BioSystems 164 (2018) 121–127

Contents lists available at ScienceDirect

BioSystems

journal homepage: www.elsevier.com/locate/biosystems

Causation, constructors and codes

Jan-Hendrik S. Hofmeyr

Centre for Complex Systems in Transition and Department of Biochemistry, University of Stellenbosch, Private Bag X1, Matieland 7602, South Africa

ARTICLE INFO

Article history:
Received 24 August 2017
Received in revised form 7 September 2017
Accepted 8 September 2017
Available online 13 September 2017

Keywords:
Aristotelan causation
Formal cause
Universal constructor
Rosen's paradox
Organic codes

ABSTRACT

Relational biology relies heavily on the enriched understanding of causal entailment that Robert Rosen's formalisation of Aristotle's four causes has made possible, although to date efficient causes and the rehabilitation of final cause have been its main focus. Formal cause has been paid rather scant attention, but, as this paper demonstrates, is crucial to our understanding of many types of processes, not necessarily biological. The graph-theoretic relational diagram of a mapping has played a key role in relational biology, and the first part of the paper is devoted to developing an explicit representation of formal cause in the diagram and how it acts in combination with efficient cause to form a mapping. I then use these representations to show how Von Neumann's universal constructor can be cast into a relational diagram in a way that avoids the logical paradox that Rosen detected in his own representation of the constructor in terms of sets and mappings. One aspect that was absent from both Von Neumann's and Rosen's treatments was the necessity of a code to translate the description (the formal cause) of the automaton to be constructed into the construction process itself. A formal definition of codes in general, and organic codes in particular, allows the relational diagram to be extended so as to capture this translation of formal cause into process. The extended relational diagram is used to exemplify causal entailment in a diverse range of processes, such as enzyme action, construction of automata, communication through the Morse code, and ribosomal polypeptide synthesis through the genetic code.

1. Introduction

One of Robert Rosen's seminal contributions to science was the rehabilitation and formalisation of Aristotle's four causes, in terms of which he was able to formulate the fundamental theorem of relational biology as "A natural system is an organism if and only if it closed to efficient causation" (Rosen, 1991). This concept of organisational closure also underlies Maturana and Varela's concept of autopoiesis (Maturana and Varela, 1980). The distinguishing feature of organisms is therefore the attribute of autonomous self-fabrication (Hofmeyr, 2007, 2017), an attribute which is also claimed for Neumann's kinematic self-reproducing automaton (Von Neumann and Burks, 1966).

When Rosen (1959b) recast Von Neumann's description of the self-reproducing kinematic automaton into the formalism of sets and mappings, he detected a logical paradox that, if true, would make the existence of such an automaton untenable. To date this paradox has not been resolved, although there have been attempts, e.g., Guttman (1966). The core of the kinematic automaton is a so-called universal constructor, A, that builds a machine X from component parts S according to $\phi(X)$, the description of X. As will be shown in this paper, the crux of the problem lies in how formal cause, the description of $\phi(X)$, is incorporated into Rosen's formalism of sets and mappings when it is a separate object from the efficient cause, the constructor A.

The core of this paper is therefore a re-examination of how formal cause is related to the other three Aristotelean causes (material, efficient, final), in particular how formal cause should be incorporated in the graph-theoretic relational diagram of a mapping, which is the fundamental unit on which relational biology is built (Louie, 2009, 2013). The realisation that efficient and formal cause act together as a unit, instead of formal cause being treated on the same level as material cause, leads to a formulation of the relational diagram that, when applied to the Von Neumann kinematic automaton architecture, avoids Rosen's paradox.

I also consider an associated problem, one that has been ignored by all of the foregoing treatments of self-fabricating systems, including the Von Neumann automaton. If formal and efficient cause are separate entities, then formal cause, as information, must exist in some descriptive (encoded) form which the efficient cause must be able to read and decode if it is to translate the information into action. This makes a code that translates signs into meaning, to use the semiotic description of a code, a logical necessity. After pre-

E-mail address: jhsh@sun.ac.za

https://doi.org/10.1016/j.biosystems.2017.09.008
0303-2647/

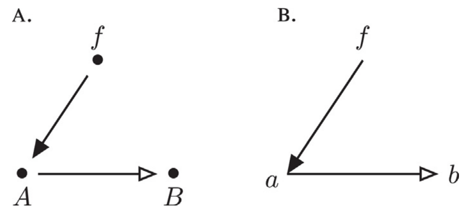

Fig. 1. Graph-theoretic relational diagram (A) of the mapping $f: A \rightarrow B$. (B) Element-chasing form of diagram (A).

senting the formal definition of codes in general, and organic codes in particular, I show how the relational diagram of a mapping can be extended to incorporate the code that interfaces between formal and efficient cause. This establishes a crucial link between relational biology (Rashevsky, 1954; Rosen, 1991; Louie, 2009, 2013) and the burgeoning field of code biology (Barbieri, 2003, 2015).

2. Rosen's formalisation of Aristotelean causation

Aristotle (1992, 1998) regarded science as being concerned with "the why of things", and formulated four different ways of replying "because" to the question "why X?", insisting that all four answers were needed for full understanding. These four *aitia*, as he called them, are now known as material, efficient, formal, and final causes, but they are not causes in the common sense of a prior event causing a later event, but rather "becauses" or explanatory factors, each corresponding to a different category of information (Ackrill, 1981). Together, these independent and inequivalent categories are sufficient for the understanding of the material phenomenon in question (Rosen, 1989). To explain material objects, Cohen (2008) suggested replacing the noun *cause* with the verb *make*, so that to explain object X in Aristotle's sense one should ask:

1. What is X *made out of*? (its material cause)
2. What *makes* (in the sense of *what is it to be*) X? (its formal cause)
3. What *makes* (in the sense of *what produces*) X? (its efficient cause)
4. What is X *made for*? What is its *purpose* or *function*? (its final cause)

