
How Do Biomolecules “Know” What To Do?

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Physicists, before recovering their balance after all the turbulence roiling their discipline during the first half of the twentieth century, faced “insane” questions seemingly without coherent answers. But they eventually turned their perplexity into an exhilarating freedom of thought. Having broken through the narrow confines of pre-quantum era (nineteenth century), solid-particle, materialistic thinking, they — or some of them anyway — allowed their imaginations to soar into previously inaccessible realms. So it was that in 2005 a Johns Hopkins University professor of physics and astronomy, Richard Conn Henry, could publish in *Nature* — that dignified matriarch of scientific reporting — an article with the risqué title, “The Mental Universe.” Referring to lessons learned during the quantum revolution, including the primacy of observation over theorizing about submicroscopic “things” — things that seem inherently non-observable — he remarked:

Someone who has learned to accept that nothing exists but observations is far ahead of peers who stumble through physics hoping to find out “what things are.”

Urging the importance of educating the wider public about the changes in physics, Henry expressed the hope that physicists can “pull a Galileo,” so as to change the way people think about the world around them (Henry 2005).

I cannot vouch for Henry’s vision of material reality. And I don’t know who among physicists, or what confluence of events, will sooner or later “pull a Galileo” with the general public. But I do have some suspicions about the “insane” questions that just might transform biology in a wonderfully bracing way. And I am convinced that here, too, transcending the limitations of materialistic thought is the decisive opportunity — and may prove even more transformative than it has in physics. After all, problems of mentality, consciousness, thought, and intention are more obviously central to biology than they are to physics.

Here I wish to articulate just one of the “impossible” questions. A question, if it is truly a question and not part of a disguised brief for a ready-made answer, is always open-ended; one is free to take it up or not, and never

knows for sure where it might lead.

Of course, no inquiry is ever *completely* open-ended. To begin with, the choice of a topic says something about the direction of thought motivating the inquiry. And I have just now admitted that I am already convinced about our need to leave behind an older, materialistic way of thinking. I will realize that if this admission encourages some few to engage with the thoughts I am putting forward, it will discourage very many others. Fair enough. It will presumably turn out that the one group or the other will be on the side of history. We will see.

Meanwhile, there is (for me, anyway) the joy of the pursuit — the wrestling with perplexities that, one way or another, need to be penetrated by human understanding. This is despite the difficulty of glimpsing, at the moment, how the penetration might even be possible. But I am convinced that every question disturbing the human heart will sooner or later find its answer.

Let’s begin by looking briefly at two research topics in molecular biology:

Example 1: Topoisomerases

As the usual comparison has it, packing the DNA of a human cell, with its 21,000 or so genes, into the cell nucleus is like stuffing 24 miles (40 kilometers) of thread into a tennis ball, with the thread divided into 46 separate pieces (chromosomes) averaging roughly a half mile each in length. Appropriate gene expression entails an elaborate, three-dimensional structuring of these chromosomes into loops and different sorts of contact domains that bring specific genes and regulatory DNA sequences into relationship with one another and also with endlessly diverse collections of effector molecules in the nucleus.

If you or I were managing the thread, it’s fair to say that we would be clueless about how to establish and maintain the intricate and intertwined functional relationships among the millions of significant loci along these strings. But there are enzymes called “topoisomerases” that somehow manage just fine as they deal expertly with one part of the problem — namely, with the knots, tangles, and the ever-changing (and potentially disruptive) helical twist

of the two-stranded chromosomes. Some topoisomerases cut one of the two DNA strands of a single chromosome, allowing the cut strand to unwind or wind (untwist or twist) further around the uncut strand, then “healing” the cut. Other topoisomerases untangle knots by cutting both strands, passing a loop of the chromosome through the gap, and then sealing the gap.

