetics to focus on a figure that may help us understand the field afresh, a figure central to the development of this scientific field: the "epigenetic landscape." This book follows the cultural trail of the epigenetic landscape, a visual image developed by Waddington as the central figure for the scientific field of epigenetics, "the causal analysis of development" (Waddington 1940). As a scientific model, the epigenetic landscape fell out of use in the late 1960s, returning only with the advent of big-data genomic research in the twenty-first century; however, the figure of the epigenetic landscape is now being used across the life sciences because it enables scientists to think about, visualize, and communicate across disciplines and model development creatively.

Moving from the first version of the image—a landscape drawing created by the modern artist John Piper—to its later, more schematic versions, this book explores what the artistic and design elements of the image contributed to the meanings it held during the lifetime of its creator. Exploring the vital role the epigenetic landscape plays in fields beyond the life sciences, this study reveals that it has been used to model the intersecting complex systems that link scientific and cultural practices or, more precisely, reveal them as never having been separate or distinct. By examining three cases of such use—in graphic medicine, landscape architecture, and bioArt—this study reclaims the broader significance of this figure formed at the nexus of art, design, and science. It challenges the reductive understanding of epigenetics and argues instead for a more complex and varied view of biological development at all scales.

Waddington chose this visual image—in its first version, a charcoal drawing of a riverine landscape by Piper, and in its second and third iterations, schematic images of a ball on a contoured hillside—as a conceptual and methodological resource for those engaged in the "causal analysis of development" (Waddington 1940, 1). If we trace the significant aspects of this visual image through several different cultural realms, we can discover the broader conceptual and practical territories that are available to us when we explore development beyond the gene. I take a feminist science studies approach to my subject, inspired by Donna Haraway's "ongoing process of refiguring what counts as nature" and her commitment to escaping the "deadly fantasy of the literal," the "fantasy of 'the one true meaning'" (Haraway in Davis and Turpin 2015, 257). I hope to serve the same ends, by exploring the multiple meanings that epigenetics can hold for us as a field that is simultaneously visual and narrative, mathematical and sensual. By engaging with the figure at its center, I want to offer a new perspective on the scientific field of epigenetics and demonstrate that its complex, multidisciplinary origins have significant implications for the ways we understand and work with development more broadly.

The concept of epigenetics was formulated by the British geneticist Conrad Hal Waddington (1905–75), the son of the Quaker first cousins Hal Waddington and Mary Ellen Warner. His story is a striking mix of orthodox patriarchal British upbringing and maverick intellectual and social daring, and it will be helpful to have this in mind as we navigate the terrain of the epigenetic landscape.[3] Waddington saw his parents infrequently during his childhood; from his fourth year, they lived in southern India as tea planters while he was raised by an aunt and uncle back in England. As a child and young man, Waddington had very wide-ranging interests; inspired by relatives and friends with scientific and botanical interests, his passions ranged from naturalism and fossil collecting to visual art, poetry, and philosophy. At Cambridge University he studied paleontology and philosophy, writing his thesis on the mechanist-vitalist controversy. At and after Cambridge, Waddington demonstrated an interdisciplinary, synthetic approach to knowledge nourished by the intellectual catholicity of a good friend, the anthropologist, semiotician, and cyberneticist Gregory Bateson, as well as the artistic and design interests of the women he married. His first marriage took place during his Cambridge years, to a woman named Lascelles; when that marriage ended in 1936, he wed the architect Justin Blanco White. A close friend remembers evening discussions at the Waddington home in Cambridge that "used to cover not only science, but philosophy, modern art, music and the Dance." Waddington was an avid Morris dancer and an expert "exponent of its techniques" (Robertson 1977, 577). These marriages produced three children: Jake (later a physics professor), Caroline (a social anthropologist), and Dusa (a mathematician specializing in symplectic geometry and topology).