One of Robert Rosen's seminal scientific contributions was the formalisation of Aristotelean (be)causation (Rosen, 1991, 2012). Whereas Aristotle only listed his four causes hierarchically, Rosen realised that they stand in a particular relation to each other, a relation that is captured by a mathematical mapping, more generally a morphism in category theory. If B is regarded as the entity to be explained (the effect), then in the mapping $f: A \rightarrow B$ the *material cause* of B is A, and the *efficient cause* of B is f. There is, however, nothing in the mapping $f: A \rightarrow B$ that can be identified with the final cause of B, and there is nothing in the mapping that can explain A and f in terms of material and efficient causes. The *final cause* of B relates to what is entailed by B, i.e., something for which B is either the material or efficient cause (or formal cause, which we will come to in due time). The final cause of B would be something outside the mapping, such as C in a paired mapping $g: B \rightarrow C$, where B is the material cause of C. In the mapping $f: A \rightarrow B$ only A and f entail something, namely B, which therefore acts as their final cause; this is equivalent to saying that the *function* of A and f is to entail B, just as the function of B is to entail C.

The mapping $f: A \rightarrow B$ may also be expressed in category theoretical terms as $f \in H(A, B)$, where the hom-set $H(A, B)$ is a set of mappings from A to B. In element-chasing terms the mapping is $f: a \mapsto b$, where $a \in A$ and $b \in B$ are related by $b = f(a)$ (Louie, 2013). Fig. 1(a) shows a relational diagram of the mapping in graph-theoretic form, which was introduced by Rosen (1991) and refined by Louie (2009, 2013). Fig. 1(b) shows the element-chasing form of the diagram.

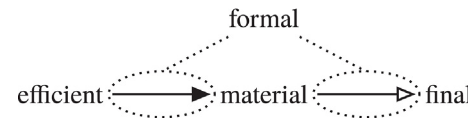

Fig. 2. The relationship between the four Aristotelean causes proposed by Louie and Kercel (2007). The labelling of the effect of the mapping as final cause (B in the mapping $f: A \rightarrow B$), relates to what entails that effect, namely the material, efficient and formal causes. As discussed in the text, its own final cause, that which is entailed by it, would lie outside the diagram to the right.

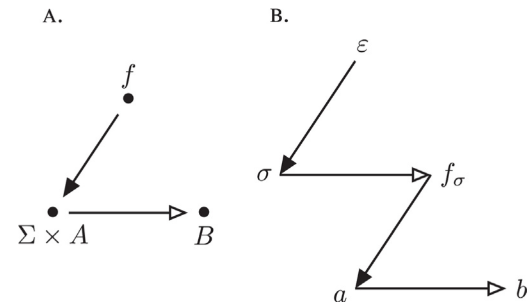

Fig. 3. Graph-theoretic relational diagrams of the expanded mapping $f: \Sigma \times A \rightarrow B$. Diagram (A) unfolds to hierarchical composite diagram (B), in which $\varepsilon: \sigma \rightarrow f_\sigma$ is a "choice mapping" that selects $f_\sigma \in H(A, B)$ for each parameter set $\sigma \in \Sigma$.

3. A formal representation of formal cause

Whereas the material cause and efficient cause of B (or b) can clearly be identified with A (or a) and f respectively, it is not obvious where the *formal cause* of B (or b) fits in. Louie and Kercel (2007) took the structure of the mapping itself, i.e., the ordered pair of solid-headed and hollow-headed arrows, to represent the formal cause, leading them to propose the diagram in Fig. 2 as a representation of the relationship between the four causes.

For the purpose of this paper this conception of formal cause is unsuitable, and I return to Rosen for an alternative view of how formal cause fits into the relational diagram, and where the formal cause can be identified with a particular entity, as can the other causes. Rosen (1989) considered the situation where f is defined on the larger set $f: \Sigma \times A \rightarrow B$, so that $f \in H(\Sigma \times A, B)$. In the category of sets and mappings **Set** there is a natural isomorphism

$$H(\Sigma \times A, B) \cong H(\Sigma, H(A, B))$$

that allows a mapping $f \in H(\Sigma \times A, B)$ in the left-hand side of the isomorphism (Fig. 3(a)) to unfold into its isomorphic image on the right-hand side of the isomorphism, namely the hierarchical composite diagram in Fig. 3(b) (Louie, 2009). The mapping $\varepsilon: \sigma \mapsto f_\sigma$ is a "choice mapping" that selects $f_\sigma \in H(A, B)$ for each parameter set $\sigma \in \Sigma$. In the language of relational biology, $\varepsilon: \sigma \mapsto f_\sigma$ is the *functional entailment* of the mapping $f_\sigma: A \rightarrow B$ (Rosen, 1991; Louie, 2009).

Each $\sigma \in \Sigma$ therefore determines a mapping $f_\sigma: A \rightarrow B$, defined by $f_\sigma = f(\sigma, a)$. If, for example, $f(\sigma, a) = \sigma a$ and parameter $\sigma \in \mathbb{N}$, where $\mathbb{N} = \{0, 1, 2, 3, \ldots\}$, then each value of σ determines a particular function f_σ in the family of parameterised functions $H(A, B) = \{f_0, f_1, f_2, \ldots\}$, where $f_0 = 0, f_1 = a, f_2 = 2a$, etc.

It is clear that the relation of σ to effect $b = f_\sigma(a)$ is quite different and independent from that of a and f, and, upon reflection, can be identified with the *formal cause* of $b = f_\sigma(a)$.

