NATURAL TRANSFORMATION MODELS IN MOLECULAR BIOLOGY

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ABSTRACT

Molecular models in terms of Categories, Functors and Natural Transformations are introduced for uni-molecular chemical transformations, multi-molecular chemical and biochemical transformations. Novel approaches to realization of Relational Biology Models of Complex System Biology are introduced in terms of Natural Transformations between Functors of Molecular Categories. Several applications of such natural transformations are then presented to protein biosynthesis, embryogenesis and nuclear transplant experiments. Other possible realizations in Molecular Biology and Relational Biology of Organisms are also suggested. Future developments will include: Fuzzy Relations in Biology; Categories of Lukasiewicz Logic Algebras and Intuitionistic Logic Algebras for Modeling of Complex Neural Network Processes; Stochastic, Genetic Networks in Lukn-Algebras, and Relational Biology Models of Complex Hormonal Controls.

1. MOLECULAR MODELS IN CATEGORIES

A simple introduction of such a synthesis is based on set-theoretical models of chemical transformations (14). Consider the simple case of uni-molecular chemical transformations (14):

$$\mathbf{T : A \times I \rightarrow B \times I} \qquad (1)$$

where A is the original sample set of molecules, I = [0, t] is a finite segment of the real time axis and A x I denotes the indexing of each A-type molecule by the instant of time at which each molecule $a \in A$ is actually transforming into a B-type molecule (see also eq.3 in ref.14). B x I denotes the set of the newly formed B-type molecules which are indexed by their corresponding instants of birth.

MOLECULAR SET -**A**, with f: A →A are ENDOMORPHISMS that belong to H(A,A)

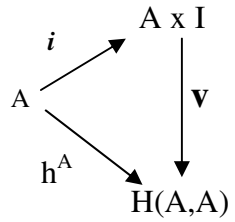
THE CATEGORY OF MOLECULAR SETS AND THEIR TRANSFORMATIONS is : M .

THE h^X FUNCTOR: h^A: ***M*** → ***Set*** is defined as:

$h^A(X\} = H(A,X)$ for any X in ***M***
$h^A(t) = m: H(A,A) \rightarrow H(A,B)$ for any t: A→B, where:

A = MOLECULAR SET
B= MOLECULAR SET OF REACTION PRODUCTS OF TYPE "B", RESULTING FROM a DEFINITION OF the MOLECULAR SET VARIABLE (m.s. v.), defined as follows.

The flexible notion of molecular set variable (m.s.v) is exactly represented by the morphisms **v** in the following diagram:

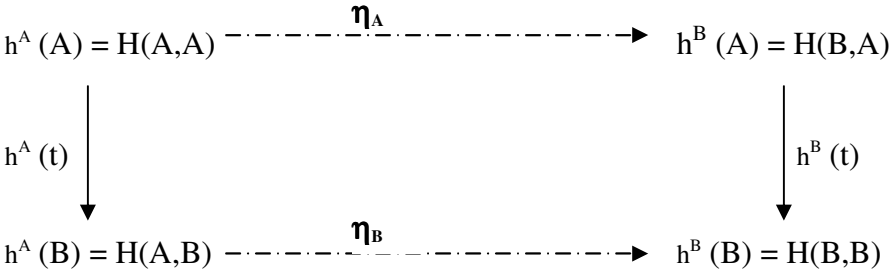


where morphisms v are induced by the inclusion mappings ***i***: A→A x I and the commutativity conditions $h^A = v \circ i$. The naturality of this diagram simply means that such Conditions hold for any functor h^A defined as above.

THE REPRESENTATION OF UNIMOLECULAR CHEMICAL REACTIONS AS **NATURAL TRANSFORMATIONS**:

The unimolecular chemical reaction can be thus represented by the natural

transformations $h^A \xrightarrow{\eta} h^B$, as one can readily check in the commutative diagram :



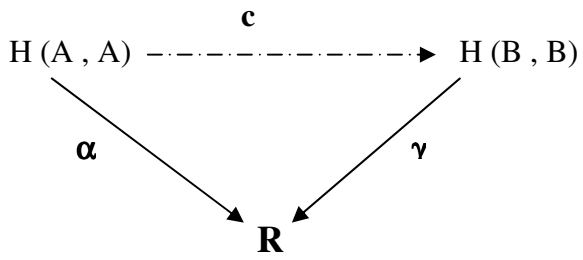
if the states of the molecular sets $A_u = a_1, \ldots, a_n$ and $B_u = b_1, \ldots b_n$ are represented by certain endomorphisms in H(A,A) and H(B,B), respectively.