No one knows how it is possible for a “dumb” molecule to perform these chores sensibly amid all the seemingly unreadable complexities of the dense mass of chromosomes. James Wang, currently a Harvard biochemist, discovered the first topoisomerases in the 1970s and has more recently written about the function of the enzymes:

When we think a bit more about it, such a feat is absolutely amazing: An enzyme molecule, like a very near-sighted person, can sense only a small region of the much larger DNA to which it is bound . . . How can the enzyme manage to make the correct moves, such as to untie a knot rather than make the knot even more tangled? How could a nearsighted enzyme sense whether a particular move is desirable or undesirable for the final outcome? (Wang 2009, p. 41)

Or, for that matter, what can we make of the enzyme’s capacity to “sense” anything at all? What is implied by that casual and oh-so-natural — yet oh-so-unnatural — use of words? And then there is the problematic reference to an outcome that is either desirable or undesirable. “Desirable” and “undesirable” are not physical categories. Yet here is a perfectly competent physical scientist driven to use such words. Perhaps we should pay attention.

In any case, we can assure ourselves that, sooner or later, someone will trace all the physically lawful activity through which the task is accomplished. It will make sense. Everything will turn out to be “routine” and “as expected” from a physical point of view. And because we find it so easy to interpret lawfulness as offering a more encompassing necessity than it can actually underwrite, we may then think that everything has been properly accounted for.

Does Biological Organization and Coordination Require Special Explanation?

It is true that the lawfulness of physical interactions reflects a kind of necessity. But this is an extremely limited sort of necessity. A rather fantastic thought might help to clarify the matter. Suppose there is a small, squirrel-sized hole in the left-field fence of a baseball stadium, and suppose further that a batter hits a line drive that passes precisely through the hole. It’s a very low-probability event. Yet it could happen.

And if it did happen, we would rightly think that everything must have been lawful, from the velocity and

spin of the pitched ball, to the angle of impact of the ball upon the bat, to the ball’s flight through the resistance of the air, to the lack of any bird or insect in the flight path, and so on to every smallest detail of muscular performance of the batter and pitcher. The pattern of lawful interactions would reflect a certain “chain of necessity,” even though what we mean by “necessity” in this case seems rather difficult to pin down. (The batter *could* have swung the bat slightly differently; a bird or insect *could* have gotten in the way; the ball *could* have encountered an unusual little gust of wind; a fan in the stands above the fence hole *could* have dropped a glove that interfered with the ball . . .)

But now suppose that, during practice, a batter hits 257 successive pitches as line drives striking the left field wall. Suppose further that chalk marks on the fence indicating the places of impact neatly spell out the sentence, “WHAT IS THE MEANING OF LIFE?” Given such an occurrence, it’s safe to say we would feel a need for explanation going beyond the physical lawfulness of each of those 257 drives. If someone suggested that a djinn suddenly emerged from a bottle and coordinated everything, we would doubtless reject the idea as ludicrous. And if we were told that this was one of the most amazing magician’s tricks ever pulled off — we knew not how — then we just might believe it. It would be either that or else keep looking for another explanation.

But what good does it do, you may be asking, to summon such an impossible picture? How could a falsely imagined occurrence help us with a real biological problem?

It’s true that the 257 line drives just now hypothesized would never happen, so that we would never actually need the looked-for explanation. The story was given in fantastic form only to point out as vividly as possible the difference between two varieties of explanation. An explanation beyond the lawfulness of physical interactions is required whenever we need to account for a kind of coordination or organization or meaning of events that physical lawfulness seems unable to support — *if indeed such coordination ever occurs*.

It is perhaps relevant here that magicians, unlike djinns, really do exist, and sometimes present us with perplexingly clever performances. When we try to understand those performances, most of us assume that everything was physically lawful. But we still want to know, “How did the magician pull this off?” The *trick* is not explained by its lawfulness.

So now we return to biology. What about the “trick” of the topoisomerases — whose accomplishment in managing complex and deeply contextualized meanings we still need to make sense of, and whose difficulty for human understanding we still need to remove. Unlike in the fanciful case of the baseball batter, we know that

the “impossibly” intelligent and meaningful management of knots, tangles, and twists by topoisomerases actually occurs. Although everything is physically lawful, this lawfulness, by all accounts, knows nothing of the needs, interests, and purposes of the cell and organism, which the topoisomerases seem to be “aware” of. The purposive and intricate coordination of molecular events by topoisomerases in service of the cell’s needs is well attested, so we can’t simply reject the picture as fantastic and unbelievable.