Consider as an example the question *Why a table?*: its *material* cause is the wood, glue and screws, its *efficient* cause the carpenter, and its *formal* cause some plan showing a flat top with legs. The

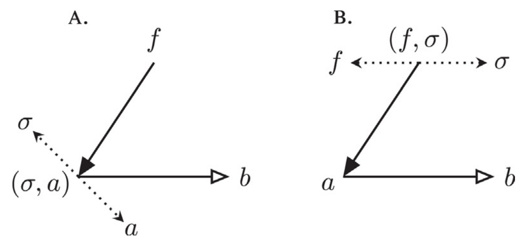

Fig. 4. Two possible ways to depict a relational diagram in which the efficient cause and formal cause are separate entities. In diagram A the pair (a, σ) is an element in the Cartesian product $A \times \Sigma$, while in diagram B the pair (f, σ) is an element in the Cartesian product $f \times \Sigma$. The dotted arrows are projection maps that allow a, f and σ to appear as individual entities in the diagram, which in turn would allow them to be the source or target of other arrows in an expanded diagram. The reason for preferring diagram B is discussed in the text.

final cause of the table could be a surface to write or eat on; the table would then serve as material cause for such a surface. Recall that if $f : a \mapsto b$ were to be paired with the mapping $g : b \mapsto c$, then b (table) would be the material cause of c (surface), and c the final cause of b. The carpenter is a general "operator", or "processor" such as f in the mapping $f : \Sigma \times A \to B$. While the table can be identified with both $b = f(\sigma, a)$ and $b = f_\sigma(a)$, it is only in the latter that σ can be unambiguously identified with formal cause; in $b = f(\sigma, a)$, parameter set σ is not causally distinguishable from a because both are stipulated at the level of the material cause of b. In contrast, σ in the hierarchical composite diagram in Fig. 3(b) plays the role of material cause of f_σ, as part of which it acts as the formal cause of that which is entailed by f_σ, namely b. How should one interpret this dual nature of σ? Consider again the example of the table: think of σ as a concrete drawing of the table that the mapping $\varepsilon : \sigma \mapsto f_\sigma$ "plants" in the head of the carpenter, f, as an image of the table (the σ in f_σ), so "informing" the carpenter who can then construct the table b from materials a without further consulting the drawing. One should therefore think of σ as a concrete category of information that "informs" f, thereby making f_σ the "informed" efficient cause of b. This makes clear that efficient cause and formal cause should be thought of as acting together as one: without being informed by formal cause the efficient cause has operator potential but no agency. Without a plan the carpenter is unable to function; without a carpenter the plan remains unimplemented.

Efficient cause and formal cause can be associated with the same entity, as would be the case when the carpenter works only from a table plan in his head (Fig. 3(b)), or they can be separate entities, such as when the carpenter works only from a concrete drawing of the table and not from the image in his head. In the latter case the question arises of how formal cause should be incorporated into the relational diagram. Fig. 4 shows the two possibilities. Just as Fig. 3(b) makes the fusion of efficient and formal cause into a single entity clear, so Fig. 4(b) shows the association between efficient and formal cause when they are separate entities but still combine to operate as one. In fact, the mapping for this situation would be $(f, \sigma) : A \to B$, where (f, σ) is a mapping in the family of mappings $H(A, B) = f \times \Sigma$. As in Fig. 3(a), σ in Fig. 4(a) cannot be causally distinguished from the material cause a of effect b. One could of course argue that formally these two descriptions are equivalent, and there is no reason to prefer one over the other. However, in the next section we shall see that the logical paradox that Rosen (1959a) found in Von Neumann's (1951) description of a self-reproducing automaton resulted from Rosen's use of the mapping $f : \Sigma \times A \to B$, and that this paradox evaporates when the mapping $(f, \sigma) : A \to B$ is used instead (as suggested by Hofmeyr (2007)). This example will place the two representations in stark relief against each other and provide a decisive argument in favour of the diagram in Fig. 4(b).

Fig. 5 summarises the two ways in which formal cause can be incorporated into the relational diagram of a mapping, depending

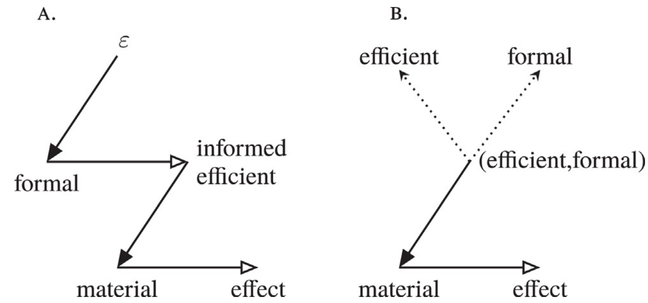

Fig. 5. Incorporating formal cause into the graph-theoretic relational diagram of a mapping. (A) Formal cause and efficient cause are associated with a single entity, the "informed" efficient cause (Fig. 3(b)). (B) Formal cause and efficient cause are separate entities that combine to form the mapping (Fig. 4(b)). The dotted arrows are projection maps.

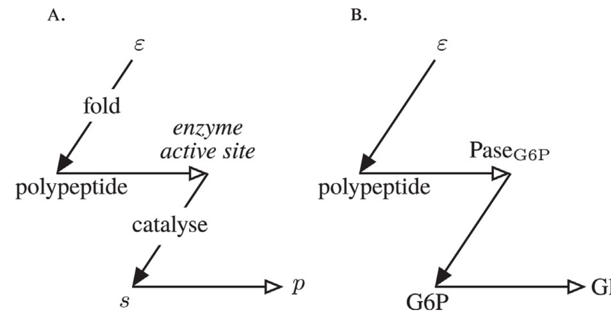

Fig. 6. Hierarchical composite diagram (A) of an unfolded, non-functional polypeptide serving both as material cause of an enzyme and, through the substrate specificity of the enzyme active site, as formal cause of the enzyme product, p. The intracellular milieu, ε, is the efficient cause of the folding of the polypeptide into the functional enzyme, which catalyses the conversion of substrate s to product p. (B) The same diagram for the enzyme glucose-6-phosphatase, $\mathrm{Pase_{G6P}}$, discussed in the text. G6P: glucose-6-phosphate; Glu: glucose.

on whether formal cause and efficient cause are fused in a single entity, or whether they are separate entities working together as one. It now remains to show examples of how the two forms of the diagram are realised.