In his post-Cambridge years Waddington moved from paleontology to embryology and the investigation of biological development, working at the Strangeways Research Laboratory under Honor Fell.[4] Later, he served in the Operations Research Section of the Royal Air Force, supervising photoreconnaissance during World War II, before turning his attention in the postwar period to problems of population biology and animal genetics. He moved to Edinburgh in 1946 to head up the genetics section of the Institute of Animal Genetics. Waddington's fiftieth birthday was celebrated in 1955 with songs and poems, including one composed by the communist epidemiologist and geneticist Barnet Woolf, who also contributed music to works in the precursor of the Edinburgh fringe festival.[5] In his "Magic Words," a chorus of men explained epigenetics to the assembled celebrants (though they were probably already in the know):

If you want the correct explanation
Why embryos grow into men
The Alsatian begets an Alsatian
A hen's egg gives rise to a hen
Why insects result from pupation
Why poppies grow out of a seed
Then just murmur 'canalization'
For that is the word that you need.

Chorus Then three cheers for canalization
Oh, come on now, hip hip hooray
A stiff dose of canalization
Will drive all your troubles away.
(Robertson 1977, 582–83)

The birthday gathering even featured "an epigenetic landscape constructed as a pinball machine, with the ball mostly travelling down the main valley to produce normal phenotypes but on occasions being diverted into a secondary valley and producing a mutant" (Robertson 1977, 583; see also Goldberg et al. 2007). Waddington's birthday party offers a whimsical glimpse of the variety of subjects before us in this study: canalization and hen's eggs, entomology, botany, and embryology. We will come to all of these aspects of epigenetics, as well as to poetry, song, and the chance-laden factors that direct development into one or another valley, whether microscopic or macroscopic, metaphoric or material.

Ironically, what should have been the culmination of Waddington's career, the creation of an Epigenetics Laboratory and an Epigenetics Research Group at Edinburgh of which Waddington would be "honorary director," was disappointingly derailed by the discovery of techniques for hybridizing DNA and RNA. This decisively redirected scientific inquiry from the study of development to the growing field of molecular biology. Waddington ended his career as an Albert Einstein Chair in Science during a two-year stint as visiting scholar at the State University of New York, Buffalo, where he taught a course titled "The Man-Made Future" (Robertson 1977, 584). His daughter Dusa testified to that broad vision of his later years, remembering her father in her Satter Prize acceptance speech as "a Professor of Genetics who travelled all over the world and wrote books on philosophy and art as well as developmental biology and the uses of technology."[6]

"Epigenetics" is a portmanteau word; Humpty Dumpty introduces this concept to Alice in *Through the Looking Glass* when she seeks his help with some words she cannot understand: "You see it's like a portmanteau—there are two meanings packed up into one word."[7] Perhaps Waddington paid homage to Lewis Carroll when he coined the term in the 1930s, for Carroll was among his good friend Gregory Bateson's favorite references.[8] The two meanings packed into this neologism fused the old Aristotelian expression for emergence, "epigenesis," with the rising field of genetics.[9] Waddington formulated this new field in his *Organisers and Genes* (1940). It would offer an analytic approach to development rather than the taxonomical and descriptive approach of embryologists up to that time. It was also in this work that Waddington presented the first version of his epigenetic landscape, a visual metaphor for the role played by stable pathways (later to be called "chreods") in the process of development. He elaborated on this theory in his later *The Strategy of the Genes* (1957).

The epigenetic landscape had only a brief heyday in its first run as a valuable scientific model. By 1961, when François Jacob and Jacques Monod discovered the *lac operon* (the combination of different genes involved in the metabolism of lactose), it was fading from use, seeming far too analogue and ambiguous to model processes that were increasingly capable of precise description (Baedke 2013; Gilbert 1991; Grene and Depew 2004).[10] Yet this changed when, in 2003, scientists and government officials at the National Human Genome Research Institute of the National Institutes of Health announced the completion of the Human Genome Project, asserting, "In addition to introducing large-scale approaches to biology, [it] has produced all sorts of new tools and technologies."[11] The challenges posed by "whole-genome" technologies, from biobanks and human genome databases to high-throughput screening techniques, catalyzed a return to the epigenetic landscape because it had the capacity to model the probabilities of change on a large scale.

