Computation capacities of a broad class of signaling networks are higher than their communication capacities

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Abstract
Due to structural and functional abnormalities or genetic variations and mutations, there may be dysfunctional molecules within an intracellular signaling network that do not allow the network to correctly regulate its output molecules, such as transcription factors. This disruption in signaling interrupts normal cellular functions and may eventually develop some pathological conditions. In this paper, computation capacity of signaling networks is introduced as a fundamental limit on signaling capability and performance of such networks. In simple terms, the computation capacity measures the maximum number of computable inputs, that is, the maximum number of input values for which the correct functional output values can be recovered from the erroneous network outputs, when the network contains some dysfunctional molecules. This contrasts with the conventional communication capacity that measures instead the maximum number of input values that can be correctly distinguished based on the erroneous network outputs.

The computation capacity is higher than the communication capacity whenever the network response function is not a one-to-one function of the input signals, and, unlike the communication capacity, it takes into account the input–output functional relationships of the network. By explicitly incorporating the effect of signaling errors that result in the network dysfunction, the computation capacity provides more information about the network and its malfunction. Two examples of signaling networks are considered in the paper, one regulating caspase3 and another regulating NFκB, for which computation and communication capacities are investigated. Higher computation capacities are observed for both networks. One biological implication of this finding is that signaling networks may have more ‘capacity’ than that specified by the conventional communication capacity metric. The effect of feedback is studied as well. In summary, this paper reports findings on a new fundamental feature of the signaling capability of cell signaling networks.

Introduction
Intracellular signaling networks in a cell respond to incoming signals to regulate some target molecules, to properly control the cell function. In general, signaling networks have multiple inputs and multiple outputs. The inputs can be ligands that, upon binding to their receptors on the cell membrane, create a chain of interactions through some intermediate signaling molecules, such as receptors, kinases, phosphatases, etc. This way the network outputs, typically target proteins such as transcription factors, are collectively regulated to produce an appropriate response.

One possible way to model a signaling network is to consider it as a communication channel [1, 2]. From this point of view, a signaling network...
communicates and conveys signals from its inputs to the outputs.

An alternative approach for modeling a signaling network is to envision it as a computing machine. In this approach, a signaling network makes some computations on the incoming signals and produces some responses at the outputs, accordingly.

Each modeling approach can reveal certain features of signaling networks. While the communication channel framework has been applied to signaling networks [1, 2], the computing machine approach does not seem to have been explored so far. As demonstrated later in this paper, the developed computing machine framework appears to be advantageous for studying signaling failures and malfunctions in pathological signaling networks.

More specifically, in the introduced molecular computing machine framework, a signaling network is a molecular system that under normal conditions correctly computes the outputs based on the applied inputs. In other words, under normal conditions, a signaling network maps the inputs to outputs via a mapping or transformation \( f \). Examples of this mapping for some experimentally-verified signaling networks are provided later in the paper. However, for an abnormal signaling network that contains some dysfunctional molecules due to mutations or some structural/functional abnormalities, its mapping is generally different from \( f \). We call the abnormal mapping \( F \). The developed computing machine approach focuses on both \( f \) and \( F \), and hence on comparing the ways a signaling network computes its outputs under normal and abnormal conditions.

The difference between the normal and abnormal network mappings \( f \) and \( F \), respectively, is caused by dysfunctional molecules. This means abnormal deviation of the signaling network from its normal function, when some molecules become dysfunctional due to mutations or some structural/functional abnormalities.

A key concept in the computing machine framework is the computation capacity, which is fundamentally different from the communication capacity previously studied in signaling networks [1, 2]. The computation capacity provides a measure of the accuracy of the computation of a desired function \( f \). As demonstrated later in the paper, the computation capacity is generally larger than the communication capacity, and it directly accounts for the functional task carried out by the network, rather than focusing on input–output information transfer.

