AUTOPOIESIS AND (*M,R*) SYSTEMS IN METABOLIC NETWORKS

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Abstract: Metabolism-repair systems ((*M,R*)) were introduced by Robert Rosen as an abstract representation of cell metabolic activity. The representation was obtained in the context of Relational Biology, which means that organization prevails over the physico-chemical structure of the components involved. This fact was determinant for algebraically formalizing (*M,R*) systems using the theory of categories.

Two elements are considered in the construction of (*M,R*) systems: the metabolic activity (*M*) and the repair functions (*R*) acting on the unities of the metabolic process.

The metabolic system M is considered as an input-output system. In the categorical representation, inputs and outputs are the objects of the category and the processes connecting these elements are represented by the arrows of the category.

Autopoiesis is a concept developed by Humberto Maturana and Francisco Varela in order to analyze the nature of living systems. It takes into account the circular organization of metabolism and it redefines the concepts of structure and organization.

Any system can be decomposed into processes and components, which interact through processes to generate other components. The definition of an Autopoietic system considers that "it is organized as a bounded network of processes of production, transformation and destruction of components that produces the components which: a)through their interactions and transformations continuously regenerate and realize the network of processes (relations) that produced them and b)constitute it (the machine) as a concrete entity in the space in which they (the components) exist by specifying the topological domain of its realization as such a network".

Both concepts were recently connected in a paper of J.C. Letelier et.al., determining that the set of autopoietic systems is a subset of the set of general abstract (*M,R*) systems. In fact, every specific (*M,R*) system is an autopoietic one, being the boundary the main element of autopoietic systems which was not formalized in Rosen's representation of (*M,R*) systems.

This paper introduces the definition of the boundary - the physical boundary and the functional one - for (*M,R*) systems in the context of the categorical representation, inducing then the same kind of formalization for autopoietic systems.

The concept of complete (*M,R*) system is also introduced as well as evidences for the functoriality and universality of the completion process.

Key-words: Autopoiesis - (*M,R*) Systems- Relational Biology- Metabolic Networks- Theory of Categories.

1.INTRODUCTION

This paper is about metabolism. The concept of metabolism cannot be separated from the definition of life. It concerns the role of matter and energy in real organisms, in contrast with other terms which may also be connected with life, such as self-organization, emergence, autonomy, growth, development and others. (Boden 1999). Following Boden, "metabolism is a type of material self organization which involves the autonomous use of matter and energy in building, growing, developing and maintaining the bodily fabric of a living system".

This conception of metabolism is broadly equivalent to the definition of life given by Humberto Maturana and Francisco Varela (1980) as "autopoiesis in the physical space". This expression comes from the identification that these authors do of a living system. They claim that it is impossible to identify a living system unless it is known what a living system is like.

Main concepts to understand what a living system is are *unity, background, organization, structure and space.*

It is considered that an observer defines a *unity* by specifying the operations of distinction that separate a discrete entity from a background. Unities may be simple or composite. A composite unity is made of components.

The definition of unity implies the definition of *background*. They are both endowed with the properties that the operations of distinction that separate them specify.

Organization refers to the relations between components that define a composite unity as one of a particular class. *Structure* refers to the actual components and relations that realize a particular composite unity as a concrete case of a particular class of unities.

The domain defined by the properties of a unity in which it can be distinguished is *the space*. A simple unity exists in the space defined by its properties and a composite unity exists in the space defined by its components.

Autopoietic systems constitute a class of systems. Their members are composite unities conforming a *network of production of components* which:

a) through their interactions recursively constitute and realize the network of productions that produced them,
b) constitute the boundaries of the network as components that participate in its constitution and realization.
c) constitute and realize the network as a composite unity in the space in which they exist.

Robert Rosen (1991) also worked on the organization of living systems in the context of Relational Biology, concerning with qualitative interactions. He was looking for principles which could connect the different physical phenomena and could express the biological unity of the organism and of the organic world as a whole.

Rosen studied the cellular system taking into account two elements: the metabolic activity (*M*) – in the cytoplasm of the cell – and the repair functions (*R*) acting on the unities of the metabolic process. The repair functions are connected with the basic functions of the nucleus of the cell. (Rosen 1958 a, 1959, 1972).

The metabolic system *M* was conceived as a system consisting of *components* which have *inputs* and *outputs*. A component transforms a set of input materials into a set of output materials. Components represent the action of metabolism, producing output materials acting on input ones.

The simplest such system may be seen in Figure 1.