Yet as the epigenetic landscape has come back into widespread use, it has done so with a difference. Now its scientific importance lies not in its representation of Waddington's "conceptual legacy," which was frequently overlooked in the rush to a molecular scale, but rather as a set of heuristic and methodological prompts (Baedke 2013, 756). The philosopher of science Jan Baedke has argued that during Waddington's research practice, the epigenetic landscape functioned heuristically in four ways: as visualization tools, as strategies for communicating across disciplines, as creative stimulation, and as methodological and modeling guides. In the post-Waddington era, Baedke argues, beyond the epigenetic landscape's primary utility for visualization, these same basic functions have continued in a wide range of fields across the life sciences, reaching even into the human and social sciences.[12] The epigenetic landscape functions in each case as a "tool" to "support transdisciplinary research; . . . stimulate visual thought [; and] guide modeling efforts and theory formation" (756).

In this book, I argue that the role of the epigenetic landscape extends beyond the life sciences. The inherent ambiguity of the epigenetic landscape as a metaphor gives it the potential to be a more productive model for the intersecting complex systems that are now understood to link scientific and cultural practices—or, more precisely, to reveal them as never having been separate or distinct. Historians, philosophers, and rhetoricians of science have demonstrated that metaphor plays an important epistemological and rhetorical role in scientific thought, for good and ill, by transferring meaning from one context to another; preserving aspects of previous thought styles in new areas; consolidating or disrupting gender relations; catalyzing experiments; and generating new frames for thinking, reading, and writing, as well as foreclosing others. Models, too, exist in the liminal zone between scientific theory building and scientific practice, where they can induce thought, touch, and movement to draw the model user into a conceptual space and engage her with its questions (Keller 2000; Myers 2015). Indeed, Evelyn Fox Keller (2000, S77) argues that "metaphors, like models (indeed a crucial component of many models), can themselves function as tools for material innovation."[13] I track some of these innovations in the body of this book.

* * *

My aim in what follows is to recover the expansive reach that epigenetics had as Waddington worked with the term over the course of his life. With his conceptual legacy obscured, the meaning of the term "epigenetics" since his death has been increasingly focused—indeed, it has been narrowed. Now the term refers primarily to the specific mechanisms by which epigenetics works on a molecular level, particularly DNA methylation and chromatin modification (Feinberg 2008, 1345; Jablonka et al. 2014, 393). When the term "epigenetics" appears in research exploring development in fields as widespread as oncology, environmental toxicology, prenatal medicine, nutrition, and psychiatry, its meaning usually tilts away from the macro meaning it once had and toward the micro realm. Contemporary epigenetics research frequently affirms a linear, gene-centered, and "programmed" approach to development, a kind of "somatic determinism," according to the historian of science Sarah S. Richardson (2015, 217, citing Locke 2013, 1896).[14]

This contemporary narrowing of epigenetics has already inspired critiques of the field from a feminist perspective. Let me give some examples. Findings about the role of epigenetics in sex and gender differences are often interpreted to endorse existing conceptions of sex and gender as binary, programmable, and stably retained over time (Richardson 2015). Epigenetic research is being directed—one could even say contained—to the kinds of studies that can add new tools or explanations to our existing framework for understanding development (Richardson, forthcoming). Similarly, some scientists working in evolutionary-developmental ecological biology (evo-devo-eco) or eco-devo-evo (the order of the abbreviations packs a partisan punch) are turning to epigenetics because they hope its study will enable them to identify how an organism integrates its genetic, environmental, and developmental processes, information they then plan to integrate into existing evolutionary theory (Abouheif et al. 2014). Even when researchers do seem willing to confirm the paradigm-shattering implications of epigenetics, acknowledging the complex and nonlinear view of development their research has revealed, they may actually be engaged in a rhetorical holding action, trying to reorient the program of epigenetics research toward their specialty to cope with increasingly scarce resources and rising demands for concrete results (Panovsky 2015, citing Arribas-Ayllon et al. 2010).

There has been a tension in the understanding of epigenetics: should it be framed narrowly or broadly? In terms of gene action or of developmental plasticity? Although the dominant strategy of the field has been to use epigenetic findings to support the mainstream gene-centered view, the feminist and postgenomic critique cited above reflects the view of other researchers that epigenetics could support a new understanding of biological organization that stresses plasticity rather than genetic determinism (Love 2010; Shapiro 2015; Sullivan 2013; Van Speybroeck 2002, 61, 79).