THE OBSERVABLE OF AN m.s.v, B, CHARACTERIZING THE CHEMICAL PRODUCTS "B" OF A CHEMICAL REACTION IS A MORPHISM:

γ: H (B , B) ------> R

where R is **THE SET OF REAL NUMBERS** .

THIS OBSERVABLE IS SUBJECT TO THE FOLLOWING COMMUTATIVITY or NATURALITY CONDITION:



(5)

with $c : A_u^* \longrightarrow B_u^*$, and A*, B* being specially prepared FIELDS OF STATES, within a measurement uncertainty range, $\underline{\delta}$.

DEFINITION OF A ***MULTI-MOLECULAR REACTION*** :

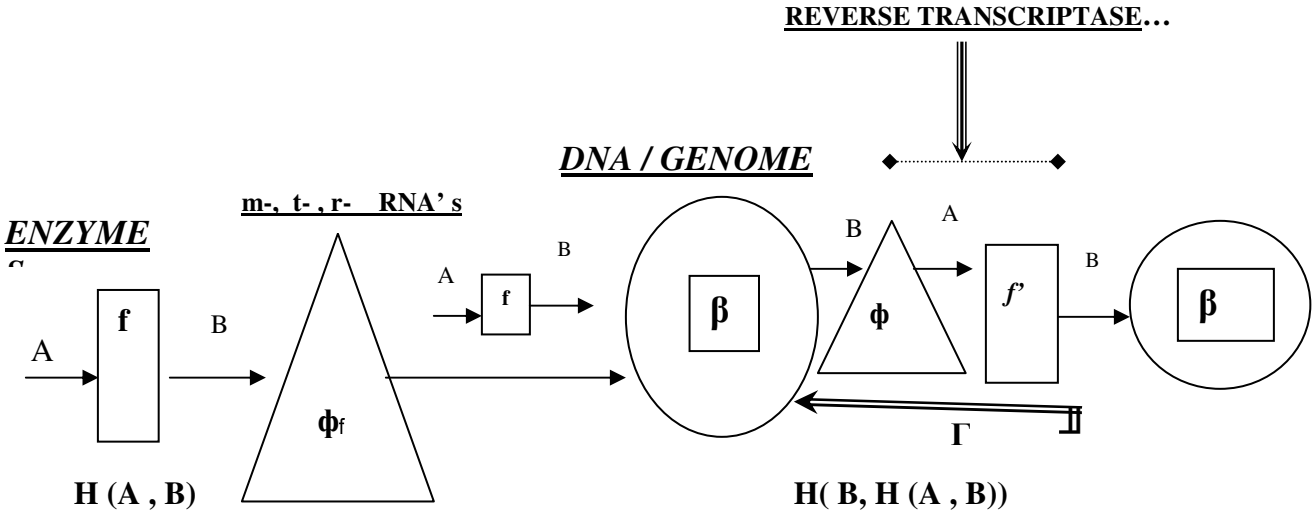
In the case of ***multi-molecular reactions***, the canonical functor of category theory:

$h : \underline{M} \dashrightarrow [M, Set]$ (4)

assigns to each molecular set $\underline{A}$ the functor $h^{A,}$ and to each chemical transformation

t: A ⟶ B, the natural transformation $h^A \xrightarrow{\eta} h^B$.

The simplest METABOLIC-REPAIR (M, R)-System with REVERSE TRANSCRIPTION.



