### CHAPTER 6 Context: Dare We Call It Holism?

The centrality of living wholes within biology seems beyond argument. These have not been "put together" or built by an external agency. They are never the *results* of a physical activity that starts with non-wholes. Biology gives us nothing but beings that have never existed except as wholes possessing the formative powers that enable them to pass through further stages of physical development.

The one-celled zygote is already a functioning whole. It does not gain further cells through the addition of "building blocks" assembled by an engineer or designer, but rather through an internal power of reorganization and subdivision in which the entire organism participates. All the parts are orchestrated in a unified performance that yields (through division of existing cells) new cells, and particular kinds of cells, just where they are needed. The orchestrating power of the whole can hardly be determined by the particular parts it in this way brings into being and orchestrates.

Where the physicist may prefer unambiguous, isolated, and well-defined "point" causes, the biologist never has such causes to theorize about. A biological whole is never absolute, and never perfectly definable as distinct from its environment. Further, its actions are always multivalent, and they interpenetrate one another, like the meanings of events in a story.

The wonderfully insightful, twentieth-century botanist, Agnes Arber (Arber 1985, p. 59), captured well the polar tension between organic wholeness, on one hand, and contextual embeddedness, on the other:

The biological explanation of a phenomenon is the discovery of its own intrinsic place in a nexus of relations, extending indefinitely in all directions. To explain it is to see it simultaneously in its full individuality (as a whole in itself), and in its subordinate position (as one element in a larger whole).

Every ecological setting, every organism within that setting, every organ within the organism, and every cell within the organ is a whole providing a context for its own interrelated parts, and at the same time is itself contextually embedded within larger wholes. "Context", "whole", and "part" can never be rigid, absolute terms in biology. They are bound up with interweaving spheres of activity.

We need to gain some practice in thinking, not with the single, distinct point-causes of the physicist (or at least the classically minded physicist), but rather with the actual <u>narrative</u> qualities of biological activity. The perplexing issues surrounding attempts at <u>holistic</u> thought may thereby lend themselves more easily to our efforts at understanding.

# Which comes first, the cell or its niche?

Every cell in an organism lives in a sufficiently distinctive way — is enough of a whole in its own right — to pose the question of identity. What makes this particular cell of my skin a keratinocyte rather than a melanocyte? Does identity imply constancy of cellular character? To what degree does a cell's environment the larger community of cells — shape its

identity and character?

Current researches are showing us how the fate of any given cell in our bodies is bound up with that of nearby cells in the same local environment, or "niche".<sup>1</sup> Consider, for example, the basal stem cells of the mammalian airway. (*Basal cells* are epithelial cells constituting the lowest layer of epidermis, and *stem cells* are relatively undifferentiated cells capable, at need, of dividing and differentiating into more specialized cell types.)

One research group found that when airway basal stem cells were in demand as a result of injury, there was a "surprising increase in the proliferation of committed secretory cells". It turned out that many of these latter, fully differentiated (specialized) cells, were, so to speak, reversing their specialization and becoming basal stem cells. The "de-differentiated" cells "were morphologically indistinguishable from stem cells and they functioned as well as [normal stem cells] in repairing epithelial injury ... This capacity of committed cells to de-differentiate into stem cells may have a more general role in the regeneration of many tissues" (Tata et al. 2013).

Further, direct contact with a single basal stem cell was enough to prevent secretory cells from de-differentiating and becoming stem cells. Clearly, then, the identity of these fully matured secretory cells is not rigidly fixed, and at the same time their transformation potential is delicately sensitive to context. We can hardly separate the question of a cell's identity from that of the niche's identity, or from the changing needs of the moment.

This point is driven home by a second study concerning mouse hair follicles.<sup>3</sup> The researchers explored how a cell's location within various compartments of the niche affects its fate. For example, stem cells in the bulge (see <u>Figure 6.1</u>) tend to stay quiescent — that is, they remain in a resting state without cell division — whereas those in the hair germ are continually differentiating into more specialized cell types. And even within the bulge, stem cells in the upper half remain much more consistently quiescent, whereas those in the lower half are more proliferative.