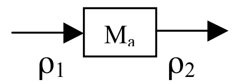

Figure 1

Here M_a is the component and ρ_1 and ρ_2 are the input and output of M_a, respectively.

Naturally, some outputs of one component may be inputs of other components, giving block diagrams as the one in figure 2.

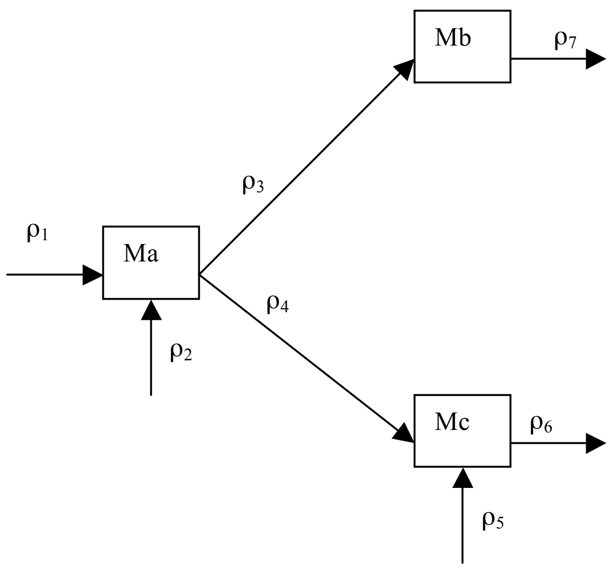

Figure 2

In real living systems, the components M_i have a finite life, and then there must be a subsystem R, where R_i repairs M_i. The subsystems Ri have then components and input and output materials, with the particularity that the output of R_i is the component M_i.

The block diagrams were reformulated in terms of abstract block diagrams, which allowed the study of the former ones with the formalism of the theory of categories (Rosen 1958 b, 1959, 1972).

Category Theory is a mathematical theory (Eilemberg and Mac Lane 1971).

A *category* has *objects* and *morphisms* between them. There must be an identity morphism for every object and morphisms may be composed and the composition must be associative. A *functor* associates categories; so, in fact, it associates objects with objects and morphisms with morphisms, preserving identities and the composition of morphisms. Comparisons between functors are carried out by *natural transformations*. For details about Category Theory the book of Eilemberg and Mac Lane may be consulted.

In an abstract block diagram inputs and outputs of a component are the objects of the category and the components are represented by the arrows (morphisms).

The abstract block diagram corresponding to Figure 2 may be seen in Figure 3.

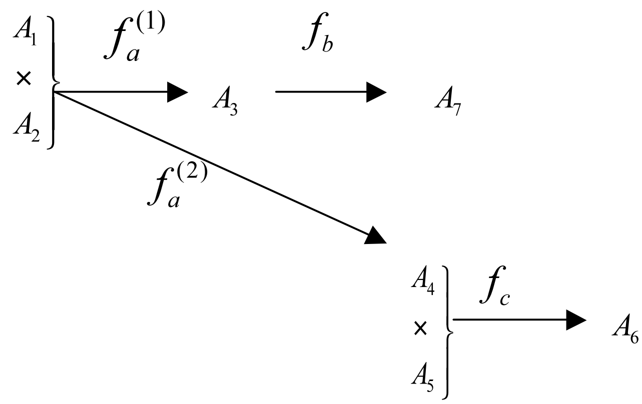

Figure 3

Formally, in the category of (*M,R*) systems, if A and B represent the set of inputs and outputs to a component, then the metabolic activity is represented by $f \in H(A,B)$, with $H(A,B)$ the set of arrows connecting A with B. The repair component is represented then by ϕ_f and the following diagram is obtained:

$$A \xrightarrow{f} B \xrightarrow{\phi_f} H(A,B)$$

with $a \in A, f(a) = b, \phi_f(b) = f$. This means that the output of ϕ_f is the metabolic component (f).

The next question is: how are these components R_i produced? Rosen found that in these systems, a mapping β exists such that $\beta(f) = \phi_f$, completing a circle given by:

$$A \xrightarrow{f} B \xrightarrow{\phi_f} H(A,B) \xrightarrow{\beta} H(B, H(A,B))$$

Both theories – Autopoiesis and Rosen´s about (*M,R*) systems were connected by Letelier, Marín and Mpodozis (2001). It is concluded there that (*M,R*) systems have the circular organization (operational closure) of autopoietic systems, but there is no element suggesting that (*M,R*) systems can generate a distinguishable unity. Both (*M,R*) and Autopoietic systems produce all the efficient causes needed for their realization and, therefore, Autopoietic systems are included in the class of (*M,R*) systems. Moreover, any specific (*M,R*) system is an autopoietic one. But (*M,R*) systems did not have, until now, a formalism for the generation of its own border.