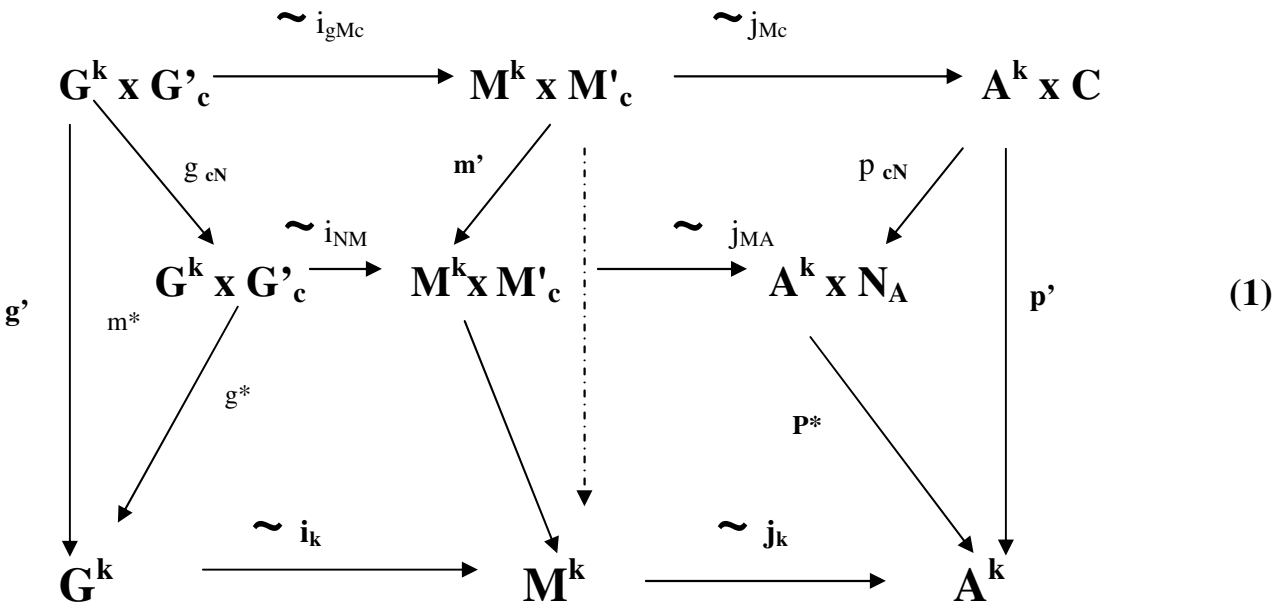
DNA Duplication and Cell Division follows next in this *linear* categorical diagram:
β : H(A,B) ⟶ H[B,H(A,B)].

FIGURE 1. The simplest (M, R)-System model of a Primordial Organism.

Possible molecular candidates are indicated at the top of the diagram in Figure 1, above the corresponding metabolic (f) or repair/ transcription (ϕ_f) components.
Living organisms have ***non-linear*** diagrams *with* **feedback** and **feedforward**. note in this case, the **'closure', functional mapping, Γ,** that physically regenerates the telomere and closes the DNA-loop at the end of the chromosome. (note also that the above diagram in fig.1 was updated in 2004; the original diagram in 1983 was completely linear, and did not have the **closure map Γ,** the telomere, the **reverse transcriptase, and the DNA duplication:** *they are now all represented in the updated diagram).*. ***Adding to this diagram an*** **hTERT** ***suppressor gene would provide a FEEDBACK mechanism for simulating the control of cell division and the possibility of cell cycle arrest that is present in somatic cells. The other alternative—which is preferred—is the addition of an*** **hTERT promoter gene that may need to be activated in order to begin cell cycling.** ***It would also allow us to introduce simple models of cancer cells and how they transform during Oncogenesis..***

STRUCTURAL 'HOMOLOGY' OF C- and Nu3-PROTEINS is caused by THE OVERLAP OF THE GENE C WITH THE GENE Nu3 IN THE BACTERIOPHAGE

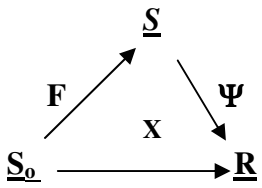
The mathematical representation of this Homology-like Sequence is given in Diagram (1):



(1)

The "homology" is mathematically represented by the isomorphisms i_{gMc}, i_{NM}, i_k, j_{Mc}, j_{MA}, j_k Regardless of the algebraic structure with which A^n , A^m, M'_c , M^k, M'_N, G^k, G'_c and G_N are endowed, the projections, p', p*, m', m*, g' and g* will always be defined. It is apparent from diagram (1) that transcription of the overlapping genes and the biosynthesis of the proteins for which they code will involve certain multi-molecular reactions. As shown in diagram (4) of ref. (l) these processes will lead to certain natural transformations, η, as specified in diagram (4) .