This tension flared into a firestorm in the response to an article published in the *New Yorker* magazine in May 2016 by the cancer researcher Siddhartha Mukherjee. In a Lewis Carroll–like bit of wordplay, Mukherjee's essay, "Same but Different," used his twin aunts to illustrate the impact of environmental factors in development, drawing parallels to the social behavior of the jumping ants studied in the New York University School of Medicine laboratory of the epigeneticist Danny Reinberg (Mukherjee 2016b). When Mukherjee's article appeared in print, the forces of disciplinary normalization came out in force, with more than one hundred scientists issuing accusations that he overemphasized epigenetic mechanisms and neglected the role of genetics (Mukherjee 2016b). As Chris Woolston reported in *Nature*, Mukherjee acknowledged his mistake: "He put too much emphasis on the 'speculative roles' of histone modification and DNA methylation. 'This was an error,' he says, adding that a mention of transcription factors could have helped to avoid 'an unnecessarily polarizing reading of the piece,' " (Woolston 2016, 295).

Woolston also described the attempt by John Greally to put the episode in context: "Greally adds that it's hard for anyone to talk about epigenetics without stirring up controversy. Different researchers have different definitions for the term, and there are still many questions about the mechanisms behind the regulation of gene expression. 'We're in a bit of a mess in epigenetics,' Greally says. Mukherjee is 'a thoughtful guy,' he adds. 'But he's beginning to realize that he stepped on a land mine.' " A land mine, indeed. The very next month, in June 2016, Greally and his fellow researchers published their article in *PLoS Genetics* sounding the alarm about EWAS and calling for a major reassessment of epigenetic research. Earlier in this chapter I quoted the interview in which he jokingly suggested he had been driven to drink by the methodological problems he found in those studies. Yet the *New Yorker* may have helped Greally pack the explosives into that land mine by choosing as the subtitle to Mukherjee's article "How Epigenetics Can Blur the Line between Nature and Nurture."[15]

The phrase seems to allude to an incisive and influential entry into the discussion of epigenetics, Keller's slim volume *The Mirage of a Space between Nature and Nurture* (2010).[16] There, Keller charges that the ambiguity, confusion, and general muddle in our understanding of nature and nurture can be attributed to shortcomings in the language of genetics. The problem is not only the discourse of "gene action," which Keller has so powerfully critiqued, but the "chronic slippage between the two meanings—ordinary and technical—of *heritability*" (or, to think of it in Mukherjee's framing of the problem, between his aunts and the jumping ants). "Heritability" is an ambiguous word, Keller points out, because the means of transmission of traits between the generations can be "genetic, epigenetic, cultural, or even linguistic." Writing of geneticists and molecular biologists, she observes, "When the words they use have multiple meanings, meaning is not so easy to control. . . . Consciously or not, slippage happens; it is not only easy to mean two—or even three—things at once, it may be unavoidable. What is difficult is meaning only one thing" (Keller 2010, 71). For Keller, it is not precisely the ambiguity that causes the problem but our failure to recognize it. "The problem is that, as the different meanings of the term travel back and forth between different kinds of arguments, different logics, and different disciplines," she writes, "the ensemble becomes knitted together into a seemingly coherent whole, giving rise to a seemingly coherent argument" (75–76). "Seemingly," here, is the keyword.

While linguistic ambiguity can be confounding or productive, depending on whether we are attentive to its presence or sink into the delusion that the word or phrase in question means "only one thing," the visual ambiguity of figures can be epistemologically enabling, complicating our thinking, encouraging us to cogitate, meditate, or just "[hang] out with ideas" and helping us to "avoid the fantasy of 'The One True Meaning'" (Haraway in Davis and Turpin 2015, 257; Keller 2010, 76). "Images function effectively at drawing viewers in, confounding them, and prodding them to ask questions" (Allen 2015, 141). Models provoke engagement, temping people to touch them, explore their surfaces, and even move with them (Myers 2015). Sensual, visual, narrative, and even mathematical, Haraway reminds us, figures can help us figure things out. Taking advantage of their epistemologically productive ambiguity, this study focuses on the three major visual images of the epigenetic landscape that Waddington used in his scientific publications between 1940 and 1957: "the river," "the ball on the hill," and "the view from underneath with guy wires."[17] In what follows, I explore the dramatic differences among the three versions in origin, subject matter, mode of composition, semiotics, and, most of all, the epistemology and ontology they imply.