What is a conscientious biologist to do, if not look for the missing aspects of a proper understanding? Fortunately, she might not warm to the idea of a djinn (or of a magician, or of any other external agent or designer). But what then? Ought we at least to keep the explanatory problem in mind? What is it about the current state of biology that so easily allows such problems to drop out of sight?

Example 2: DNA damage repair

The DNA of a human cell incurs, on average, tens of thousands of molecular lesions per day. These can occur through internal agents such as reactive oxygen species, or

environmental agents (smoke, radiation, natural toxins, or man-made mutagenic chemicals). Without the cell’s ability to repair nearly all this damage, our lives would be extremely short, if we even survived to birth.

The various means of repair that a cell can bring to bear upon these diverse sorts of damage are so unthinkable complex and difficult for the human mind to follow that I would not attempt to capture that complexity here even if I were capable of it. I merely present in Figure 1 a biologist’s summary representation of two methods employed in dealing with a single kind of DNA damage — double strand breaks. Figure 2 is an elaboration of a small section at the lower right of Figure 1. The highly schematized figures, completely devoid of the massively complex biochemical details, are intended for those with training in genetics, and I imagine that trying to follow the depicted pathways of coordinated molecular surgery must have caused innumerable headaches in graduate students of molecular biology.

I would advise readers not to bother much with these figures. A vague and general impression is enough. But I will have a few things to say, usefully I hope, about the problem of DNA damage repair.

Figure 1, below (Note to readers: This figure and the following one don’t need to be understood. See main text.) Figure 1 depicts two general pathways for the repair of DNA double-strand breaks: non-homologous end-joining (NHEJ) and homologous repair (HR). Each pair of blue or gray horizontal lines represents the two strands of one complexly structured DNA molecule (double helix). Sections of these strands may be swapped around, and one molecule may be employed in the repair of a second, damaged molecule. Each of the steps shown may be accomplished by a large number of protein molecules working cooperatively. Figure 2 expands slightly on just one of the steps of homologous repair, involving the formation of a Holliday junction.¹

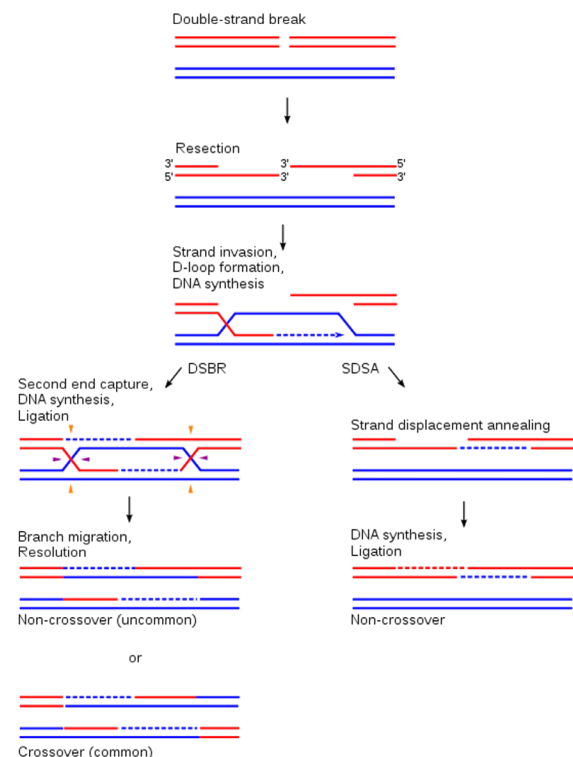
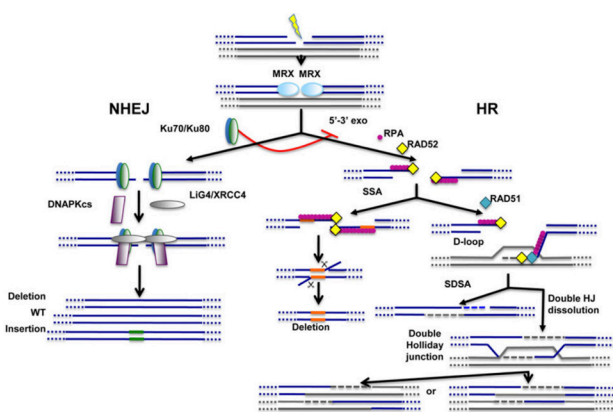


