
Relational Biology

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Abstract

Relational biology is a study of life in terms of the organization of entailment relations in living systems, independent of any particular physical mechanism or material realization. Anticipation is the pivot on which the relational study of life revolves. An organism is the very example of an anticipatory system. Robert Rosen's systematic study of anticipation was founded under the auspices of his determined journey in relational biology, a quixotic adventure that is now continuing in the next generation and beyond.

Keywords

Relational biology • Living system • (M,R)-system • Clef system • Anticipatory system • Impredicative system • *Function dictates structure* • Closure to efficient causation • Metabolism–repair • Material entailment • Functional entailment • Hierarchical cycle

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Life Anticipates

Anticipation is a necessary condition of life: *a living system anticipates*. This connection ultimately explains how the mathematical biologist Robert Rosen (1934–1998), in his lifelong quest of general principles that would answer the question “What is Life?”, happened to write, en passant, many papers on anticipatory systems, culminating in his book *Anticipatory Systems: Philosophical, Mathematical, and Methodological Foundations* (Rosen 1985a).

Rosen was a stalwart of a specific school of mathematical biology called *relational biology*, the study of biology from the standpoint of ‘organization of relations’. It was founded by Nicolas Rashevsky (1899–1972) in the 1950s, thence continued and flourished under his student Rosen (who was, incidentally, my PhD supervisor). The essence of reductionism in biology is to keep the matter of which an organism is made and throw away the organization, with the belief that, since physicochemical *structure implies function*, the reconstitution of the organization from the analytic material parts may be attempted. Relational biology, on the other hand, keeps the organization and throws away the matter; *function dictates structure*, whence material aspects are synthetically entailed.

For a thorough exploration of the Rashevsky–Rosen school of relational biology (and for a comprehensive illustration of the powers of our approach to the study of life), the reader is cordially invited to read the two books that I have (so far) written on the subject. The exploratory journey begins with the monograph *More Than Life Itself: A Synthetic Continuation in Relation Biology* (Louie 2009) and continues with the monograph *The Reflection of Life: Functional Entailment and Imminence in Relational Biology* (Louie 2013). The themes of the two books are, respectively, “What is life?” and “How do two lifeforms interact?”. This present chapter of the *Handbook* is a terse introduction to relational biology, with emphasis on its connection to anticipation, the topic at hand.

Respectus

Rashevsky, in 1939, founded the *Bulletin of Mathematical Biophysics* (now the *Bulletin of Mathematical Biology*) after having been taken to task by the editor of a physiology journal because his submitted (and accepted) paper on nervous

excitation did not contain “original experimental observations”. Rashevsky, as a physicist, began, as was the norm at the time, with an essentially reductionistic view of the relation of biology to chemistry and physics. His successes at modeling specific biological processes, however, instead of reinforcing his reductionism began to gnaw at him in an increasingly something-is-missing sense. As he wrote in Rashevsky (1954):

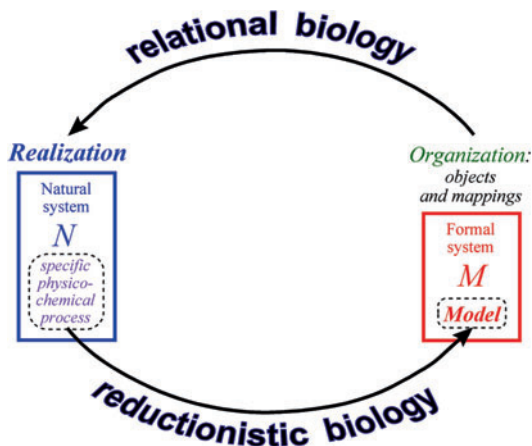
There is no record of a successful mathematical theory which would treat the integrated activities of the organism as a whole... this integrated activity of the organism is probably the most essential manifestation of life... These fundamental manifestations of life drop out from all our present theories of mathematical biology... We must look for a principle which connects the different physical phenomena involved and expresses the biological unity of the organism and of the organic world as a whole.

This now-classic 1954 paper (“Topology and Life”) is generally acknowledged as the origin of relational biology. Indeed, Rashevsky first discussed therein the ‘relational aspects’ of biology. By ‘relational’ he meant an approach that was based on the algebraic, topological organizations of functions, as opposed to one based on the analytic, metric, mechanistic, physicochemical organizations of structures, the latter approach having theretofore dominated his subject of ‘mathematical biophysics’.

Here is Rashevsky’s basic idea: instead of starting with a mishmash of reductionistic fragments and attempting to find some a posteriori way of fitting them together to generate integrated biological behavior, he might try to represent this integrated behavior from the outset. Organisms are recognized as such because one can recognize homologies in their behaviors, regardless of the physical structures through which these behaviors are implemented. All organisms seek and ingest food, metabolize it to generate energy, adapt, reproduce, etc. Rashevsky sought to represent the integrated manifestation of these biological functions, common to all organisms, in mathematical terms. Through the basic and ubiquitous manifestation of such functions, organisms could be mapped (‘biotopologically’) into one another in such a way as to preserve these basic relations, and we could in fact hope to construct a unified theory of organisms in this fashion. In this way, he was led to an abstract topological structure that served as a kind of functional bauplan manifested by any system that might be called an ‘organism’. Stated otherwise, one *begins* with an abstract structure, of which any specific organism constitutes a *realization*. The manner in which particular organisms relate to (or map onto) the bauplan then establishes their relations to one another.

Rashevsky coined the term *relational biology* to characterize this qualitative approach, as distinct from the quantitative approach that is *metric biology*. One of its crucial premises is this: experimenters (e.g., biochemists or molecular biologists) proceed by initially destroying all higher-level biological organization, leaving behind a purely physicochemical system to be studied entirely by physicochemical means. In other words, they proceed by abstracting away all organizational properties, hoping to recapture them in due course by synthetic arguments based on encoded data from their analytic models. The relational approach, on the other hand, proceeds in an exactly converse way; in effect, it initially abstracts away all

Fig. 1 Relational biology decodes; reductionistic biology encodes



purely physicochemical aspects, leaving behind a pure organization to be represented and studied entirely by mathematical means. The detailed physics and chemistry of such a system are to be recaptured later by a decoding process of *realization*. (For a detailed explication of encoding, decoding, model, and realization, consult the exposition on the modeling relation in the chapter on “► [Mathematical Foundations of Anticipatory Systems](#)” in this *Handbook*.)

Premise

The principles of relational biology may thus be considered the operational inverse of reductionistic ideas. Relational biology is mathematical organization seeking realizations, and reductionistic biology is physicochemical process seeking models (Fig. 1).

One must understand that the ‘relational’ in ‘relational biology’ is not just an adjective with its common-usage sense of ‘having an effect of a connection’ (sometimes even misinterpreted as ‘relative’). ‘Relational’ is more importantly used in its mathematical sense that ‘a mathematical relation (subset of a product set) exists’.

Operational inverses relational biology and reductionistic biology may be, but it is important to note that we in the former are not antagonistic in any sense toward practitioners of the latter. One does not argue with success. Molecular biology, the poster child of reductionistic biology, is useful and has enjoyed popular success and increased our understanding of life by parts. It is, however, also evident that there are incomparably more aspects of natural systems that the physics of mechanisms is not equipped to explain. It is the overreaching reductionistic claim of genericity (that only material-based biology is biology) that is a misrepresentation and a falsehood.

In relational biology we often propose not one model for a specific biological process, but many entirely different models that share a common formalism. It is the

commonality that makes them all models for a particular biological process which is the true item of interest and not the detailed properties of any one of them. Thus our interest is not on the details of individual mechanisms (as important as these might be in many contexts), but on qualitative concepts of *behavior*, which may be variously realized: what needs to be isolated is what these mechanisms share that allows them to be realizations of a behavior.