The original epigenetic landscape was a work of landscape art, commissioned by Waddington from his friend John Piper. We will look much more closely at it in a later chapter, but for now I will just describe it briefly: in shades of gray, white, and black, it shows a turbulent river flowing through brush-bordered banks. As its caption as the frontispiece in *Organisers and Genes* reveals, this version of the epigenetic landscape also has an element of fantasy: "Looking down the main valley towards the sea. As the river flows away into the mountains it passes a hanging valley, and then two branch valleys, on its left bank. In the distance the sides of the valleys are steeper and more canyon-like." Despite the gravitational paradox—how can a river flow away into the mountains?—Waddington judges it "an amusing landscape to picture to oneself; and I think it expresses, formally at least, some characteristics of development which are not easy to grasp in any other way" (Waddington 1940, 93).[18]

While the ball on the hill and the view from underneath with guy wires are quite different visually and compositionally from the first version, the second and third versions of the epigenetic landscape also express its three central principles: canalization, homeorhesis, and scaling. We will encounter these processes later in much more detail, but for now here is a brief definition of each. Canalization, or developmental robustness, is the ability to sustain a developmental direction despite environmental disruptions. Waddington termed these dedicated developmental pathways "chreodes" (another coinage). Homeorhesis, which is related to the physiological concept of homeostasis, or the maintenance of equilibrium, in contrast, is the ability of a dynamic system to sustain its rate of change or flow. Temporal and spatial scaling are the perceptual/conceptual properties that make this developmental model of the "biological picture" inclusive of life from conception to death and meaningful at the scale of a cell, an embryo, or a population.[19]

Figures are sensual, Haraway tells us. As a model that is also a metaphor, the epigenetic landscape engages our senses, as an example from Waddington's late-life writings can reveal. In his final, posthumously published book, *Tools for Thought: How to Understand and Apply the Latest Scientific Techniques of Problem Solving* (1977), Waddington included a set of instructions for "Exploring a Landscape." Inspired by a paper by the Russian mathematicians Israel Gel'fand and Michael Tsetlin (translated from the Russian by his daughter, the mathematician Dusa McDuff), Waddington imagined using kinesthetic strategies to investigate the unknown in the epigenetic landscape. "An important question about the epigenetic landscape and branching pathways is this: When we are confronted with an unknown system, how do we find out what the shape of the landscape is?" he writes. "One suggestion, due to . . . Gel'fand and Tsetlin, is to proceed as follows. We find ourselves doing something to a system which we believe has certain stability characteristics, which could be described as an epigenetic landscape; but we have no idea where we are on the landscape when we first start trying to affect the system" (Waddington 1977, 113).

The entire passage repays careful reading for its vigorous kinetic language. Waddington imagines himself "going out into the landscape," moving uphill and downhill, following the slope into the valley, and then taking "quite a large jump" across the landscape "onto the opposite hillside lower down the valley," where "a local exploration around that spot may show us the slope going in the opposite direction." The exploration works by trial and error. As he explains, "One can't, of course, give any general rules for doing this. It has got to be largely a method of 'suck it and see.' A point of general principle is that in exploring such a landscape it would take too long to walk all over it step by step. . . . It is better to alternate between (a) local exploration . . . and (b) a jump in the dark to try to change some quite different aspect of the system" (Waddington 1977, 113–14).

This combination of local exploration and the jump in the dark with which Waddington proposes to explore the epigenetic landscape is familiar to me from years of my own research. In an earlier book, I thought of it in terms of escaping the academic culture of expertise, giving myself the holiday of curiosity, or "poach[ing] on academic territory in which I can claim at best amateur competence."[20] Now I think of it as the strategy of refusing critique to follow concern instead (Latour 2004).