A particularly clear biological realisation of Fig. 5(a) is an enzyme that catalyses a reaction in which substrate(s) from set S are converted into product(s) in set P, assuming that, as for almost all biochemical reactions, the reaction rate in the absence of enzyme is negligible. The enzyme protein is synthesised as a chain of amino acids, a polypeptide, which in its unfolded state is non-functional. The particular chemical environment provided by the intracellular milieu acts as efficient cause of the folding of the polypeptide into the conformation that contains the active site where substrate binding and catalysis takes place (Fig. 6(a); see Hofmeyr (2017) for a detailed discussion of the role of the intracellular milieu in the closure to efficient causation of the cell).

Enzyme action always has two aspects, both associated with the active site, namely catalytic specificity and substrate specificity. Catalytic specificity determines the type of reaction that the enzyme catalyses; substrate specificity determines which substrate(s) it binds. For example, the catalytic specificity of a phosphatase determines that it catalyses hydrolytic dephosphorylation, while its substrate specificity determines on which particular phosphorylated substrate it acts. So, glucose-6-phosphatase is the enzyme in the phosphatase family $H(S, P)$ that is specific for glucose-6-phosphate, i.e., $\mathrm{Pase_{G6P}} \in H(S, P)$ (Fig. 6(b)). "Pase" denotes the broad enzyme family of phosphatases, while the subscript "G6P" picks out a specific enzyme from within that family on the basis of its substrate specificity: it instantiates a particular phosphatase, giving it an identity, just as σ above instantiated a particular map-

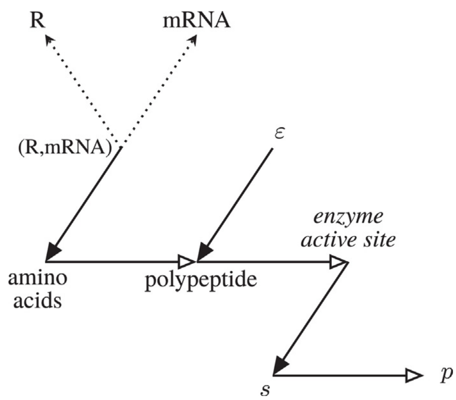

Fig. 7. The relational diagram on the left is of a mapping in which formal cause and efficient cause are associated with separate entities, here ribosome, R, and mRNA respectively, that together polymerise amino acids into a polypeptide (equivalent to Fig. 5(b)). This figure also shows how the enzyme catalysis diagram in Fig. 6(a) links to the synthesis of the enzyme's polypeptide.

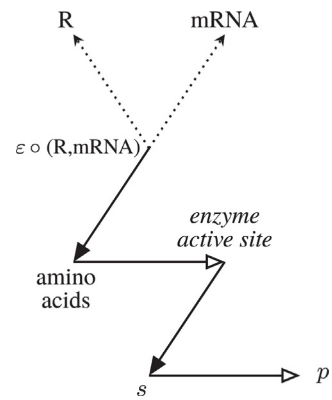

Fig. 8. The relational diagram Fig. 7 in which the two left-most mappings have been composed to form the mapping $\varepsilon\circ$ (R,mRNA).

ping f_σ, singling it out from the hom-set of mappings $H(A, B)$. This allows us to refine our conception of formal cause of an enzyme reaction by identifying it with substrate specificity, while the efficient cause is identified with catalytic action.

We saw previously that σ in the hierarchical composite diagram in Fig. 3(b) is at the same time the material cause of f_σ and, by informing f, the formal cause of that which is entailed by f_σ, namely b. Here we have an exact analogue: the unfolded polypeptide not only serves as the material cause of the enzyme protein, but its specific amino acid sequence provides the information for the substrate specificity of the active site, the formal cause of the product of the active site, namely p.

In phosphatases, as in most enzymes, both catalytic and substrate specificity are determined by the same active site, but there are enzymes, such as proteases, in which catalytic and substrate specificity are determined by distinct sites on the enzyme. Even so, both efficient cause (catalytic action) and formal cause (substrate specificity) still remain associated with the same material entity (the enzyme protein).

A biochemical analogue of the situation in Fig. 5(b), where efficient and formal cause are separate entities, is the production of a polypeptide from amino acids by a ribosome (efficient cause) using the sequence information in an mRNA (formal cause); see Fig. 7. On its own the ribosome is non-functional: it needs to be associated with an mRNA to become functional and to be formally describable as a mapping (the mapping on the left in Fig. 7). The direct substrates for the synthesis of polypeptides are of course aminoacyl-tRNAs and not free amino acids; I come back to this later. Fig. 7 also shows how this diagram directly links with the previous example of an enzyme-catalysed reaction. The combined diagram shows a nested cascade of formal causes: sequence information in mRNA as the formal cause of the amino acid sequence of the polypeptide, which in turn through folding determines the substrate specificity of the active site, which is the formal cause of the product, p, of the enzyme-catalysed reaction.

Up to now I have only considered the "becauses" of the question *Why b?*, i.e., the Aristotelean causes of the effect of the mapping $f_\sigma: a \mapsto b$ (for the sake of simplicity I stick to the element-chasing form of the mapping). In the same vein we may of course also ask what the causes are that functionally entail the mapping $f_\sigma: a \mapsto b$. Just as we had to look for at least the material, efficient and formal causes of b in the mapping $f_\sigma: a \mapsto b$, so should we look for these causes of f_σ in the functional entailment mapping $\varepsilon: \sigma \mapsto f_\sigma$. Material and efficient causes are clear: respectively they are σ and ε. Because f_σ itself entails something—it is the efficient cause of b—it also has a final cause, namely b. Formal cause is not made explicit in the mapping $\varepsilon: \sigma \mapsto f_\sigma$, but in keeping with what has gone before, it must be informing the efficient cause ε, i.e., it must be something that either parameterises ε or associates with ε as a separate entity. I refer to the diagram in Fig. 8 to explain the latter situation. In this diagram the two left-hand mappings in Fig. 7 have been composed into the mapping $\varepsilon\circ$ (R,mRNA). The question *Why f_σ?* is now *Why enzyme active site?* Amino acids are the material cause; the ribosome, R, operating in the correct intracellular milieu, ε, is the efficient cause; and mRNA is the formal cause—the nucleotide sequence information in mRNA ultimately determines the identity of the enzyme in terms of what it does and on what it acts.

