# An Application of Category Theory to the Study of Complex Networks

Taichi Haruna

Department of Earth and Planetary Sciences, Graduate School of Science,
Kobe University, 1-1, Rokkodaicho, Nada, Kobe, 657-8501, Japan
PRESTO, JST, 4-1-8 Honcho Kawaguchi, Saitama, Japan
tharuna@penguin.kobe-u.ac.jp

**Abstract**

We propose a new data analytical tool for directed networks by using category theory. We develop a category theoretical treatment of directed networks in order to obtain functional networks for real networks. By applying our method to concrete data on real information processing biological networks, we find a distinguishing global structure of functional networks. A possibility of a new hypothesis on network motifs is also indicated based on our theory and data analysis.

**Keywords** : Directed Networks, Category Theory, Presheaves, Information Processing, Network Motifs.

## 1 Introduction

A network represented as a directed graph consists of a set of nodes and a set of arcs between each pair of nodes. A node is just a point, both structure-less and function-less. However, nodes in real networks often have structures or functions. For example, a node in a gene transcription regulation network consists of a gene and a protein coded by that gene (Arcs are regulation relations). There is information processing from DNA to protein in each node, which can be seen as a function of each node. Such aspect is usually neglected in the study of complex networks since the statistical property of the entire network is the main focus in this field [4, 17].

It would be useful for further understanding of real networks if we can obtain a formal representation including a function of nodes. In this paper we develop a general way to associate a function with each node in a network. In particular, we focus on information processing as a function of nodes. We simply represent information processing in a node by a directed graph. We use category theory to construct our theory [13].

In the previous work on applications of category theory to theoretical biology, category theory is used to describe general framework to describe general organization of biological systems [7, 8, 18, 19, 21]. In contrast our aim in this paper is to show that category theory can provide a new tool in order to analyze concrete biological networks.

This paper is organized as follows. In section 2 we develop a category theoretical treatment of directed networks and obtain functional networks for real networks. In section 3 we apply our theory to real network data. In section 4 we suggest a possibility of a new hypothesis on network motifs based on our theory and data analysis. In section 5 we give conclusions.

## 2 Construction of Functional Networks for Directed Networks

In this section we develop a category theoretical treatment of directed networks. We describe how to associate a function with each node in a directed network so that we obtain functional networks for real networks.

### 2.1 Networks as Presheaves

We consider networks that can be represented as directed graphs. A directed graph is a quartet $G = (A, O, \partial_0, \partial_1)$ where $A$ is a set of arcs, $O$ is a set of nodes and $\partial_i (i = 0, 1)$ are functions from $A$ to $O$ taking a source of each arc $(i = 0)$ or a target of each arc $(i = 1)$. A directed graph $G = (A, O, \partial_0, \partial_1)$ can be seen as a presheaf in the following way. Let $\mathbf{C_2}$ be a finite category defined by the following diagram:

$$0 \underset{m_1}{\overset{m_0}{\rightrightarrows}} 1.$$

We can make $G$ a functor from $\mathbf{C_2}^{\mathrm{op}}$ to the category of sets $\mathbf{Set}$ by setting $G(1) = A, G(0) = O$ and $G(m_i) = \partial_i (i = 0, 1)$. Thus $G$ is a presheaf on the category $\mathbf{C_2}$.

A homomorphism $D$ from a directed graph $G = (A, O, \partial_0, \partial_1)$ to a directed graph $G' = (A', O', \partial_0', \partial_1')$ is a pair of two maps $D_A : A \to A'$ and $D_O : O \to O'$ satisfying $\partial_i' \circ D_A = D_O \circ \partial_i (i = 0, 1)$. That is, $D$ preserves sources and targets. If we think of $G$ and $G'$ as presheaves then $D$ is a natural transformation from $G$ to $G'$. Thus we can identify the category of directed graphs $\mathbf{Grph}$ with the category of presheaves on $\mathbf{C_2}$ denoted by $\mathbf{Set}^{\mathbf{C_2}^{\mathrm{op}}}$. Indeed they are isomorphic categories.

In the following we make use of category theoretical structures in order to study directed graphs. Hence we shall use the presheaf notation to denote directed graphs.

