ARTISTS' ARTICLE

Drawing to Extend Waddington's Epigenetic Landscape

GEMMA ANDERSON, BERTA VERD AND JOHANNES JAEGER

ABSTRACT

The authors, an artist, a mathematician and a biologist, describe their collaboration examining the potential of drawing to further the understanding of biological processes. As a case study, this article considers C.H. Waddington's powerful visual representation of the "epigenetic landscape," whose purpose is to unify research in genetics, embryology and evolutionary biology. The authors explore the strengths and limitations of Waddington's landscape and attempt to transcend the latter through a collaborative series of exploratory images. Through careful description of this drawing process, the authors touch on its epistemological consequences for all participants.

> *When artists have tried to learn direct lessons from science, copying the visual phenomena turned up by scientific research or technically based industry, not much of value or profundity has been produced. The notions which have been more fructifying are those which have been absorbed by empathy, through the pores, as it were. And they have been expressed again by the artists not so much in any explicit exposition or diagramming of scientific ideas, but rather by living a life of implicit incorporation into a work of art—an artefact—from which the spectator again absorbs them by in-feeling more than by analysis. It is at the deep levels of the human psyche, where these kinds of communications operate, that there is the closest unity between science and art* [1].

This paper presents a transdisciplinary collaboration between a visual artist (Anderson), a mathematician (Verd) and a biologist (Jaeger). It aims to realize and highlight the potential of drawing to further the understanding of biological processes: We use drawing as an epistemic tool to generate new images to think with [2].

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In the very first volume of *Leonardo*, published in 1968, Waddington stated that

> science is something more than a collection of conceptual or practical results. It is also an activity; and its practice involves, as a very important part, the exercise of the faculties of insightful perception of natural phenomena and of the imaginative creation of new concepts [3].

In fact, both scientists and artists must be able to explore concepts before they are fully and explicitly formulated, prelinguistically. The release from scientific constraints in artistic practice makes collaborative image-making a mind-opening experience that can mutually benefit scientist and artist.

Here we build on previous epistemological inquiries by Anderson [4] to develop and demonstrate the use of drawing in representing biological process, informed by Anderson's experience of morphological and topological drawing, Verd's training in dynamic systems theory and evolutionary developmental biology and Jaeger's process-based approach to living systems. We integrate methods by artists such as Paul Klee, who have pioneered techniques for the representation of dynamics [5]. Alongside this practical development of drawing, we aim to stimulate discussion toward revitalizing the practice of hand-drawing in contemporary scientific practice.

Our complementary perspectives brought us to reconsider and extend one of the most powerful visual representations of biological process: Conrad Hal Waddington's "epigenetic landscape" [6] (Fig. 1). Beyond visualizing the paths of organisms' embryonic development, the iconic image shown at top right was meant to reunify embryology with genetics and evolution by showing how complex genetic changes affect the topography of the landscape. Here we recount creating an extended version of this representation [7] through a series of six collaborative images that identify and address challenges for visualizing the complex, multidimensional dynamics of evolving biological systems.

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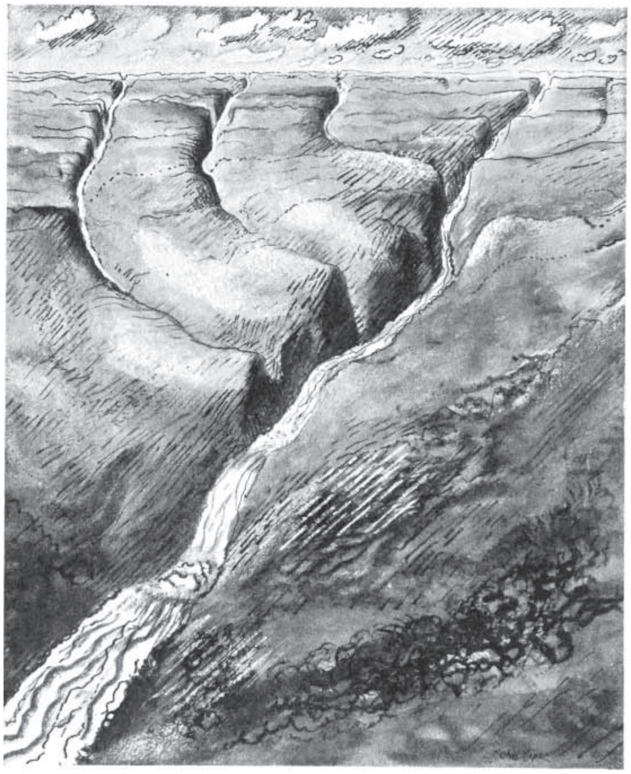

