Shape, Time and Chemistry: Some Platonic Meditations

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Abstract

The shape of a protein molecule determines its functionality. Until very recently, a protein's three-dimensional shape—what chemists call its "secondary structure"— was thought to result from its "primary structure," the sequence of amino acids that compose it. Current research has challenged this seemingly firm and reasonable assumption. In late-2006, cancer researchers speculated that the *timing* and *pace* of protein production can affect its shape without changing its amino acid sequence. This finding indicates an interesting connection between the molecule's temporal structure (i.e., history) and its shape. We examine the possibility that space-binding and time-binding processes (i.e., molecular structure and bond-formation) are closely linked and that learning to manipulate time by influencing timing may be at least as effective as nanotechnological manipulation of the spatial location of individual atoms and molecules.

The shape of a protein molecule determines its functionality, i.e., its selective reactivity and other important properties. Proteins are constructed within living cells by genes that link basic building blocks, namely amino acids, into a specific sequence that is unique to each protein. Until very recently, a protein's three-dimensional *shape*—what chemists call its "secondary structure"— was thought to be a result its "primary structure," its sequence of amino acids. This is a fact of special interest to protein scientists because a small structural or compositional change results in drastically different functionalities. In 2006, cell biologists [1] working on the knotty research problem of multi-drug-resistance, speculated that the *timing* and *pace* of protein production affects its shape without changing the amino acid sequence. The *MDR1* (for *m*ulti-*d*rug-*r*esistance) gene constructs *p-glycoprotein*, a protein which performs the function of a "toxin pump" that ejects foreign molecules, thus rendering cancer cells drug resistant. Current research has challenged the seemingly firm and reasonable assumption that a protein's shape and thus its function derive from its amino acid sequence. It turns out that *mutant* MDR1 genes can construct p-glycoprotein with the identical primary structure and composition of a p-glycoprotein constructed by regular MDR1, but, surprisingly, its secondary structure (i.e., its 3-D shape) is different. The protein constructed by a mutant gene is incapable of imbedding itself in the cell membrane to function as a toxin pump, thus preventing the cell's multi-drug resistance. The proposed role of *timing* indicates an interesting connection between (a) the molecule's temporal structure, or history, (b) its spatial structure, and (c) its functionality vis a vis interactions with other molecules. The relationship between space-binding processes (structure-building) and time-binding processes (history, development, emergence) has been observed in a variety of complex systems (e.g., cells and ecosystems) and bears further examination.

In the classical framework of science, time plays a small but key role as a metric, and historicity plays virtually no role. Einstein noted that "people…who believe in physics, know that the distinction between past, present, and future is only a stubbornly persistent illusion." Newton's equations do not distinguish between past and future, nor do Einstein's: both treat time as just another dimension of a coordinate system. French philosopher Henri Bergson[2] criticized this tendency to "spatialize time," to reduce it to an extrinsic measure of change. In classical physics, structure is defined primarily as spatial, not temporal.

The science of complex systems exemplifies an alternative paradigm for science, and for the philosophy of science. It presents an opportunity to recognize key limitations of the classical perspective. We may recall that at the end of the 19th century most physicists thought that the science of physics was nearly complete, only minor inconsistencies remained. But they had missed some important aspects of the world: within a few decades, relativity and quantum theory re-opened the world of physics. Science is prone to such episodes of premature closure. The attempt to reduce chemistry and biology to physics, for example, is an implicit effort to make physics function as the ontological and epistemological foundation of all science. But a change of focus has begun and its effects are profound. *Process* ontology[3] becomes prominent as science begins to account for the *creation and emergence* of increasingly complex structure. This trend is best exemplified in Nobel Laureate Ilya Prigogine's work on complex systems in far-from-equilibrium states[4]. Self-organization is a basic ordering principle in complex systems. Chronobiology, which is concerned with the variety of cycles of living cells (e.g., the circadian cycle), attests to the fact that temporal pattern is as *formative* a factor as spatial structure[5]. This idea has ancient roots.

Plato's *Timaeus*[6] is the first text to present the basis of mathematical physics about 2500 years ago[7]. It is also a creation story that envisions a cosmos in which creatures are co-creators. In Plato's cosmos, space, is the "receptacle of becoming," a closed net of mathematical relations embodied in the five "Platonic solids." Of these regular solids, four constitute the microcosmos (fire=tetrahedron, earth=cube, air=octahedron, water=icosahedron), the fifth (dodecahedron) encompasses the macrocosmic whole. Plato's creator god, an "artisan" and geometer, weds the transformational geometry of the 4-element microcosm to planetary orbital geometry: the planets as the "instruments of time" are mathematically related to the motion of atoms. Plato likens planets to the shuttles of a loom, weaving warp and weft into an indissoluble union. The creative power of the Divine Artisan is conveyed to our minds through our senses as we "see through" the cosmos to the patterns it embodies. Plato's myth further suggests that science began with the realization of mathematical order in the timing of celestial events. In doing science we continue the Divine Geometer's creative act by extending the reach of order deeper into the world.

In the *Timaeus*, as in Book VII of his *Republic*[6], Plato subordinates the intelligible framework of science to that of moral and esthetic ideals. Platonic cosmology has an indelible ethical and esthetic agenda. Constructivist, feminist and post-colonial critiques of science have demonstrated that value-neutral science is a chimera. Does this invalidate the findings of western science? Not necessarily. It does, however, obligate us to recognize the limits of objective science. For example, it is clear that medical science and ecosystem restoration are unapologetically agenda-driven; it would be irresponsible to pretend neutrality. Until relatively recent times, we have maintained the myth of science's objectivity. Plato was never dogmatic on this point: he explicitly presents mathematical physics as a cosmic *myth*, and does so in a self-reflexive manner. In the myth and in the telling, both cosmos and cosmology strive continuously, if unsuccessfully, to embody the eternal ideals most readily exemplified in mathematics… and, Plato would hasten to add, all for the sake of the good and the beautiful.

The central problematic of classical physics is: starting from unchanging laws and matter, how do we explain the emergence of new structures? For Plato, Bergson, Whitehead[3], and Prigogine, emergence is the central principle. Their central problematic is: how can we re-order the creative advance of time such that it may better embody the good and the beautiful? Recent approaches to understanding the shape of proteins, as described above, are consistent with a process ontology and suggest that experimental manipulation of timing may be as valuable to chemistry as it is to chronobiology. This alternative mode of science is a "new dialogue with nature," for in self-organizing worlds, creation is dynamic co-creation.

References

[1] Grottesman, et al, "Silent Polymorphism in the *MDR*1" *NIH NEWS* December 21, 2006 (http://www.nih.gov/news/pr/dec2006/nci-21.htm).
[2] Bergson, Henri, *Time and Free Will* (NY: Geo. Allen,1913); *Creative Evolution* (NY: Dover,1911).
[3] Whitehead, A.N., *Process and Reality,* (NY: McMillan, 1927/1976).
[4] Prigogine, I., Stengers, I., *Order out of Chaos: Man's New Dialogue with Nature* (NY: Bantam,1984).
[5] Strogatz, S., *Sync: The Emerging Science of Spontaneous Order* (NY: Hyperion, 2001).
[6] Plato, *The Collected Works,* (NY: Hackett, 1997).
[7] As noted by Heisenberg, Friedlander, Cornford, Vlastos, Folse, and others.