With a clear understanding of how the four Aristotelean causes fit together we now see whether we can use this to resolve the paradox that Rosen detected in Von Neumann's description of a self-reproducing kinematic automaton.

4. Von Neumann's universal constructor and Rosen's paradox

Towards the end of his life John von Neumann turned to the study of self-reproduction, which his untimely death from cancer in 1957 prevented him from completing. In Von Neumann and Burks (1966, Fifth Lecture) he described an automaton that could reproduce itself. In his notation, the automaton $A+\phi(X)$ consists of a *universal constructor* A combined with the description $\phi(X)$ of a machine X. A builds X from component parts S according to $\phi(X)$. Supplied with its own description $\phi(A)$, A builds a copy of itself. To give automaton $A+\phi(X)$ the ability to not only build X but also copy $\phi(X)$, Von Neumann added a description copier B and a controller C, so that the automaton becomes $(A+B+C)+\phi(X)$ (see Fig. 9). Supplied with its own description, $\phi(A+B+C)$, A can build $(A+B+C)$ and B can make a copy of $\phi(A+B+C)$, which, when assembled, creates a new copy of the full automaton $(A+B+C)+\phi(A+B+C)$, amounting to self-reproduction of the automaton. Von Neumann and Burks (1966) described this particular architecture as the *kinematic model of self-reproduction*. Fig. 10 sums up this self-reproduction process.

When Rosen (1959b) recast the universal construction aspect of Von Neumann's architecture—$A+\phi(X)$ constructs X from component parts S according to description $\phi(X)$—in terms of sets and mappings, he detected a logical paradox in the self-construction process where A is provided with its own description $\phi(A)$, which, if proved impossible to resolve, would make the existence of a self-reproducing automaton untenable.

Previously, Rosen (1958) had shown that an arbitrary single-output automaton can be represented by the mapping $f: A \rightarrow B$, where A is the set of admissible inputs and B the set of admissible outputs. In Rosen's formulation f is equivalent to X in Von

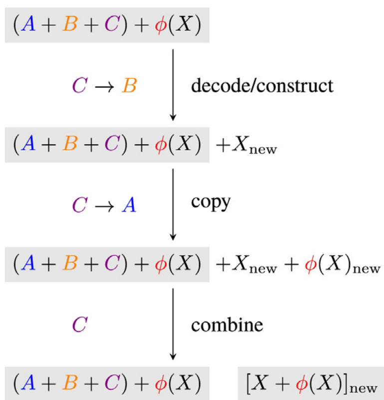

Fig. 9. Von Neumann's universal constructor. *A* is the constructor, *B* the description copier, and *C* the controller that switches the system from construction mode, to description-copying mode, to assembly mode.

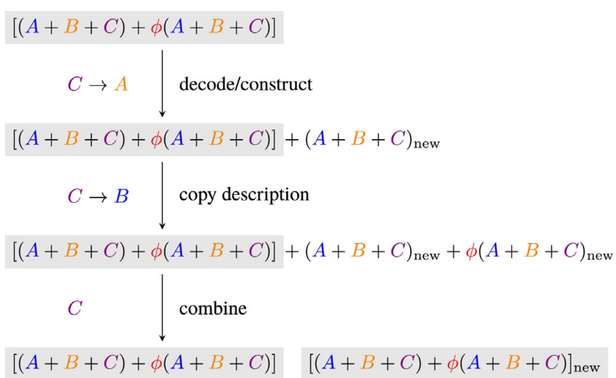

Fig. 10. Von Neumann's self-reproducing kinematic automaton in which the automaton $(A+B+C)$ is supplied with its own description $\phi(A+B+C)$.

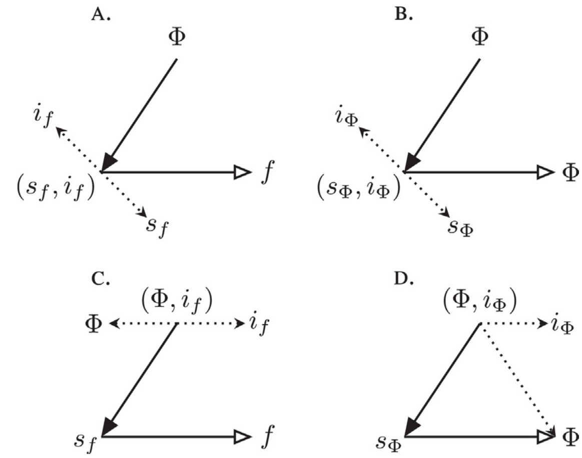

Fig. 11. Two possible ways to depict the relational diagram of a universal constructor, using Rosen's (1959b) symbolism. (A) and (C) diagram the construction of *f*, while (B) and (D) diagram the construction of Φ. Diagrams A and B correspond to the diagram in Fig. 4(a). When the output of the mapping is Φ itself, as in diagram B, it leads to Rosen's paradox. Diagrams C and D correspond to the diagram in Fig. 4(b). When the output of the mapping is Φ itself, as in diagram D, there is no paradox, since Φ itself is not a mapping.

Neumann's description. Rosen now considered what he called a *universal automaton* Φ that can construct automaton *f* from a set of environmental materials S_f when provided with the description i_f of *f*. In Rosen's formulation this output automaton would be $f = \Phi(S_f, i_f)$; the relational diagram is given in Fig. 11(a). When Φ is supplied with its own description i_Φ it would seem that it can construct itself from materials S_Φ; the output of the process would be $\Phi = \Phi(S_\Phi, i_\Phi)$ (Fig. 11(b)). But this is exactly where the logical paradox arises: on the one hand, no mapping can be defined before its domain and codomain are stipulated; on the other hand, the range, since it contains the mapping Φ itself as an element, cannot be stipulated before the mapping is given. Thus, in the words of Rosen (1959b), "neither the mapping Φ nor its range can be specified *until the other is given* [italics in original]." Previously, Wittgenstein also reasoned that no function can be its own argument (Wittgenstein, 1921, aphorism 3.333). Kampis (1991, p. 212) discussed this situation under the heading "self-acting functions" and noted the formal problem that "no mathematical function can belong to its own domain or range".