Dramatically, the authors also show that "hair follicle stem cells are dispensable for regeneration, and that epithelial cells, which do not normally participate in hair growth, repopulate the lost stem-cell compartment and sustain hair regeneration" — provided, however, that "the overall integrity of the niche is maintained". When the stem cell population in the bulge or hair germ is destroyed by laser ablation, distant epithelial cells flow toward the damaged compartment and go through a transformation of identity enabling them to replace the lost cells. As the authors summarize it, "The overall structure and function of the tissue is maintained because cells are capable of adopting new fates as dictated by their new niche

microenvironment".

Clearly, the different elements of the hair follicle niche are not rigidly fixed entities. Rather, their changing forms and relationships are choreographed by the larger environment. So the goings-on in the hair follicle niche illustrate very well how the context helps to "decide" what sorts of elements it will have, how they will be formed and transformed, how they will flow toward the places where they are needed, and how they will come into mutual relationship. Nothing could be further from the common picture of an organism being constructed, bottom-up, from an available collection of well-defined building blocks capable of determining outcomes. It appears, rather, that the desirable outcome determines the "building blocks".



And we need to remember that the humble hair follicle represents just one of millions of distinct niches within a mouse or human being. Liver, kidney, heart — every organ embraces countless micro-environments, none of which is exactly like any other. In every one of those micro-environments a unique, evolving collection of cells is caught up in the wholeness of its governing context. And the same demand for flexible coordination, but now at a higher level, is repeated as all those niches are assimilated to the unity of a single organ, and again in the way the organs are brought into harmony within the functioning of the whole organism.

Embryos in general exhibit this power of flexible coordination to an extraordinary degree. Harvard biologist Richard Lewontin once described how you can excise the developing limb bud from an amphibian embryo, shake the cells loose from each other, allow them to reaggregate into a random lump, and then replace the lump in the embryo. A normal leg develops. Somehow the form of the limb as a whole is the ruling factor, redefining the parts according to the larger pattern. Lewontin went on to remark:

Unlike a machine whose totality is created by the juxtaposition of bits and pieces with different functions and properties, the bits and pieces of a developing organism seem to come into existence as a consequence of their spatial position at critical moments in the embryo's development.

A developing organism, Lewontin adds, "is like a language whose elements ... take unique

meaning from their context" (Lewontin 1983).

## 'More than the sum of its parts': clarifying a cliché

The foregoing illustrates how a biological context defines its parts — lends them their meaning — not the other way around. However hard it may be for us to conceive, there seems to be something fundamentally *causal* about a context. It *governs* its parts, bringing them into existence, transforming them, and coordinating their activity. But

there is another, closely related way to look at the matter. For this we can turn to the preeminent cell biologist, Paul Weiss, whose work extended from the 1920s into the 1970s, when he was awarded the National Medal of Science by President Jimmy Carter.

As a life-long observer of cells and tissues, Weiss pointed out something obvious, simple, and yet revolutionary for today's biology. When we examine the form and physiology of an organism, we see how "certain definite rules of order apply to the dynamics of the *whole* system ... reflected [for example] in the orderliness of the overall architectural design, which cannot be explained in terms of any underlying orderliness of the constituents" (Weiss 1971, p. 286).

That is, despite the countless processes going on in the "heaving and churning" interior of the cell (Weiss 1973, p. 40), and despite the fact that each process might be expected to "go its own way" according to the myriad factors impinging on it from all directions, the actual result is quite different. Rather than becoming progressively disordered in their mutual relations (as indeed happens after death, when the whole dissolves into separate fragments), the processes come together in a larger unity. The behavior of the whole "*is infinitely less variant from moment to moment than are the momentary activities of its parts*":

Small molecules go in and out, macromolecules break down and are replaced, particles lose and gain macromolecular constituents, divide and merge, and all parts move at one time or another, unpredictably, so that it is safe to state that at no time in the history of a given cell, much less in comparable stages of different cells, will precisely the same constellation of parts ever recur ... Although the individual members of the molecular and particulate population have a large number of degrees of freedom of behavior in random directions, the population as a whole is a system which restrains those degrees of freedom in such a manner that their joint behavior converges upon a nonrandom resultant, keeping the state of the population as a whole relatively invariant (Weiss 1962, p. 6).

