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## **BIOSEMIOTICS AND THE RELATIONAL TURN IN BIOLOGY**

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### **ABSTRACT**

This contribution attempts to synthesize and expand ideas previously presented at these meetings by placing them into a wider framework at the intersection of biosemiotics and current philosophy of biology. In previous investigations I aimed mainly at exploring the connections between two special kinds of relational structures: the networks of self-referential circular loops that appear pervasively in living systems, and the triadic relational structures that Peircean semiotics envisions as the basis of all semiotic transactions.

On the present occasion I attempt to place these concerns within a wider set of emerging ideas that have recently coalesced through both new and concurrent tendencies in separate areas of biology and the philosophy of science. For lack of a better expression, I characterize these partially overlapping trends as the outcomes of a “relational turn” in these disciplines. Indeed, one of the salient commonalities connecting these developments is a shift of attention away from objects and things and towards relational structures and processes, both as the central targets of experimental research, and as the principal conceptual vehicles for explanatory modeling and theorizing.

Increasingly sophisticated research technologies of molecular biology have generated an enormous quantity of experimental data, subsequently sparking a renewed need for relational approaches that help to discern recurrent patterns. Earlier conceptions of relational biology and cybernetics, once deemed too abstract and speculative to make contact with experimental praxis, are now being resurrected and applied through the application of methods made possible by current computational, modeling and simulation tools.

With this in mind, I briefly review aspects of systems biology and some new directions in evolutionary theory, such as epigenetic inheritance, niche construction and ecological engineering. My focus is on the role of circular, downward and reciprocal causation in the constitution of relational structures and dynamical circuits or networks.

Finally, I explore possible avenues of integration and conceptual cooperation between ideas and goals of biosemiotics and ones emerging from the examined new currents in biology. For this purpose I sketch the main features of a parallel relational turn presently manifest in the philosophy of science, rooted in the philosophy of physics and mathematics. This relational turn is a main, explicit tenet of different varieties of structural or relational realism and informational realism. I attempt to assess the potential of this philosophical platform for grounding the integration of biosemiotics with the rest of biology, as well as natural philosophy in general, across disciplinary boundaries.

## Systems biology

There seems to be a quiet revolution afoot within the life sciences. New theoretical and experimental approaches now emerging under the wide – encompassing label of **systems biology** may radically transform the very foundations of the life sciences as well as their relations to other branches of intellectual life. If successful, these perspectives may do for this new century's biology what quantum physics and relativity did for 19<sup>th</sup>-century classical physics. Just as in the case of physics, this portended revolution stems from a philosophical examination and reformulation of basic concepts and implicit beliefs. Such reflections often result in the rejection or modification of notions once deemed fruitful and successful, but which later—as they were pressed to their limits—revealed unsuspected shortcomings.

**One basic standpoint** of systems biology is that there is **no privileged level of functionality**, either within organisms or within the systems they create through their complex interactions: parts act on the wholes they integrate, and these wholes in turn act in a circular fashion upon their components.<sup>1</sup> This view sits in stark opposition to the ideology of genetic determinism and physical and chemical reductionism—an ideology that became entrenched in the life sciences through the enormous success of concepts, methods and techniques applied by molecular biology and other sub-disciplines.

**A second major standpoint** of systems biology is a **shift** from the traditional study of statically-defined structures towards the identification of **dynamical networks** or **circuits** of biochemical processes and the detailed mapping of the regulatory loops that control and maintain biological functions.

While the systems approach to biology has been around for decades (see e.g. von Bertalanffy 1950, Rosen 1958), there are multiple reasons why many experimental biologists have recently re-embraced it. Most notable is the need to

synthesize enormous accumulations of experimental data which result from the outputs of new high-throughput technologies. The ensuing methodologies have opened up the study of living systems, spanning an intricate hierarchy of levels ranging from subcellular systems (e.g., multiprotein complexes and signaling networks) to organelles, cells, tissues and entire organisms and their associations.

These complex systems are modeled by synthesizing experimental data with the aid of mathematical and computational tools capable of revealing unprecedented levels of complexity and compositional detail. Such innovative techniques make it possible for the first time to probe the causal relations connecting microscopic processes (initiated by individual molecules) with their macroscopic effects at the cellular and organismal levels. They also enable researchers to trace back the reciprocal causal nexus from the higher to the lower strata of these hierarchies of complexity.

Such circumstances encourage the tendency to shift focus away from individual parts and structures, and instead to seek ways to discern recurrent patterns and networks of relations among them. This perspective enriches biology through the application of concepts and modeling devices originally conceived by systems engineers, physicists and mathematicians for other unrelated applications.