In the rest of this chapter, I shall illustrate how relational biology attempts to answer the ultimate biological question, “What is life?”. I will show how the concept of anticipation arises in this process. “What is life?” is a very terse ontological question. A slightly more explicit ontological formulation is “How is a living system different from a non-living one?” or, epistemologically, “What are the defining characteristics of a natural system for us to perceive it as being alive?”. A relational-biologic answer will be of the form: “an organism is a material system that realizes a certain kind of relational pattern (whatever the particular material basis of that realization may be)”. The exercise, then, is to find this specific relational pattern that defines life.

It is opportune here to point out the subtle difference between a *material system* (or a physical system) and a *natural system*. A material system is ontological, it being simply any physical object in the world. A natural system, on the other hand, is a part, whence a subset, of the external world and a collection of qualities, to which definite relations (of causal entailment) can be imputed. A natural system is, therefore, epistemological, since the partitioning of the external world and the formation of percepts and their relations are all mental constructs (and are therefore entailed by the bounds of mental constructs). In short, a natural system is a subjectively defined representation of a material system. Note also that the existence of causal entailment in a natural system is ontological, but the representation of causality, by arrows (i.e., as mappings), is epistemological.

Pegmata

I need some set-theoretic scaffolding to proceed.

Axiom of Specification For any set U and any statement $p(x)$ about x , there exists a set P , the elements of which are exactly those $x \in U$ for which $p(x)$ is true.

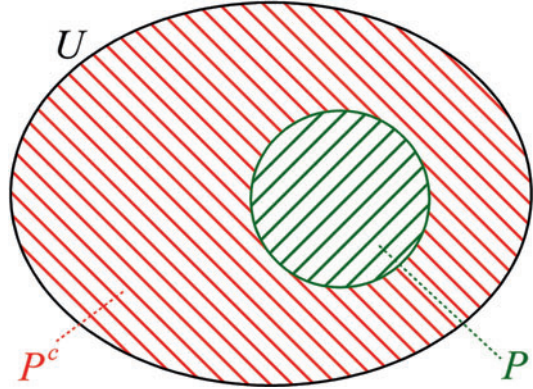
To indicate the way P is obtained from the ‘universe’ U and the defining property p , the customary notation is

$$P = \{x \in U : p(x)\}. \quad (1)$$

The ‘ $p(x)$ ’ in (1) is understood (with the conventional omission of the predicate) to mean “‘ $p(x)$ ’ is true”; it may also be read as “ x has the property p ”. The axiom of specification says that a set is defined by the property that its elements must satisfy.

The set specified by the property p , $P = \{x : p(x)\}$, has as its *complement* the set specified by the property $\neg p$ (*not p*); i.e.,

Fig. 2 A subset P and its complement P^c partition U



$$P^c = \{x : \neg p(x)\} [= \{x \in U : x \notin P\} = U \sim P] \quad (2)$$

[the set consisting of elements of U that do *not* have the property p].

A property p is more interesting if both P and P^c are nonempty. If either every $x \in U$ or no $x \in U$ satisfies $p(x)$ (which means, respectively, that $\langle P = U, P^c = \emptyset \rangle$ or $\langle P = \emptyset, P^c = U \rangle$), then property p defines no new subset of U . More importantly, the pair $\langle P, P^c \rangle$ of sets that is a subset and its complement defines a *partition* of the universe U , in the sense that for each $x \in U$, either $x \in P$ or $x \in P^c$, but not both; for each $x \in U$, either x has the property p or it does not, but not both:

$$\forall x : [p(x) \vee \neg p(x)] \wedge [\neg(p(x) \wedge \neg p(x))]. \quad (3)$$

Stated otherwise, the ‘barrier’ between P and P^c is ‘nonporous’ (Fig. 2).

In our discourse (that of relational biology), the universe is the collection N of natural systems. An organism (in the sense of a general lifeform, a living system) is a natural system. So, if L is the collection of all organisms, then (Fig. 3)

$$L \subset N. \quad (4)$$

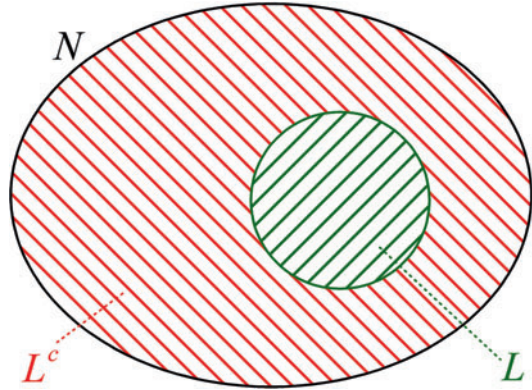
And trivially both L and $L^c = N \sim L$ are nonempty.

Now, the answer to the “What is life?” question should consist of a property ℓ such that a natural system x is alive if and only if $\ell(x)$ is true, i.e., iff ‘ x has the property ℓ ’:

$$L = \{x \in N : \ell(x)\}. \quad (5)$$

Let $P = \{x : p(x)\}$ and $Q = \{x : q(x)\}$, then

Fig. 3 The partition of life from nonlife



$$P \subset Q \text{ if and only if } \forall x p(x) \Rightarrow q(x). \tag{6}$$

The equivalence (6) may be read as $P \subset Q$ if and only if p is *sufficient* for q , and also $P \subset Q$ if and only if q is *necessary* for p .

Thus, the quest to answer the “What is life?” question is the search for a precise definition of the ‘living condition’ ℓ that is necessary and sufficient. Explicitly, if q is *necessary* for ℓ , i.e., if

$$\forall x \ell(x) \Rightarrow q(x), \tag{7}$$

i.e., if a living system must have the property q , then (Fig. 4)

$$L \subset Q. \tag{8}$$

The exercise is then to further restrict the ‘necessity’.

Conversely, if p is sufficient for ℓ , i.e., if

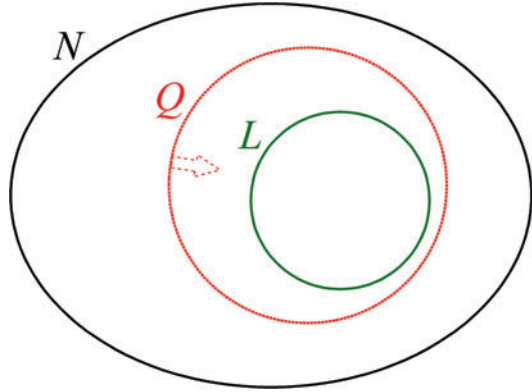
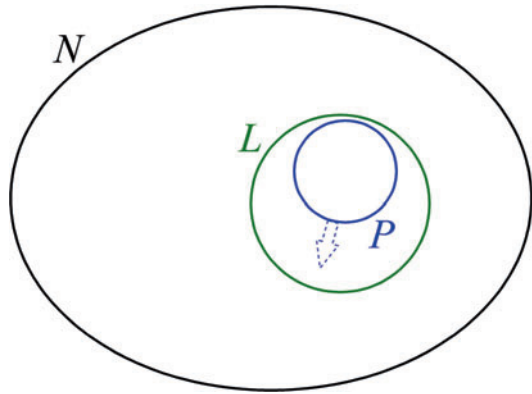
$$\forall x p(x) \Rightarrow \ell(x), \tag{9}$$

i.e., if a natural system has the property p , then it is living, and then (Fig. 5)

$$P \subset L. \tag{10}$$

In this case, the exercise is then to relax the ‘sufficiency’ to make it less stringent. Also, if one knows a sufficient condition for life, then it is in principle possible to realize the sufficiency thence fabricate life.