**Descriptive comparison of computation and communication capacities**

The communication capacity is the maximum amount of information that can be reliably transferred from the input of a communication channel to its output. The goal is reliable communication, i.e. correct recovery of the input message from the erroneous output. This is a reasonable model for a network that just transfers the information from its inputs to its outputs, without any processing or computation on the information. This is typically the case in man-made communication channels [3]. In such systems, the output and input are ideally the same, if there is no transmission error [3]. In contrast, in signaling networks, outputs are typically computed from inputs, and there is a desired function that maps the inputs to the outputs (examples are provided later in the paper). The goal of signaling systems therefore can be considered to be reliable computation, i.e. mapping inputs to correct outputs. In other words, the goal of a reliable computing network is ensuring that its erroneous outputs\(^7\) are as close as possible to the correct outputs. This necessitates a new definition for the capacity, and the computation capacity, introduced in [4], provides a useful choice. As defined rigorously later in the paper, the computation capacity of a signaling network is the maximum number of input values for which the functionally correct outputs, corresponding to the case when there is no dysfunctional molecule, can be recovered from the erroneous network outputs, which are affected by errors due to dysfunctional molecules. Later in the paper we provide examples of signaling networks and calculate both their communication and computation capacities. We will show that the predictions and interpretations obtained from the computation capacity provide novel insights on signaling networks. Communication capacity is more suitable to analyze the transduction noise in a network [1, 5], whereas computation capacity is well suited to study signaling failures in abnormal signaling networks.

The computation capacity is first introduced in the present paper for normal and abnormal networks, i.e. non-diseased and diseased (with dysfunctional molecules) networks. On the other hand, the communication capacity of non-diseased and diseased networks was previously introduced and studied in [2].

**Computation capacity of signaling networks—basic definitions**

Consider a system such as a signaling network, with \( X \) as its input, which computes the output according to the error-free mapping \( f \). So, the error-free output is \( f(X) \). When the system is erroneous due to the presence of the dysfunctional node in the network, output values can become different from correct output values. That is why we call them incorrect or erroneous output values, or in short, erroneous outputs (resulted from errors introduced by the dysfunctional node and propagated to the network output).
of some dysfunctional molecules, the mapping is called \( F \), so the erroneous output is \( F(X) \). If we consider the system as a communication channel, following the regular definition of channel capacity [6], the communication capacity of this system can be written as [7]

\[
C(F) = \max_{P(X)} \{ H(X) - H(X|F(X)) \} = \max_{P(X)} \{ I(X;F(X)) \},
\]  

(1)

where the maximization is over all input distributions \( P(X) \), the \( H \) symbols represent entropy and conditional entropy, respectively, and \( I(X;F(X)) = H(X) - H(X|F(X)) \) is the mutual information between \( X \) and \( F(X) \). The entropy \( H(X) \) measures the variability in the input, whereas the conditional entropy \( H(X|F(X)) \) measures the equivocation, or uncertainty, about the input given the erroneous output [6]. Following standard nomenclature, we will also refer to \( R(F) = H(X) - H(F(X)) \), for a fixed input distribution \( P(X) \), as the communication rate. Overall, equation (1) is the commonly-used maximum mutual information between the input and output, which is well justified in the context of communication, i.e., situations where, in the absence of electronic noise, the output is intended to reproduce the input [3]. However, in systems where the output \( f(X) \) is different from the input \( X \) even in the absence of any type of noise, the definition in equation (1) may underestimate the capacity of the system to reproduce the function \( f(X) \). Intuitively, in computing systems where the error-free function \( f(X) \) is not a one-to-one mapping, this \( H(X|F(X)) \) measure of equivocation generally overestimates the relevant uncertainty at the output, since the goal is recovering \( f(X) \), and not the input \( X \). As a result, the communication capacity may underestimate the true functional ‘capacity’ of the system to reproduce \( f(X) \). We demonstrate this later in the paper, using some experimentally-verified signaling networks. This motivates the introduction of the computation capacity concept. Note that with \( Y = F(X) \) being the erroneous output, the conditional entropy or equivocation in equation (1) is given by \( H(X|F(X)) = H(X|Y) = - \sum_y P(Y = y) \sum_x P(X = x|Y = y) \log_2 P(X = x|Y = y) \), where \( P \) and \( \log_2 \) stand for probability and the base 2 logarithm, respectively. This equivocation definition is modified in what follows, to obtain a new capacity definition which is more suitable for signaling networks.