Tuning in to this basic picture — if we could really take it seriously — might change just about everything in biology. It is therefore worth hearing the voice of one other competent authority who emphatically echoed Weiss' remarks, despite writing from a very different specialist's angle. In a 1985 paper Guenter Albrecht-Buehler, a biophysicist at Northwestern University, wrote this:

During the course of uncountable simultaneous biochemical and biophysical events, information is copied, received, transmitted, and stored as hormones, mRNAs,

neurotransmitters, pre- and postsynaptic potentials, post-translational modifications, covalent links between macromolecules. Different kinds of cyclic events keep time and synchronize other cellular events, eventually generating mitotic cycles and circadian rhythms. Materials such as proteins and RNAs or much larger structures such as viruses or organelles that carry the information around are transported, produced, exchanged, recycled, modified, inhibited, or stored.

And he concluded: "All these events occur in a microscopically small world of violent and random thermal fluctuations. Yet, cytoplasm can keep its complex actions accurate in the midst of drowning thermal noise all around and within" (Albrecht-Buehler 1985).

We might say that a given type of cell (or tissue, or organ, or organism) insists upon maintaining its own recognizable identity with "unreasonable" tenacity, given the relative freedom, in purely physical terms, of its molecular constituents as they make their way through a watery medium.

The same principle holds when we look at the "erratic" placement of individual cells within a larger tissue that exhibits beautiful order. In Weiss' summary:

While the state and pattern of the whole can be unequivocally defined as known, the detailed states and pathways of the components not only are so erratic as to defy definition, but, even if a Laplacean spirit<sup>4</sup> could trace them, would prove to be so unique and nonrecurrent that they would be devoid of scientific interest.<sup>5</sup>

"This", Weiss remarks, "is exactly the opposite of a machine", where the pattern of the product "is simply the terminal end of a chain of rigorously predefined sequential operations of parts. In a [biological] system, the structure of the whole coordinates the play of the parts; in the machine, the operation of the parts determines the outcome" (Weiss 1973, p. 41). So it happens, in Weiss' words, that "molecules can contribute to 'the control of cellular activity' only insofar as 'cellular control' prevails over their individual activities" (Weiss 1962, p. 62). In other words, it doesn't make much sense to speak at all of molecules as *controllers* of cellular activity.

Everything here might well remind us of what we heard from E. S. Russell in <u>Chapter 2</u>: in living activity, the end is more constant than the means. Or: the *purposive* end is more constant than the *physical* means. And it can hardly be disputed: the imposition of order upon the cell that we have been describing seems impossible to understand without an element that looks much more like intention than like the physical lawfulness through which that intention realizes itself. (As I have tried to make clear since the first chapter of this book, and hope to make clearer still in what follows, I am not necessarily speaking of human-like awareness, concious planning, and intention.)

So, anyway, it turns out, with a touch of irony, that *less* change is what shows the whole cell, or any organic whole, to be *more* than the sum of its parts. It's as if there were an active, coordinating agency subsuming all the part-processes and disciplining their separate variabilities so that they remain informed by, and caught up in, the greater unity. The coordination, the ordering, the continual overcoming of otherwise disordering impacts from the environment so as to retain for the whole a particular character or organized way of being, expressively unique and different from other contexts — this is the "more" of every organism and every context that cannot be had from the mere summing of discrete, causal parts.

So the center holds, and this ordering center — this whole that is more than the sum of

its parts — cannot itself be just one or some of those parts it is holding together. When the organism dies, the parts are all still there, but the whole is not.