It is usually easier to discover necessary conditions q for life. The experimental verification simply consists of: remove condition q and the organism dies. Sufficient conditions are more difficult to come by.

Fig. 4 Necessity for life**Fig. 5** Sufficiency for life

In any event, our strategy is to derive a set of individually necessary and jointly sufficient conditions for life. The set-theoretic motivation is that a set is the intersection of all its supersets:

$$A = \bigcap_{B \supset A} B. \quad (11)$$

We strive for a set of individually necessary conditions, viz.:

$$\ell \Rightarrow q_1, \quad \ell \Rightarrow q_2, \quad \ell \Rightarrow q_3, \quad \dots; \quad (12)$$

i.e.,

$$L \subset Q_1, \quad L \subset Q_2, \quad L \subset Q_3, \quad \dots \quad (13)$$

Then from these supersets Q_i of L , one may construct a descending chain of intersections,

$$Q_1 \supset Q_1 \cap Q_2 \supset Q_1 \cap Q_2 \cap Q_3 \supset \dots \supset L, \quad (14)$$

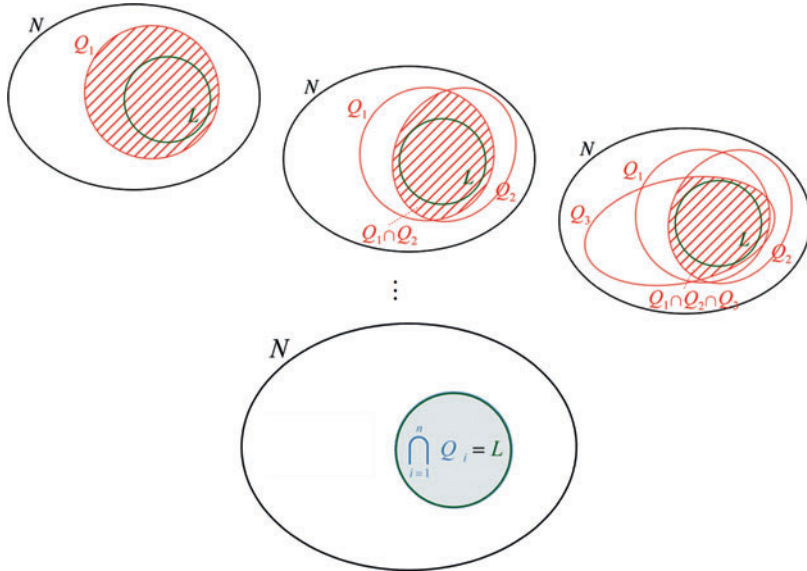


Fig. 6 Individually necessary and jointly sufficient conditions for life

that will ideally converge to L in the limit. In practice, however, one may not get the (necessarily finite) sequence to converge to L . All one can do is to find supersets $Q_1 \supset L, Q_2 \supset L, Q_3 \supset L, \dots, Q_n \supset L$ (corresponding to necessary conditions $q_1, q_2, q_3, \dots, q_n$), so that their intersection $\bigcap_{i=1}^n Q_i$ is as close to L as one can achieve. Then one defines

$$\ell = \bigwedge_{i=1}^n q_i \tag{15}$$

(whence

$$L = \bigcap_{i=1}^n Q_i \tag{16}$$

and declares the joint sufficiency that all natural systems satisfying simultaneously the conditions $q_1, q_2, q_3, \dots, q_n$ are alive. This may include some natural systems that are not obviously alive, but one defines them to be (Fig. 6).

Opera

Consider the following three properties of a natural system $x \in N$:

$$\begin{aligned} q_1(x) &= x \text{ is } \textit{impredicative}; \\ q_2(x) &= x \text{ is } \textit{anticipatory}; \\ q_3(x) &= x \text{ is } \textit{closed to efficient causation}. \end{aligned}$$

Each defining term, of course, requires explanation, which I shall do presently. But let me first give an overview of the argument. It turns out that each of the three properties is a necessary condition for life, i.e.,

$$\ell \Rightarrow q_1, \quad \ell \Rightarrow q_2, \quad \ell \Rightarrow q_3. \quad (17)$$

But more than that, they are related by sequential implications:

$$\ell \Rightarrow q_3 \Rightarrow q_2 \Rightarrow q_1. \quad (18)$$

This means $Q_2 = Q_1 \cap Q_2$ and $Q_3 = Q_1 \cap Q_2 \cap Q_3$, and the three supersets Q_1 , Q_2 , and Q_3 of L form a descending chain:

$$Q_1 \supset Q_2 \supset Q_3 \supset L. \quad (19)$$

One then declares the sufficiency of q_3 for life that Q_3 is the closest that one gets to L in the relational-biologic approach and defines

$$L = Q_3, \quad (20)$$

which is the bold statement of

The Fundamental Theorem of Relational Biology *A natural system is an organism if and only if it is closed to efficient causation.*

Robert Rosen's lifetime's opera are embodied in his trilogy:

- *Fundamentals of Measurement and Representation of Natural Systems* (Rosen 1978)
- *Anticipatory Systems: Philosophical, Mathematical, and Methodological Foundations* (Rosen 1985a)
- *Life Itself: A Comprehensive Inquiry into the Nature, Origin, and Fabrication of Life* (Rosen 1991)

The following additional references are also notable milestones:

- "Some relational cell models: the metabolism–repair systems" (Rosen 1972)
- "Organisms as causal systems which are not mechanisms: an essay into the nature of complexity" (Rosen 1985b)
- *Essays on Life Itself* (Rosen 2000)

Historically, the condition q_2 (anticipation) was introduced in Rosen (1985a, although the first draft of the book was completed in 1979); condition q_1

(impredicativity) first appeared in Rosen (1985b) and then was explicated in detail along with condition q_3 (closure to efficient causation) in Rosen (1991). The various essays in Rosen (2000) further illustrate these conditions and their connections. Metabolism–repair systems, the very picture of closure to efficient causation, were the topic of Rosen’s PhD thesis and his first published paper (Rosen 1958), and Rosen (1972) remains the most comprehensive treatise on this subject.

Anticipation

As mentioned at the outset, anticipation is a necessary condition for life: *a living system anticipates*. In Rosen (1985a), the Foreword contains the passage:

... biology is replete with situations in which organisms can generate and maintain internal predictive models of themselves and their environments, and utilize the predictions of these models about the future for purpose of control in the present. Many of the unique properties of organisms can really be understood only if these internal models are taken into account.

and in Section 1.1:

... obvious examples of anticipatory behavior abound in the biosphere at all levels of organization, and that much (if not most) conscious human behavior is also of this character.

One proclaims the

Axiom of Anticipation *Life is anticipatory.*

Anticipation is, of course, the *raison d’être* of the present *Handbook*. I shall provide a comprehensive exposition on Robert Rosen’s theory of anticipatory systems in the chapter on “► [Mathematical Foundations of Anticipatory Systems](#)”. For now, as a stepping stone toward a characterization of life, it suffices to give a terse

Definition A natural system is an *anticipatory system* if

- (i) it contains an *internal predictive model* of itself and its environment, and
- (ii) in accordance with the model’s predictions, *antecedent actions* are taken.