### Table 1. Summary of communication and computation capacity-related metrics and definitions and results.

| X: input signal \( f(X) \); error-free network output \( F(X) \); erroneous network output \( H \): entropy | Equivocation | Capacity | 2Capacity |
| --- | --- | --- | --- |
| Communication metrics | \( H(X(F(X))) \) | \( C(F) = \max \{H(X) - H(X|F(X)) \} \) | Max number of \( X \) values such that \( X \) can be correctly recovered from \( F(X) \), i.e., max number of decodable or distinguishable inputs |
| Computation metrics | \( H(f(X)|F(X)) \) | \( C_c(F) = \max \{H(X) - H(f(X)|F(X)) \} \) | Max number of \( X \) values such that \( f(X) \) can be correctly recovered from \( F(X) \), i.e., max number of computable inputs |

For signaling networks, a more appropriate capacity metric is one that depends on the normal network mapping function \( f \) as well. We propose to use the following equivalent definitions for signaling networks

\[
C_c(F) = \max_{P(X)} \{ H(X) - H(f(X)|F(X)) \}
\]

\[
= \max_{P(X)} \{ I(f(X);F(X)) + H(X|F(X)) \},
\]  

(2)

where \( C_c(F) \) is the computation capacity of the erroneous function \( F \) with respect to the error-free function \( f \) [4]. In analogy with the communication rate \( R(F) \), we will refer to \( R_c(F) = H(X) - H(f(X)|F(X)) \), for a fixed input distribution \( P(X) \), as the computation rate. Recall that we have two different input–output network mappings: the error-free correct mapping \( f \) and the erroneous incorrect mapping \( F \). For modeling and analysis of abnormal signaling networks with some dysfunctional molecules, equation (2) is a more suitable metric than equation (1). This is because it emphasizes the differences between the correct and incorrect outputs of a network, caused by some abnormal conditions and dysfunctional molecules. This is reflected in the new equivocation term \( H(f(X)|F(X)) \) in the first definition in equation (2), which represents the ambiguity on \( f(X) \), the correct network output, given \( F(X) \), the incorrect network output. Note that this is different from the traditional equivocation term in equation (1), \( H(X|F(X)) \) defined in the paragraph after equation (1), which measures the ambiguity on \( X \), the network input, given \( F(X) \), the incorrect network output. The equivocation model \( H(X|F(X)) \) is more suitable for communication channels, where ideally one would like to have the incorrect outputs as close as possible to the inputs. In contrast, the equivocation model \( H(f(X)|F(X)) \) is more appropriate for mapping networks and computing systems such as signaling networks, where ideally it is desired to have the incorrect outputs as close as possible to the correct outputs.

The second definition in equation (2), developed in supplementary material (stacks.iop.org/PhysBio/16/064001/mmedia), provides another way to relate computation and communication capacities. It shows that the computation capacity equals the maximum mutual information between correct and incorrect outputs \( I(f(X);F(X)) \), and the uncertainty on the input given the correct output \( H(X|F(X)) \). The former
is a measure of accuracy of the incorrect output with respect to the correct output, whereas the latter measures the degree of ‘non-invertibility’ of the function $f$, i.e. the degree of the function $f$ ‘not being one-to-one’. Mathematical details and some numerical examples are provided in supplementary material.

The summary illustrative table 1 and figure 6 presented at the end of the paper, summarizing our results and findings, further assist with understanding the differences between the computation and communication capacities and their implications for signaling networks.

### A relation between computation and communication capacities

An interesting property of the computation capacity in equation (2) is that it is greater than the communication capacity in equation (1), i.e. $C_f(F) > C(F)$ [4], as long as $f$ is not a one-to-one function (no one-to-one correspondence between the elements of domain and co-domain of $f$). This is because the ambiguity of $f(X)$ given $F(X)$ is less than the ambiguity of $X$ given $F(X)$, i.e. $H(f(X)|F(X)) < H(X|F(X))$ by the data processing inequality [6]. Therefore, upon comparing equation (2) with (1), we observe that $C_f(F) > C(F)$, i.e. computation capacity is greater than communication capacity. In signaling networks with lots of redundancies and many cross-linked pathways from inputs to outputs [8], most often the network response function $f$ is not a one-to-one function of the input signals, and therefore the computation capacity is higher than the communication capacity. This is further verified and demonstrated in this paper for two examples of caspase3 and NFκB signaling networks (other networks can be similarly analyzed). Note that only for the special case of $f$ being a one-to-one function, the two capacities become equal.

