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Secrecy of Signals by Typing in Signal Transduction*

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Abstract. We discuss secrecy of signals in signal transduction. As we have developed a basic concurrent language with interferencial coefficients, *Iπ-calculus*, to describe aberrance in biological models, a typing system for *Iπ-calculus* is proposed for achieving secrecy of signals in signal transduction. We show that this typing system guarantees that, if signal transduction typechecks, then it does not leak aberrance of signals.

1 Introduction

Signal transduction, short for ST, is the key to uncover the wild growth of cells. Aberrant ST is the cause of many diseases challenged by modern medicine, including cancers, inflammatory diseases, and so on. Formal method is one of approach to research ST. Process algebra, such as *pi* calculus and its variation, is a way to model ST system. There are several pieces of related work about modelling ST [4, 5, 2, 3], based on *pi calculus* [1, 6]. *Interference pi calculus* [8], (*Iπ- calculus*) is proposed to model aberrant ST.

When a signal mutates aberrantly, we want to know what will happen in the whole ST. We used a typing system [9], to replace the tag system which is used to label the existence of aberrance by sets computation, such as union, disjoint [8]. This typing system is simple enough to be enforced statically. It had been proved to be equivalent to the tag system in the capability of labelling the existence of aberrance [9].

In this paper, we emphasis on this typing system. An informal principle is developed for achieving secrecy of signals in ST. In particular, in the analyzing aberrance of ST, we label each protein(its domains) and each signal as either normal or aberrant. A signal-receiver can not find the signal from signal-sender is normal or aberrant during the transduction of signals. That is to say, the

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whole ST does not leak aberrance of signal. The notion of leaking is formalized in terms of testing equivalence. We point out, if ST typechecks, then it does not leak the aberrance of signals.

2 Secrecy of Signals in Signal Transduction

Signal transduction is a manner to answer the stimulation of cells outside. It is the key to uncover the wild growth of cells leading to many diseases. When the whole ST works perfectly, decisions of growth and death of cells are also made by rule and line. When some signals mutate aberrantly, however, the whole ST could be interfered. Cancers are some diseases resulting from this kind of interference of ST.

The sequel that the ST is interfered is, the growth of a cell is never controlled by growth factors outside. There exist many methods to get it, one of which is that some aberrant proteins make the cell release the growth factors into the environment. These factors can stimulate the cell which sets them free, and make it grow. Another is the aberrance of *Ras* protein. Normal *Ras* protein in the inactive state is waiting for the signal. It is activated when it receives the signal, and then sends signal to the others. After that, it could be inactivated to return the initial state. This kind of inactivity make assure that the cell just can receive finite signals.

Aberrant *Ras* protein has some difference with normal *Ras* protein. Aberrant *Ras* protein can be activated and send a signal to the others, as same as normal *Ras* protein. Aberrant *Ras* protein however can not be inactivated any more. That means, it will be always in the active state and always sends the signal to the others, even there is no real signal coming.

In a word, whatever is chosen, aberrant proteins pretend the normal proteins to transduce stimulation signals. In another word, a carrier waiting for signals does not know the category of signals.

Therefore, we have an important property about aberrance:

In signal transduction, a sender does not leak aberrance of signals.

This is also a principle in the studying of signal transduction.

3 The Pure $I\pi$-*calculus*

$I\pi$-*calculus* is proposed to describe aberrant ST. This section presents the pure version of $I\pi$-*calculus* that serves as the preliminary setting for our formal work.

We assume an infinite countable set $\mathcal{A}$ of values, an infinite countable set $\mathcal{N}$ of names and an infinite countable set $\mathcal{V}$ of variables. Let σ, ρ be functions from $\mathcal{N}$ to $\mathcal{A}$. One can think of σ as an interference function and that $\sigma(a)$ as the interference degree of a. The function ρ is a critical function and that $\rho(a)$ is the critical value of the interference degree of a. The interferential coefficient can be defined below:

Definition 1 (Interferential Coefficient). *For $a \in \mathcal{N}$, let i_a be $|\rho(a) - \sigma(a)|$. We say that i_a is the interference coefficient of a.*

Intuitively, when i_a is equal to zero, we take that a is in an aberrant state; when i_a is not zero, we think that a is still in a normal state.