Let

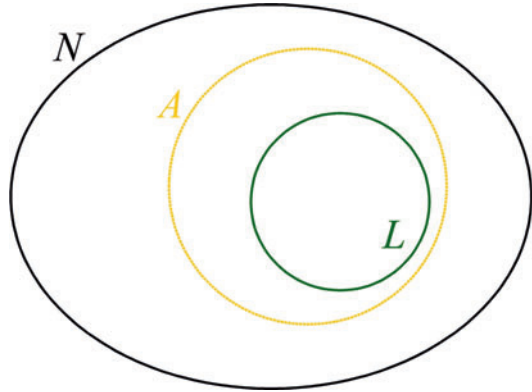
$$a(x) = x \text{ is an anticipatory system } (= q_2(x)), \quad (21)$$

whence

$$A = \{x \in N : a(x)\} = \text{the collection of all anticipatory systems.} \quad (22)$$

The axiom of anticipation thus says

$$\forall x \ell(x) \Rightarrow a(x) \quad (23)$$

Fig. 7 Life is anticipatory

and (Fig. 7)

$$L \subset A. \quad (24)$$

One notes that all complementary sets are nonempty: for example, a simple mechanism is not anticipatory: $\text{umbrella} \in A^c = N \sim A$, and a socioeconomic system is a nonliving anticipatory system: $\text{SES} \in A \sim L$ (Fig. 8).

Impredicativity

In logic, the *predicate* is what is said or asserted about an object. It can take the role as either a property or a relation between entities. Thus *predicate calculus* is the type of symbolic logic that takes into account the contents (i.e., predicate) of a statement. The defining property $p(x)$ in $P = \{x \in U : p(x)\}$ (cf. (1) above) is an example of a predicate, since it *asserts* unambiguously the property that x must have in order to belong to the set P .

Contrariwise, a definition of an object is said to be *impredicative* if it invokes (mentions or quantifies over) the object itself being defined or perhaps another set which contains the object being defined. In other words, *impredicativity* is the property of a *self-referencing definition*. Impredicative definitions usually cannot be bypassed and are mostly harmless. But there are some that lead to paradoxes and may *entail ambiguities*.

Let the property i be defined thus

$$i(x) = x \text{ is an } \textit{impredicative} \text{ system}; \quad (25)$$

then

$$I = \{x \in N : i(x)\} = \text{the collection of all } \textit{impredicative} \text{ natural systems}. \quad (26)$$

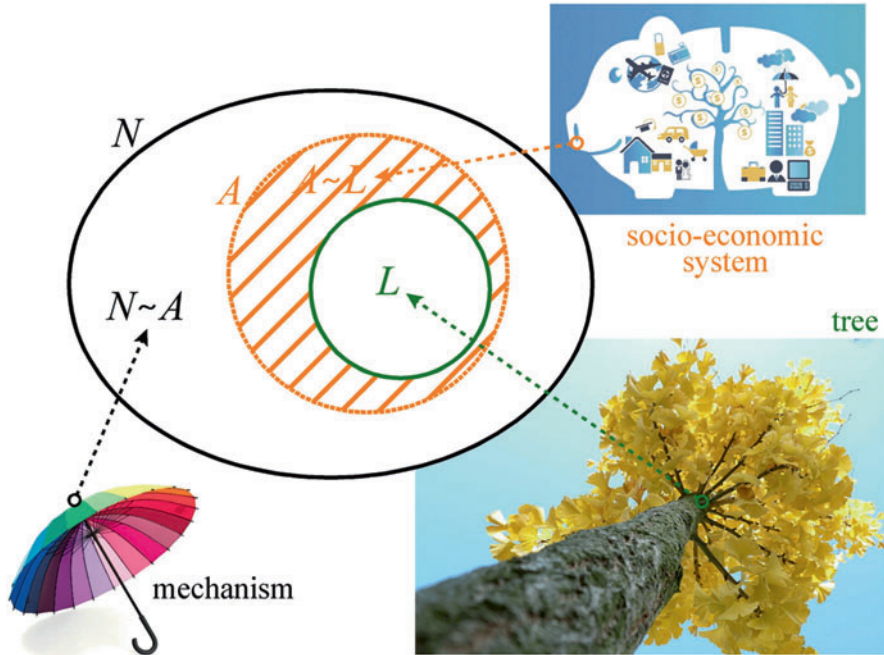


Fig. 8 Anticipatory and non-anticipatory systems

A natural system that is *not* impredicative is called *predicative*, whence

$$\begin{aligned}
 I^c &= \{x \in N : \neg i(x)\} \\
 &= \text{the collection of all } \textit{predicative} \text{ natural systems.}
 \end{aligned}
 \tag{27}$$

Recall that there is a ‘nonporous’ boundary between I and I^c , which cannot be crossed at all in either direction. The partition is built into the set-theoretic logic. There are no purely syntactic operations, i.e., no finite number of rote repetitions that will produce predicativity from impredicativity, or vice versa (Fig. 9).

In Rosen’s lexicon, members of I^c are *simple* systems (also called mechanisms), and members of I are *complex* systems. There are, alas, unfortunate derogatory connotations of the burdened terms: physics deals with simple systems; biology deals with complex systems. The dubious ordering ‘complex > simple’ entails an implied hierarchy of importance. Indeed, to have one’s subject labeled ‘simple’ may be seen as a slight. Also, there are almost as many definitions of complexity as schools involved in the study of the topic, and the overused term ‘complex(ity)’ is consequently rendered quite meaningless. It is perhaps better off sticking with the ‘neutral’ adjectives of $I^c = \textit{predicative}$ systems and $I = \textit{impredicative}$ systems. An added advantage is that since ‘predicativity’ and ‘impredicativity’ are not words of common usage, there is less chance of equivocation. For an alternate exposition on ‘complex systems’, see the chapter on “► [Complex Systems](#)” in this *Handbook*.

Fig. 9 I and I^c partition N

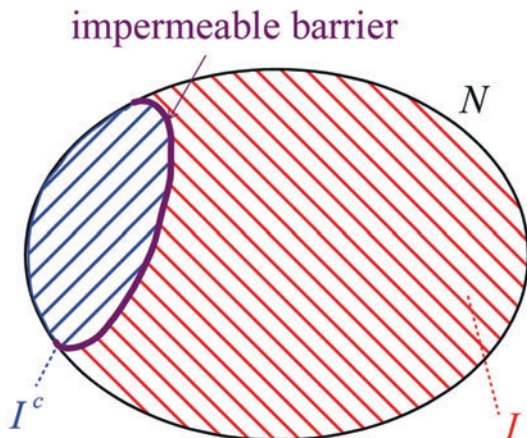
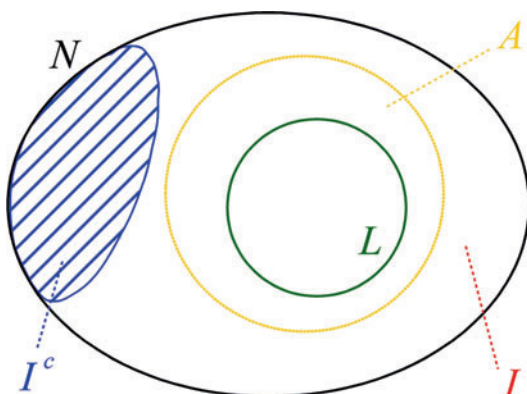


Fig. 10 $L \subset A \subset I$



For our purpose here of reaching a characterization of life, it is sufficient to consider the

Theorem *An anticipatory system must be impredicative; an impredicative system may (or may not) be anticipatory.*

(See the chapter on “► [Mathematical Foundations of Anticipatory Systems](#)” in this *Handbook* for further discussion of this implication, $\forall x a(x) \Rightarrow i(x)$.) Thus one has the proper containment:

$$A \subset I. \quad (28)$$

Together with the containment $L \subset A$ from (24) above, one has the containments shown in Fig. 10.