### Case study (1) caspase3 signaling network

Here we calculate the communication and computation capacities of an experimentally-verified signaling network, the caspase3 network (figure 1). Caspase3 is an important molecule and a key regulator of apoptosis. Signaling pathways from the ligands EGF, epidermal growth factor; insulin and TNF, tumor necrosis factor, to caspase3 (figure 1) are extensively characterized and experimentally verified [9]. Based on the experimental results [9], the network output caspase3 is active, when the inputs EGF and insulin are inactive and the input TNF is active. Otherwise, the output is inactive. When a molecule in the network is dysfunctional, one can consider that the activity state of that molecule does not change in response to its regulators [10]. Here we consider the scenario where the dysfunctional molecule remains inactive [10]. This gives rise to a signaling network that can be considered as an erroneous computing machine. The input–output functional relationship $F$ of the abnormal network can be different from $f$ of the normal network, and depends on which molecule is dysfunctional, as shown in supplementary material, section A. We observe that when AKT or EGFR or MEKK1ASK1 is dysfunctional in the network, the input–output abnormal mapping function $F$ is different from $f$ of the normal network; whereas $F$ is the same as $f$, when other molecules in the network are dysfunctional.

In what follows, to quantify the amount of impact of each dysfunctional molecule on communication and computation capacities of the caspase3 signaling network, we consider a model where each single molecule can be dysfunctional with a probability $p$, such that $0 \leq p \leq 1$.

### Communication capacity $C(F)$ of the caspase3 signaling network

Using the network transition probability matrices of the caspase3 network, equations (2)–(5) of [11], and based on equation (1) in this paper, the communication capacity of the caspase3 network is plotted in figure 2, when one of its molecules is dysfunctional (see supplementary material for the method). Interestingly, the communication capacity metric overlooks the differences between the molecules and classifies them into two groups. It appears that the communication capacity provides less information about the network and its abnormal behavior, when it contains dysfunctional molecules. This is in contrast to the computation capacity, as discussed next.

### Computation capacity $C_f(F)$ of the caspase3 signaling network

Using the network transition probability matrices of the caspase3 network, equations (2)–(5) of [11], and based on equation (2) in this paper, the computation capacity of the caspase3 network with respect to the error-free output $f$ is plotted in figure 3, when one of its molecules is dysfunctional (see supplementary material for the method). Comparing with the communication capacity in figure 2, we notice two remarkable points:

1. The computation capacity magnitude is larger than the communication capacity. This is because the input–output mapping function $f$ of the caspase3 network (supplementary material, equation (s1)) is not a bijective function, i.e. is not a one-to-one correspondence. This makes the computation capacity larger than the communication capacity, as stated earlier in the paper. Intuitively, this indicates that the number of input values that can be correctly computed on is larger than the number of input values that can be correctly recovered given the output of the network.
**Figure 1.** Caspase3 signaling network (the node ComplexI includes TNFR and TRADD-RIP-TRAF2, and ComplexII represents TRADD-RIP-TRAF2 and FADD [9]. The edges ending in an arrowhead or a blunt line indicate activation or inhibition, respectively).

**Figure 2.** Communication capacity in equation (1) versus the dysfunction probability $p$ for each molecule in the caspase3 network.

**Figure 3.** Computation capacity in equation (2) versus the dysfunction probability $p$ for each molecule in the caspase3 network.
(ii) The computation capacity classifies the network molecules into four groups. This indicates that the computation capacity can have more predictive power than the communication capacity, which identifies only two groups of molecules. In other words, the computation capacity can recognize the roles and functions of different molecules in the network more precisely than the communication capacity.

Case study (2) NFκB signaling network

Now we study some communication and computation characteristics of a network that has feedback and hence defines an input–output mapping $f$ with memory. Consider the network in figure 4, where tumor necrosis factor (TNF) and nuclear factor κB (NFκB) are input and output molecules, respectively. The molecule A20 has an inhibitory feedback effect, whereas TRC stands for TNF receptor complex [5]. A comprehensive stochastic differential equation model is developed in [12] and its accuracy is extensively verified via experimental data. It is well known that the activity of NFκB first increases with TNF, but the upregulation of A20 by NFκB inhibits TRC, which in turn decreases the activity of NFκB. Consider that the inactive and active states of a molecule are represented by 0 and 1, respectively (see [10, 13–15] for an overview and examples of this modeling approach in systems biology). In supplementary material, sections C–E, we first present activity models for the network output in term of the input activity, under normal (wild type) and abnormal (A20-deficient) conditions, and show how the input–output models are corroborated by biological data. Afterwards, we present a system formulation and discuss its biological relevance in section F of supplementary material. The system formulation allows to calculate and compare communication and computation rates and capacities of the NFκB network.