This paper describes a way of introducing the representation for the boundary of (*M,R*) systems in a categorical framework and, by its means, it gives a construction which provides a completion for abstract (*M,R*) systems.

2. NEW ASPECTS OF (*M,R*) SYSTEMS IN CONNECTION WITH AUTOPOIESIS.

2.1.The digraph of an (*M,R*) system.

In a categorical language, an (*M,R*) system has the following elements: each metabolic component M_a is represented by an arrow f_a.

$$f_a = (f_a^1, f_a^2, ..., f_a^n)$$

This means that M_a has n outputs. The domain (*dom*) of each f_a^i is:

$$dom(f_a^1) = dom(f_a^2) = ... = dom(f_a^n) = A$$

with $A = A_1 x ... x A_m$, the input of M_a consisting of the simultaneous input of $A_1, A_2, ..., A_m$.

The codomain (*codom*) of each f_a^i is an object C_a^i representing an output of the component f_a^i. Then

$$codom(f_a^i) = C_a^i$$

For each metabolic component M_a there exists a repair component R_a represented by an arrow ϕ_{f_a}.

$$\phi_{f_a} = (\phi_{f_a}^1, \phi_{f_a}^2, ..., \phi_{f_a}^n)$$

with n the number of outputs of M_a.

$$dom(\phi_{f_a}^1) = dom(\phi_{f_a}^2) = ... = dom(\phi_{f_a}^n) = B$$

with $B = \prod C_i^j$, being C_i^j outputs of the metabolic system (each $C_i = codom(f_i)$).

The codomain of each $\phi_{f_a}^i$ is the part of the metabolic process that this $\phi_{f_a}^i$ reproduces.

Then:

$$codom(\phi_{f_a}^i) = H(A, C_a^i)$$

$H(A,B)$ is the set of arrows with domain A and codomain B.

With the elements (A_i, f_a, ϕ_f) an (*M,R*) system may be represented by a digraph: the set of vertices is the set of inputs and outputs of each component and the set of arrows is the set of processes (components).

The digraph of the (*M,R*) system is then the digraph of the metabolic system *M* where only the inputs to the corresponding repair components (the domains of ϕ_f) must be identified. It is not necessary to add the output of each repair component , because that output is the component itself and it is completely determined.

An example of the digraph of an (*M,R*) system (in fact, the corresponding *M* system) may be seen in figure 4.

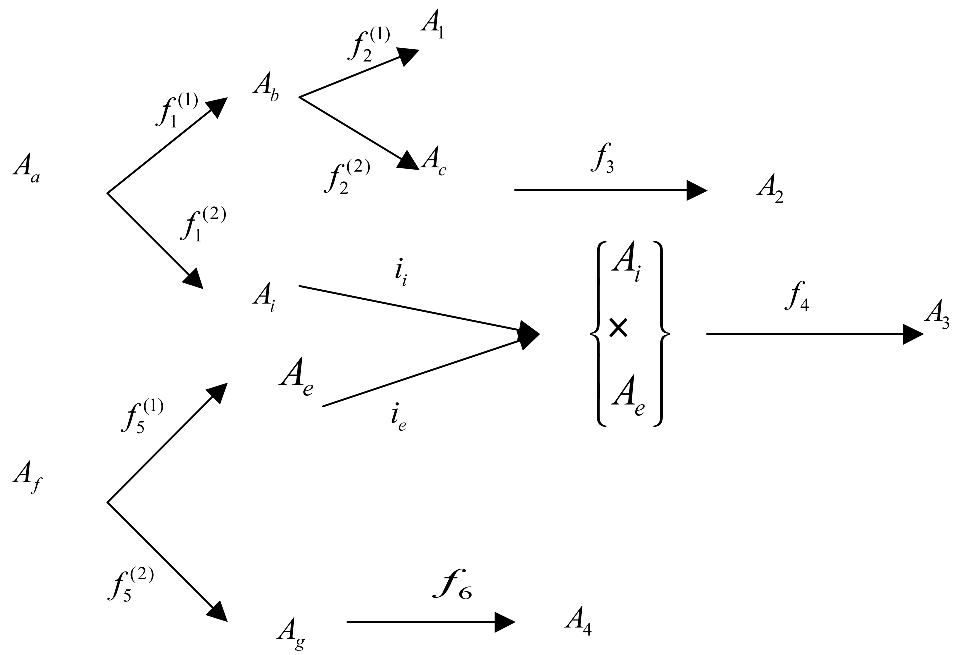

Figure 4

The arrows i_j were introduced in the representation as theoretical arrows in order to identify the connections corresponding to each factor of a Cartesian product. Then i_j is the immersion of A_j in $A = A_1 x ... x A_j x ... x A_m$.