### 2.2 Representation of Function of Nodes

We focus on information processing as a function of nodes in a network. We do not consider what information is processed but treat patterns of information flow. We consider a unit for patterns of information flow consists of the following three aspects: receiving, transformation and sending of information. We represent this by a directed graph consisting of two distinct nodes and an arc between them:

$$\bullet \to \bullet.$$

Thus any directed graph would represent a pattern of information flow. Now we would like to associate a pattern of information flow to each node in a network. We can achieve this by considering a functor called distributor in category theory.

Let $\mathbf{A}, \mathbf{B}$ be small categories. A *distributor* (or *module*) from $\mathbf{A}$ to $\mathbf{B}$ is just a functor $D : \mathbf{A} \to \mathbf{Set}^{\mathbf{B}^{\mathrm{op}}}$ [5]. The notion of distributor is considered as a generalization of binary relation. They form a bicategory. However, we consider only a special case with $\mathbf{A} = \mathbf{B} = \mathbf{C_2}$ in this paper.

In the case $\mathbf{A} = \mathbf{B} = \mathbf{C_2}$ we call a distributor $M : \mathbf{C_2} \to \mathbf{Set}^{\mathbf{C_2}^{\mathrm{op}}}$ *information processing pattern*. In this case $M$ consists of the following data: two directed graphs $M(0), M(1)$ and two directed graph homomorphisms $M(m_0), M(m_1) : M(0) \to M(1)$. $M(0)$ is a representation of a function of each node, which we call a pattern of information flow at the beginning of this subsection. $M(1)$ is for an arc in a network which represents how functions of two nodes are related when there is an arc between two nodes. $M(m_0)$ and $M(m_1)$ specify a source part and a target part in $M(1)$ respectively by mapping $M(0)$ into $M(1)$.

Let us consider gene transcription regulation networks as an example. If a protein coded by a gene $X$ regulates a gene $Y$ then there is an arc from $X$ to $Y$. There is complicated chemical information processing from DNA to protein including transcription, translation and synthesis in a node. However, here we focus on an overall pattern of information flow. We represent information flow from DNA to protein by a directed graph consisting of two distinct nodes and an arc between them. Thus we put

$$M(0) = \bullet \to \bullet.$$

The source node in $M(0)$ is an abstraction for DNA whose function is considered as receiving information and the target node in $M(0)$ is an abstraction for protein whose function is considered as sending information. If there is an arc from $X$ to $Y$ then we could imagine the sending of information in $X$ contacts to the receiving of information in $Y$. We represent this situation just by identifying them as a node. Thus we define

$$M(1) = \bullet \to \bullet \to \bullet.$$

$M(m_0)$ is defined by sending the unique arc in $M(0)$ to the left arc in $M(1)$. $M(m_1)$ is defined by sending the unique arc in $M(0)$ to the right arc in $M(1)$.

The above argument can be applied to not only gene transcription regulation networks but also the other information processing biological networks such as neuronal networks, signal transduction networks and so on.

One may consider more complicated directed graphs for $M(0)$ and $M(1)$. However, in the following we mainly consider the information processing pattern $M$ defined above since its intuitive meaning is obvious and it is mathematically easy to tractable. We denote this information processing pattern by $M_0$.

## 2.3 Functional Networks for Real Networks

First let us consider a general situation. Let $\mathbf{C}$ be a small category and $D$ be a distributor $\mathbf{C} \to \mathbf{Set}^{\mathbf{C}^{\mathrm{op}}}$. $D$ induces a Hom-tensor adjunction on $\mathbf{Set}^{\mathbf{C}^{\mathrm{op}}}$ in the following way. Define a functor $R_D : \mathbf{Set}^{\mathbf{C}^{\mathrm{op}}} \to \mathbf{Set}^{\mathbf{C}^{\mathrm{op}}}$ by sending $G$ to $R_D(G) = \mathrm{Hom}(D(-), G)$. For an object $c$ in $\mathbf{C}$ $R_D(G)(c) = \mathrm{Hom}(D(c), G)$, which is the set of all natural transformations from $D(c)$ to $G$. Given a morphism $u : c' \to c$ in $\mathbf{C}$, $R_D(G)(u)$ is a map from $\mathrm{Hom}(D(c), G)$ to $\mathrm{Hom}(D(c'), G)$ defined by composition from right $(-) \circ D(u)$:

$$D(c') \overset{D(u)}{\to} D(c) \to G.$$

$R_D$ has a left adjoint $L_D$ defined as follows. Let $G$ be a presheaf on $\mathbf{C}$. The *category of elements for $G$* denoted by $\int_{\mathbf{C}} G$ is defined by the following data: Objects are pairs $(c, x)$ where $c$ is an object in $\mathbf{C}$ and $x \in G(c)$. A morphism from $(c', x')$ to $(c, x)$ is a morphism $u : c' \to c$ in $\mathbf{C}$ with $G(u)(x) = x'$. Let $\pi_G$ be a functor $\int_{\mathbf{C}} G \to \mathbf{C}$ defined by $\pi_G(c, x) = c$. Then we define $L_D(G)$ as the following colimit:

$$L_D(G) = \mathrm{Colim} \left( \int_{\mathbf{C}} G \overset{\pi_G}{\to} \mathbf{C} \overset{D}{\to} \mathbf{Set}^{\mathbf{C}^{\mathrm{op}}} \right).$$

In other words, $L_D$ is a left Kan extension of $D$ along Yoneda embedding $\mathbf{y} : \mathbf{C} \to \mathbf{Set}^{\mathbf{C}^{\mathrm{op}}}$.

For a presheaf $G$ on $\mathbf{C}$ and an object $d$ in $\mathbf{C}$ we have

$$L_D(G)(d) = \left( \sum_{c \in \mathbf{C}} G(c) \times D(c)(d) \right) / \sim,$$

where $\sim$ is an equivalence relation generated by $(\alpha \cdot u, y) \sim (\alpha, u \cdot y)$, $\alpha \cdot u = G(u)(\alpha)$ and $u \cdot y = D(u)(d)(y)$ for $\alpha \in G(c)$, $y \in D(c')(d)$ and a morphism $u : c' \to c$ in $\mathbf{C}$. We write $\alpha \otimes y$ for an equivalence class containing $(\alpha, y)$.

We have a natural isomorphism $\mathrm{Hom}(L_D(F), G) \cong \mathrm{Hom}(F, R_D(G))$ for any presheaves $F, G$ on $\mathbf{C}$. Since $L_D$ is a left adjoint to a Hom functor $R_D$, we may write $L_D(F) = F \otimes D$. Indeed we have a property of usual tensor products for modules, associativity for "coefficients", namely $(\alpha \cdot u) \otimes y = \alpha \otimes (u \cdot y)$. For the proof of the adjunction $L_D \dashv R_D$ see [9, 12].

Now we go back to our finite category $\mathbf{C_2}$. Given an information processing pattern $M : \mathbf{C_2} \to \mathbf{Set}^{\mathbf{C_2}^{\mathrm{op}}}$ and a directed graph $G$ (recall that a directed graph is a presheaf on $\mathbf{C_2}$), $R_M(G)$ is also a directed graph. How can we interpret $R_M(G)$? $R_M(G)(0) = \mathrm{Hom}(M(0), G)$ is the set of nodes for $R_M(G)$. Each node is a homomorphism from $M(0)$ to $G$. Hence each image of $M(0)$ in $G$ is collapsed into a node in $R_M(G)$. Similarly each image of $M(1)$ in $R_M(G)$ is collapsed into an arc in $R_M(G)$. In short, we can say that $R_M$ collapses $M$ in $G$.
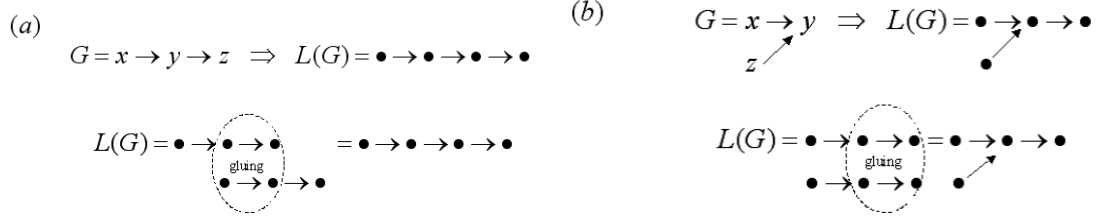
**Fig. 1**: Two examples for the calculation of $L_{M_0}$ (subscript $M_0$ is omitted in the figure).