However, in the light of the previous discussion of the role of formal cause in the relational diagram of a mapping, it is clear that the paradox can be avoided by recasting the problem in the form of Fig. 11(c) and (d). The crucial point is that in Rosen's formulation Φ is a mapping that acts on the pair (S_f, i_f), as in Fig. 11(a), while in Von Neumann's terms the automaton $A+\phi(X)$, translated into Rosen's notation, is actually the mapping $\Phi + i_f$, or better, the pair $(\Phi, i_f) \in f \times I$ acting on S_f, as in Fig. 11(c). This implies that Φ becomes functional (a mapping) only when combined with a description; on its own Φ is just an inert object and cannot act as an operator. This is analogous to carpenter needing a plan before he can construct a table, or a ribosome needing an mRNA before it can construct a polypeptide. While Rosen was of course correct that it is logically impossible for Φ to entail itself if it is cast as the mapping in Fig. 11(b), it is logically perfectly possible for mapping (Φ, i_Φ) to produce object Φ (Fig. 11(d)). One can define Φ and i_Φ as individual objects in their own right and then combine them to form the mapping (Φ, i_Φ); since Φ by itself is not a mapping, nothing prevents the range of (Φ, i_Φ) containing Φ. Whether such a system is physically realisable is quite another matter, but that is not at issue here. What is nevertheless clear is that there is no logical paradox in Von Neumann's description of a universal constructor.

You may have noticed that in the scheme of Von Neumann's self-reproducing automaton (Fig. 10) the first step consisted not only of construction but also decoding—the constructor must be able to "read" and "understand" (decode) the description before it can build the automaton in question, i.e., the constructor must be able to translate the language in which the description is written into action. This requires a set of rules, a convention or code, that forms an interface between formal and efficient cause. In both Von Neumann's and Rosen's treatments this aspect seems to be implicitly accepted as obvious and is not mentioned at all, but when we turn to biology and the organic codes that play this translation role, we cannot sweep it under the carpet. And so it is to codes, their formal representation, and their organic manifestations that we now turn.

5. The formal representation of a code

A good starting point for a discussion of codes is the definition given by Barbieri (2003): a code is a set of rules that establishes a correspondence (or a mapping) between two independent worlds. Furthermore, the rules of a code are arbitrary in the sense that they are not dictated by physical laws, so that there is potentially an unlimited number of such arbitrary relationships between the two independent worlds. This feature allowed Barbieri (2015) to refine his definition: *A code is a small set of arbitrary rules selected from a potentially unlimited number in order to ensure a specific correspondence between two independent worlds.*

In order to relate codes to the foregoing discussion I turn to formal language theory (Eilenberg, 1974) to provide an definition of a code. Consider two finite sets *S* and *T*, respectively called the *source* and *target alphabets*, the *code* being a mapping $C: S \to T^*$ that

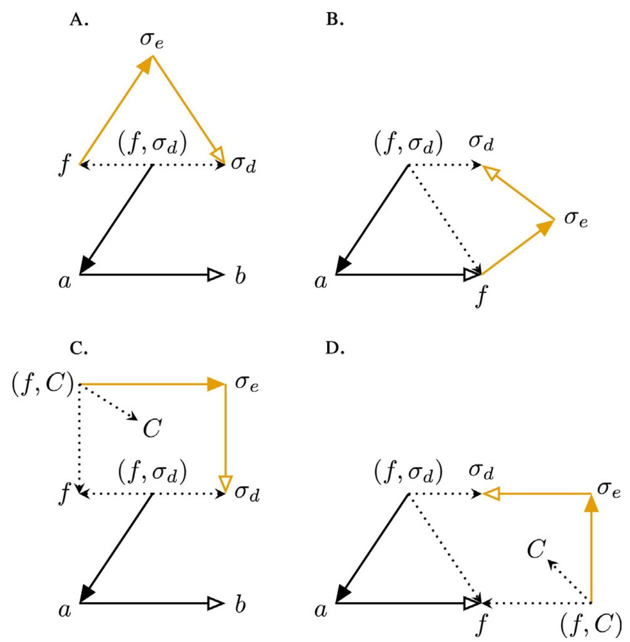

Fig. 12. Extended form of the diagram in Fig. 4(b) showing how the encoded form of the formal cause, σ_e, is decoded by f to σ_d (orange arrows), which then combines with f to form the mapping (f, σ_d). In diagrams A and B the fact that f must use a code mapping to translate σ_e to σ_d is implied, while in diagrams C and D it is made explicit by incorporating the code mapping C as an object that combines with f to form the decoding mapping (f, C). Diagrams B and D are the self-constructing forms of diagrams A and C in which σ_e is the formal cause of f itself, and are the extended forms of diagram D in Fig. 11. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

maps each symbol in S to a sequence of symbols (words) in T^*, where T^* is the so-called Kleene star (the set of all sequences over the alphabet T, of which T itself is of course a subset). The *extension* of C is a mapping $E: S^* \to T^*$ that uniquely translates sequences of source symbols into sequences of target symbols.