Some vertices represent *environmental inputs (A_a* and *A_f)* or *environmental outputs (A_1, A_2, A_3* and *A_4)*. Following Rosen, the first ones are those inputs which are not produced by any metabolic activity of the system. The environmental outputs are the ones which are not incorporated again to the metabolic activity (Rosen 1972).

2.2.The physical border: *inside* and *outside*.

One of the facts we will use in this paper is the connection between (*M,R*) systems and autopoietic ones. Letelier et.al (2001) showed that every autopoietic system is, at least conceptually, an (*M,R*) system and that after realization, every (*M,R*) system is autopoietic. This result leads to the following property:

Property 1

Every (*M,R*) system has a physical border.

Proof

As (*M,R*) systems are autopoietic, then, as such, (*M,R*) systems must have an operational closure and must generate their own border, that is, a physical boundary making of that system a distinguishable unity □.

As the border exists, then through the metabolic activity of the system, some elements will cross this border, going from *outside* to the *interior* of the system and viceversa. To reach the real exterior of the system the *functional border* must also be traversed.

In order to describe the traversion of the physical boundary the components (arrows in categorical language) of the system must be characterized.

Each system and its surrounding environment conforms a network of physical elements and components acting on them, to get more physical elements.

In the language of categories these physical elements are objects A_i of the category and the components are arrows f connecting them: $A_i \xrightarrow{f} A_j$. These components represent processes affecting A_i and producing A_j. In the corresponding digraph, the components f are the arcs of the digraph and the objects A_i are the vertices.

But not all the processes are of the same kind. We can distinguish three kind of processes in (*M,R*) systems: processes of *transformation*, *translocating* processes and *signals*.

Definition 1: A process $f: A_i \to A_j$ is a *transformation process* if $x \in A_i \Rightarrow x \notin A_j$.

Definition 2: A process $f: A_i \to A_j$ is a *signal* if it exists at least one (but not all) $x \in A_i$ such that $x \in A_j$.

Definition 3: A process $f: A_i \to A_j$ is a *translocating process* if $\forall x \in A_i \Rightarrow x \in A_j$.

Other resources different from a process f like the ones just described may participate of the production of A_i.

Two facts can be set immediately in order to characterize which elements conform the interior of the system and which ones are outside it:

i) *if* A_i *is obtained by means of a resource not involving one of the processes* f, *then* A_i *does not belong to the interior of the system.*

ii) *if* A_i *is obtained by a transformation process* f, *then* A_i *belongs to the interior of the system.*

Let now be $f: A_i \to A_j$ a translocating process. If A_i is a product of a process of transformation, then f is an internal process and A_i and A_j are internal objects of the metabolic network.

But A_i may not be produced by a process of transformation. If A_i is produced through a resource which is not one of these processes f then A_i is an environmental input and $f: A_i \to A_j$ traverses the physical boundary. In this case f is a border process.

If A_i is produced by a translocating process $g: A_k \to A_i$ then: $A_k \xrightarrow{g} A_i \xrightarrow{f} A_j$ and the physical boundary is traversed by g.

If $f: A_i \to A_j$ is a signal then:

a)If $g: A_k \to A_i$ is a transformation process, then f is an internal process and A_i, A_j are internal objects.

b)If $g: A_k \rightarrow A_i$ is not a transformation process, then f is an internal process (modulable) and A_i, A_j are external objects.

2.3.The functional border

In this interplay and exchange of elements, it clearly appears that the network does not end at the physical boundary. We will be also interested in those objects and arrows which are outside the physical boundary but they belong to the network as well. This idea will lead us to the concept of *functional boundary*.

The system exchanges different elements with the environment, in direct connection with the interior of the metabolic network. Though these elements do not belong to the interior of the system they are, for sure, part of the network. We can consider that the external world - the world where the observers live - is beyond this functional limit.