We consider the network to be abnormal, when it has A20 deficiency. It is demonstrated that an A20-deficient mouse develops severe inflammation and dies prematurely [16]. This is because cells with this deficiency cannot stop the NFκB response caused by TNF, as is evident in figure 4, when there is no feedback. It is also known that the dysfunction of A20 is involved in a number of diseases such as multiple sclerosis, lupus, rheumatoid arthritis, etc [17]. To model A20 deficiency in the network, we consider A20 as a molecule which has a chance to be dysfunctional with a probability $p$. More specifically, consider that the probability of A20 to remain 0, inactive, regardless of the signal from NFκB is $p$. This model is consistent with the fact that A20 is inactive in several hematological malignancies [18], and also as shown below, it allows to calculate and compare communication and computation rates and capacities of the NFκB network, when A20 is dysfunctional.

Communication rate of the NFκB signaling network

Due to the feedback in the network, the network has a memory such that its output (NFκB) activity state depends on the present and past input (TNF) activity states (see section G of supplementary material). Calculation of the communication capacity in the presence of memory requires to optimize over the distribution of sequences of inputs. In order to gain some insight into the communication capacity of systems with memory, we first evaluate the communication rate, i.e. the mutual information between two successive values of the input and the corresponding output values for a fixed uniform distribution of the input.

To elaborate, let $Y_1$ and $Y_2$ represent the activity states of NFκB at two consecutive time instants $t = 1$ and $t = 2$, respectively, i.e. $Y_1 = NFκB(t = 1)$ and $Y_2 = NFκB(t = 2)$. Note that $t = 1$ and $t = 2$ represent early and late signaling events, respectively. Similarly, we have $X_1 = TNF(t = 1)$ and $X_2 = TNF(t = 2)$. Clearly $X$ and $Y$ variables refer to the network input and output in figure 4, respectively. The communication rate evaluated as the mutual information between the network input sequence $(X_1, X_2)$ and the network output sequence $(Y_1, Y_2)$ can be shown to be (see section G of supplementary material for the method)

$$R(F) = I(X_1, X_2; Y_1, Y_2) = H(X_1) + H(X_2) - H(X_1, X_2) = 2 - 0.25(2 - p)\log_2(2 - p) + 0.25(1 - p)\log_2(1 - p),$$

where $\log_2$ is logarithm to the base 2 and $p$ is the probability of A20 to be dysfunctional. As seen in figure 5, the communication rate, i.e. the mutual information, increases with $p$. This means the network output in figure 4 has more information about the
input, when A20 becomes more dysfunctional. In other words, as A20 becomes more dysfunctional, the network behaves closer to a linear pathway with no feedback, and the input activity state can be determined with less ambiguity from the output activity state.

Computation rate of the NFκB signaling network

Using the notation introduced earlier, i.e. $Y_1 = \text{NFκB}(t = 1)$, $Y_2 = \text{NFκB}(t = 2)$, $X_1 = \text{TNF}(t = 1)$ and $X_2 = \text{TNF}(t = 2)$, the computation rate of the network with respect to the error-free output can be shown to be (see section G of supplementary material for the method)

$$R_f(F) = H(X_1, X_2) - H(f(X_1, X_2)|Y_1, Y_2) = 2.$$ (4)

As seen in figure 5, the computation rate for the NFκB network is greater than its communication rate. Moreover, its constant value implies that regardless of $p$, correct outputs can be inferred from erroneous outputs (supplementary material, section G).

Communication and computation capacities of the NFκB signaling network

Let $C(F)$ represent the communication capacity of the NFκB network. It can be shown that (see section H of supplementary material for the methods)

$$C(F) = \begin{cases} \log_2 \left( \frac{1 + \sqrt{5}}{2} \right) \approx 0.7, & 0 \leq p < 1, \\ 1, & p = 1 \end{cases}.$$ (5)

Interestingly, the term $(1 + \sqrt{5})/2$ is the well-known golden ratio [19]. Another noteworthy observation is that the calculated communication capacity of about 0.7 bits for the TNF-NFκB system is based on early and late NFκB responses, respectively [5].

On the other hand, let $C_f(F)$ stand for the computation capacity of the NFκB network with respect to the error-free output $f$. It can be shown that (see section I of supplementary material for the methods)

$$C_f(F) = 1, \quad 0 \leq p \leq 1.$$ (6)

Note that since the function $f$ here is not one-to-one (see the second column of table S2), the computation capacity, 1 in equation (6), is higher than the communication capacity, 0.7 in equation (5). Only for the special case of $p = 1$, A20 being completely dysfunctional with unit probability, the NFκB network (figure 4) becomes a linear pathway in the absence of A20 feedback. This makes $f$ a one-to-one function that results in equal capacities for the special case of $p = 1$.