This definition allows us, for example, to formally describe the Morse code as a mapping between the symbols in the source set $S = \{a, b, c, \ldots, z, 0, 1, 2, \ldots, 9\}$ and sequences of the symbols in the target set $T = \{\bullet, -\}$. The Morse code $C_M : S \to T^*$ can be written as the set

$$C_M = \{a \mapsto \bullet\,-,\ b \mapsto -\bullet\bullet\bullet,\ c \mapsto -\bullet-\bullet,\ \ldots,\ 9 \mapsto ----\bullet\}$$

The extension of the Morse code $E_M : S^* \to T^*$ contains element-chasing mappings such as

$$\begin{aligned} \text{the} &\mapsto -, \bullet\bullet\bullet\bullet, \bullet \\ \text{morse} &\mapsto --, ---, \bullet-\bullet, \bullet\bullet\bullet, \bullet \\ \text{code} &\mapsto -\bullet-\bullet, ---, -\bullet\bullet, \bullet \end{aligned}$$

In the *semiotic* definition of a code it is a mapping from a *sign* into its *meaning*. What is sign and what is meaning depends on the context, and is in practice associated with the act of decoding. So, in decoding a Morse-encoded sequence the signs would be the dot-dash sequences and their meanings the corresponding alphanumeric symbols. Similarly, at a traffic light the signs {*red*, *orange*, *green*} decode into their corresponding meanings {*stop*, *slow*, *go*}.

Organic codes can be treated in exactly the same way. An organic code is a molecular system for translating an organic sign into its biological meaning (Barbieri, 2015). In many organic codes both the signs and their meanings are molecules or parts of molecules, such as mRNA codons and their corresponding amino acids in the genetic code, or first messengers and their corresponding second messengers in signal transduction codes. But there are also examples where the signs and their meanings are biological effects, such as histone modifications corresponding to post-transcriptional regulation, structural modifications or even post-translational modifications of other histones (Kühn and Hofmeyr, 2014).

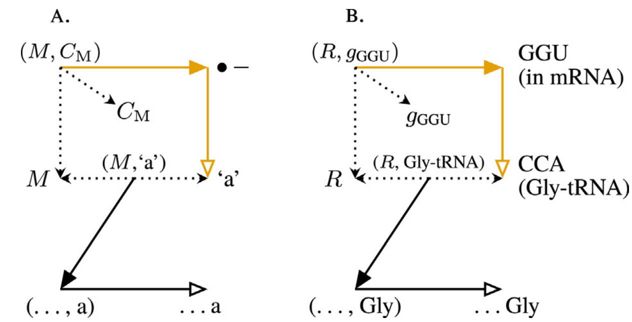

Fig. 13. Two concrete examples of the diagram in Fig. 12(c). (A) The Morse code; (B) the genetic code. See text for discussion.

The genetic code is a mapping from the source alphabet of 64 triplet sequences (codons) formed from the four nucleotides in mRNA (A, G, C, U) to the target alphabet of the twenty amino acids found in proteins plus the stop signs:

$$C_G = \{\text{GGU} \mapsto \text{Gly},\ \text{GGC} \mapsto \text{Gly},\ \text{GCU} \mapsto \text{Ala},\ \text{UUA} \mapsto \text{stop}, \ldots\}$$

where the Morse code C_M is a monomorphism (one-to-one but not onto), the genetic code C_G is an epimorphism (onto but not one-to-one) and is therefore a degenerate code that can only be decoded in the direction from triplet codon to amino acid. The extension of the genetic code translates sequences of codons into sequences of amino acids, for example,

$$\begin{aligned} &\text{GUU UUA} \mapsto \text{Val-Leu} \\ &\text{UCU UAU GCU} \mapsto \text{Ser-Tyr-Ala} \end{aligned}$$

The individual rules of an organic code are implemented in molecules called *adaptors*. The 64 rules of the genetic code, for example, are realised in 64 tRNAs, each carrying one of the 64 anticodon triplets. Each tRNA is charged with its corresponding amino acid by a specific aminoacyl-tRNA synthetase, which can be said to "write" the rule molecularly, just as you can be said to write down a rule of the Morse code on paper. An aminoacyl-tRNA is a molecular interface between a codon on an mRNA molecule (organic sign) and the amino acid (organic meaning) on the tRNA carrying the complimentary anticodon. Similarly, the transmembrane receptor-protein complex that binds the first messenger (organic sign) at the extracellular membrane surface and catalyses the intracellular production of the second messenger (organic meaning) is the adaptor that instantiates a rule in the signal transduction code. All organic codes are realised in this way (Barbieri, 2003, 2015).

While an organic code such as the genetic code C_G can of course be formally defined by a single mapping, it would be more correct to define each rule of the code (instantiated in a specific adaptor) as a mapping in a family of mappings that together comprise the code. For example, each rule in the genetic code is an individual mapping g_{codon} : codon → amino acid associated with a unique molecular adaptor, such as g_{GGU} : GGU → Gly, g_{GGC} : GGC → Gly, g_{GCU} : GCU → Ala, etc.

6. From code definition to code implementation

Up to now we have only considered the mapping that describes a code, albeit a cultural or an organic code, but the use of that mapping is but one in the sequence *recognise-translate-act* that comprises the implementation of that code by an agent. Consider yourself a ship's radio operator, a "sparky", listening to the transmission of a Morse-encoded message. You hear and recognise a dot-dash sequence, translate it into a alphanumeric symbol using the Morse code mapping C_M, and then write or type the letter or number, adding it to the previously translated sequence. All organic codes are implemented in the same way. For example, a first messenger binds to the external binding site of its membrane receptor-protein (recognition), the membrane protein (adaptor) produces an intracellular second messenger (translation), and this molecule has an intracellular biological effect (action). Similarly, an mRNA codon recognises the anticodon on an aminoacyl-tRNA that embodies the translation of the codon to the amino acid, which the ribosome then incorporates into the polypeptide.

Recall that our discussion of codes originated from the realisation that a code is required to translate the description of an automaton before a Von Neumann constructor can build an automaton: the code forms the interface between formal and efficient cause, translating the encoded form of the formal cause into its decoded form. Fig. 12 shows how the relational diagram of the constructor, whether for automaton construction (Fig. 11(c)) or self-construction (Fig. 11(d)), can be extended to incorporate code implementation. The details are provided in the figure legend.