### **Relational structures and processes**

Theoretical inclinations to favor relational structures over their individual relata are not an exclusive characteristic of systems biology—they seem to be emerging throughout many spheres of intellectual pursuit, including:

- the **philosophy of science** (structural or relational realism, informational realism)<sup>2</sup>

- **mathematics**, where category theory acts as a relational bridge between mathematical sub-disciplines and offers an alternative to set theory in foundational issues<sup>3</sup>
- **physics**, with the emergence of the relational interpretations of quantum mechanics<sup>4</sup>

This relational turn in biology naturally generates interdisciplinary and meta-disciplinary approaches and methodologies. One and the same network of relations may organize disparate systems at totally different scales or levels, from molecules to ecosystems or societies. It can also make its appearance across traditional disciplinary boundaries (e.g. as embodied in electronic circuits as well as in living systems). Teamwork is frequently needed for the simultaneous application of ideas and techniques that have been imported from previously isolated specialties. It seems likely that concepts and discoveries of mathematics and the physical sciences will become integral to the theoretical fabric of biology, and graduate from the primarily ancillary roles to which they have usually been relegated. Consequently, this seems an auspicious time to incorporate biosemiotics' ideas and research results into such an expanded framework.

For our purposes it is important to consider another characteristic of systems biology that may open novel possibilities for integration with biosemiotics: the **radically temporal** and dynamic nature of many of the most important relational structures deployed in living systems. As Pedro Mendes notes:

Data is now becoming available consisting in simultaneous measurements of thousands of cellular components such as mRNA and proteins. If sequences of these are put together they will form movies of the cellular machinery in action, and it should be possible to build dynamic models that describe it. (Mendes 2001).

In cellular biology great progress has been made in the elucidation of the network structure and regulation patterns found in the key biochemical reactions and interactions intrinsic to metabolic and genetic processes. These circuits invariably involve highly complex cascades of signaling events, such as those displayed in signal transduction and propagation. Network interaction diagrams are extremely difficult to map and interpret because of the impact of such factors as noise, history dependence and the actions of feedback loops. Static diagrams, while quite useful, often fail to fully represent temporal event sequences and the interconnected flow of information, matter and energy that is channeled through labyrinthine biochemical circuits.

Similarly, in evolutionary theory and ecology some recent relational trends emphasize temporal relations, historical considerations and a form of circular causality. **Niche construction** is the self-referential and history-driven process by which organisms reciprocally transform each other's niches, influencing their own and each other's evolution. Their actions progressively alter their interrelations of competition and cooperation and transform their relations to the abiotic environment and to the changing selection pressures **simultaneously created by these very activities** (see e.g. Laland *et al.*1999).

A parallel feedback action surfaces in **ecosystems engineering**, a new approach that has recently emerged in ecology. Here organisms are seen as engineers that direct and partially control the flow of energy and matter within their environments. Other new developments in biology, including the recognition of the critical role of non-genomic (epigenetic) transmission of information across generations, likewise reveal the presence of complex, temporal nets of relations. Here again, as with cellular physiology, the tangled, interconnected networks of dynamically changing processes must be depicted by means of intricate diagrams that represent both spatial and temporal relations.<sup>6</sup>

## Biosemiotics and irreducibly triadic relations

From a philosophical point of view, the focus on relations in preference to objects—arising independently in several scientific disciplines, as well as in the philosophy of science—marks a remarkable (if tacit) departure from a widespread, enduring metaphysical trend in modern philosophy and science: **nominalism**. It seems to me that this pervasive nominalistic bias has been a considerable impediment to the reception and assimilation of semiotic ideas into biology.

One of nominalism's most characteristic tenets is the denial of the reality of relations or, at best, their ontological subordination to the reality of their individual relata. In fact, from nominalism's medieval inception through its reception and elaboration by 17<sup>th</sup>-century natural philosophers, the subsistence of entities through the destruction of relations was taken as a criterion of reality. When Ockham applied what Funkenstein calls the "principle of annihilation," real things were identified as those that could be created independently of any other thing, those that would survive the annihilation of everything else in the universe ("*toto mundo destructo*"). (See e.g. Funkenstein 1975, 1986).