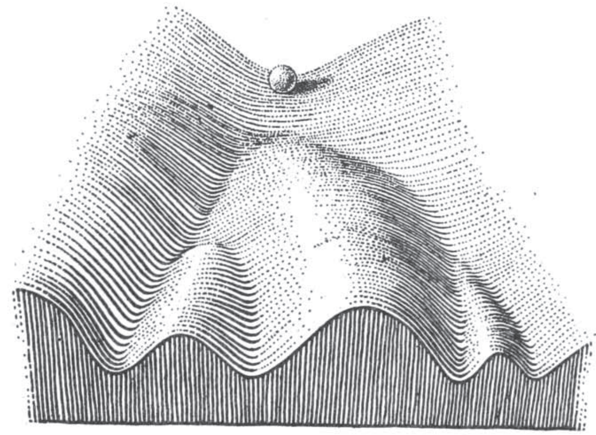

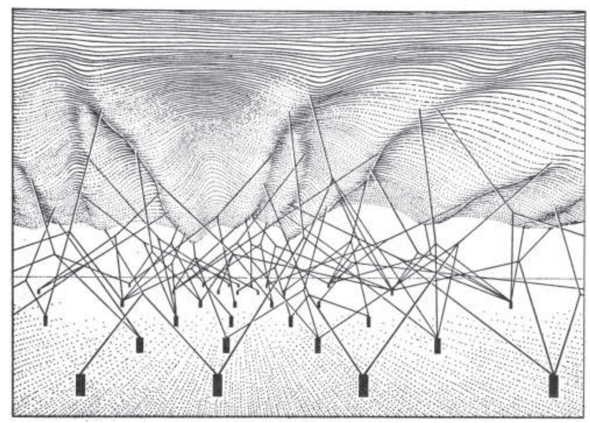

Fig. 1. C.H. Waddington's epigenetic landscape. (above left) John Piper, drawing for Waddington's *Organisers and Genes* [26], captioned: "Looking down the valley towards the sea. As the river flows away into the mountains it passes a hanging valley, and then two branch valleys, on its left bank. In the distances the sides of the valleys are steeper and more canyon-like." (© Cambridge University Press, 1940); (right) Waddington's classical depictions of his landscape from *The Strategy of the Genes* [27]. (top right) Top view of the landscape; the path followed by the ball represents a developmental trajectory (or chreode). The valleys represent alternative paths depicting different developmental potentials—e.g. differentiation into various cell types. (bottom right) Depicting the underside of the surface, Waddington illustrated the idea that genes can change the landscape during evolution. The pegs underneath represent genes acting on the landscape by tugging on the intertwined web of guy ropes, thereby changing the topography of the valleys and ridges above. (© Taylor & Francis, courtesy tandfonline.com)

WADDINGTON'S LANDSCAPE: INFLUENCE AND LIMITATIONS

Waddington's visualization works as follows: There is a ball on an abstract surface. This ball represents the current state of a developing biological system. The ball rolls downhill along valleys—called *chreodes*—that determine the system's possible trajectories. There are branching points in these valleys, one for each developmental decision—for example, whether to become a neuron or a skin cell. Each valley is bounded by steep slopes, keeping the ball on track despite perturbations diverting it from its default path. This represents the robust or, per Waddington, canalized nature of development [8]. The landscape is not fixed: Underneath the surface, we see pegs connected to it by a network of guy ropes, which pull and alter the topography in complex, nonintuitive ways. The pegs represent genes and the webbed ropes their influence on the developmental system. In this way, Waddington graphically combined developmental dynamics (the ball rolling down the landscape) and evolutionary dynamics (the landscape shifting underneath the ball).