Figure 2. Schematic diagram showing Holliday junctions in two pathways of homologous DNA repair: the double-strand break repair pathway (top and left), and synthesis-dependent strand annealing pathway (top and right).²

Huge numbers of protein molecules are involved, directly or indirectly, in the intricate repair. Perhaps the first task for each molecule is to “understand” with which of many possible repair pathways, for which of many types of damage, and with which of countless possible cooperating repair molecules, it is “supposed” to engage itself. Then there are the other molecules that must “know” how to repeatedly modify these protein molecules along the way, so as to make them “fit” for the successive stages of their work. Then there are all the molecules that need to “watch” the process from outside so that they can collectively “decide” how well the whole process is proceeding in all its aspects, and whether the damage is too great for repair, so that a process of cell death “needs” to be initiated.

If we were to think that genes hold the secret of life, this thought would immediately be contradicted by the companion thought that, whatever the complex capabilities of genes, the cell must stand “knowledgeably” above them, with its ability to repair such complex entities and recommit them to their “proper” roles — or else to “decide” that the irreparably damaged genes are not up to their job and that the cell therefore needs to “sacrifice” itself and recycle its contents for the general “good.”

The quoted terms in the preceding descriptions should be taken as mere placeholders. They are (as often read, anyway) improper — hard to reconcile with the language of respectable scientific description. As placeholders they are merely reminders that we need *some* terms in those places — either by investing the given words with proper meaning, or by finding better words. And it is the clarifying task of biologists to find those meanings and words. With this understanding I will continue using such terms, both quoted and unquoted.

Recognitions of the Problem

It feels misleading to single out examples such as the ones given above, since all physiological processes, when looked at in sufficient depth, involve something like the same complexity, meaning, and end-directedness. The general capacity of biological molecules to contribute holistically and lawfully to functional order and organization rather than to go their own disinterested ways could be considered definitive of life. The molecules are continually “spelling out,” as it were, the open question governing all biological research: “What is the meaning of life?”

The opportunity for biologists is to ask themselves, “What can we say about the not-yet-understood wisdom that shines through organic activity at every level of observation?” The question remains after the physical lawfulness of all the activity is demonstrated, since it is not a question about this lawfulness, but rather about the meaningful and expressive organization of the activity. It seems clear enough that biological processes require us to seek principles of understanding that go beyond the non-violation of physical laws.

We don’t see the same sort of organizing in the non-organic cosmos or in earth’s solar system, or in the sciences of geology and chemistry. But we see it everywhere in biology. No textbook describes DNA damage repair without central reference to the purposiveness of the entire process — the wholeness and healthy functioning of the genome being “aimed at.” Cells and organisms achieve this aim only with a considerable expenditure of energy — that is, only by making a well-directed “effort.”

As I’m sure nearly all biologists would agree, the coherence of such well-organized activity needs a proper scientific accounting. And, in fact, there is a common thought that, somehow, evolution by natural selection must give us the required account. However slowly and however indirectly, it must have supervised the emergence of all the necessary capabilities.

Evolution is said to be a tinkerer, and over time (so the thought goes) it tinkered with all the biological mechanisms constituting the present organism until those mechanisms became more or less efficient at doing the needed thing, whatever that might be. After all, organisms that do the right thing are the ones that survive and reproduce best, so it is not surprising that we see everywhere organisms that have the basic tools for survival. How could it be otherwise? So where’s the problem in that?