Waddington's instructions for "Exploring a Landscape" also bring to mind the philosopher Michel Serres's *tiers-instruit*: a third mode of learning that operates not through critique and subordination to one reigning epistemological category, but as a wandering, translational commentary that ranges across disciplines and disciplinary languages. Rather than dividing and subordinating fields, Serres multiplies them and disturbs their boundaries, preferring disorder and fertility to sterile order. In my thinking about the epigenetic landscape, I am also inspired by Serres's method of inquiry, which, as Bruno Latour has explained in a useful pair of images, differs from the standard Western epistemological model (Latour 1987, Serres and Latour 1995). Because one of the main points of this book is the importance of attending to the productive expressiveness of figures, I include them here (figure I.1).

The first image, a circle marked by arrows extending both outward toward the periphery and inward through the "intermediary" to the center, represents "a powerful critique . . . that ties, like a bicycle wheel, every point of a periphery to one term of the centre through the intermediary of a proxy" (Latour 1987, 90). Latour describes this as the mode of the "Critique philosophers," who "firmly install their metalanguage in the center, and slowly *substitute* their arguments to every single object of the periphery" (90). The second image represents Serres's "pre-critical philosophy," a series of parallel lines stacked one above the other, with the tiered labels "Language 1, 1.2, 1.3, and 1.4" and wavering and straight vertical lines linking the tiers. "Crossover from one repertoire to another," the caption reads. Latour defines Serres's method not as critique but as commentary, a "cross-over, in the genetic sense, whereby characters of one language are crossed with attributes of another origin" (90–91).

Beneath the linguistic layering, there is something topographic in this image, an anticipation of the contour grooves we will encounter in the second image of the epigenetic landscape. The negotiation of the tiers in Latour's second image (a process both linguistic and spatial) resembles the challenge posed by another medium to embody the perspective of

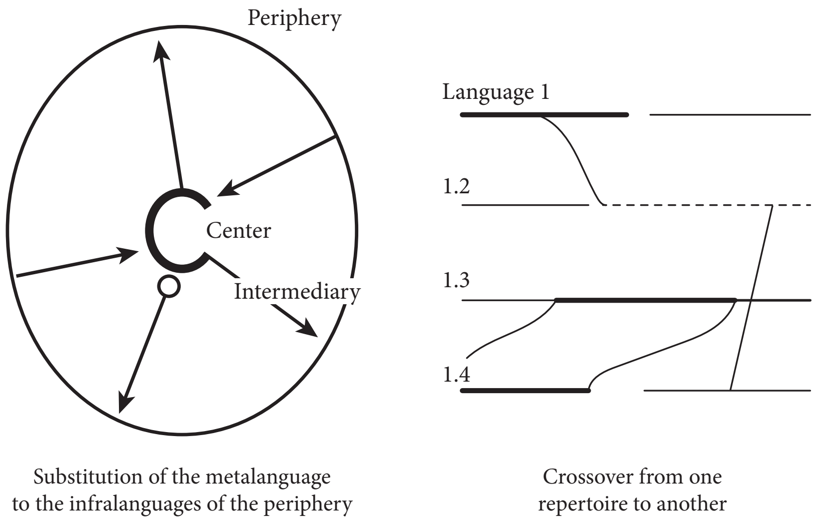

FIGURE I.1 Michel Serres's method of inquiry, as imaged by Bruno Latour (1987, 90).