While the extent of Waddington's conceptual impact on developmental and evolutionary biology is debated, his pictorial legacy is wide-ranging and profound [9]. His landscape is used to integrate and structure thinking across disciplinary boundaries. René Thom put Waddington's visual intuitions on a firm mathematical basis [10]. More recently, landscape images have become widespread in stem cell biology, where they are used to connect experimental molecular biology with systems-level models [11]. In general, Waddington's landscape is used by researchers who apply dynamic systems theory to the study of developmental or other regulatory processes and their evolution [12]. The landscape brings into visual focus the particular dynamic nature of biological processes and facilitates the transdisciplinary communication required to study these dynamics in an integrative and systematic way.

These examples highlight that Waddington's landscape was successful in a role that would have pleased its originator: It stimulates visual thought, enabling us to contemplate biological processes in new ways that are not yet explicitly conceptualized. Waddington's artful representation helps to "loosen the joints of [the scientist's] psyche," creating a space for the associative play required to introduce new concepts in theory formation [13].

Despite its success, Waddington's landscape suffers from several important limitations. First, it may be too abstract to be helpful, visually informative or imaginatively stimulating, and it is certainly difficult to connect to the experimental study of specific morphogenetic processes [14]. For example, it is not clear how the position of the ball within the landscape—representing the state of the developing system—connects to morphological changes or other indicators of system state that can be observed and measured in the laboratory. Moreover, while the particular topography Waddington uses in his illustrations is intuitive, it does not hold up under mathematical scrutiny [15].

Finally, and most importantly in our context, Waddington's landscape cannot visualize a key property of biological systems: His two-dimensional representation of the topographical surface does not accommodate complex behavior such as oscillatory dynamics. In the landscape, the ball must always run downhill, while in oscillatory dynamics, the system revisits the same state or topographical location periodically. Oscillations are at the core of many fundamental cellular and developmental processes [16]. One important example of oscillatory patterning is somitogenesis, the process by which vertebrate animals form their body segments (called somites)—adding them one by one as they grow longer during embryogenesis [17]. We use this developmental process as biological anchor and motivation for our own creative process.

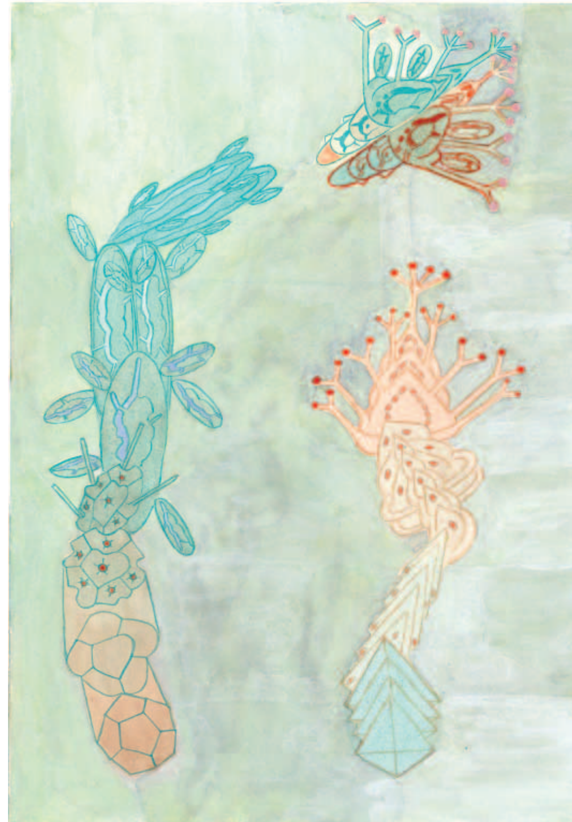

Fig. 2. Gemma Anderson, *Isomorphogenesis No. 2*, watercolor on paper, 18 × 26 cm, 2014. Image from the Isomorphogenesis series, exploring the potentialities of representing morphology as a dynamic and formative process. (© Gemma Anderson)