But this line of thought leaves untouched the problem we’re looking at now. An evolutionary tinkering with mechanisms that are preserved into the future so that they can be perfected through further tinkering is hardly relevant. All these interacting molecules in a fluid medium must coordinate their intricately organized activity on the fly and in this very moment, without the external guidance of any evident gears, levers, or mechanical contrivances engineered in the distant past.

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the activity of topoisomerases or DNA repair enzymes, we are out of luck. There are no such mechanisms to be found, and I am not aware of anyone claiming to have found them. It seems impossible even to conceive the existence of such devices. So what enduring material *mechanism* is evolution supposed to have been working on, and where do we see any such mechanism guiding the topoisomerases in their second-by-second “brain surgery”?³ To say that evolution fosters the development of needed traits, *whatever they might be* (regardless of their physical implausibility), is much the same as appealing to magic, or saying “Everything is as it is because God made it so.”

The question all this molecular activity poses is not about the prior evolutionary selection of particular mechanisms or structures, but rather about an apparent wisdom that must be brought to bear in a currently unknown fashion upon exactly this moment’s ever-changing, somewhat chaotic, and evolutionarily unprecedented configuration of diverse molecules within the cell’s swirling plasm. Everything must proceed discriminately and without the guidance of any accessible record of historical transactions in similar (but never identical) situations. And this unscripted performance must continue, unpredictably, past the present moment and on to the next, and the next, and the next, without end (until death) — all in order to keep the organism healthily functioning. It is an amazing choreography without an evident choreographer. Yet, just such a performance is uniquely inherent in every different sort of organism. What are we to make of this?

Paul Weiss and the “Restraint” of the Whole

There are two angles I haven’t mentioned yet, from which we might look at the puzzle we are confronting. One was offered to us by the twentieth-century cell biologist and National Medal of Science honoree, Paul Weiss. Reflecting on the degrees of freedom molecules possess in a fluid medium, he concluded that it made no sense, physically, for collections of organic molecules not to go their own way, as opposed to carrying out an endless series of stunningly detailed, functionally efficient, expertly organized performances.

But Weiss had no desire to go beyond the observed facts or to explain them from a position of ignorance. He merely remarked rather dryly that “The resultant behavior of the population [of cellular constituents] as a whole is infinitely less variant from moment to moment than are the momentary activities of its parts.” And so “the system *as a whole* preserves its character” (Weiss 1962, p. 6). That is what he observed.

Or, in somewhat different words: 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)

Weiss sums up the situation in a way that highlights the non-mechanical uniqueness of the molecular configuration in a cell at every moment of the cell’s existence:

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)

We are particularly invited to pause and weigh our ignorance in the presence of these words: “the population as a whole is a system which restrains those degrees of freedom.” What do we actually know, in our present science, about such restraint? Here, perhaps, is one of the opportunities for future biologists to “pull a Galileo” (as Richard Conn Henry put it above) and move biology into a new era of previously unimagined thinking.

The Decisive Role of Context

A second additional angle on our topic is expressed in a current mantra recited time and again in molecular biological writing: just about every molecular interaction in a living cell, we’re told, is context-specific (or context-dependent, or context-sensitive). An alternative word would be “holistic,” if it weren’t anathema in biology. After all, being sensitive to a context just means acting consistently with, or in harmony with, the larger whole in which one finds oneself.

The phrase “context-specific” makes no sense unless it refers to some kind of top-down (“formal”) causation — that is, causation relating to the part’s participation in, and conformity to, the pattern or form or meaning of the whole. This is not the kind of causation that old habits of thought encourage us to acknowledge. That’s why “context-specific,” despite occurring almost everywhere in the biological literature, is defined almost nowhere.

The idea that the whole interpenetrates its parts, thereby helping them to become what they are, reminds us of the way the meaning of speech and text works. It's as if individual words "pay attention" to the meaning of their context, and adapt themselves to it — or, we might say, the context imposes its own meanings upon the words. Or perhaps the adapting and imposing are really a single, harmonious, and indivisible play of meaning. This play must, of course, occur both in the actual production of the speech or text, and in our understanding of it.