Processes evolve by performing actions. In process algebra actions capabilities are introduced by prefix capabilities. In *$I\pi$-calculus*, we introduce two capabilities in addition to the prefix defined by *pi calculus*.

Let $a, b, \cdots$ range over the names and $x, y, \cdots$ range over the variables. We also define two symbols § and ♯ to represent the aberrance capability. Here § represents the suicide capability and ♯ the propagation capability. When a process has the suicide capability, it terminates its action immediately. And when a process has the propagation capability, it will duplicate its action infinitely.

Definition 2 (Prefix). *The prefix of $I\pi$-calculus are defined as follows:*

$$\pi ::= \overline{a}(b) \mid a(x) \mid \overline{a} \mid a \qquad \pi_i ::= \pi \mid [i_{\pi_i} = 0]\S(\pi_i) \mid [i_{\pi_i} = 0]\sharp(\pi_i)$$

The capability of π is the same as in *pi calculus*. $[i_{\pi_i} = 0]\S(\pi_i)$ and $[i_{\pi_i} = 0]\sharp(\pi_i)$ are the substitution capabilities. They are respectively the capabilities § and ♯ if the subject of π_i is in an aberrant state.

Definition 3 (Process). *The $I\pi$-calculus processes are defined as follows:*

$$P ::= 0 \mid \pi_i.P \mid \pi_i.P + \pi_i'.P' \mid P|P' \mid (\nu a)P$$

Intuitively the constructs of *$I\pi$-calculus* processes have the following meaning: 0 is the inert process. The prefix process $\pi_i.P$ has a single capability imposed by π_i, that is, the process P cannot proceed until that capability has been exercised. The capabilities of the sum $\pi_i.P + \pi_i'.P'$ are those of $\pi_i.P$ plus those of $\pi_i'.P'$. When a sum exercises one of its capabilities, the other is rendered void. In the composition process $P|P'$, the components P and P' can proceed independently and can interact via shared channel. In the restriction process $(\nu a)P$, the scope of the name a is restricted to P.

We write $fn(P)$ for the set of free names in process P, and $fv(P)$ for the set of free variables in P. An expression is closed if it has no free variables. Notice that a closed expression may have free names.

The reaction relation, introduced initially by Milner [1], is a concise account of computation in the pi calculus. In addition to the well-known interaction rule(Com-N), our reaction relation also includes two new rules about reactions with aberrance(Pre-§ and Pre-♯).

A *barb* is a name m, a co-name $\overline{m}$ or two primitives § and ♯. An action is a barb or the distinguished *silent action* τ. We range α, β, $\cdots$ over actions.

$$\frac{}{[i_{\pi_i} = 0]\S(\pi_i).P \xrightarrow{\S} 0}\ \text{Pre-§ ;} \qquad \frac{}{[i_{\pi_i} = 0]\sharp(\pi_i).P \xrightarrow{\sharp} \pi_i.[i_{\pi_i} = 0]\sharp(\pi_i).P}\ \text{Pre-♯ ;}$$

$$\frac{}{\overline{a}(b).Q \mid a(x).P \xrightarrow{\tau} Q|P\{b/x\}}\ \text{Com-N;} \qquad \frac{}{\overline{a}.Q \mid a.P \xrightarrow{\tau} Q \mid P}\ \text{Com-SN}$$

$$\frac{P \xrightarrow{\alpha} P'}{P + Q \xrightarrow{\alpha} P'} \text{Sum;} \qquad \frac{P \xrightarrow{\alpha} P'}{P \mid Q \xrightarrow{\alpha} P' \mid Q} \text{Com;}$$

$$\frac{P \xrightarrow{\alpha} P' \quad a \neq \alpha}{(\nu a)P \xrightarrow{\alpha} (\nu a)P'} \text{Res;} \qquad \frac{Q \equiv P \quad P \xrightarrow{\alpha} P' \quad P' \equiv Q'}{Q \xrightarrow{\alpha} Q'} \text{Stc.}$$