EXTENDING WADDINGTON'S LANDSCAPE THROUGH COLLABORATIVE IMAGE-MAKING

We explore the limits of Waddington's landscape and extend it to accommodate oscillatory and other complex dynamics through a process of collaborative image-making that involves artist and scientist in equally crucial roles. Here, we reflect on the dynamics of this collaboration. We refer back to the epistemological nature of drawing, emphasizing its role in transdisciplinary communication and the formulation of new concepts. Finally, we discuss how our collaborative process informs both artistic and scientific methodology for the study and understanding of biological processes.

We developed our collaboration through a series of six images—each involving a unique process of creating and exchanging knowledge through drawing. Iterative in nature, each image builds on critical discussions of the previous one.

The process began in September 2016, when Anderson was visiting the Konrad Lorenz Institute for Evolution and Cognition Research (KLI) in Klosterneuburg, near Vienna. She had been invited by Jaeger, whose interest was piqued by meeting with Anderson at a process philosophy workshop and discovering her depiction of morphological transformation in her Isomorphogenesis project. This project is an exercise in theoretical morphology consisting of a series of drawings that represent an analog simulation of the dynamic possibilities of form (Fig. 2). It integrates D'Arcy Thompson's grid transformations, Klee's color gradation method and William Latham's FormSynth system for the generation of form [18]. What is missing from the Isomorphogenesis series is a Waddington-style landscape shaping and constraining

Fig. 3. Gemma Anderson, *Isomorphogenesis Embedded in Waddington's Epigenetic Landscape*, watercolor on paper, 26 × 36 cm, 2016. (© Gemma Anderson)

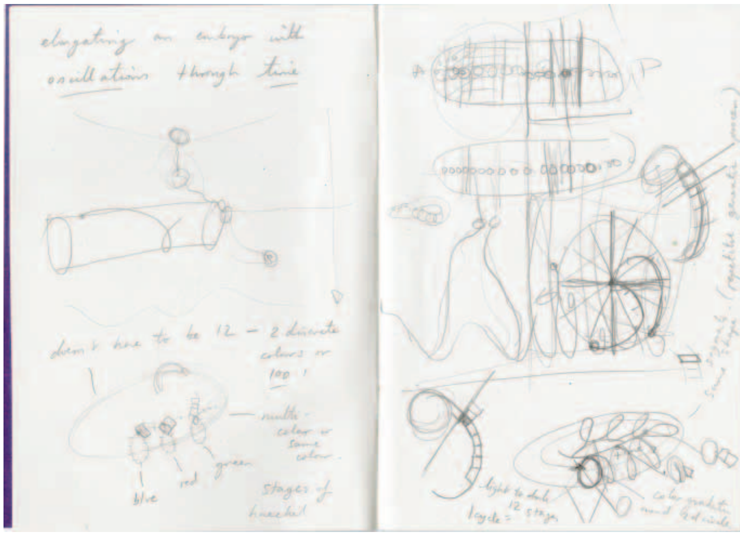

Fig. 4. Gemma Anderson and Berta Verd, *Somitogenesis/Oscillations*, pencil on paper, 18 × 26 cm, 2016. (© Gemma Anderson)