## Every biological context is a a complex of embodied ideas

Curiously, "<u>holism</u>" has almost become a dirty word in biology. It commonly connotes loose thinking, vagueness, obscurantism, and perhaps even an unfortunate tendency toward mysticism. I say "curiously" because the fact is that biologists speak incessantly about

holism. You might almost think they were, in recent years, becoming fanatical about it. It's just that they prefer to honor holism under the more acceptable (and obscure) slogan, "context matters". This latter idea occurs like a mantra in the contemporary technical literature, so that it would be hard to find any physiological or behavioral process that is not routinely (and rightly) said to be "context-dependent" or "context-specific".<sup>6</sup>

Strangely, despite the almost universal employment of the pregnant term "context" in molecular biology, it is rarely if ever defined, and the unwelcome meanings implicit in the use of the term seem never to become explicit. And yet the word can hardly mean anything at all if it is not a close synonym for "larger whole". The frequent appeal to context as a decisive determining factor, then, looks rather like an under-the-table invocation of the unmentionable concept of holism. It allows biologists to import the seemingly inescapable idea of the causal whole into their descriptions and theorizing, while outwardly pursuing a style of explanation that pretends to disdain holism in favor of purely physical analysis into parts — the parts whose sum supposedly gives us the whole.

Let's not forget: when we say that what happens in a cell is "context-dependent", we are talking about a watery expanse populated by untold billions of molecules in unsurveyable variety. The need is for just the right combinations of molecules to do just the right things "in the moment" — and to do them *in light of the overall state of the entire cell within its particular tissue*. Is this cell just now committing itself to cellular division? Then what these molecules here and those molecules over there must do is now being radically redefined. Their new "assignments" depend not only on their location in the cell, but also on their necessary functional participation in lengthy, complex, temporal sequences of interaction that require the choreographing of countless other molecules as well.

Something is always going on contextually, and all the molecular interactions, taken together, must reflect whatever that something happens to be — must reflect the meaning of the encompassing <u>narrative</u>.

Appeals to context are necessary because transient, local, physical causes are unable to explain the purposive and narrative *significance* of whatever is going on. A broader, orchestrated performance is always playing out — a performance to which local processes are made to conform. This seems to imply that a kind of cause is being directed from the context, or whole, toward the parts. (See Chapters 9, "A Mess of Causes", and 10, "What Is the Problem of

Form? — and especially the section, "The problem of organic form", in <u>Chapter 12</u>, "Is a Qualitative Biology Possible?") The parts, being *caught up* in the form and activity of the larger context, receive from it their shifting identities and meanings.

The word *context* refers etymologically to that which has been woven together, and is commonly applied today to language, thought, and intention, and, in general, to the connections that weave through the elements of meaningful conceptual expression, making a coherent whole out of them. But, whether we have recognized it or not, this meaning remains precisely the same when the word is used in biology. Narrative connections of language, thought, and intention are what make a biological context the characteristic whole that it is, lending it its form and meaning.

All this may be easier to grasp by looking at our own experience.

The activity on and around a football field during a game differs as a context from the activity on and around a baseball field. The difference could neither exist nor be articulated if it weren't for the distinct *ideas* and *intentions* establishing the two contexts, including all the rules of the games, the organization of Box 6.1

#### Some Call It Holism

The yearning for a means to recognize and understand the whole organism seems to have surfaced with more or less intensity throughout all of modern history — but perhaps at no time more insistently and wisely than during the first half of the twentieth century. The great neurosurgeon, Kurt Goldstein, wrote in his masterpiece, *The Organism*, first published in 1934:

By virtue of [an] isolating, dismembering procedure one can readily abstract and single out from living phenomena those phenomena on the physico-chemical "plane." But the attempt to reintegrate the elements thus abstracted, to reorganize these split-off segments into the reality of living nature, is doomed to fail. ... it is not possible to comprehend the whole on the basis of the parts (Goldstein 1995, p. 378).

Likewise, the leading embryologist, F. R. Lillie, wrote in 1906: Cells are subordinate to the organism, which produces them, and makes them large or small, of a slow or rapid rate of division, causes them to divide, now in this direction, now in that, and in all respects so disposes them that the latent being comes to full expression ... The organism is primary, not secondary; it is an individual, not by virtue of the cooperation of countless lesser individualities, but an individual that produces these lesser individualities on which its full expression depends (quoted in Russell 1930, pp. 243-44).

The eminent physiologist, John Scott Haldane:

When we endeavour to treat physiological phenomena as separable events we only reach unintelligible chaos to which there is no end. When we seek to understand them as manifestations of life regarded as a whole we find that we can make them intelligible and predictable (Haldane 1931, p. 69).