The first two rules deal with reactions with aberrance: the former says that the resulting process is terminated; the latter declares that the resulting process duplicates its action infinitely. The third reaction rule deals with the interaction in which one sends a message with a channel while the other receives a message with the same channel so that they have an interactive action. Each of the reduction rules are closed in the summation, composition, restriction and structural congruence.

Next, we represent some preliminaries of testing equivalence. These notions are belong to Martín Abadi [7].

A *test* is a pair (Q, β) consisting of a closed process Q and a barb β. We say that P *passes* a test (Q, β) if and only if $(P \mid Q) \xrightarrow{\tau} Q_0 \cdots \xrightarrow{\tau} Q_n \xrightarrow{\beta} A$

For some $n \geq 0$, some processes $Q_0, \cdots Q_n$, and some process A, we obtain a testing preorder $\sqsubseteq$ and a testing euqivalence $\simeq$ on closed processes:

$P \sqsubseteq P' \stackrel{\triangle}{=} for\ any\ test\ (Q, \beta),\ if\ P\ passes\ (Q, \beta)\ then\ P' passes\ (Q, \beta)$

$p \simeq P' \stackrel{\triangle}{=} P \sqsubseteq P'\ and\ P' \sqsubseteq P$

A *strict barbed simulation* is a binary relation $\mathcal{S}$ on closed processes such that $P\mathcal{S}\mathcal{P}'$ implies:

(1) for every barb β, if $P \xrightarrow{\beta} A$ for some A, then $P' \xrightarrow{\beta} A'$ for some A',
(2) for every P_1, if $P_1 \xrightarrow{\tau} P_1$ then there exists $P_1{}'$ such that $P' \xrightarrow{\tau} P_1{}'$ and $P_1 \mathcal{S} P_1{}'$.

A *strict barbed bisimulation* is a relation $\mathcal{S}$ such that both $\mathcal{S}$ and $\mathcal{S}^{-1}$ are strict barbed simulations.

The following lemma provides a method for proving testing equivalence:

Lemma 1. *If for every closed process Q there exists a strict barbed bisimulation $\mathcal{S}$ such that $(P \mid Q)\mathcal{S}(P' \mid Q)$, then $P \simeq P'$*

In [7], Martín Abadi gave a simple direct proof.

4 The Typing System

This section describes rules for controlling information flow in *Iπ-calculus* calculus. Here we embody them in a typing system for *Iπ-calculus* calculus. The typing system was firstly introduced by Martin Abadi in studying security protocols [7].

In order to represent the aberrance of ST we classify signals into three classes:

– A *Normal* signal is one that takes part in the normal processes.

– An *Aberrant* signal is one that takes part in the aberrant processes.
– An *Unknown* signal could be any signal.

To simplify we define a reflexive order relation <: among these three classes:

$$Normal <: Unknown; \; Aberrant <: Unknown.$$

For convenience of representation, we denote M as a name or a variable. M is called *term*. Corresponding to these three classes the typed system has three kinds of assertions:

– "$\vdash \Gamma$ well formed" means that the environment Γ is well-formed.
– "$\Gamma \vdash M : T$" means that the term M is of the class T in Γ.
– "$E \vdash P : ok$" means that the process P typechecks in E.

Typing rules are given under an environment. An environment is a list of distinct names and variables with associated classifications.

Definition 4 (Typed Environment). *Typed environments are given by the following rules:*

$$\frac{}{\vdash \emptyset \; well \; formed} \textit{Environment Empty}$$

$$\frac{\vdash \Gamma \; well \; formed, M \notin \Gamma}{\vdash \Gamma, M : T \; well \; formed} \textit{Environment Term}$$

Having defined the environments, one can define rules for terms and processes.