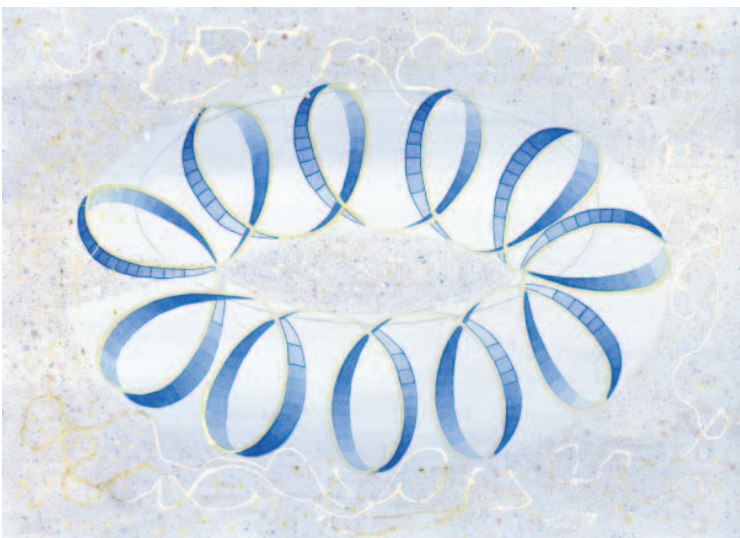

Fig. 5. Gemma Anderson, *Somitogenesis/Oscillations:Torus*, watercolor and pencil on paper, 26 × 36 cm, 2016. (© Gemma Anderson)

the morphological transitions taking place. This observation provided a natural starting point for our exploration.

The ball in Waddington's landscape (Fig. 1) remains the same over time as it rolls down its valley. It does not undergo any morphological transformations. We imagined overcoming this limitation by replacing the ball moving through the landscape with an Isomorphogenesis transformation. The resulting experimental image by Anderson is shown in Fig. 3. It reduces the level of abstraction of Waddington's representation by explicitly showing the trajectory of morphological change (the chreode) through the valleys of the landscape. On the other hand, it provides context for the developmental processes in the Isomorphogenesis series through its explicit depiction of the landscape. However, it remains unsatisfactory, still limited to a two-dimensional landscape surface that restricts its ability to portray complex developmental processes more realistically.

Inspired by a mutual interest in topology, Anderson and Verd decided to experiment with different geometrical structures as landscapes on which to draw developmental processes. The idea was that topologically complex landscapes would allow us to depict an expanded range of developmental dynamics. In particular, we wanted to find a landscape topology that enabled us to represent the oscillatory dynamics involved in somitogenesis (Fig. 4). The addition of somites to the growing vertebrate body involves repeating waves of genes being activated and repressed, creating oscillatory patterns of gene product synthesis and hence dynamic waves of cell state changes moving through the tissue [19].

How to represent such periodic oscillations? A torus is the natural surface topology choice. In *Somitogenesis/Oscillations:Torus* (Fig. 5), the developmental trajectory wraps around the torus like a string. The chreode is now free to oscillate. Its cyclic color gradation represents the oscillating levels of gene products involved in somitogenesis. A new somite is formed after each of these cycles, elongating the embryonic axis one segment at a time. We have mentioned above that chreodes are canalized—buffered against perturbations—which Waddington summarized under the concept of "developmental noise." Anderson integrates a visual interpretation of such noise using artistic methods such as watercolor speckling, splashes and gestures in the image.

The torus topology turned out to be extremely useful as a visual tool for thought. It successfully marries mathematical intuition and observation (landscape and oscillations) by releasing the landscape from the constraint of a strictly two-dimensional surface. It allows experimentation with parameters such as frequency and period of the oscillations, or diameter and length of the torus, which creates intuitions for comparing the formation of somites in different organisms, from snakes to mice. The image thus constitutes a powerful tool for visualizing the evolution of vertebrate somitogenesis.

Somitogenesis/Oscillations:Torus is the final product of Anderson's first visit to the KLI. Although satisfied with the advances provided by this image, we remained aware of its limitations: It prioritizes gene expression patterns over accurate representation of morphological transformations. In April 2017, Anderson returned to the KLI in the context of a KulturKontakt Austria residency. In the meantime, she had developed a more systematic approach to creating and depicting developmental noise. Her drawing system Noise/Form/Gradation provides formal components for creating image texture with relationships analogous to biological complexity [20] (see e.g. Figs 6, 7 and Color Plate A). In

Fig. 6. Gemma Anderson, *Somitogenesis/Oscillations:Knot*, watercolor on paper, 18 × 26 cm, 2017. (© Gemma Anderson)