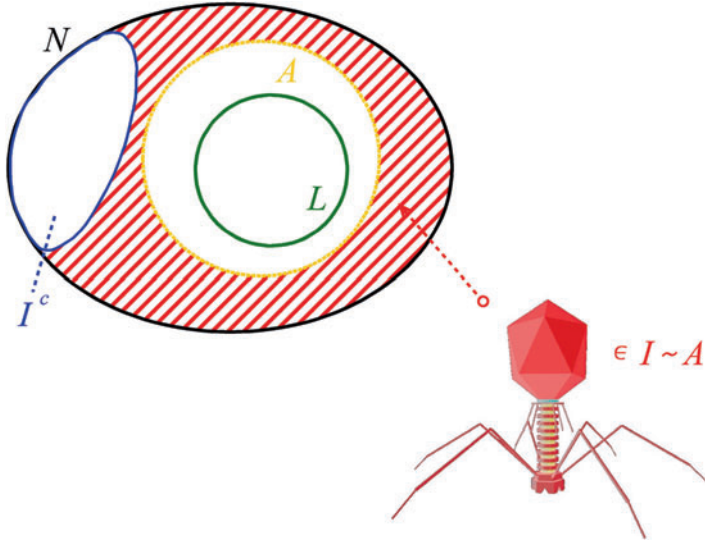


Fig. 11 Relational virology

A virus is impredicative but not anticipatory: $\text{virus} \in I \sim A$. This is because it is an isolated repair component (more on this later), but only uses the host’s anticipatory processes to reproduce itself when joined (Fig. 11).

The proper containments (24) and (28) together say

$$L \subset (A \subset)I, \tag{29}$$

whence

Rosen’s Theorem *An organism must be impredicative; an impredicative system may (or may not) be an organism.*

Impredicativity is a necessary condition of life, but not life itself.

Mappings and Their Relational Diagrams

Let $f : A \rightarrow B$ be a mapping from set A to set B ; this situation may also be denoted $f \in H(A, B)$, where $H(A, B) \subset B^A$ is a *hom-set* (of mappings from A to B). When f is represented in the element-chasing version $f : a \mapsto b$ (where $a \in A$ and $b \in B$), its *relational diagram* may be drawn as a network with three nodes and two directed edges, i.e., a directed graph (or *digraph* for short):

$$f \longrightarrow a \longrightarrow b \tag{30}$$

The *hollow-headed arrow* denotes the *flow* from input (material cause) $a \in A$ to output (final cause) $b \in B$, whence the final cause of the mapping may be identified also as the hollow-headed arrow that terminates on the output:

$$\longrightarrow \triangleright b \quad (31)$$

The *solid-headed arrow* denotes the induction of or constraint upon the flow by the *processor* (efficient cause) f , whence the efficient cause of the mapping may be identified also as the *solid-headed arrow* that originates from the processor:

$$f \longrightarrow \blacktriangleright \quad (32)$$

The formal cause of the mapping may be identified as the *ordered pair* \langle processor, flow \rangle of the two kinds of arrows:

$$\longrightarrow \blacktriangleright \longrightarrow \triangleright \quad (33)$$

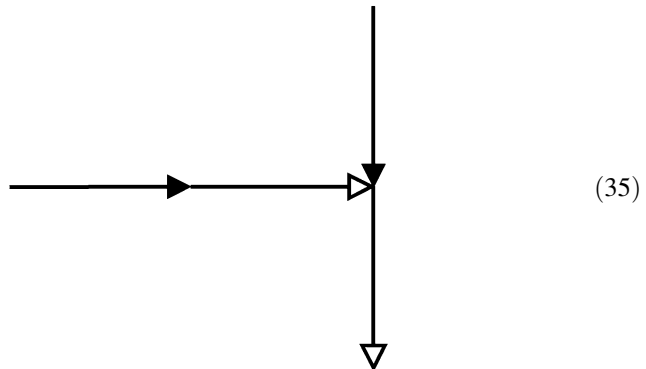
The processor and output relationship may be characterized '*f entails b*', denoted by

$$f \vdash b \quad (34)$$

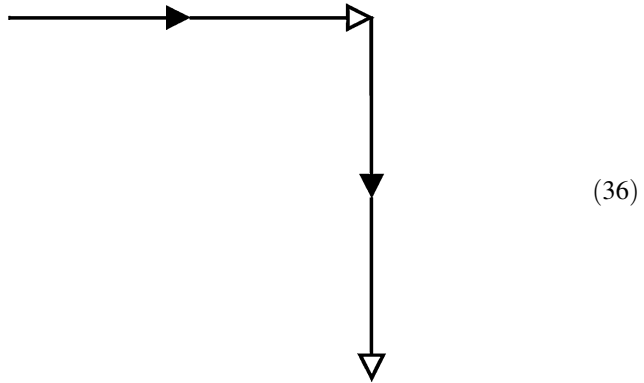
where \vdash is called the *entailment symbol*. The efficient cause f , the processor of entailment \vdash and at the tail of the solid-headed arrow, is *that which entails*. The final cause b , the target of entailment \vdash and at the head of the hollow-headed arrow, is *that which is entailed*. A relational diagram is also called an *entailment network*.

The relational diagrams of mappings may *interact*: two mappings, with the appropriate domains and codomains, may be connected at different common nodes. (For an in-depth study on the various modes of connections, see Chapter 5 of Louie 2009 and Chapter 10 of Louie 2013.)

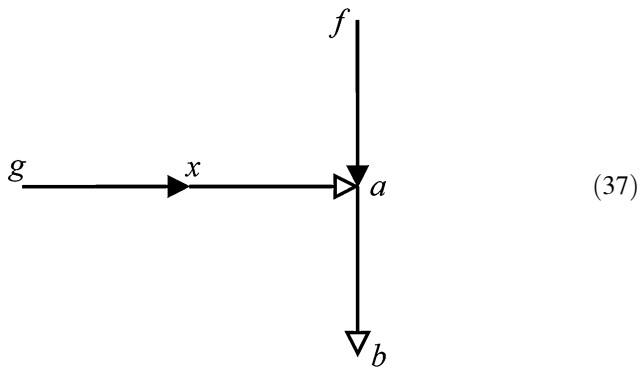
Composition of two mappings involves the combination of their digraphs in such a way that a final cause of one is relayed to become an ingredient of the other; i.e., when one mapping entails some component of the other. Two of the interactions of two mappings may be considered as compositions:



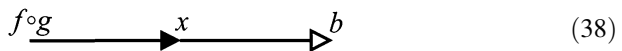
and



The relational interaction (35) arises when one has two mappings $f \in H(A, B)$ and $g \in H(X, A)$, whence *the codomain of g is the domain of f* . Let the element chase be $f : a \mapsto b$ (thus $f \vdash b$) and $g : x \mapsto a$ (thus $g \vdash a$), whence *the final cause of g is the material cause of f* . When that which is entailed is used as material cause (by another process), as is the case for ‘ $\vdash a$ ’ in $g : x \mapsto a$ followed by $f : a \mapsto b$, the entailment is called *material entailment*. The relational diagrams of these two mappings connect at the common node a as in



This *sequential composition* of relational diagrams represents the composite mapping $f \circ g \in H(X, B)$ with $f \circ g : x \mapsto b$ and has the abbreviated relational diagram:

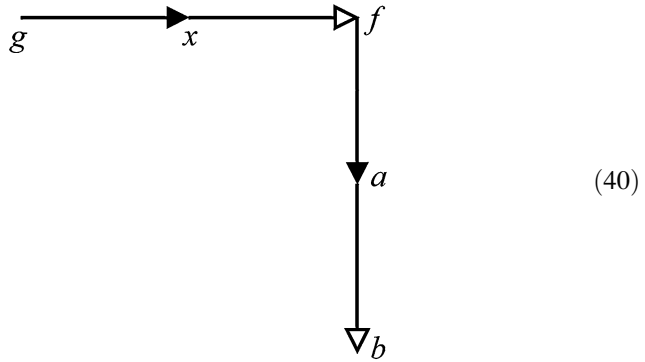


whence the corresponding entailment diagram is



($f \circ g$ entails b).