A common feature of structural realism in philosophy and of emerging relational interpretations of quantum mechanics is the recognition of the **relational nature of physical reality**, thereby reversing the views of nominalistic ontology. In several of these proposals, relations no longer have a reality subordinated to that of their relata; rather, the reality of any related individual entities becomes dependent on the reality of the relations. Moreover, in some interpretations **reality is relational** in the precise sense that an entity is real only in relation to the other entities with which it interacts. The ultimate elements of physical reality are thus the **relations of interaction between systems**, instead of some ontologically preexistent individuals. According to Carlo Rovelli:

Quantum mechanics is a theory about the physical description of physical systems relative to other systems, and this is a complete description of the world. (Rovelli 1996, p. 1650).

Since the earliest stages of its development, numerous researchers have attempted to ground biosemiotics on the basic ideas of Peircean semiotics (see e.g. Kull *et al.* 2008). Much of the power of Peirce's theory of semiosis stems from **his special brand of relational realism**, based on a sharp distinction between dyadic and triadic relations. Genuine (non-degenerate) triadic relations are not reducible to combinations of dyadic ones, while all other higher-order relations can be constructed out of dyadic and triadic components. Physical interactions (forces) as well as their mathematical representations (vectors, lengths) are paradigmatic instances of dyadic relations, while signs, rules and habits exemplify triadic structures.

Nowadays, within the various disciplines that appear to be undergoing a relational turn, the importance or validity of distinguishing between different orders of relations is rarely considered. Likewise, the assumption that binary combinations of binary relations are sufficient for the depiction of all processes is implicitly made. Yet making and justifying such distinctions would be instrumental in bringing biosemiotics (at least in its Peircean orientation) into the fold of other relational approaches. A few ideas that may help us reach this aim are briefly sketched in the following section.

### **Triadic relations, temporality and self-reference**

Peirce's conception of the triadic structure of semiosis is fundamental for his entire system and intimately tied to the third of his universal categories. Yet he was apparently unable to bring to a satisfactory synthesis his several suggestive insights on the nature of triadicity and, consequently, on the sign relation. Some of these insights, which are hinted at in several places during his later career, are

undeveloped and hard to disentangle from writings addressing such contentious problems as the nature of continuity, modal realism and the final proof of pragmatism.<sup>5</sup> At any rate, and whether or not they turn out to be faithful to the direction of Peirce's thought, I will advance some ideas congenial to those Peircean intimations. I hope they may prove useful to the task of characterizing triadic relations in a way that might foster the integration of biosemiotics within other relational trends in biology and elsewhere. I will concentrate on two unique features of triadic relations, which bear on **the passage of time** and the phenomenon of **self-reference**.

As indicated earlier, the iconic depiction of intrinsically temporal processes in static diagrammatic form tends to obscure the sequences' dynamic character, concealing their before-after relations behind a simultaneous presentation of their relata. This tendency is not confined to diagrams—it appears to be innate in our visual habits of attention and conceptualization.

Early in the last century, Bergson criticized modern science and relativity theory especially, for “spatializing” time. Einstein disagreed but nevertheless recognized the phenomenon here described and considered it the root of errors that marred many defective presentations of his theories.<sup>7</sup> I think spatialization is a special case of a more general tendency that inclines us to reduce higher order relations to (dyadic combinations of) dyadic relations. Dyadic relations are easily and naturally represented as spatial configurations in ordinary diagrams. Genuine triadic relations and some temporal relations, on the other hand, do not seem amenable to complete depiction by such means. Our penchant for visualization appears to seduce us into the “spatialization” of such patterns.

I propose as a working hypothesis that irreducible triadic relations share two important characteristics that Peirce somewhat obliquely indicated: they are **irreducibly temporal** (their relata do not exist simultaneously)<sup>8</sup> and they involve a **self-referential nexus** (their relata relate to themselves through their relations

to the other relata).<sup>9</sup> These two features of temporality and self-reference appear to be intimately interconnected, as was originally discovered by George Spencer-Brown (see Spencer-Brown 1979).

Independently of triadicity the coordinated emergence of temporality and self-reference, along with its logical, mathematical, physical, biological and philosophical implications, has been developed by numerous authors (see e.g. Goudsmit 2007, 2009; Varela 1979; Kauffman 1987, 2002, 2005; Kull 1997).

Some have pointed out its connections with the need to employ imaginary numbers in temporal representations (e.g. Kauffman 1987, 2002, 2005; Shoup 1995; Kampis 1995) and with the presence of feedback loops in computational and biological circuits (e.g. Thomas and Rösler 2006, Bernot *et al.* 2004). These developments are far too complicated and technical to be discussed in this brief communication, but point to some promising avenues for embedding semiotic ideas within a full-fledged relational biology of the future.