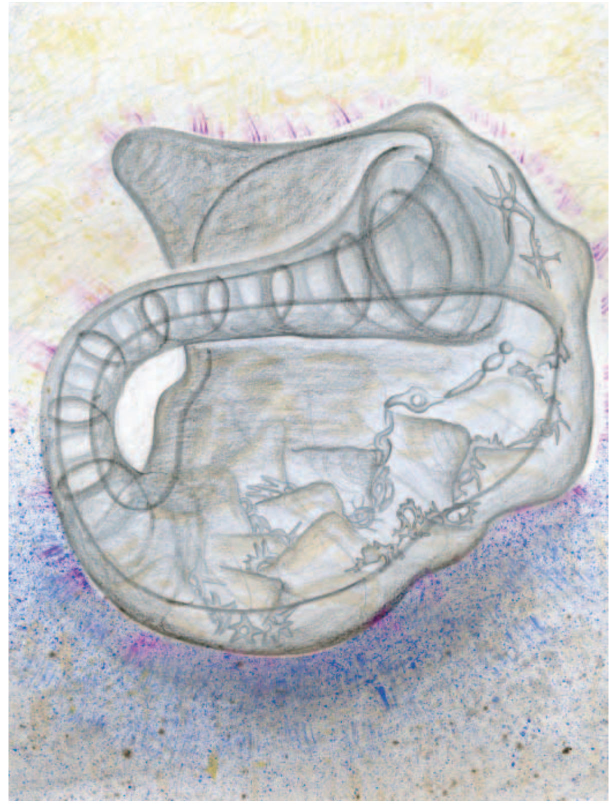

Fig. 7. Gemma Anderson, *Klein Bottle Landscape*, watercolor and colored pencil on paper, 31 × 41 cm, 2017. (© Gemma Anderson)

addition, we wanted to experiment with even more complex topologies to enable Anderson to more accurately represent morphogenesis in her drawings. As a first step, we attempted to symbolize the complex, convoluted nature of organismic development by introducing knots into the torus (Fig. 6).

Knots deliver an increase in complexity, a more comprehensive exploration of the image space on the page and an expansion of the surface area that can be occupied by the chreode. Different loops within the knotted structure could be thought of as representing different stages in a life cycle (embryo, larva, adult), each of which is subjected to variable levels and kinds of noise as indicated by the background. A complex knotted topology can also convey the sense of multiple simultaneous oscillations—for instance, cell divisions and oscillatory waves of gene expression in the case of somitogenesis. Such combinations are extremely common in developmental biology. Knotted loops thus provide an aesthetically pleasing compromise between complexity and simplicity. And yet, this representation still does not convey developmental trajectories in a truly realistic manner, as it does not incorporate branching or interacting paths. Anderson therefore decided to experiment with a network of spiraling tubes as a next step.

Somitogenesis/Oscillations:Pathways (Color Plate A) shows a tangled web of helical trajectories in intermittent focus. It highlights features of development complementary to those represented in the previous images. Figures 5 and 6 convey the cyclic and periodic nature of biological processes. The trajectories shown in Color Plate A may form loops as well, but only outside the focal plane of the image. Here, different processes (marked through distinct color gradation) connect and mutually influence direction and morphogenetic transformations (drawn as simplified Isomorphogenesis-like series in some of the grey-shaded tubes). This represents induction, an important and fundamental type of developmental event, in which one tissue signals to another to alter its fate. Waddington called inductive signaling “evocation” of a competent tissue [21]. An example is the induction of lens formation by the optic cup during the development of the vertebrate eye [22].

A satisfactory synthesis of Figs 5, 6 and Color Plate A requires a landscape topology combining cyclic aspects with different intertwined processes. Verd suggested a topological structure including both: the Klein bottle [23]. Like its better-known cousin the Möbius strip, a Klein bottle is a two-dimensional surface with one side only. We can understand the Klein bottle as having a main body that narrows to form a “handle.” The handle forms a cylindrical tube intersecting the side of the main body, looping back to connect the inside surface to its outside at the bottle’s base. This topology makes it possible for handle and main body to represent interactions of different processes within an intertwined cyclical trajectory (Fig. 7).