PHYSICOCHEMICAL MEASUREMENTS ON ORGANISMIC STRUCTURES, **S_o**, YIELD CERTAIN ***OBSERVABLES*** **F**: S_o ----> ***S*** ; these are defined NATURALLY, such that the DIAGRAM OF CATEGORIES AND ALGEBRAIC THEORIES :



is ***commutative*** .

Such observables of **S**$_o$ associate to each of its elements, e_j, at each moment, the biological activities of **S**$_o$ and the products made as a result of such activities. **S** was shown to be an **algebraic theory** and is built from *cartesian products* of the sets describing the biological activities and biochemical products of such activities. Physicochemical measurements on **S$_o$** produce real numbers so that certain general observables X: **S**$_o$ → R are defined naturally.

AN ALTERNATIVE , QUANTITATIVE APPROACH TO RELATIONAL BIOLOGY IS PROVIDED BY **LATTICE-VALUED RELATIONS**, L.V.R' s (introduced by MUIR AND WARNER in ref. 8) :

λ : A x B →LATTICE
λ = FUNCTION
A = SET, B= SET.

EXAMPLES:

l) λ: A x A → **[0,1]** is a **FUZZY RELATION** ;

2) λ: S x S → **H(L,I)** is a **MARKOV PROCESS WITH CONTROLS**

(S =state-space, L= **LATTICE** OF MEASURABLE SETS IN A PROBABILITY SPACE,
I = SET OF INPUTS to the AUTOMATON,
p:L →I is a **MAPPING** in the SET **H(L, I)** ;

3) **λ: Luk$_n$ x Luk$_n$ → H(L , I)**

is a STOCHASTIC,GENETIC NETWORK , **Luk$_n$ = L-ALGEBRA**, and **H(L ,I)** is defined as in the MARKOV PROCESS WITH CONTROLS.

L .V. R' s measure the **STRENGTH OF RELATIONS** in ORGANISMIC STRUCTURES, and were applied to study HORMONAL CONTROL AND SEVERAL METABOLIC PROCESSES.

FUTURE **L.V.R**. DEVELOPMENTS will include **L.V.R- MORPHISMS**, **GROUP L.V.R's**, **L.V.R-HOMOLOGY**, and **N-ARY** L.V.R's to model METABOLIC PROCESSES such as **RIBOSOME BIOGENESIS AND PROTEIN BIOSYNTHESIS IN CELLS .**

NATURAL TRANSFORMATIONS IN PROTEIN BIOSYNTHESIS AND EMBRYOGENESIS.

THE SET OF r-PROTEINS is H (A,B)

THE SET OF r-PROTEIN mRNA's is H(B, H(A,B))

THE GENOME TRANSCRIBED INTO r-PROTEIN mRNA is then H(H(A,B), H(B,H(A,B))

(SEE ALSO FIGURE 1 FOR CLARITY)

Consider: { TWO SETS X and Y in THE METABOLIC CATEGORY, M
THE MAPPING t: X → Y of M

DEFINITION OF THE SPECIAL FUNCTOR h^X : M → Set

$h^X(Y) = H(X,Y)$ for any set Y in M;

$h^X(t) = m : H(X,X) \rightarrow H(X,Y)$ for any t: X → Y;

$h^X(g)(t) = g \circ t : H(X,X) \rightarrow H(X,Y')$ for any g: Y → Y' in M ,

where X is a certain fixed object in M. The functor h^X carries Y into H(X,Y)

CONSTRUCTION OF THE SET H (B, H (A, B) of r-PROTEIN mRNAs USING THE CANONICAL FUNCTQR h : M → [M, Set]

Is defined as

$S \sim\sim\rightarrow h^X$ and $\mathbf{t} \sim\sim\rightarrow h^X \xrightarrow{\eta_t} h^Y$,

Where t: X→ Y and [M, Set] is a category of functors from M to Set.