In pursuit of this goal one immediate task is to characterize semiotic relations by drawing their contrasts to other types of relations that occur in biological networks. Another concomitant endeavor is to make explicit the peculiar features that distinguish semiosis from other temporal relations (e.g., different kinds of causal actions) that are embedded within the relational fabric of living systems. In the wake of these two undertakings a third desideratum may perhaps be fulfilled: forging a universal concept of *information*; capturing, subsuming and reconciling this notion's multiple roles and acceptations in logic, physics, technology, biology and semiotics.

### **In conclusion**

The current relational trends in science, particularly their present emergence in the life sciences under the label of **systems biology**, afford a welcome opportunity for integrating biosemiotics into the theoretical underpinnings of these disciplines. A clarification and development of the peculiar relational patterns

underlying semiotic transactions (i.e., triadicity, temporality, and self-reference) and of their roles in the overall dynamics of living systems (e.g., metabolism, gene expression, self-regulation, etc.) may propel biosemiotics from its present marginal status into an exalted role within the explanatory core of biology and, more generally, of a genuinely meta-disciplinary natural philosophy. Such a progression would fulfill an ideal first advanced by some of the early founders of systems theory, such as Rashevsky, von Bertalanffy and Rosen: the rising of an authentic **relational biology**.

## Notes

<sup>1</sup> Several recent monographs review the basic ideas and methods of systems biology, with different philosophical biases (see e.g. Kitano 2001, Konopka 2007, Rigoutsos 2007). Denis Noble's *The Music of Life: Biology beyond the Genome* is a very readable non-technical introduction and eloquent manifesto (Noble 2006). Philosophical issues concerning special forms of causation in living systems underlay the systems approach. Recent analyses and key references concerning top-down causation can be found in Auletta *et al.* 2008. Mossio *et al.* 2009 offer a review and a new analysis of the relation of Rosen's conception of "closure to efficient causation" and the issue of computability, backed by an extensive bibliography.

<sup>2</sup>Structural realism encompasses a group of related positions in the philosophy of science that coincide on emphasizing the role of **relational structures**, both in nature and in our theories about nature, updating and reassessing the arguments of some 19<sup>th</sup> and 20<sup>th</sup> century thinkers, such as Poincaré, Duhem, Weyl and Cassirer, whose ideas are closely associated with the importance of focusing on relational notions. Current debates about structural realism stem from a seminal article by Worrall (Worrall 1989). An excellent review of issues and positions is given in Ladyman 2009. An important form of structural realism of special interest for biosemiotics is presented in Floridi 2008. Fernandez 2008 considers other issues relating Peirce's philosophy, structural realism and biosemiotics.

<sup>3</sup>Category theory was incipiently applied by Robert Rosen in his earlier versions of relational biology. A recent introduction to the subject with possible applications to biology can be found in Ellerman 2007. Further discussions on the possible role of these and related mathematical notions in the structure of systems biology are presented in Bailly and Longo 2006.

<sup>4</sup>There are several interpretations of quantum mechanics that fall under this rubric. They have diverse origins but they seem to converge into the same basic idea for overcoming the interpretational problems of the theory: subordination of the notion of objects to that of relational systems. Physical states exist only in relation to other states, including that of the "observer" (which does not need to be a human being or even an organism). A recent review by two prominent advocates is given in Laudisa and Rovelli 2008.

<sup>5</sup> Under the heading of “Peirce’s modal shift” Robert Lane analyzes in detail the tangled interconnections of these issues in Peirce’s later thought. See Lane 2008.

<sup>6</sup> In ecosystems the circuits of nutrients, energy and other transports are usually depicted as trophic networks, or separated following the major cycles (nitrogen, carbon, water), or as global processes, such as primary production and respiration. At present many authors postulate a global time directionality impressed by an ultimate thermodynamic constraint, the maximization of entropy production (see e.g. Ulanowicz 2004, Kleidon 2009, Trefil *et al.* 2009).

<sup>7</sup> In a review of Meyerson’s *La déduction relativiste* Einstein praises the author because he rightly insists “... on the error of many expositions of relativity which refer to the ‘spatialization of time’. Time and space are fused in one and the same continuum, but the continuum is not isotropic. The element of spatial distance and the element of duration remain distinct in nature... The tendency he denounces, although often latent, is nonetheless real and profound in the mind of the physicist, as is unequivocally shown by the extravagances of the popularizers and even of many scientists in their expositions of relativity” (Einstein 1928, cited by Stachel 2007).