The mathematician and student of form, D'Arcy Thompson: We tend, as we analyze a thing into its parts or into its properties, to magnify these, to exaggerate their apparent independence, and to hide from ourselves (at least for a time) the essential integrity and individuality of the composite whole (Thompson 1917, p. 712).

And, finally, the neurophysiologist Sir Charles Sherrington: The living creature is fundamentally a unity. In trying to make the "how" of an animal existence intelligible to our imperfect knowledge, we have, for purposes of study, to separate its whole into partaspects and part-mechanisms, but that separation is artificial. It is as a whole, a single entity, that the animal, or for that matter the plant, is finally and essentially to be envisaged (quoted in Russell 1930, p. 166).

There are countless other examples of the same sort. And today we see a resurgent defense of holism in some quarters. But I think it is fair to say that the proponents of holism have yet to make their point in a way that faces up to all the issues and effectively communicates these to the larger scientific community. And two of

leagues into teams, and the competitive framework. Those ideas and intentions enable us to predict the kinds of activity we will observe. And the the key issues, which will figure in later chapters, are (1) the necessity to speak of a type of causation other than physical causation, and (2) the role of idea, or thought, in the phenomena of life.

predictions are possible because, one way or another, the activities occur with implicit reference to the ideas. The physical facilities, the equipment, and the players — all the activities, viewed physically — do not *produce* the ideas; rather, the activities are *governed* by the ideas. Even the very same physical checkerboard differs as a context, depending on whether the governing ideas are those of checkers or chess.

When a player runs from first base toward second and the catcher throws the ball to the second baseman, we understand the narrative sense of it because we understand the relevant ideas and intentions. Similarly, when we say that the fate of two nearly identical cells will diverge radically depending on their locations in the hair follicle niche, or that a particular chromosomal modification is "cell-type-specific" — neuron or muscle cell? — we have in mind the distinct *character* of the different contexts, their unique ways of being, and what they *need* in order to proceed through their different stories within the still larger context of the organism as a whole.

And so — as we already saw in <u>Chapter 2</u> ("The Organism's Story") — whenever we speak of beings rather than things, we necessarily turn to a language of directed intention (*respond*, *develop*, *adapt*, *regulate*, and so on); a normative and aesthetically colored language (everything relating to health and disease, order and disorder, rhythm and dysrhythmia, harmony and disharmony, error and error correction); and a language of wholeness (*context*, *coordination*, *integration*, *organization*).

Not surprisingly, then, the biologist finds herself directly invoking the language of meaning in terms such as *message*, *information*, *communication*, and *signal*. But, again, she usually tries to do so in a mathematized, *de-meaned* manner intended to conceal the inwardness of the organism. Yet her recourse to the ubiquitous idea of context is a dead giveaway: if the word does not signify an ideational, aesthetic, and directive coherence, it refers to nothing living at all. Things just "being there" without an integral unity expressed in relational ideas — things without a describable role in a story that matters — do not make a living context.<sup>7</sup>

## Contextual wholes and living narratives

We saw in "<u>The Organism's Story</u>" that every animal's life has a <u>narrative</u> quality through which the meanings of its life are expressed. It pursues its own needs and interests; it interprets, responds to, and re-shapes its environment; and it exhibits a certain biological end-directedness or purposiveness in its activity, from the molecular level on up. It is always "up to something" or

"going somewhere".

So long as we are content to look only at the sum of physical causes, we miss this narrative. The same would be true if we read a novel while attending only to the physical causes underlying all the events. If we then said that the unbroken connection of these causes proves the absence of the narrative — the absence of the meaningful living activity and the ideas that the story is actually *about* — then we would merely be asserting our fierce determination to see nothing but physical causes.

At this point the reader, perhaps growing impatient, has every right to ask: "If the organism's life is a narrative in the sense you speak of, then who is the narrator? And how does that narrator achieve its 'governing' or 'coordinating' role — if, indeed, you are not suggesting some sort of vital force?"