Next, the relational interaction (36) happens when one has two mappings $f \in H(A, B)$ and $g \in H(X, H(A, B))$, whence *the codomain of g contains f* . Because of this ‘containment’, the mapping g may be considered to occupy a higher ‘hierarchical level’ than the mapping f . Let the element chases be $f: a \mapsto b$ and $g: x \mapsto f$, whence *the final cause of g is the efficient cause of f* . When that which is entailed is an efficient cause (of another process), as is the case for ‘ $\vdash f$ ’ in $g: x \mapsto f$ (with $f: a \mapsto b$ in turn), the entailment is called *functional entailment*. In functional entailment, one has the *hierarchical composition* of relational diagrams



with the corresponding composition of entailment diagrams

$$g \vdash f \vdash b. \quad (41)$$

Note that diagram (41) shows an iterative *entailment of an entailment*. A comparison of (39) and (41) reinforces the graphical differences of diagrams (35) and (36) and shows that sequential composition and hierarchical composition are different in kind: they are different both *formally* and *in content*.

Hierarchical Cycle

A formal system is an object in mathematics. The chapter on “► [Mathematical Foundations of Anticipatory Systems](#)” in this *Handbook* contains a more detailed explanation. Here one may simply consider a formal system as a set S with a collection $\kappa(S)$ of mappings, so a formal system is the ordered pair $\langle S, \kappa(S) \rangle$. The mappings may compose to form a very complicated pattern of inferential entailment in a network. The various network topologies are explored in Chapter 6 of Louie 2009.

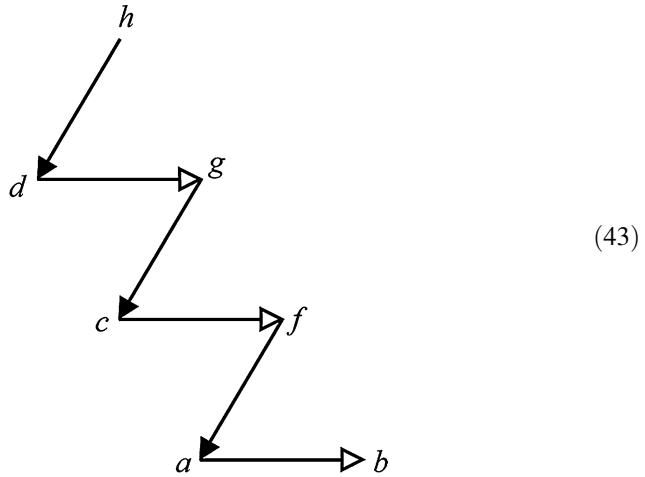
There is one mode of connection that is of special interest: when *two or more* hierarchical compositions are involved in a *cycle*, i.e., a closed path. (Note that a closed path in the directed graph sense means the arrows involved have a consistent direction.) This is called a *closed path of efficient causation*. In other words, a closed path of

efficient causation is an entailment cycle that contains two or more efficient causes. Both the hierarchy of containment and the cycle are essential attributes of this closure.

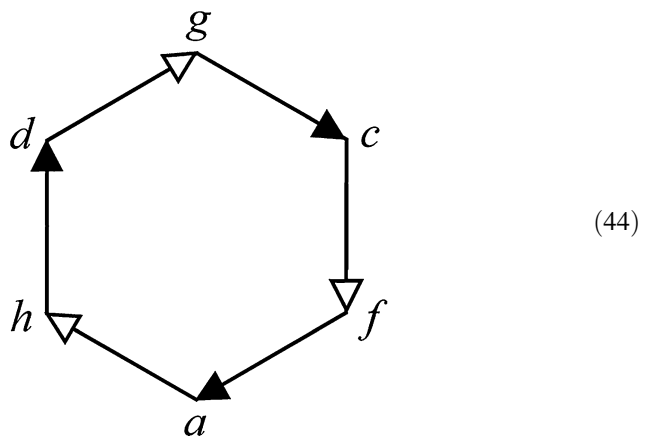
For example, consider three mappings from a hierarchy of hom-sets,

$$f \in H(A, B), \quad g \in H(C, H(A, B)), \quad h \in H(D, H(C, H(A, B))). \quad (42)$$

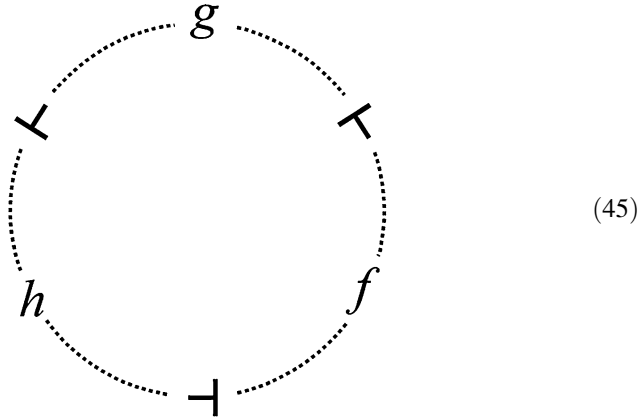
Their hierarchical compositions form the relational diagram:



(where, naturally, $a \in A$, $b \in B$, $c \in C$, and $d \in D$). Now suppose there is a correspondence between the sets B and $H(D, H(C, H(A, B)))$. Then an isomorphic identification between b and h may be made, and a cycle of hierarchical compositions results



In diagram (44), one may say that the hierarchical compositions of the three maps $\{f, g, h\}$ are in *cyclic permutation*. The corresponding cyclic entailment pattern is



One may say that the diagram (45) represents the *cyclic entailments*:

$$\{g \vdash f, h \vdash g, f \vdash h\}. \quad (46)$$

Formally, one has the

Definition A *hierarchical cycle* is the relational diagram in graph-theoretic form of a closed path of efficient causation.

Impredicativity and Clef

Note that in a hierarchical cycle (e.g., arrow diagram (44)), there are *two or more solid-headed arrows* (since a closed path of efficient causation is defined as a cycle containing *two or more* hierarchical compositions). A hierarchical cycle is by definition the formal system representation (i.e., encoding) of a closed path of efficient causation in a natural system, so trivially one has the following

Lemma *A natural system has a model containing a hierarchical cycle if and only if it has a closed path of efficient causation.*

Because of this equivalence of a closed path of efficient causation in a natural system and a hierarchical cycle in its model, the term *hierarchical cycle*, although defined for formal systems, sometimes gets decoded back as an alternate description of the closed path of efficient causation itself. In other words, one may speak of a hierarchical cycle of inferential entailments as well as a hierarchical cycle of causal entailments.

Having a hierarchical cycle turns out to be equivalent to impredicativity:

Theorem *A natural system is impredicative (i.e., ‘complex’) if and only if it contains a closed path of efficient causation. A natural system is predicative (i.e., ‘simple’) if and only if it contains no closed path of efficient causation.*

Stated otherwise, a natural system is impredicative if and only if it has a model that contains a hierarchical cycle.