As it was defined before, the (*M,R*) system is represented by a directed graph (digraph) G which is part of a network of elements related to it.

Let be $EI = \{v \in G \,/\, v \text{ is an environmental input of } G\}$

$EO = \{v \in G \,/\, v \text{ is an environmental output of } G\}$

If $v \in EI$ we define I_v as the set of in-neighbors of v. Then, if $x \in I_v, x$ is adjacent to v and there exists an arc $t: x \rightarrow v, x \notin G$.

In a similar way, if $w \in EO$ we define O_w as the set of out-neighbors of w. Then, if $y \in O_w, y$ is adjacent to w and there exists an arc $j: w \rightarrow y, y \notin G$.

<u>Definition 4</u>: The *functional border* of G (∂ G or L_G) is defined in the following way: if z is a vertex of L_G then $z = I_v$ or $z = O_w$, $\forall v \in EI, \forall w \in EO$. The sets of neighbors (in and out) are not empty given the definition of environmental input and output.

<u>Surmise</u>: If two elements of L_G are connected, there is an indirect connection through elements of G or through elements out of $G \cup L_G$.

Property 2

If a metabolic network contains its functional border, then it contains its physical border.

Proof

In order to define the functional border, environmental inputs v_i, environmental outputs w_j and their in-neighbors $I_{v_i} (I_{v_i} \rightarrow v_i)$ and out-neighbors $O_{w_j} (w_j \rightarrow O_{w_j})$ respectively, are identified. Then, if z is any other object of the system and there is a walk from I_{v_i} to z or from z to O_{w_j} this walk must traverse the physical border. If not, I_{v_i} or O_{wj} would be in the interior of the system. This fact is in contradiction with the definition of I_{v_i} and O_{wj} □.

2.4.Going back to categories.

Taking into account all the elements involved, a new category of representation is defined.

Let us work in *G*, the category of (directed) graphs (Mac Lane 1971). Let G be a digraph representing an (*M,R*) system as it was defined before. Then G=(V,A). V is a set of objects (vertices) and A is a set of arrows f (arcs). There is a pair of functions from A to V:

$$A \xrightarrow{\partial_o} V \text{ and } A \xrightarrow{\partial_1} V$$

such that $\partial_o f = domain\ f$ and $\partial_1 f = codomain\ f$.

A morphism $D: G \to G'$ of graphs is a pair of functions $D_V: V \to V'$ and $D_A: A \to A'$ such that

$$D_V \partial_0 f = \partial_0 D_A f \text{ and}$$

$$D_V \partial_1 f = \partial_1 D_A f$$

for every arrow $f \in A$.

As these digraphs represent (*M,R*) systems following Rosen's definition and now it is considered that each system has a boundary, this element must be incorporated to the representation.

Because of property 2, the functional boundary is a real limit with the external world. So, the representation of an (*M,R*) system may be the one given by Rosen or may be one including the elements of the boundary as well.

Definition 5: An (*M,R*) system is *complete* if the metabolic network contains its functional border.

The digraph G represents metabolic systems without boundaries. In order to represent a complete system, the border must be added.

The purpose now is to formalize this completion in a categorical representation. The idea follows Harris (1998, 2001).

Let X be the category of digraphs containing complete and non-complete systems.

Let be X_0 the subcategory of complete objects (digraphs). Let $U: X_0 \to X$ be the forgetful functor (the inclusion) and I the identity functor on X. A *completion operator* consists of the following:

i) A functor $C: X \to X_0$

ii) A natural transformation $i: I \to UC$

iii)The fact that X (via i)is left adjoint to U

By a natural transformation i it is meant that for each object A in X, $i_A: A \to C(A)$ is a map in X, and for $f: A \to B$ in X, $C(f)i_A = i_B f$. Conceptually: any object is embedded in its completion, and maps in X are extended to maps of the completed objects.

By left adjoint it is meant that for any objects A in X and B in X_0, and any map $f: A \to U(B)$, there is a unique map $f_0: C(A) \to B$ with $U(f_0)i_A = f$. U can be ignored to have a simpler expression: for any $f: A \to B$ with B already complete, there is a unique

$f_0 : C(A) \to B$ with $f_0 i_A = f$. Conceptually: any map into a complete object extends uniquely to the completion of the domain.

Left adjoints are unique up to natural equivalences (that is, natural transformations consisting of isomorphisms) (Mac Lane 1971). The consequence of this fact is that the functor C may be considered "the" completion operator with respect to the notion of completion embodied by the subcategory X_0.