The Klein bottle provides a combination of torus and Waddington landscape, accommodating both oscillatory and branching dynamics. The handle and body of the bottle can be interpreted as different stages of development with fundamentally different levels of noise and canalization. The handle resembles one of the tubes in Figs 5, 6 and Color Plate A. It contains a spiraling undifferentiated path, corresponding to early stages of embryogenesis. In contrast, the surface of the main body provides space for branching Isomorphogenesis transformations across an underlying Waddington landscape with valleys and peaks. This landscape is drawn on the "outside" surface of the body of the bottle. The looping topology of the Klein bottle makes it possible to represent many iterations of these processes: a representation of the life cycle of an organism.

There are vastly different levels of developmental noise on different sides of the bottle. The representation of canalization and noise is much more sophisticated in this image compared to Figs 5, 6 and Color Plate A. Not only do extrinsic noise levels vary, but so do the intrinsic canalizing constraints. The narrow cylinder of the handle prevents branching morphogenesis but allows for variation in the period or amplitude of the oscillation. It is difficult to predict where exactly a specific cell will exit the handle. This represents the stochastic behavior of undifferentiated stem cells [24]. On the main body of the bottle, branching morphogenesis does occur, but is tightly canalized by the topography of the landscape on its outer surface. It represents the more diversified, but also more canalized, late development of distinct differentiating cell populations.

In summary, the Klein bottle allows us to represent a complex knotted cyclical path with a representation of branching morphological transformations. In artistic terms, it enables Anderson to extend her Isomorphogenesis method onto a landscape in combination with a depiction of stochastic oscillatory dynamics in the handle of the bottle. Seen in this light, Fig. 7 provides a powerful synthesis of our explorations into a realistic, yet still intuitive, pictorial representation of developmental dynamics through our collaborative image-making process. In addition, it demonstrates the power of using complex topologies to represent high-dimensional developmental dynamics.

CONCLUSIONS

Our collaborative approach to extend Waddington's landscape through drawing is an ongoing iterative and creative process in the space between art and science. The result is not illustration of a scientific concept but novel insights into the nature of life's processes. This does not happen through explicitly formulated conceptual analysis, as is usual within the framework of the scientific method, but rather through absorption of our images "by in-feeling," as Waddington fittingly puts it above. It is a two-way exchange to which artist and scientist contribute equally. On the one hand, drawing is an epistemological tool and point of convergence that enables artist and scientist to jointly develop their knowledge of the world. It provides images to think with. Complex landscape topologies such as tori and Klein bottles enable Verd and Jaeger to develop new intuitions and concepts regarding transformation of morphogenesis during evolution. This is achieved not only through new techniques for visualization of dynamic processes but also through the contemplative, interactive and iterative process of drawing itself. Drawing allows us to selectively highlight and explore salient features of a phenomenon. It is also a powerful constructive method for sharing insights across disciplines. On the other hand, our project reveals how the artist can make use of scientific concepts and processes—such as using complex landscape topologies to represent oscillatory dynamics—to develop new approaches and methods for the visualization of dynamic form.

Modern neuroscience confirms the age-old intuition that creativity—the formation of new associations and concepts—requires the playful abandoning of preconceived notions. To be creative we must let our minds wander [25]. Sadly, our rush for productivity, and the loss of space and time for contemplative practices—especially the decline of drawing in scientific practice—make this sort of creative work increasingly hard to achieve, thus hampering the creative potential of modern scientific inquiry. Our collaborative image-making process is an effort to reestablish focused creative contemplation in scientific practice. Hand-drawing must not be allowed to disappear. We say this not because of its use in scientific illustration but because of its potential as an epistemological tool to form insight and understanding, to share this understanding and to enhance creativity among artists and scientists alike.