Diagram C in Fig. 12 is particularly useful because it can be used to depict code implementation in general. In Fig. 13 it is used to generate relational diagrams for two of the examples that have been discussed above: the Morse code and the genetic code. In Fig. 13(a) a "sparky" M implements a rule in the Morse code C_M by translating the •– sign into its meaning (the symbol 'a'), and then adds the letter a to the growing sequence of alphanumericals. Fig. 13(b) is a step in ribosomal polypeptide synthesis: ribosome R implements the genetic code rule g_{GGU} by binding an mRNA and associating the GGU codon at the binding site with Gly-tRNA that carries the CCA anticodon and the associated Gly amino acid. The ribosome then adds the Gly to the growing polypeptide chain.

7. Conclusion

The main aim of this study was to develop a graph-theoretic relational diagram of a mapping which relates all four of the Aristotelean causes, with particular emphasis on formal cause, which has hitherto been neglected in relational biology. While this study was originally prompted by a re-examination of Rosen's paradox, and was instrumental in resolving the paradox, it has led to a conception of formal cause that could prove very useful in future studies in relational biology. I therefore regard the relational diagrams in Fig. 5 and their biological realisations as its most important results. The application of these insights to Rosen's paradox also explicated the fact that a code is needed to translate from formal to efficient cause when these causes are separate entities, and allowed the embedding of the decoding mapping in the relational diagram.

Acknowledgements

I thank Roberto Poli, John Kineman, Ilkka Tuomi, Mario Giampietro, Marcello Barbieri, and Joachim de Beule for fruitful discussions on the topic of this paper and related issues. Olaf Wolkenhauer was my intellectual sparring partner when I started thinking about some of the ideas explored here, and Aloisius Louie in particular has helped me refine the translation of my intuitions into the mathematics of relational biology; to both of them I am eternally grateful. Part of this work was initiated while on a Fellowship of the Wissenschaftkolleg zu Berlin.

References

Ackrill, J.D., 1981. Aristotle the philosopher. In: Explanation in Natural Science. Clarendon Press, Oxford, pp. 35–54 (Chapter 4).
Aristotle, 1992. Physics Books I and II. Clarendon Aristotle Series. Clarendon Press, Oxford, Translated with Introduction, Commentary, Note on Recent Work, and Revised Bibliography by William Charlton.
Aristotle, 1998. The Metaphysics. Penguin Books, London, Translated by Hugh Lawson-Tancred.
Barbieri, M., 2003. The Organic Codes: An Introduction to Semantic Biology. Cambridge University Press, Cambridge.
Barbieri, M., 2015. Code Biology: A New Science of Life. Springer, Heidelberg.
Cohen, S.M., 2008. The four causes (Philosophy 433 lecture notes) (accessed 19-07-17) https://faculty.washington.edu/smcohen/433/FourCauses.pdf.
Eilenberg, S., 1974. Automata, Language and Machines, vol. A. Academic Press, New York.
Guttman, B.S., 1966. A resolution of Rosen's paradox for self-reproducing automata. Bull. Math. Biophys. 28 (2), 191–194.
Hofmeyr, J.-H.S., 2007. The biochemical factory that autonomously fabricates itself: a systems-biological view of the living cell. In: Boogerd, F.C., Bruggeman, F., Hofmeyr, J.-H.S., Westerhoff, H.V. (Eds.), Systems Biology: Philosophical Foundations. Elsevier, Amsterdam, pp. 217–242 (Chapter 10).
Hofmeyr, J.-H.S., 2017. Basic biological anticipation. In: Poli, R. (Ed.), Handbook of Anticipation: Theoretical and Applied Aspects of the Use of Future in Decision Making. Springer International Publishing, Cham, pp. 1–15.
Kampis, G., 1991. Self-modifying Systems in Biology and Cognitive Science: A New Framework for Dynamics, Information and Complexity. Pergamon Press, Oxford.
Kühn, S., Hofmeyr, J.-H.S., 2014. Is the "histone code" an organic code? Biosemiotics 7, 203–222.
Louie, A.H., 2009. More than Life Itself. A Synthetic Continuation in Relational Biology. Ontos Verlag, Heusenstamm.
Louie, A.H., 2013. Reflection of Life: Functional Entailment and Imminence in Relational Biology, Vol. 29 of Systems Science and Engineering. Springer, New York.
Louie, A.H., Kercel, S.W., 2007. Topology and life redux: Robert Rosen's relational diagrams of living systems. Axiomathes 17, 109–136.
Maturana, H.R., Varela, F.J., 1980. Autopoiesis and Cognition: The Realisation of the Living. D. Reidel Publishing Company, Dordrecht, Holland.
Rashevsky, N., 1954. Topology and life: in search of general mathematical principles in biology and sociology. Bull. Math. Biophys. 16, 317–348.
Rosen, R., 1958. The representation of biological systems from the standpoint of the theory of categories. Bull. Math. Biophys. 20, 317–341.
Rosen, R., 1959a. On a logical paradox implicit in the notion of a self-reproducing automaton. Bull. Math. Biophys. 21, 387–394.
Rosen, R., 1959b. Some further comments 0n the DNA-protein coding problem. Bull. Math. Biophys. 21 (3), 289–297.
Rosen, R., 1989. The roles of necessity in biology. In: Casti, J.L., Karlqvist, A. (Eds.), Newton to Aristotle. Birkhäuser, New York, pp. 11–37.
Rosen, R., 1991. Life Itself: A Comprehensive Inquiry into the Nature, Origin, and Fabrication of Life. Columbia University Press, New York.
Rosen, R., 2012. Anticipatory Systems: Philosophical, Mathematical, and Methodological Foundations. Springer, New York.
Von Neumann, J., 1951. The general and logical theory of automata. In: Jeffres, L. (Ed.), Cerebral Mechanisms of Behavior. John Wiley and Sons, New York, pp. 1–41.
Von Neumann, J., Burks, A.W., 1966. Theory of Self-reproducing Automata. University of Illinois Press, Urbana, IL.
Wittgenstein, L., 1921. Tractatus Logico-Philosophicus. Routledge and Kegan Paul (English Edition 1961), London.