On the other hand, we can say that $L_M$ embeds $M$ into $G$. Indeed we have the following representation of $L_M(G)$ if $G$ has no isolated node. Assume that for any $x \in G(0)$ there is $\alpha \in G(1)$ such that $\alpha \cdot m_0 = x$ or $\alpha \cdot m_1 = x$. Then we have

$$L_M(G)(i) \cong G(1) \times M(1)(i)/\sim$$

for $i = 0, 1$, where $\sim$ is generated by $(\alpha, \psi) \sim (\alpha', \psi') \Leftrightarrow \exists y \in M(0)(i) \; \exists j_0, j_1 \in \{0, 1\}$ such that $\alpha \cdot m_{j_0} = \alpha' \cdot m_{j_1}, \psi = m_{j_0} \cdot y, \psi' = m_{j_1} \cdot y$ for $(\alpha, \psi), (\alpha', \psi') \in G(1) \times M(1)(i)$. We can read this equation for $L_M(G)$ as follows: first make a copy of $M(1)$ for each arc in $G$ and second glue them according to how arcs are connected in $G$. Some examples for the calculation of $L_{M_0}(G)$ is given in Figure 1.

Given any directed network $G$ we obtain a directed graph $L_M(G)$ constructed by embedding $M$ into $G$. Since we consider that $M$ represents a function, we would like to call $L_M(G)$ a *functional network* for $G$.

In the next section we obtain functional networks for real information processing biological networks by applying $L_{M_0}$ to them. We will find a distinguishing global structure of functional networks for real networks.

## 3   Data Analysis

In Figure 2 we apply $L_{M_0}$ to five real information processing biological networks provided at [1]. Explanations for these networks are found in [16]. A number associated with each $L_{M_0}(G)$ is the largest number of self-loops on a single node. It is typically on the pivot node for the largest fan.

In order to characterize the feature of functional networks for real networks quantitatively, we calculate two indices. The first index is the ratio of the number of nodes in $L_{M_0}(G)$ (denoted by $n'$) to the number of node in $G$ (denoted by $n$). The second index is the ratio of the maximum degree of a node in $L_{M_0}(G)$ (denoted by $d'_{\max}$) to $n$. The degree of a node is calculated by just summing in-degree and out-degree for the node. If there is a self-loop then it is counted only once. We can prove that $0 \le n'/n \le 2$ and $0 \le d'_{\max}/n \le 1$.