So, a completion functor C must be defined on a category X having both metabolic networks and "metabolic networks that have boundaries attached to them". The next step is to show that this boundary is a functorial, natural and universal construction. To demonstrate universality it will be shown that this construction is the essentially unique way of completing metabolic networks in such a way that any other completion process can naturally be compared by means of a map from the boundary defined here to the other boundary.

The next step is then to define the completion functor $C : X \to X_0$. As it is a functor, it must be defined on the objects and on the arrows of X.

If G is an object of X, $C(G) = G \cup L_G$.

If $f : G \to G' \Rightarrow C(f) : C(G) \to C(G')$. Then $C(f)$ is a morphism between graphs in X_0. This means that $C(f) : G \cup L_G \to G' \cup L_{G'}$. Then $C(f) = (C(f)_V, C(f)_A)$ and it must be defined on the vertices and on the arcs of $G \cup L_G$.

Let be $v \in V(G)$ a vertex of G. Then $(C(f))_V(v) = f(v)$.

Let now be $v \in L_G$, the functional border of G. If $v = I_z$ then v identifies the in-neighbors of z for z an environmental input of G. We take $f(z)$. If $f(z) \notin EI \wedge f(z) \notin EO$, we define $(C(f))_V(v) = f(z)$.

If $f(z) \in EI(EO) \Rightarrow \exists v' = I_{f(z)}(v' = O_{f(z)}) \in L_{G'}$. In this case, we define $(C(f))_V(v) = v'$. That is to say:

$$(C(f))_V(v) = \begin{cases} f(v) & \text{if } v \in G \\ f(z) & \text{if } v \notin G, f(z) \notin EI, EO; v = I_z(O_z) \\ & \\ v' & \text{if } \quad f(z) \in EI\ (f(z) \in EO) \text{ with } v' = I_{f(z)}(v' = O_{f(z)}) \end{cases}$$

Now we define $C(f)_A$ on the arcs of $G \cup L_G$.

a)If $r : v_1 \to v_2; v_1, v_2 \in G \Rightarrow C(f)_A(r) = f(r) = r'$ in the usual way the morphisms of graphs are defined.

b) Let be $r : I_z \to z$ (The same idea may be applied if $r : z \to O_z$). Then,

b1)If $f(z)$ is not related with $I_{f(z)}$ ($O_{f(z)}$ would be similar), then $C(f)_V(I_z) = f(z)$ and r' is defined in such a way that:

$$C(f)_V(\partial_0(r)) = \partial_0(C(f)_A(r))$$
$$C(f)_V(\partial_1(r)) = \partial_1(C(f)_A(r))$$

b2)If $f(z)$ is related with $I_{f(z)}$ ($O_{f(z)}$ would be similar), then $C(f)_V(I_z) = I_{f(z)}$ and r' is defined as in b1). The only difference is that in there, $r': f(z) \to f(z)$ and in b2) it is $r': I_{f(z)} \to f(z)$.

The technical aspects to show the functoriality and naturality of this construction is subject of another paper.

Let us say some words about universality. To prove universality means that if G is any object of X, G_0 is a complete object of any kind and $f: G \to G_0$, then there exists one and only one $f_0: C(G) \to G_0$ such that $f = f_0 \circ i_G$ with $i_G: G \to C(G)$ defined as $i_G(v) = v$ and $i_G(r) = r$ if $v \in V(G)$ and $r \in A(G)$.

By definition, this completion functor C adds all the elements of the functional border to the representation of the system. By the surmise made before, no arc is completely embedded in this border. If a system G is completed by any other means, it must contain the system itself and the elements of the functional border, to begin with. So, it must contain the completion of G given by C. Then C provides the smallest completion that it can (naturally) be got.

3.CONCLUSIONS

(*M,R*) systems were represented with the additional elements coming from the condition of being autopoietic systems. The connection between both types of systems has the double objective of incorporating the boundaries to concrete (*M,R*) systems and besides, it provides a way of having a formalization of autopoietic systems within the theory of categories.

The definition of a new category having as objects metabolic networks allows to use categorical tools to analyze them as a unity, incorporating the concept of complete system. Until now, though the categorical representation of Rosen in terms of abstract block diagrams was useful to analyze characteristics of the relations among the components of a metabolic system, in the present formulation each system is a unity, it constitutes an object in a category and it becomes clearer its condition of autopoietic. Then all its elements may be expressed in categorical terms, providing new formal tools of analysis.

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