In formal systems, closed paths of efficient causation, i.e., cycles of entailment, are manifested by impredicatives (or ‘self-references’). In science, where entailment means causality, causal cycles empower a rigorous study on categories of final causation, whence on *function* and *anticipation*. To say that something is a final cause of a process is *to require the process to entail something*. Final cause thus requires something of its effect. Indeed, a final cause of a process must *entail the entailment of the process itself*. (See, in particular, the discussion on ‘immanent causation’ in the last few sections of Chapter 5 of Louie 2009.) It is this peculiar reflexive character of final causation that links it intimately to impredicative, hierarchical cycles, in which the hierarchical compositions are precisely ‘entailments of entailment’.

Note that an impredicative system only requires the *existence* of a hierarchical cycle that contains two or more processes. There may be many of its constituent processes that are not part of hierarchical cycles.

Definition *A natural system is closed to efficient causation if its every efficient cause is entailed within the system.*

Theorem *Closure to efficient causation for a natural system means it has a formal system model in which all of the efficient causes in its causal entailment structure are contained in closed paths; i.e., all efficient causes are components of hierarchical cycles.*

This theorem allows the description *closed to efficient causation* to be used on formal systems, those with all efficient causes involved in hierarchical cycles.

Let me emphasize that the predicates ‘contains a closed path of efficient causation’ and ‘closed to efficient causation’ are *not* equivalent. The class of systems that are closed to efficient causation forms a *proper subset* of the class of systems that contains a closed path of efficient causation. Members of the latter class, i.e., impredicative systems, are required to have only *some*, and not necessarily *all*, processes involved in hierarchical cycles.

Instead of the verbose ‘closed-to-efficient-cause system’ or ‘systems that are closed to efficient causation’, in Louie and Poli (2011), we have introduced a new term ‘clef system’ (for *closed to efficient causation*) with the

Definition *A natural system is clef if and only if it has a model that has all its processes contained in hierarchical cycles.*

Analogously, a *clef* formal system is one that has all its mappings contained in hierarchical cycles. The word ‘clef’ means ‘key’, so this terminology has the added bonus of describing the importance of the class of *clef systems*.

Let

$$c(x) = x \text{ is a clef system.} \quad (47)$$

Then

$$C = \{x \in N : c(x)\} \subset I \quad (48)$$

with proper containment. In other words, the class of clef systems forms a proper subset of the class of impredicative systems.

Metabolism and Repair

As mentioned above, Robert Rosen, a stalwart in relational biology, devised in the 1950s a class of relational models called *metabolism–repair systems* ((M,R)-systems).

Relational biology has a functional view of life, expressed in terms of processes that organisms manifest, independent of the physical substrata on which they are carried out. An organism, being a system open to material causation, must have processes that are modes of interaction with the world. It must have inputs from the world, typical material inputs which supply energy and which provide the capacity for renewing the structure of the organism, whatever it might be. So it is a *sine qua non* that one has to have a *metabolic* apparatus. The word *metabolism* comes from the Greek *μεταβολή*, ‘change’, or *μεταβολισμός*, ‘out-throw’, i.e., an alteration or a relay of materials. Metabolism, in its most general form, is thus a mapping $f : x \mapsto y$ in which $\vdash y$ is material entailment.

An organism must also have a *genetic* apparatus, information carriers that tell how the products of metabolism are to be assembled. The genetic apparatus serves two functions: to produce the metabolic apparatus of the organism and to *reproduce* it. Rosen called the genetic processes *repair*, which, in its most general form, is a mapping $f : x \mapsto y$ in which $\vdash y$ is functional entailment.

The English word ‘repair’ comes from the Latin *re + parare*, ‘make ready again’. It is, of course, a word in common usage and means ‘restore to good condition or proper functioning after damage or loss’; ‘renovate or mend by replacing or fixing parts or by compensating for loss or exhaustion’; ‘set right or make amends for loss, wrong, or error’. Rosen defined the technical usage of the term ‘repair’ in relational biology, precedently back in the beginnings of (M,R)-systems in the 1950s, to mean a hierarchical process for which ‘the output of a mapping is itself a mapping’. This is the general *telos* of ‘repair’, that of an action taken to generate another action. The entailed process may possibly be previously existing, but repair does not have to be a ‘return to normalcy’ or ‘restore to original condition’; the goal of ‘the fix works’ is more important. It is unfortunate (but ultimately irrelevant) that the technical term now, alas, suffers semantic equivocation because of its usage in molecular biology to insularly mean biochemical repair of a specific molecule, that of ‘DNA (and sometimes RNA) repair’. This restricted usage is a very example of the meager appropriating the generic. Since the word ‘repair’ is not a specially coined word, its

biological definition is not entitled to a universal decree. And in the absence of a default, Humpty Dumpty’s rule applies: “When I use a word, it means just what I choose it to mean – neither more nor less.”

To recap, our Unabashed Dictionary of Relational Biology defines

$$\begin{aligned} \textit{metabolism} &= \text{material entailment,} \\ \textit{repair} &= \text{functional entailment.} \end{aligned} \tag{49}$$

Anything that one would want to call ‘alive’ would have to have at least these two basic functions of M and R. (M,R)-systems began as a class of metaphorical, relational paradigms that define cells. It is, however, not much of a hyperbole to declare that all of Rosen’s scientific work – his lifelong quest being the answer to the question “What is life?” – has arisen from a consideration of topics related to the study of (M,R)-systems.

Definition

- (a) An *(M,R)-network* is an entailment network of a finite collection of metabolism and repair components.
- (b) An *(M,R)-system* is an (M,R)-network that is closed to efficient causation.

Not every system is an (M,R)-network. This is because the terse definition (a) above has hidden some connection details; it has the verbose (and mathematically technical) expansion thus:

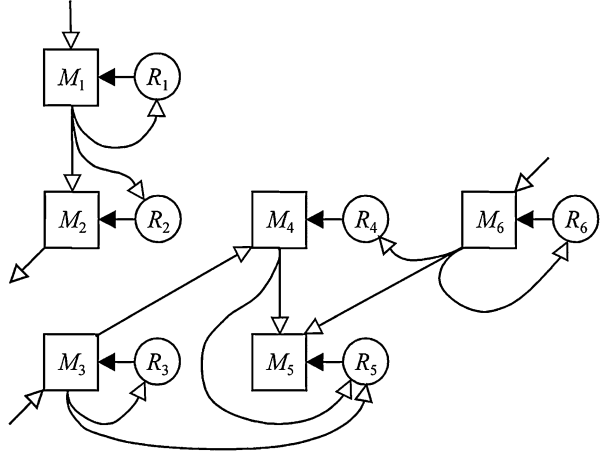
Definition *Metabolism* and *repair* are input-output systems that are connected as *components* into a network. They are formal systems with the following further category-theoretic structures.

- (i) A *metabolism component* is a formal system $M_i = \langle A_i, H(A_i, B_i) \rangle$.
- (ii) A *repair component* is a formal system $R_i = \langle Y_i, H(Y_i, H(A_i, B_i)) \rangle$.
- (iii) A *metabolism–repair network*, i.e., an *(M,R)-network*, is a finite collection of pairs of metabolism and repair components $\{(M_i, R_i) : i \in I\}$, connected in a model network. In particular, the outputs of a repair component R_i are observables in $H(A_i, B_i)$ of its corresponding metabolism component M_i . The metabolism components may be connected among themselves by their inputs and outputs (i.e., by $B_k \subset A_j$ for some $j, k \in I$). Repair components must receive at least one input from the outputs of the metabolism components of the network (i.e., $Y_i = \prod_{k=1}^n B_{i_k}$ with $n \geq 1$ and where each $i_k \in I$).