We plot the pair of indices $(n'/n, d'_{\max}/n)$ for five real networks in Figure 3 (black squares). For comparison, we also plot the pair of values for random networks (small
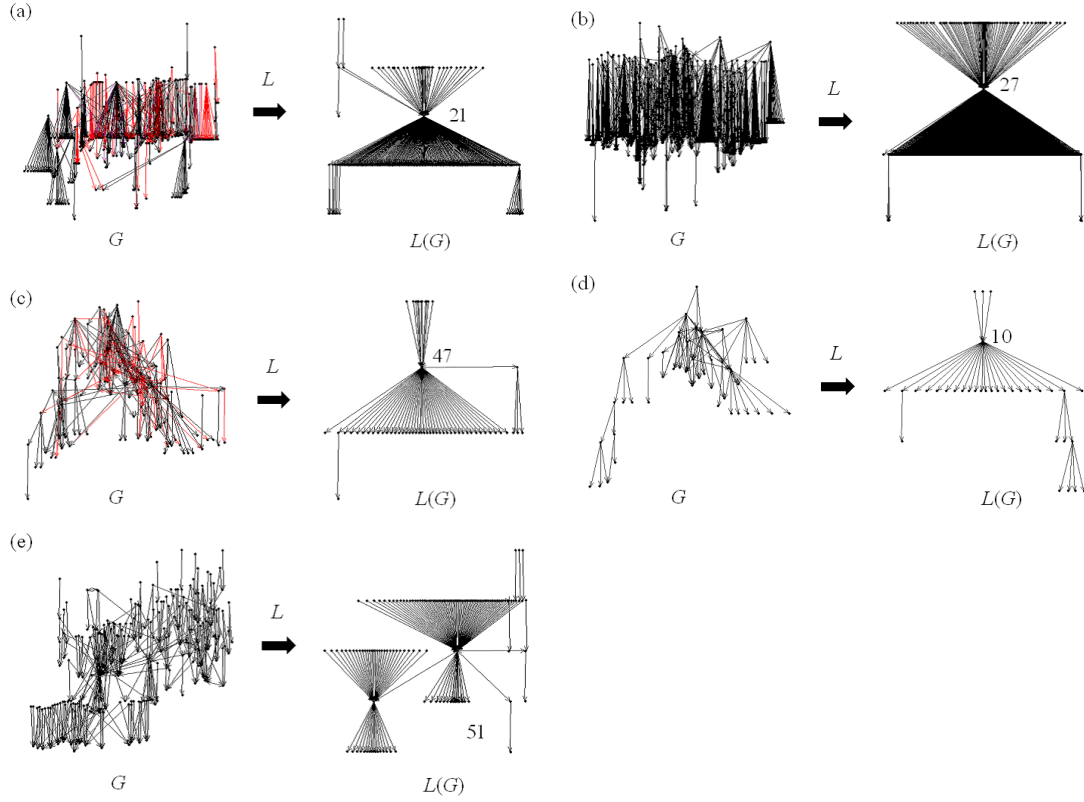
**Fig. 2**: Functional networks $L_{M_0}(G)$ for real information processing biological networks $G$ (subsript $M_0$ is omitted in the figure). A number associated with each $L_{M_0}(G)$ is the largest number of self-loops on a single node. (a) Gene transcription regulation network of *E. coli*. (b) Gene transcription regulation network of *S. cerevisiae*. (c) Developmental gene transcription regulation network of drosophila. (d) Developmental gene transcription regulation network of sea urchin. (e) Neuronal synaptic network of *C. elegans* (only synaptic connections with more than or equal to 5 synapses are included). All network data used are provided at [1].
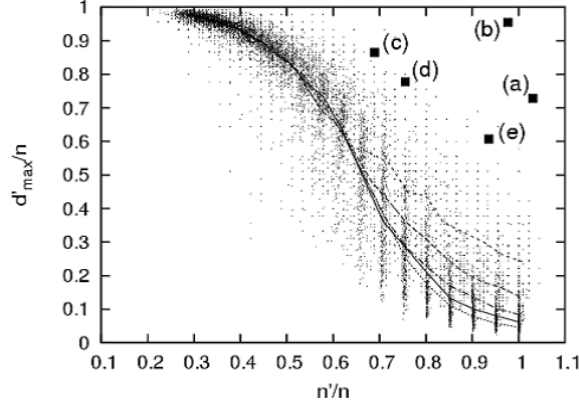
**Fig. 3**: Plot for $(n'/n, d'_{\max}/n)$ where $n$ is the number of nodes in real (and random) networks, $n'$ is the number of nodes in functional networks and $d'_{\max}$ is the maximum degree of a node in functional networks. Real networks (black squares) and random networks (small dots) are shown. Symbols for real networks correspond to those in Figure 2. See text for detail.

dots). Random networks are prepared as follows. For each real networks, we fix $n$ and vary the number of arcs $a$ from $n$ to $2n$. For each pair $(n, a)$ we generate 100 random networks that have $n$ nodes and $a$ arcs with no isolated node. Lines are averages of random networks for each real network.

One can see a trade-off between the two indices for random networks. This can be roughly understood as follows. If $a$ is close to $n$ then copies of $M_0(1)$ are hard to be glued. Hence random networks with $n$ nodes and $a$ arcs have relatively high values of $n'$ and low values of $d'_{\max}$ in their functional networks. On the other hand, if $a$ is large (close to $2n$) then copies of $M_0(1)$ tend to be glued into a few nodes with many self-loops. Hence we obtain functional networks with low values of $n'$ and high values of $d'_{\max}$.

Obviously real networks are deviated from the trade-off curve for random networks. Their typical tendency is that their functional networks have nearly the same number of nodes as that for real networks and have a high maximum degree of a node. Combining with visual inspections for Figure 2, we suggest a distinguishing global structure of functional networks for real networks (Figure 4). Functional networks for real networks typically have many input nodes and many output nodes together with a central node with the small number of self-loops. We would like to call such structure *bottleneck structure*.