These are essential questions, and in this chapter I have tried to take the first steps toward an answer. We have seen (in <u>Chapter 2</u>, "The Organism's Story") that biologists in general, despite the "fierce determination" just referred to — and however unconscious they are of the meanings of their words — compulsively refer to organic *contexts* as if they somehow possessed governing powers, and as if organisms really *are* engaged in purposive, or end-directed, activity. So it appears that the questions are not only mine. They are endemic to biology. Whose are the ends or purposes we find ourselves recognizing in the life of an animal?

On my part, I have tried to begin an answer with two basic recognitions. One is that every context, so far as it is a unitary and integral whole, just *is* regarded, for practical explanatory purposes, as the narrator of the story being enacted within its own domain. It informs its parts and disciplines their activity in harmony with the needs and character of the whole. If there seems to be something *causal* about this disciplinary power (and there certainly does), it differs in some respects from the causation we are familiar with in the inanimate world.

One difference is that this biological causation can never be understood in absolute and unambiguous terms. As when reading a novel, we find that unfolding events make ever clearer sense out of an organism's life. But the interwoven and qualitative *reasons* for things never have the simple character of a mathematical law. Moreover (as we heard from Agnes Arber at the outset of this chapter), every causal context is embedded in still larger contexts, without which it cannot be fully understood. Biological causes always interpenetrate one another.

The second key recognition is that a living context, or whole, exists only by virtue of a certain "<u>inwardness</u>" — an inwardness associated with ideas and intentions, and therefore with volition, cognition, and intelligence. This inwardness may not sit well with the prevailing

materialism in today's biology, but we will find in <u>Chapter 12</u> (the section on "The problem of organic form") that it gives us the key for understanding how a context might be said to *causally govern* its constituent elements.

But even before further explanation, the tantalizing fact remains: every activity with a narrative character shares at least one thing with a human-written novel: it has its own immaterial causal basis, or meaning, which alone enables us to understand and explain what is going on. This remains true even if the meanings at issue are radically different between, say, a giraffe and a politician. An implicit belief in the meaning of organic activity is what leads biologists to classify their research projects according to the significant performances of organisms — from gene expression and cell division to pursuing prey and protecting the young.

Calling these activities "functions" may be more comforting to some (because less alive and more machine-like), but what we here denote by a function typically just *is* a meaningful performance — a form of contextualized self-expression or self-realization. We would never in the same way say of a volcano (and we ought not to say of a machine) that it is *expressing* or *realizing* its own nature by how it *responds* to its surroundings.

Meanings require, and are given by, contexts. It seems way past time in biology not only to implicitly recognize the contextual meanings of biological activity, but also to say a conscious "yes" to them and thereby free ourselves to consider the difference between understanding the animate and inanimate worlds.

#### Seeing the Organism in Context

In <u>Chapter 2</u> ("The Organism's Story") the organism's life was described as story-like in the sense that it is a progressive unfolding in time of interwoven meanings expressing the needs, interests, and intentions representing a particular way of being. These meanings cease to exist, as we noted using a dog as an example, at the moment of death.

From there we went on to <u>Chapter 3</u> ("What Brings Our Genome Alive?"), where we learned about the all-but-incomprehensible skill and wisdom with which a cell manages its own genome, and to <u>Chapter 4</u> ("The Sensitive, Dynamic Cell"), where this same sort of skill and wisdom finds its expression in connection with the cytoskeleton and cellular membranes.

Then, in <u>Chapter 5</u> ("Our Bodies Are Formed Streams"), we learned how all this happens in the plastic context of the cell, where organizing powers are reflected in the "dance" of chromosomes, in "molten" regions of proteins, in continual phase transitions in the cellular plasm, and, more generally, in a free movement of molecules within the fluid cell. And now we have seen (with the help of Paul Weiss) how this relatively disordered movement contrasts with the overall order of the cell, which is imposed as if "from above".

All this has led to our present concern with the *governing* role of contexts with respect to their parts — "governing" in the sense of imposing order and meaning upon the collective parts and, in fact, bringing those parts into existence as integral and well-coordinated participants in the meaning of the whole. We heard a fine example of this priority of context over parts in the description of the changing identity of cells within the hair follicle niche.