An embedding I: M →Set and Phi: I-→ h^X are natural transformations

and define protein and mRNA's (elements of H (X, H (X, Y)))

EMBRYOGENESIS AND NUCLEAR EQUIVALENCE. NUCLEAR TRANSPLANT EXPERIMENTS

NUCLEAR EQUIVALENCE IMPLIES THE EXISTENCE OF CERTAIN DYNAMIC ISOMORPHISMS BETWEEN THE DYNAMIC SYSTEMS REPRESENTING NUCLEI AT DIFFERENT, EQUIPOTENT STAGES OF DEVELOPMENT:

$$S[A,U(B)] \tilde{\;}\!\!\rightarrow S'[K(A,B)]$$

CATEGORIES: S -GENERATES THE DYNAMIC SYSTEM ASSOCIATED WITH THE NUCLEUS AT STAGE 1; THIS IS A DYNAMIC SYSTEM D;

S' -GENERATES THE DYNAMIC SYSTEM CORRESPONDING TO NUCLEUS IN DEVELOPMENTAL STAGE 2 :

THIS IS SYSTEM D'

ADJOINT FUNCTORS: U and K (form an ADJOINT PAIR)

$$S \xrightarrow{K} S' \xrightarrow{U} S$$

THE PROGRESSIVELY RESTRICTED ABILITY OF THE NUCLEUS TO DEVELOP "NORMALLY" WHEN TRANSPLANTED FROM THE MORE ADVANCED STAGES OF DEVELOPMENT IS MODELLED BY DYNAMIC EPIMORPHISMS:

$$S\,[X,V(Y)] \overset{EPI}{\rightarrow} S'\,[W(X),Y]$$

where V and W are a PAIR OF **WEAKLY** ADJOINT EUNCTORS:

$$S \overset{W}{\longrightarrow} S' \overset{V}{\longrightarrow} S$$

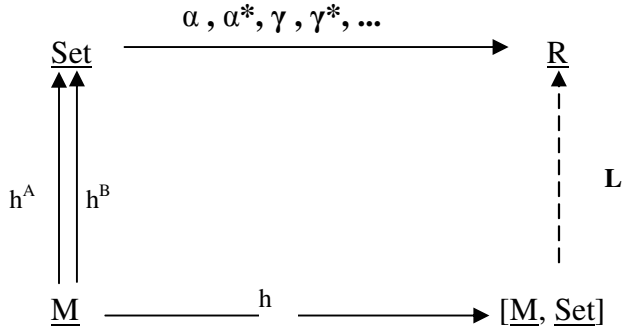
THE DYNAMIC TRANSFORMATION **d: So ---→ So** .OF AN EMBRYO

DESCRIBES THE EMBRYOGENESIS WHEN NATURAL TRANSFORMATIONS OF**d**-TYPE FUNCTORS DEFINE DEVELOPMENTAL STAGES IN MOLECULAR TERMS- AS MULTI-MOLECULAR TRANSFORMATIONS.

PROTEIN BIOSYNTHESIS DEFINED AS A MULTI-MOLECULAR REACTION VIA NATURAL TRANSFORMATIONS

SUCH MULTI-MOLECULAR REACTIONS LEAD TO GENERALIZED OBSERVABLES

Such processes induce certain natural transformations υ: α ---→α*: and ω: γ --→γ*:, with α , α*: Set →R and γ , γ*: Set→ R being certain special functors. From the definitions of natural transformations and multi-molecular reactions (see formulae (2)-(5) in Section (1) one obtains the following commutative diagram



with ***L*** playing the role of a ***generalized observable***. In this diagram, the *canonical* functor h assigns to each *molecular set A* the functor h^A and to each *chemical transformation* t: A→B, the natural transformation η : h^A → h^B.

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Note:

The Earliest Quantum Automata and Quantum Dynamics in terms of Category Theory:

It is often assumed that 'Categorification' of Quantum Field Theory, or the formal use of the Theory of Categories in Quantum Gravity and Topological Quantum Field theories (TQFTs) began in the 1990s. In fact, the concepts of Quantum Automata and Quantum Dynamics represented in terms of Categories, Functors and Natural Transformations were formally introduced as early as 1968-1973 (Bull. Math. Biophysics, 33:339-354 (1971), and references cited therein). The self-contained presentation in the earliest 1968 paper on Categorical Dynamics introduce all necessary concepts for a student just entering this 'new' field. This earliest 1968 publication is currently available on the web.

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