On the computation capacity being higher than the communication capacity

We generally discussed earlier in the paper that signaling networks with lots of redundancies and many cross-linked pathways from inputs to outputs do not possess one-to-one mapping functions, and therefore their computation capacities are proved to be higher than their communication capacities. We also verified this specifically for two signaling networks. Interestingly, it has been a surprise to researchers that information (communication) capacities of signaling networks appear to be smaller than what is typically anticipated [1, 20]. In this regard, the computation capacity concept introduced here is a new metric that can possibly shed some light on this controversy, and...
can perhaps reveal some unknown capabilities and characteristics of signaling networks.

**An illustrative comparative summary of computation and communication capacities of signaling networks**

The computation capacity is introduced in this paper for normal and abnormal networks, i.e. networks with dysfunctional molecules, whereas the communication capacity of normal and abnormal networks was previously studied in [2]. Some other studies have investigated the communication capacity of signaling networks [5, 21–23] and genetic systems [24].

To better understand the differences between the computation and communication capacity metrics, we provide an illustrative schematic in figure 6. The figure depicts a signaling network with some dysfunctional molecules, the erroneous input–output mapping function \( F \), the input signal \( X \) and the erroneous output response \( F(X) \). As graphically shown in figure 6, the communication capacity \( C(F) \) considers only \( X \) and \( F(X) \). In contrast, the computation capacity \( C_f(F) \) additionally takes into account the desired error-free input–output mapping function \( f \). In other words, the computation capacity \( C_f(F) \) considers \( X, F(X) \) and \( f(X) \) (figure 6). The transformation \( \Phi \) (figure 6) is a mapping from \( f \) to \( F \), and models the changeover from the normal response \( f(X) \) to the abnormal response \( F(X) \). In other words, \( \Phi \) represents computation/signaling errors caused by dysfunctional components and molecules. Note that the abnormal and normal states in figure 6 are symbolically shown by an irregular shape and a rectangle, respectively. Overall, this figure elucidates the concepts behind the communication and computation capacities and their differences.

Additionally, a summary of communication and computation capacity-related metrics and definitions and results that clarifies their differences is presented in table 1. The corresponding mathematical details and derivations and other numerical examples for communication and computation capacities are presented in supplementary material, sections J–L.

**On signaling network models for calculating computation and communication capacities**

In the stochastic network models considered in this paper, activity level of each molecule is a continuous-valued number between 0 and 1, indicating the probability of the molecule to be active [15] (For an overview and examples of this modeling approach in systems biology, interested readers can refer to [10, 13–15]). To model the presence of feedback in the NFκB network, a time-varying model is developed in this paper. Additionally, we have used the experimentally verified stochastic differential equation model of [12], also used in [25], to generate data. We have used the data to demonstrate the biological relevance of our developed model, which is suitable for calculating and comparing communication and computation capacities of the NFκB network, under similar conditions. Extension of the computation capacity concept to concentration-type models such as differential equation-based models is a possible next step. In this context, care should be taken when defining entropies for such models. Presence of memory and time variations in a system under study make capacity
definitions and calculations particularly difficult, due to the need to optimize over the input distribution. If not feasible to calculate the computation capacity for such scenarios, still it is helpful to calculate the computation rate instead, to gain some insights.

Conclusions

Cell signaling networks can be envisioned as computing systems that compute the outputs in response to the inputs. The system inputs can be considered to be ligands which upon binding to their receptors on the cell membrane, create chains of interactions through some intermediate signaling molecules. The system outputs are some target proteins such as transcription factors. Due to the presence of dysfunctional molecules in a signaling network, it may behave abnormally, i.e. may compute the network outputs incorrectly. In this paper, a new fundamental characteristic of signaling networks, i.e. the computation capacity, is introduced and investigated. Our results on caspase3 and NF-κB networks indicate that their computation capacities are higher than their communication capacities. Additionally, it is shown in the paper that in general, the network computation capacity is higher than the network communication capacity, as long as the network response function is not a one-to-one function of the input signals. One biological implication of this finding is that signaling networks may have more capabilities than what we presently know. Overall, this study and its findings are anticipated to advance our understanding of some fundamental characteristics of cell signaling networks.

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