the epigenetic landscape. As we will see in a later chapter, the medium of comics requires the reader/viewer to follow a verbal and visual narrative across panels, down tiers, and through gutters while continuously supplying the closure the narrative requires. While Latour's celebration of Serres emphasizes his understanding of the relations among language, biology, information theory, and thermodynamics—a view that arguably is heavily indebted to Waddington—it also illuminates the methodological choices I faced while writing this book. I could have situated my discussion of epigenetics within the broad frames of developmental systems biology, regenerative medicine, postgenomics, or bioethics, choosing one of them as the centering strategy within which to consider the epigenetic landscape as a metaphor and model. Instead, in accord with what Rick Dolphijn and Iris van der Tuin have dubbed "the transversality of new materialism . . . a nomadic traversing of the territories of science *and* the humanities, that perform[s] the agential or *non-innocent* nature of all matter," I investigate the relations between objects and subjects, states and forces customarily held in opposition (Dolphijn and van der Tuin 2012, 100–101; see also Braidotti 2006). Or, to put it more simply, I have followed my developing thoughts where they led me, even (especially) if they drew me laterally rather than linearly. After all, despite disciplinarily formed practices of denial, scientists, writers, and artists have long been thinking, learning, teaching, and inquiring collaboratively. As feminist science studies has shown, biology has been shaped all along by both aesthetic and social concerns, just as the humanities and arts have engaged with the vital process of development (Haraway 1976; Haraway in Davis and Turpin, 2015).[21] I have chosen to combine local exploration with many a jump in the dark as I investigate how the epigenetic landscape can illuminate our understanding of disciplines marginal to the life sciences and even challenge our habitus toward disciplinarity.

So much is at stake in working with the epigenetic landscape that my investigation is unavoidably incomplete.[22] While exploring the creative potential of the epigenetic landscape as an instructive third space, I have tried to stay close to the method Waddington established so I can recapture the broader implications contained not only in the epigenetic landscape, but also in the concept of epigenetics. Waddington hoped for a crossing over between embryology (which studied the impact of surgical or chemical interventions in a living embryo) and genetics (which studied the role of hereditary factors, later known as genes, in producing embryonic changes). I hope through my own post-disciplinary practice of crossing over to show how the scientific study of development can illuminate ways to work with developing life beyond those initial focuses.

Although I have restricted my attention to areas suggested by the specific images provided by the epigenetic landscape itself—the ball on the hill, the river, and the view from underneath with guy wires—I explore what each image affords as a means of orientation as I carry out a local exploration of the specific environment to which it has drawn me. As a result, while this project has been a bit of a jump in the dark, it has taken me deeply and pleasurably into very different fields of endeavor. In each field I have chosen one version of the visual image of the epigenetic landscape, the one that originally brought the field to my mind, as my prompt or tool as I explore the strategies each field uses, though at very different scales, to work with the balance of freedom and constraint, change and stability, inherent in biological development.

The ability to think about development from a number of different perspectives, visual as well as verbal, fuzzy as well as precise, is increasingly understood to be a catalyst to creativity (Meloni and Testa 2014). Such a process of exploring the unknown is even more pertinent to the power of the epigenetic landscape. This visual image was not only attractive, alluring, contradictory, and even seductive but also deeply playful, as Waddington's set of instructions for exploring it reveal. While we have learned in science studies to appreciate the epistemological values of the imprecise, the allure of the unknown "epistemic thing" that tempts us out of our comfort zone, and the challenge of forging an "epistemology of the concrete," we are only beginning to push these strategies to their limit by watching them as they play, as well as play out, beyond the realm of science (Rheinberger 2010).

Therefore, I approach these versions of the epigenetic landscape as models not merely in the sense of being predictable or testable scientific objects, but also—in Waddington's tradition—as productive engagements with the unknown. I understand them to function kinetically, affectively, and methodologically, as well as epistemologically. Just as the embryologist Wilhelm His found in the act of creating the wooden model of an embryo the capacity to integrate perceptions previously held at a distance, and just as protein crystallographers dance into the proteins whose folding they are attempting to model, so, too, the enactments of the epigenetic landscape we will look at in the chapters that follow provide opportunities to make development physiologically concrete, affectively present, and methodologically meaningful (Hopwood 1999; Myers 2015).[23]

The first two chapters of this study follow the epigenetic landscape from its origins as a nexus of Waddington's scientific and artistic interests, through the different functions it held for him in the 1960s, and finally to its methodological expansion in the work he did in his final years. I draw on the concept of canalization as I explore how the gendered and disciplining effects of different intellectual and social contexts shaped the use and reception of the epigenetic landscape. While interest in the epigenetic landscape waned during the Serbelloni Symposia, which Waddington convened to frame the discipline of theoretical biology, it returned and expanded while he was writing *Behind Appearance: A Study of the Relations between Painting and the Natural Sciences in This Century* (1970 [1969]) and still more in his late-life projects *Tools for Thought* and, with Erich Jantsch, *Evolution and Consciousness: Human Systems in Transition* (1976).