It doesn't take a lot of reflection to realize that, if biological activity is context-sensitive, the whole must have something like a causal influence on the part. This is not the usual conception of parts acting upon parts and therefore summing up to the whole. It looks rather more as if the idea or meaning of the whole informs and governs its parts. But to give idea or meaning a causal role in this way is foreign to contemporary scientific thought. Or is it, really? How easy it is to forget that a great part of conventional science consists of explanatory *ideas*, many of which nearly all scientists are perfectly happy to regard as belonging to our causal understanding of the world! This is certainly true, for example, of the mathematical ideas (equations) expressing our conventional understanding of the basic physical forces.⁴

Short of reckoning with the molecular conundrum presented by the topoisomerases as a *problem of meaning*, no one seems to have even a tentative approach to it, and so it fades into the unspoken (and, perhaps, largely unthought) background of biology. Maybe we are approaching a place where we can do better than that.

Unanswered Questions Are a Part of Any Healthy Science

We might put the question we have been dealing with this way: *How do molecules gain whatever passes for their "awareness" of — their ability to interact intelligently in light of — the meanings of the larger cellular and organismal context in which they find themselves?* The problem is that making the question explicit is enough to show that it does not sit comfortably with the acceptable explanatory apparatus of today's biology.

One option is simply to turn from biology to the sciences of the inanimate while assuming that the continuing elucidation of physically lawful processes will sooner or later carry us beyond the stubbornly persistent questions facing biologists. But this no longer looks like a solution once we have recognized the fundamental difference between questions of physical lawfulness and those of meaningful coordination and organization in

relation to an organism's needs, purposes, and interests. Perhaps the "stubborn persistence" of the questions simply reflects this fact.

Yet we must, I think, refuse the idea that molecules, or even cells, have anything we are likely to want to call "awareness" in close analogy with human awareness. But, as I mentioned earlier, we have no choice but to find *some* way to substitute for, or qualify, that word (and others like it). And we are certainly free to ask ourselves whether this problem points us toward the possibility for a refreshingly new science of biology in the future.

I have been suggesting that we cannot account for biological organization merely by tracing a sequence of physically lawful processes. Something "above" that is required. But saying that something more is required is not to explain how the requirement is fulfilled. And I am not about to explain it now, simply because I am not capable of it. It is always good to acknowledge the limits of one's current understanding.

I do, however, recognize at least some of the reasons why we should expect the question or problem we have been looking at — how do biomolecules "know" what to do? — to prove insoluble in the context of today's biology. After all, the most obvious terms in which we might approach the question have long been ruled out by the materialistic commitment implicit in today's biology. That's why the question we are considering is not even being posed by contemporary working biologists — certainly not with any clarity. Where a science lacks the resources even to pose a pressing question, we can hardly expect it to possess the resources for answering that question.

I have already mentioned one root of the problem: biologists have a great difficulty with the notion that ideas — or, more generally, what we might refer to as the *interiority* of the organism (which needn't refer to conscious awareness) — can play anything like a causal role in its life. Ideas are scarcely thought to be real in any fundamental (ontological) sense, let alone to possess some sort of causal power.

Another aspect of the problem lies in the fact that scientists since Galileo have unapologetically tried to rid science of qualities. The problem is that, if they could somehow succeed in this crazily impossible project, they would be left with no observation-based science at all, since all observation of the material world is irreducibly qualitative.⁵ Nor would they have any content from which to abstract quantities. In and of themselves, of course, quantities are not material entities. (Talbot 2023).

To whatever degree we succeed in arriving at quality-free explanatory laws (and it is never 100%), those laws become abstract, universal, and silent about particular things, because things in their particularity simply aren't

there to be recognized in the terms of such laws.

So the seemingly insuperable problem we now face is this: if respectable science can hardly bear to deal at all with observable things in their own, irreducibly qualitative terms — if the world’s lawfulness is required to be universal and detached from the qualities and meanings that distinguish one thing from another — how can we even begin to talk about the “something more” that is the unique, unfolding form and highly coordinated way of being of a trillium or snail or cellular life cycle? The problem is simply invisible to anyone raised up according to the quantitative and materialistic ideals of our present science.