Acknowledgments

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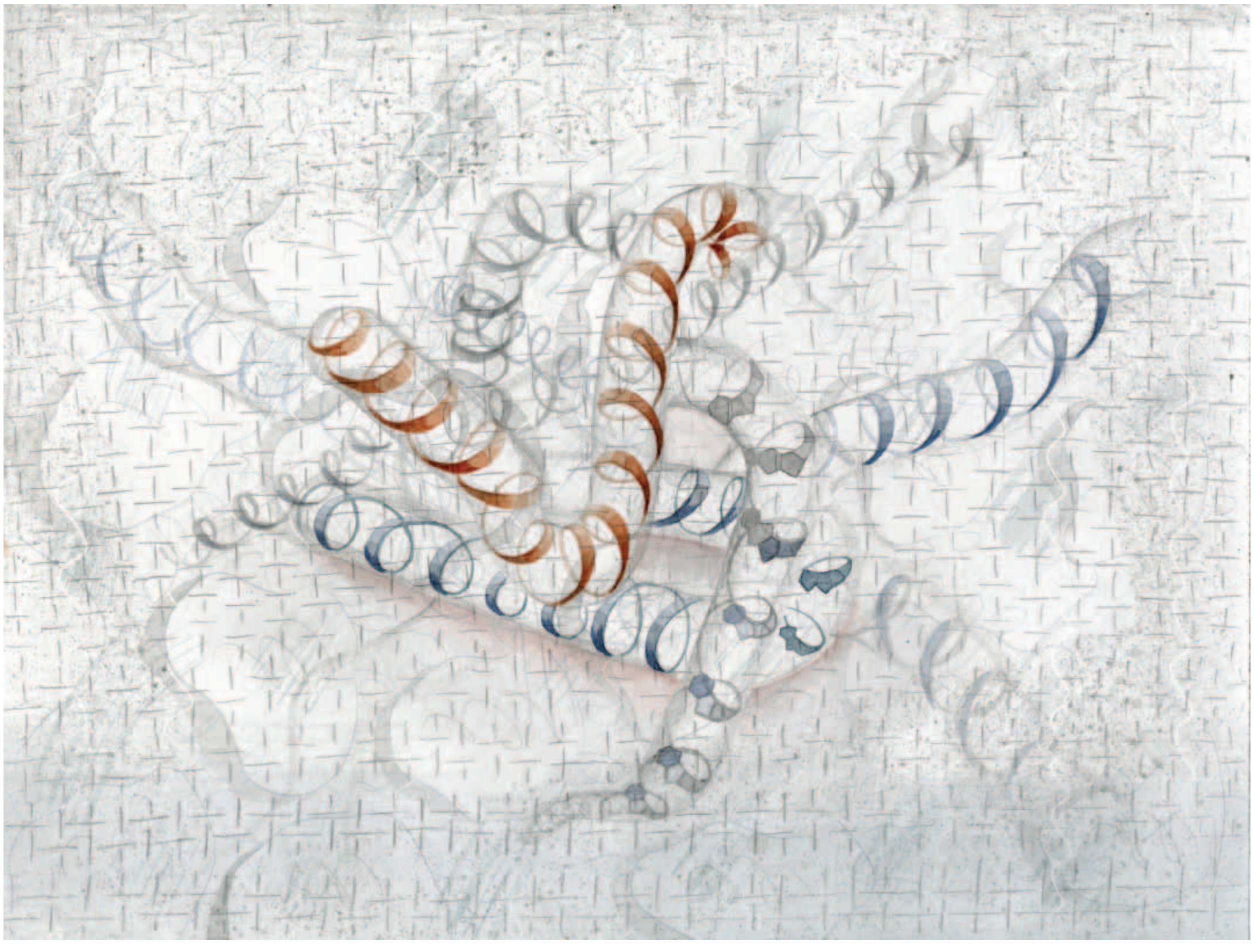
COLOR PLATE A: **DRAWING TO EXTEND WADDINGTON'S EPIGENETIC LANDSCAPE**



Gemma Anderson, *Somitogenesis/Oscillations:Pathways*, watercolor on paper, 31 × 41 cm, 2017. (© Gemma Anderson) (See article in this issue by Gemma Anderson, Berta Verd and Johannes Jaeger.)