<sup>8</sup> For Peirce time is “...that diversity of existence whereby that which is existentially a subject is enabled to receive contrary determinations in existence. Phillip is drunk and Phillip is sober would be absurd, did not time make the Phillip of this morning another Phillip than the Phillip of last night. The law is that nothing dyadically exists as a subject without the diversification which permits it to receive contrary accidents. The instantaneous Phillip who can be drunk and sober at once has a potential being which does not quite amount to existence.” From CP 1.496 (1896) in Peirce 1958. The three relata in semiosis are correlated to the three time “dimensions”: present time with the representamen, past with the object and future with the interpretant. A sign does not exist at any singular, particular instant, just as motion does not exist instantaneously. Like motion, semiosis is radically temporal, in the sense that its parts cannot coexist in the way that spatially individuated objects do.

<sup>9</sup> Peirce refers implicitly on several occasions to the self-referential nature of semiosis but I have not been able to find any explicit articulation of this important issue. The most explicit declaration I have come across reads: “The same form of distinction [as that of immediate and dynamical object] extends to the interpretant; but as applied to the interpretant, it is complicated by the circumstance that the **sign not only determines the interpretant to represent (or take the form of) the object, but also determines the interpretant to represent the sign.** Indeed in what we may, from a point of view, regard as the principal kind of signs [dicisigns], there is one distinct part appropriated for representing the object, and another for representing how **this very sign itself** represents that object [my emphasis].” (From a 1906 letter to Lady Welby, included in Peirce 1998, 477-478).

## References

- Alon, Uri (2007). *Introduction to Systems Biology: Design Principles of Biological Circuits*. Boca Raton, Fla.: Chapman & Hall.
- Auletta, Gennaro; Ellis, G. F. R.; Jaeger, L. (2008). "Top-down causation by information control: from a philosophical problem to a scientific research problem." *Journal of the Royal Society: Interface*, 5, 1159-1172.
- Bailly, Francis and Longo, Giuseppe (2006). *Mathématiques et sciences de la nature: La singularité physique du vivant*. Paris: Hermann.
- Bernot, Gilles; Comet, Jean-Paul; Richard, Adrien; Guespin, Janine (2004). "Application of formal methods to biological regulatory networks: extending Thomas' asynchronous logical approach with temporal logic," *Journal of Theoretical Biology*, 229 (3): 339-347.
- Einstein, Albert (1928). "A propos de la déduction relativiste de M. Emile Meyerson," *Revue Philosophique*, 105: 161–166.
- Ellerman, David (2007). "Adjoint and emergence: applications of a new theory of adjoint functors." *Axiomathes*, 17: 19–39.
- Fernandez, Eliseo (2008). "Peirce in 21st Century Science and Philosophy: New Prospects" III Jornadas "Peirce en Argentina" Buenos Aires, September 11-12, 2008. Available at [http://www.lindahall.org/services/reference/papers/fernandez/P\\_en\\_A\\_English.pdf](http://www.lindahall.org/services/reference/papers/fernandez/P_en_A_English.pdf)
- Floridi, L. (2008). "A Defense of Informational Structural Realism," *Synthese*, 161 (2): 219-253.
- Funkenstein, Amos (1975). "Descartes, eternal truths, and the divine omnipotence," *Studies in History and Philosophy of Science Part A*, 6 (3): 185-199.
- (1986). *Theology and the Scientific Imagination from the Middle Ages to the Seventeenth Century*. Princeton: Princeton University Press.
- Goudsmit, Arno L. (2007). "Some reflections on Rosen's conceptions of semantics and finality." *Chemistry and Biodiversity*, 4, 2427-2435.
- \_\_\_\_\_ (2009). "Sense and self-referentiality in living beings." *Biosemiotics*, 2 (1): 39-46.
- Gunji, Yukio; Nakamura, Takashi (1991). "Time reverse automata patterns generated by Spencer-Brown's modulator: invertibility based on autopoiesis," *Biosystems*, 25 (3) 151-177.
- Gunji, Yukio; Shirakawa, Tomohiro; Niizato, Takayuki (2008). "Life driven by damaged damage," *Progress of Theoretical Physics, Supplement* 173, 26-37.