Note that the connections specified in (iii) are the *requisite* ones; an (M,R)-network may have additional interconnections among its components and with its environment.

This is not the place for an exposition on (M,R)-systems. In addition to the comprehensive reference Rosen (1972), the enthused reader may like to consult Chapters 11–13 of Louie (2009) and Chapter 7 of Louie (2013). For illustrative purposes, here is an (M,R)-network with six pairs of metabolism–repair components (Fig. 12).

Fig. 12 A sample (M,R)-network



Let

$$m(x) = x \text{ is an (M, R)-network,} \quad (50)$$

$$r(x) = x \text{ is an (M, R)-system,} \quad (51)$$

$$M = \{ x \in N : m(x) \} = \text{(M, R)-networks,} \quad (52)$$

and

$$R = \{ x \in N : r(x) \} = \text{(M, R)-systems.} \quad (53)$$

Note that

$$N \sim M \neq \emptyset \quad (54)$$

because not all systems have the requisite structure in the definition of an (M,R)-network. In Section 13.14 of Louie (2009), I have shown that, however, an anticipatory system contains the necessary entailment, that for each $i \in I$ one must have $R_i \vdash M_i$ of an (M,R)-network, so

$$A \subset M. \quad (55)$$

Theorem *A anticipatory system is an (M,R)-network.*

By definition, an (M,R)-system is an (M,R)-network that is clef:

$$R = M \cap C. \quad (56)$$

But in fact a clef system is a priori an (M,R)-network, because closure to efficient causation implies the repair \vdash metabolism entailment, whence

$$C \subset M \tag{57}$$

(cf. Section 8.28 in Louie 2013).

Theorem *A clef system is an (M,R)-network.*

Relations (56) and (57) then combine to imply

$$R = C; \tag{58}$$

that is,

Theorem *A clef system is an (M,R)-system (and vice versa).*

Sufficiency

(M,R)-systems began as a class of metaphorical, relational paradigms that define cells.

Definition *A cell is (at least) a material structure that realizes an (M,R)-system.*

The class has since been generalized to model ‘organisms’, a term which is used in the sense of general living systems, including, in particular, cells. So, by definition,

$$L \subset R \tag{59}$$

(a living system is an (M,R)-system).

In Louie (2012) (also Section 13.13 of Louie 2009), I have shown that

Theorem *An (M,R)-system is anticipatory.*

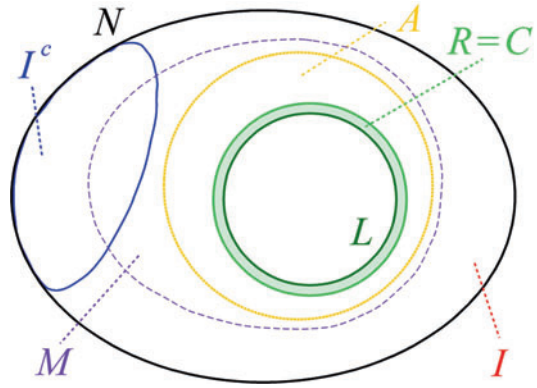
Thus with equality (58), one has

$$R = C \subset A. \tag{60}$$

The Venn diagram is now (Fig. 13)

At this point, the question is, “Is the set $R \sim L$ empty?” Stated otherwise, “Is an (M,R)-system a sufficient characterization of life?” Rosen argued (in what were in effect concluding statements of his lifetime’s work), for example, that “Any material system possessing such a graph [of an (M,R)-system] as a relational model (i.e., which *realizes* that graph) is accordingly an organism.” (Section 10C of Rosen 1991) and “*Making a cell means constructing such a realization.* Conversely, I see no grounds for refusing to call such a realization an autonomous life form, whatever its material basis may be.” (Chapter 17 of Rosen 2000). So he answered the question by *defining* (i.e., expanding) L so that

Fig. 13 Necessary and (almost) sufficient conditions for life



$$R \sim L = \emptyset, \quad (61)$$

whence

$$L = R. \quad (62)$$

This is the

Postulate of Life *A natural system is an organism if and only if it realizes an (M,R)-system.*

Thus an (M,R)-system is the very model of life, and, conversely, life is the very realization of an (M,R)-system.

A union of interacting (M,R)-systems (or better, their *join* in the *lattice* of (M,R)-systems; cf. Sections 2.1 and 7.28 in Louie 2009) is itself an (M,R)-system. A multicellular organism has a life of its own, apart from the fact that the cells that comprise it are alive. Similarly, in some sense an ecosystem of interacting organisms is itself an organism. In particular, a symbiotic union of organisms may itself be considered an organism (cf. Section 11.12 in Louie 2013).

The equalities (58) ($R = C$) and (62) ($L = R$) together imply

$$L = C, \quad (63)$$

which is

The Fundamental Theorem of Relational Biology *A natural system is an organism if and only if it is closed to efficient causation.*

Here is, then, the final taxonomy with the necessary and sufficient condition for life (Fig. 14):

$$\text{Impredicativity} \supset \text{Anticipation} \supset \text{Life}. \quad (64)$$

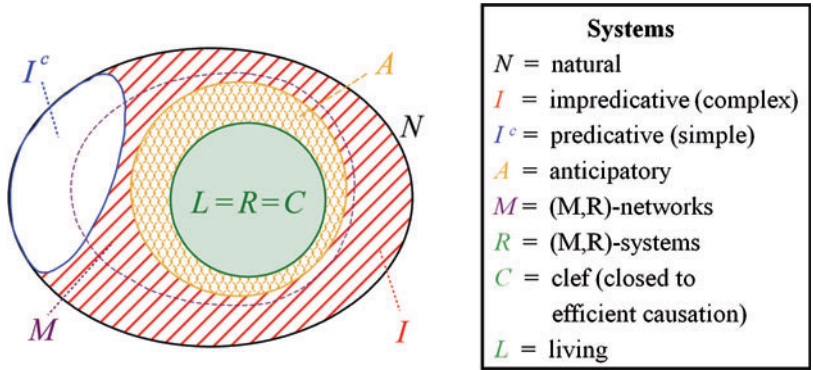
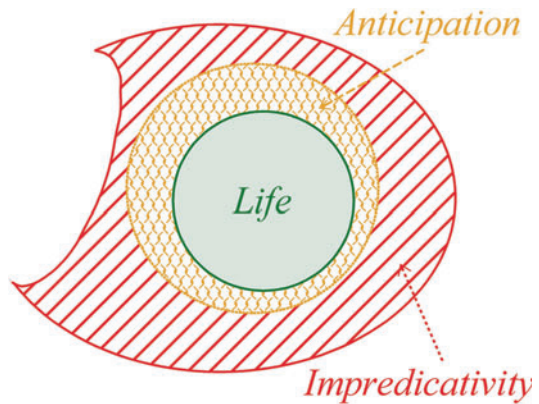


Fig. 14 The taxonomy

Fig. 15 The triumvirate



Anticipation holds a pivotal role in the relational biology exercise of the characterization of life. So hereby it is duly noted (Fig. 15).

Summary

$$\text{Life} \subset \text{Anticipation} \subset \text{Impredicativity}$$

Life anticipates. Robert Rosen’s theory of anticipatory systems arose out of his quest to characterize life using the tools of relational biology. The connection explains the presence of a chapter on “► Relational Biology” in this *Handbook*. In this chapter, I show how three necessary conditions for life – impredicativity, anticipation, and closure to efficient causation – become jointly sufficient to distinguish a living system from a nonliving one.

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