Each of the following chapters moves beyond Waddington to take one instantiation of the epigenetic landscape—the ball on the hill, the river, and the view from underneath with guy wires—as its methodological model. Working from the central image to the specific field of practice it has suggested to me, I explore what this version of the epigenetic landscape brings to that local system of thought and practice as it deals with development. Chapters 3 and 4 focus on the most familiar image of the epigenetic landscape, the ball or fertilized egg or embryo poised near the top of a contour-riven slope. Because this image suggests the field of embryology, and particularly the history of making embryos visible, I consider the temporally and spatially scaled nature—the *Russian dollness*, if you will—of developmental processes in chapter 3. I explore how the shift from descriptive and taxonomic embryology to analytic embryology not only reflected but was enabled by what Janina Wellmann (2017, 31) calls a new "epistemology of rhythm." Expressed across the entire cultural field through a mode of serial graphic display, this strategy of combining movement and stillness, image and gap, not only nurtured a newly process oriented perspective but also prepared the way for the stop-motion photography and animation that would later bring embryology to widespread public attention.

In chapter 4, I continue this analysis, turning to the nexus of contemporary popular culture and medical communication, where the comics medium provides a powerful space in which to image and enact the process of development at multiple scales. In their temporal and spatial complexity, comics recover the properties of the early twentieth-century embryo cartoons and animations that made it possible for embryologists not only to analyze development but also to share their findings widely. I describe how graphic medicine—comics about illness, medical treatment, disability, and caregiving—are providing a remedy for the narrow instrumentalism of the institution of medicine. Looking closely at what I call the graphic embryo, a comics genre grounded in the tradition of embryo imaging, I argue that as it remediates the medical image of the embryo, it provides an aesthetic and social space to reimagine development. By "unflattening" it into multidimensional time and space, the graphic embryo offers the possibility of nonlinear outcomes, diverse developmental trajectories, and a more complex model of development that includes not only embryos, but also infants, children, mothers, fathers and even a "sentient organism in [a] nearby solar system" (Sousanis 2015; Nilsen 2014).

Chapters 5 and 6 return to the first version of the epigenetic landscape, Piper's drawing of the river, and the particular epigenetic principles it expresses. Beginning with Waddington's late-life application of the epigenetic landscape model to ecology, chapter 5 traces the entangled commitments to ecological mapping and scientific control in the work of Waddington's fellow Scot Ian McHarg, founder of the field of landscape architecture. A look at several other prominent landscape architects working in McHarg's tradition reveals that the epigenetic principle of homeorhesis, the maintenance of a steady rate of flow or change, has been both harnessed and transgressed by landscape theorists as they deal with development on a macro scale. Chapter 6 continues this examination, moving from McHarg's mode of landscape architecture theory and practice; the contribution of feminist landscape architectural theory; and a more expansive understanding of development to, finally, the exciting contemporary work of Anuradha Mathur and Dilip da Cunha, who reorient the landscape architectural treatment of development from reductionist linearity to situated, kinetic complexity, with ecological and global sociopolitical significance.

Chapter 7 turns to the final version of the epigenetic landscape I explore in depth: the view from underneath. Originally designed to reveal the genes and guy wires whose interactions produce gene expression and thus shape the contours of the epigenetic landscape, this image served Waddington in his later life as a model of social and conceptual development and more recently has been adapted to represent complex sociological processes (Tavory et al. 2012, 2013). In the chapter, I profile Art Laboratory Berlin, an epigenetic landscape in its full transdisciplinary sense. I argue that in this space that entangles art and science, practitioners and members of the public model a highly speculative, kinetic, and affective multidisciplinary approach to producing knowledge about development.

The conclusion provides a brief sketch of how one contemporary feminist scientist is using cartoon animation to adapt the three images of the epigenetic landscape—the ball on the hill, the river, and the view from underneath with guy wires—to illuminate the development of gender identity and sex differences in behavior. Returning to how one life scientist is currently using the epigenetic landscape as an epistemological and