In the next section we discuss implications of the bottleneck structure in functional networks for real network structures.
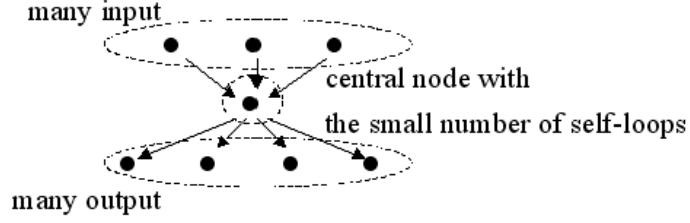
**Fig. 4**: Distinguish global feature of functional networks for real information processing biological networks.

## 4  Toward a New Hypothesis on Network Motifs

In this section we first obtain the condition that directed networks are stable under embedding of information processing pattern $M_0$. Second we suggest a possibility of new hypothesis on network motifs by combining the stability condition and the result of data analysis in the previous section.

Given an information processing pattern $M$, we say a directed graph $G$ is *stable* for $M$ if $\eta_G : G \to R_M L_M(G)$ is an isomorphism where $\eta$ is a unit of adjunction $L_M \dashv R_M$. This means that all functional constraint by $L_M(G)$ is already incorporated into $G$.

We can obtain the stability condition for $M_0$ as an explicit condition for the structure of directed graphs. We have $\eta_G : G \cong R_{M_0} L_{M_0}(G)$ if and only if (i) $G$ is a binary graph (that is, there is at most one arc from one node to another node) and (ii) if $a \to b \leftarrow c \to d$ in $G$ then $a \to d$ in $G$ where we write $a \to b$ when there is an arc from node $a$ to node $b$. In particular, we call the second condition (ii) *bifan condition*. An intuitive explanation for a proof of the "if part '' is given in Figure 5(a).

More generally, one can see that a multi-fan structure in a real network corresponds to a bottleneck structure (without self-loops) in its functional network under the stability condition for $M_0$ (Figure 5(b)).

We can prove that the bifan condition is generic in the following sense. Let $\mathbf{C}$ be a small category and $M, N : \mathbf{C} \to \mathbf{Set}^{\mathbf{C}^{\mathrm{op}}}$ be two distributors. We define a tensor product between $M$ and $N$ (denoted by $M \otimes N$) by the following composition of functors [5]:

$$\mathbf{C} \xrightarrow{M} \mathbf{Set}^{\mathbf{C}^{\mathrm{op}}} \xrightarrow{L_N} \mathbf{Set}^{\mathbf{C}^{\mathrm{op}}}.$$

Thus for any object $c$ in $\mathbf{C}$ we have $(M \otimes N)(c) = M(c) \otimes N$. If we consider the case $\mathbf{C} = \mathbf{C_2}$ then we can obtain more complicated information processing pattern $M \otimes N$ from simpler ones ($M$ and $N$). We have the following theorem:

(a)

$L$:embedding $M_0$

bifan

$R$:collapsing $M_0$

(b)

Multi-fan structure in real network    Bottleneck structure in functional network
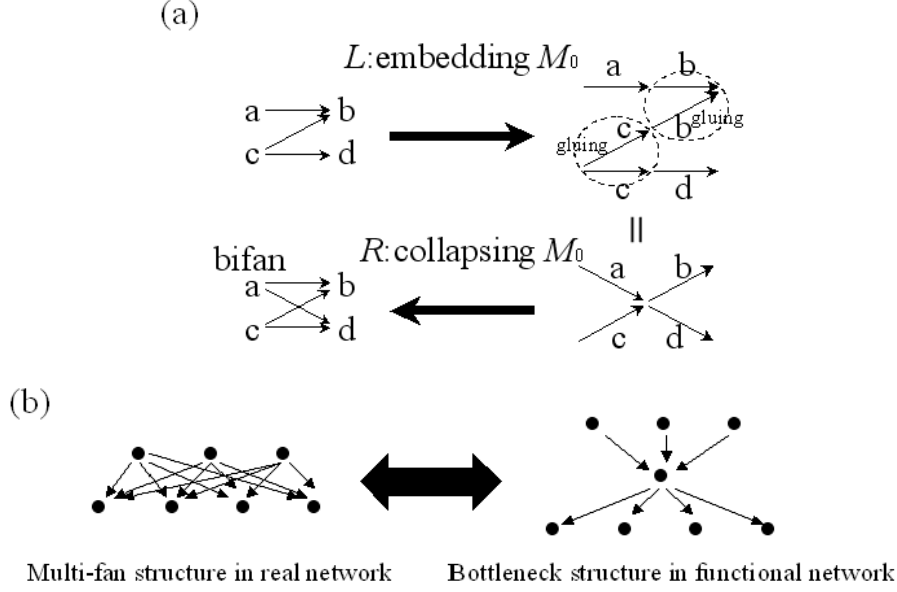
**Fig. 5**: (a) An intuitive sketch of derivation of the stability condition for $M_0$. See text for detail. (b) The correspondence between multi-fan structure in real networks and bottleneck structure in their functional networks under the stability condition.