NOTES

1. Figure 1 credit: Decottignies 2013, (CC BY-SA 3.0).
2. Figure 2 credit: emw2012 (CC BY-SA 3.0).
3. It is interesting that evolutionary discussions of physiological processes tend to focus on how new or modified proteins arise in evolutionary history. The focus is on *things*. And yet the more directly relevant question is how the proteins that are there manage to *do what they do*.
4. The ideas bearing on the force of gravity or, say, the dynamics of billiard balls are, of course, a long way from the formative ideas we see at work in organisms. But why should the ideas governing disparate realms of being all be of the same sort? No one has demonstrated inherent limits upon the kinds of ideas that might be embodied in the various phenomena of the material world. Just as we indisputably “see” the mathematics of gravity in planetary motions, we also and with equal persuasiveness “see,” for example, the striving for life evident in all organisms. This is always a species-specific striving that seems quite able to guarantee, for example, the infinitely complex, distinctive, and qualitative pathway from a tiger zygote to a mature tiger.

(Regarding the distinctive way of being for a species, see Craig Holdrege’s whole-organism studies: <https://natureinstitute.org/whole-organism-biology>. And also his book, *Seeing the Animal Whole — And Why It Matters*: Holdrege 2021.)

As far as possible, the physicist tends to seek universal laws that apply to objects without reference to their own character. Hence the appeal to abstracted, universal quantities such as mass and energy. Things with their own character are invisible to such laws. A 5-kilogram meteor and a 5-kilogram groundhog — they’re pretty much the same thing as far as the law of gravity is concerned. On the other hand, biology deals with qualitative behaviors arising from the internal and differentiated characters of the uniquely expressive, more or less individuated “objects” (organisms) it deals with. The biologist’s knowledge of a ground-

hog is not at all the same as the physicist’s knowledge of a rock. The formative ideas are very different in the two cases.

Where physics gives us universal principles of regularity, biology gives us, over evolutionary time, the ever more distinct focal agency of organisms. And this agency can be meaningfully exercised — it can actually *be* agency and culminate in freedom — only in a world of physical regularity. Without such predictable regularity, no act of an agent could mean anything since the consequences of the act could not be known in advance. This complementarity between two very different sorts of formal causation is one of the ways in which organisms and the inanimate world must be understood in relation to each other.

5. If you are thinking of an instrument that provides only a numerical output, don’t. If the reading of the instrument is to be of any scientific use, it can only be because a scientist has employed it in relation to a qualitatively describable phenomenon and then interprets the numbers in terms of that phenomenon. A presentation of numbers by themselves means nothing. Just imagine that I read off to you a series of numbers without any context. What would they mean?

REFERENCES

- Decottignies, Anabelle (2013). “Alternative End-joining Mechanisms: A Historical Perspective,” *Frontiers in Genetics* (April). <https://doi.org/10.3389/fgene.2013.00048>
- Henry, Richard Conn (2005). “The Mental Universe,” *Nature* vol. 436 (July 7), p. 29. doi:10.1038/436029a
- Holdrege, Craig (2021). *Seeing the Animal Whole — And Why It Matters*. Great Barrington MA: Lindisfarne.
- Talbott, Stephen L. (2023). “How the World Lends Itself to Our Knowing,” in *Organisms and Their Evolution: Agency and Meaning in the Drama of Life*. Available online at <https://bwo.life/bk>
- Wang, James C. (2009). *Untangling the Double Helix — DNA Entanglement and the Action of DNA Topoisomerases*. Cold Spring Harbor NY: Cold Spring Harbor Laboratory Press.
- Weiss, Paul (1962). “From Cell to Molecule,” in *The Molecular Control of Cellular Activity*, edited by John M. Allen, pp. 1-72. The University of Michigan Institute of Science and Technology Series. New York: McGraw-Hill.
- Weiss, Paul A. (1971). *Within the Gates of Science and Beyond: Science in Its Cultural Commitments*. New York: Hafner.