We hardly need to be told that, in the pages of their professional journals today, biologists constantly mention (although as if merely "in passing") the context-dependence of everything that happens in the organism. The unfortunate fact is that they really do pass such phrases by without making much of an effort to characterize what they mean by "context". So the charge of mysticism, if applied at all, should probably be leveled at the ubiquitous but unclarified use of the term "context" in today's biology.

Nevertheless, the term *can* be used with a perfectly clear awareness of its profound meaning — even if that meaning doesn't sit well with conventional thought today. We will have plenty of occasion in the chapters ahead for further reference to both "contextuality" and "holism", which are very nearly perfect synonyms. In particular, we will deal specifically with the importance of *organizing ideas* for our understanding of biological contexts in <u>Chapter 21</u> ("Inheritance, Genetics, and the Particulate View of Life"), as well as in the section, "The problem of organic form", in <u>Chapter 12</u> ("Is a Qualitative Biology Possible?").

### Notes

1. See, for example, the brief article summaries in Tan 2013.

2. Figure 6.1 credit: From Rompolas, Mesa and Greco 2013.

3. <u>Rompolas et al. 2013</u>. For an updated and more detailed report on this same research, see Xin et al. 2018.

4. Pierre-Simon, Marquis de Laplace (1749-1827) was a mathematician and physicist. The reference is to what is often referred to as "Laplace's demon", although Laplace himself did not use the word "demon":

We ought then to regard the present state of the universe as the effect of its anterior state and the cause of the one which is to follow. Given for one instant an intelligence which could comprehend all the forces by which nature is animated and the respective situation of the beings who compose it — an intelligence sufficiently vast to submit these data to analysis — it would embrace in the same formula the movements of the greatest bodies of the universe and those of the lightest atom; for it, nothing would be uncertain and the future, as the past, would be present to its eyes … The curve described by a single molecule in air or vapour is regulated in a manner just as certain as the planetary orbits; the only difference between them is that which comes from our ignorance. (Laplace 1951, p. 4)

5. Here's a way to picture the situation concretely. Imagine there were bricks with a built-in mechanism for placing themselves in position on a wall under construction. Imagine further that this placement was somewhat random, so that individual bricks stuck out this way here, and that way there, and tended in general to be precariously balanced, sometimes even falling off. If this degree of randomness held true as course after course of bricks were laid down, and if it applied to the courses themselves as well, we know very well that the variability successively added to variability would eventually bring the entire, unsightly structure to the point of collapse.

In the real-life case, the mason continually makes fine adjustments to compensate for the low-level variability that remains even under his steady hands. In this way, he reliably guides the structure toward its finished form. But he acts upon the wall as an outside force, and we see no outside force acting upon the organism so as to coordinate and continually "discipline" the degrees of freedom evident in its physiological activity. The only powers we can observe are those intrinsic to the organism itself. Our observation cannot be doubted, and we will have no hope of understanding if we lose sight of this observation due to its troubling nature.

6. Doing a quick hyperbole-check on myself, I find that a google scholar search on

#### "context dependent" gene cell

yields over 459,000 results. (I included the terms "gene" and "cell" in the search in order to ensure that the results were mostly from biological texts, with an emphasis on molecular biology.) It would be a worthwhile exercise for the reader to execute that search (by <u>clicking here</u>) and then browse down through some of the article titles and excerpts. Or go to scholar.google.com and type in the search terms.

7. It is worth mentioning here that inanimate phenomena are surely contextual as well, even if they lack those focal, organic centers of need and interest that can *respond* to context. The physicist Georg Maier once pointed this out by mentioning that the warm air in a closed room collects near the ceiling, while the air in the earth's atmosphere generally becomes cooler with elevation. The two contexts make a big difference.

Of course, the ideas evident in inanimate phenomena are very different from the ones we find in the phenomena of life. But ideas do remain ideas: we may prefer to formulate the regularities in physical events as high, mathematical abstractions, but they are ideas nonetheless. The seemingly willful blindness to this obvious fact of the ideational character of physical reality may be the central pathology of contemporary science.

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