**Theorem 1** *For any information processing pattern $N$, consider a tensor product $M_0 \otimes N$. If a directed graph $G$ is stable for $M_0 \otimes N$ then the bifan condition holds for $G$.*

*Outline of a proof.* Assume $\eta_G : G \cong \mathrm{Hom}(M_0 \otimes N(-), G \otimes (M_0 \otimes N))$ and $a \to b \leftarrow c \to d$ in $G$. We have $\varphi \in \mathrm{Hom}(M_0(1), G \otimes M)$ corresponding to a possible arc $a \to d$ in $G$. We define $\varphi_N \in \mathrm{Hom}(M_0(1) \otimes N, (G \otimes M_0) \otimes N)$ by $\varphi_N(i)(\alpha \otimes y) = \varphi(j)(\alpha) \otimes y$ for $(\alpha, y) \in M_0(1)(j) \times N(j)(i)$. Since $G \otimes (M_0 \otimes N) \cong (G \otimes M_0) \otimes N$ and $G \cong \mathrm{Hom}(M_0 \otimes N(-), G \otimes (M_0 \otimes N))$ by assumption, $\varphi_N$ corresponds to an arc $a \to d$ in $G$, which now exists. $\qquad \square$

Thus the bifan condition is a necessary condition so that a directed graph is stable for an information processing pattern of the form $M_0 \otimes N$.

Now we discuss implications of our theory and data analysis for real network structures. Network motifs are patterns found in given networks that are significantly more frequently than those in randomized networks [2, 3, 14, 15]. Bifan is a typical network motif in real networks. It is ubiquitously found in various real information processing biological networks and is most over-represented [10, 11]. In the previous work, the abundance of a motif in a real network is explained by its function considered as a dynamical system [2, 3]. Here both structure and function are considered locally. Such an explanation seems to succeed in the case of feed-forward

loop motif [2, 3]. However, function of bifan is still controversial [10, 11].

Our theory and data analysis suggests a new possibility. First the fact that bifan is over-represented in real networks suggests that real networks have a tendency toward a stabilization in our sense. Furthermore, we see that the correspondence between multi-fan structure in real networks and bottleneck structure in their functional networks under the stability condition. It suggests that a possibility that the abundance of bifan in real networks is explained in relation to the global feature of functional networks.

We should note that the meaning of our stability condition is not obvious. In particular, its relation to dynamical stability is still unknown. However, our theory and data analysis suggest a totally new direction (global perspective) different from the previous one (local perspective).

## 5   Conclusions

In this paper we proposed a new approach to the study of complex networks. By developing a category theoretical treatment of directed networks, we constructed a systematic method to obtain functional networks for real networks. We applied our theory to a few real information processing biological networks. We found a distinguishing global structure of functional networks for real networks compared to randomized networks. We suggested a possibility of a new hypothesis on network motifs based on our theory and data analysis.

Many tasks are left as future work. A few of them are listed below:

 (i) More enhanced data analysis.

 (ii) Calculation of stability condition for more general information processing patterns.

(iii) Relation to dynamical stability.

(iv) Experimental study for our approach to network motifs.