- Kampis, George (1995). "Computability, Self-Reference, and Self-Amendment," *Communication and Cognition*, 12 (1-2): 91-109.
- Kauffman, Louis H. (1987). "Self-reference and recursive forms," *Journal of Social and Biological Structures*, 10(1) 53-72.
- \_\_\_\_\_ (2002). "Time, Imaginary Value, Paradox, Sign and Space," Available at <http://www.math.uic.edu/~kauffman/TimeParadox.pdf>
- \_\_\_\_\_ (2005) "EigenForm," *Kybernetes*, 34 (1/2): 129-150. Available at <http://www.math.uic.edu/~kauffman/Eigen.pdf>
- Kauffman Stuart A.; Logan, R. K.; Este, R.; Goebel, R.; Hobill, D.; Shmulevich, I. (2008). "Propagating organization: an enquiry," *Biology & Philosophy*, 23 (1): 27-45.
- Kitano, Hiroaki (ed.) (2001). *Foundations of Systems Biology*. Cambridge, Mass.: MIT Press.
- Kleidon, Axel (2009). "Nonequilibrium thermodynamics and maximum entropy production in the Earth system," *Naturwissenschaften* 96 (6): 653-677.
- Konopka, Andrzej (ed.) (2007). *Systems biology: Principles, Methods, and Concepts*. Boca Raton: CRC Press/Taylor & Francis.
- Kull, Andreas (1997). "Self-reference and time according to Spencer-Brown," In "Time, Temporality, Now. Atmanspacher, Harald and Ruhnau, Eva (Eds.). Berlin: Springer, 71-79.
- Kull, Kalevi; Emmeche, Claus; Favareau, Donald (2008). "Biosemiotic questions," *Biosemiotics* 1 (1): 41-55.
- Ladyman, James (2009). "Structural Realism," *The Stanford Encyclopedia of Philosophy*. Available at: <http://plato.stanford.edu/entries/structural-realism/>
- Lane, Robert (2007). "Peirce's modal shift: from set theory to pragmatism," *Journal of the history of philosophy* 45 (4): 551-576.
- Laudisa, Federico and Rovelli, Carlo (2008). "Relational quantum mechanics," *The Stanford Encyclopedia of Philosophy*. Available at: <http://plato.stanford.edu/entries/qm-relational/>
- Mendes, Pedro (2001). "Modeling large biological systems from functional genomic data: parameter estimation," In Kitano 2001, 163-186.
- Mossio, Matteo; Longo, Giuseppe; Stewart, John (2009). "A computable expression of closure to efficient causation," *Journal of Theoretical Biology* 257: 489-498.
- Noble, Denis (2006). *The Music of Life: Biology beyond the Genome*. New York: Oxford University Press.

Peirce, Charles S. (1958). *Collected papers of Charles Sanders Peirce*, vols. 1–6 (1931–1935), Charles Hartshorne & Paul Weiss (Eds.); vols. 7–8 (1958) Arthur Burks (Ed.). Cambridge: Harvard University Press.

\_\_\_\_\_ (1998). *The Essential Peirce: Selected Philosophical Writings*. Volume 2 (1893–1913). Peirce Edition Project (Ed.). Bloomington & Indianapolis: Indiana University Press.

Rigoutsos, Isidore and Stephanopoulos, Gregory (eds.) (2007). *Systems Biology*. New York: Oxford University Press.

Rovelli, Carlo (1996). "Relational quantum mechanics," *International Journal of Theoretical Physics*, 35, 1637–1678. Also available at arXiv:quant-ph/9609002

Shoup, Richard G. (1995). "Space, Time, Logic, and Things," *PhysComp '94 Workshop on Physics and Computation*. (1994 : Dallas, Tex.). Los Alamitos, Calif.: IEEE Computer Society Press. Also available at <http://www.boundarymath.org/papers/SpaceTime.pdf>

Spencer-Brown, George (1979). *Laws of Form*. New York: E. P. Dutton, 3rd edition.

Stachel, John (2007). "A World Without Time: The Forgotten Legacy of Gödel and Einstein," (review) *Notices of the American Mathematical Society* 57 (7): 861–868.

Thomas, René and Rösler, Otto E. (2006). "Genèse de forme," *Revue des Questions Scientifiques*, 177 (3-4): 279–296.

Trefil, James; Morowitz, Harold J.; Smith, Eric (2009). "The Origin of Life. A case is made for the descent of electrons," *American Scientist*, 97(1): 206–213.

Ulanowicz, Robert E. (2004). "Quantitative methods for ecological network analysis," *Computational Biology and Chemistry* 28 (2004): 321–339.

Varela, F. J. (1979). *Principles of biological autonomy*. New York: Elsevier.

Worrall, James (1989). "Structural realism: The best of both worlds?" *Dialectica*, 43: 99–124.