For a theoretical issue, we would like to put a few words on (ii). For information processing pattern $M_0$, $T_{M_0} := R_{M_0} L_{M_0}$ is an idempotent monad since we have $R_{M_0} L_{M_0} R_{M_0} \cong R_{M_0}$. Hence the category of $T_{M_0}$-algebras is equivalent to the category of free $T_{M_0}$-algebras, which is equivalent to a full subcategory of **Grph** consisting of directed graphs $G$ satisfying $\eta_G : G \cong T_{M_0}(G)$ [6]. This suggests that we should obtain a condition for more general information processing patterns $M$ such that the corresponding monads $T_M$ become idempotent. One might classify information processing patterns $M$ satisfying this undiscovered condition based on the stability condition.

Applications of category theory to theoretical biology originated from the work of Robert Rosen, who is also a pioneer in the study of anticipatory systems [20]. In

one of his early papers [19], he introduced a conversion which sends input-output systems to diagrams that he called abstract block diagrams. This conversion is the fundamental basis for his work on Metabolism-Repair systems. The essence of the idea of the conversion is inversion of nodes and arcs, that is, each arc is converted to a node. One can see that this conversion is embedded in the functor $R_{M_0}$ since each arc in a directed graph $G$ is sent to a node in $R_{M_0}(G)$ when $R_{M_0}$ is applied to $G$. Although the details of Rosen's conversion and the functor $R_{M_0}$ are different, the spirit is quite similar. This connection with Rosen's work suggests a potentiality of our approach for applications to anticipatory systems.

**Acknowledgements**

# References

[1] http://www.weizmann.ac.il/mcb/UriAlon/

[2] U. Alon, *Introduction to Systems Biology: Design Principles of Biological Circuits.* CRC Press, Boca Raton, 2006.

[3] U. Alon, Network motifs: theory and experimental approaches. *Nature Rev. Genet.* 8, 450-461, 2007.

[4] R. Albert and A.-L. Barabasi, Statistical mechanics of complex networks. *Rev. Mod. Phys.* 74, 47-97, 2002.

[5] J. Benabou, Distributors at work. preprint, 2000.

[6] F. Borceux, *Handbook of Categorical Algebra: Volume 2.* Cambridge Univ. Press, Cambridge, 1994.

[7] A. C. Ehresmann, J.-P. Vanbremeersch, Hierarchical evolutive systems: A mathematical model for complex systems. *Bull. Math. Biol.* 49, 13-50, 1987.

[8] T. Haruna and Y.-P. Gunji, Duality between decomposition and gluing: A theoretical biology via adjoint functors. *BioSystems* 90, 716-727, 2007.

[9] T. Haruna, *Algebraic Theory of Biological Organization.* Doctoral Dissertation, Kobe University, 2008.

[10] P. J. Ingram, *et al.*, Network motifs: structure does not determine function. *BMC Genomics* 7:108, 2006.

[11] A. Lipshtat, *et al.*, Functions of bifans in context of multiple regulatory motifs in signaling networks. *Biophys. J.* 94, 2566-2579, 2008.

[12] S. MacLane, I. Moerdijk, *Sheaves in Geometry and Logic: A First Introduction to Topos Theory.* Springer-Verlag, New York, 1992.

[13] S. MacLane, *Categories for the Working Mathematician, 2nd edition.* Springer-Verlag, New York, 1998.

[14] R. Milo, *et al.*, Network Motifs: Simple Building Blocks of Complex Networks. *Science* 298, 824-827, 2002.

[15] R. Milo, *et al.*, Superfamilies of Evolved and Designed Networks. *Science* 303, 1538-1542, 2004.

[16] Supporting online material for [15].

[17] M. E. J. Newman, The structure and function of complex networks. *SIAM Review* 45, 167-256, 2003.

[18] R. Rosen, A relational theory of biological systems. *Bull. Math. Biophys.* 20, 245-260, 1958.

[19] R. Rosen, The representation of biological systems from the standpoint of the theory of categories. *Bull. Math. Biophys.* 20, 317-341, 1958.

[20] R. Rosen, *Anticipatory Systems.* Pergamon Press, 1985.

[21] O. Wolkenhauer, J-H S. Hofmeyr, An abstract cell model that describes the self-organization of cell function in living systems. *J. Theor. Biol.* 246, 461-476, 2007.