Definition 5 (Terms). *The rules for terms of typing system are as follows:*

$$\frac{\Gamma \vdash M : T \quad T <: R}{\Gamma \vdash M : R} \textit{Level Subsumption}$$

$$\frac{\vdash \Gamma \; well \; formed \quad M : T \; in \; \Gamma}{\Gamma \vdash M : T} \textit{Level Term}$$

Intuitively the rule Level Subsumption says that a term of level *Normal* or *Aberrant* has level *Unknown* as well.

Definition 6 (Processes). *The rules for typing processes are as follows:*

$$\frac{\Gamma \vdash a : Normal \quad \Gamma \vdash b : Normal \quad \Gamma \vdash P : Ok}{\Gamma \vdash \overline{a}(b).P : Ok} \textit{T-out}$$

$$\frac{\Gamma \vdash a : Normal \quad \Gamma \vdash x : Unknown \quad \Gamma \vdash P : Ok}{\Gamma \vdash a(x).P : Ok} \textit{T-in}$$

$$\frac{\Gamma \vdash a : Normal \quad \Gamma \vdash P : Ok}{\Gamma \vdash \overline{a}.P : Ok} \textit{T-sout} \quad \frac{\Gamma \vdash a : Normal \quad \Gamma \vdash P : Ok}{\Gamma \vdash a.P : Ok} \textit{T-sin}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash b : Normal \quad \Gamma \vdash P : Ok}{\Gamma \vdash \overline{a}(b).P : Ok} \textit{T-aout}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash x : Unknown \quad \Gamma \vdash P : Ok}{\Gamma \vdash a(x).P : Ok}\textit{T-ain}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash P : Ok}{\Gamma \vdash \overline{a}.P : Ok}\textit{T-asout} \quad \frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash P : Ok}{\Gamma \vdash a.P : Ok}\textit{T-asin}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash b : Normal \quad \Gamma \vdash P : Ok}{\Gamma \vdash [i_a = 0]\S(\overline{a}(b)).P : Ok}\textit{T-kout}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash x : Unknown \quad \Gamma \vdash P : Ok}{\Gamma \vdash [i_a = 0]\S(a(x)).P : Ok}\textit{T-kin}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash P : Ok}{\Gamma \vdash [i_a = 0]\S(\overline{a}).P : Ok}\textit{T-ksout} \quad \frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash P : Ok}{\Gamma \vdash [i_a = 0]\S(a).P : Ok}\textit{T-ksin}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash b : Normal \quad \Gamma \vdash P : Ok}{\Gamma \vdash [i_a = 0]\sharp(\overline{a}(b)).P : Ok}\textit{T-pout}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash x : Unknown \quad \Gamma \vdash P : Ok}{\Gamma \vdash [i_a = 0]\sharp(a(x)).P : Ok}\textit{T-pin}$$

$$\frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash P : Ok}{\Gamma \vdash [i_a = 0]\sharp(\overline{a}).P : Ok}\textit{T-psout} \quad \frac{\Gamma \vdash a : Aberrant \quad \Gamma \vdash P : Ok}{\Gamma \vdash [i_a = 0]\sharp(a).P : Ok}\textit{T-psin}$$

$$\frac{\vdash \Gamma \ well\ formed}{\Gamma \vdash 0 : Ok}\textit{T-nil} \quad \frac{\Gamma, a : Normal \vdash P : Ok, \quad a \notin dom(\Gamma)}{\Gamma \vdash (\nu a)P : Ok}\textit{T-res}$$

$$\frac{\Gamma \vdash P : Ok \quad \Gamma \vdash Q : Ok}{\Gamma \vdash P \mid Q : Ok}\textit{T-com} \quad \frac{\Gamma \vdash P : Ok \quad \Gamma \vdash Q : Ok}{\Gamma \vdash P + Q : Ok}\textit{T-sum}$$

$$\frac{\Gamma \vdash a : Unknown\ \Gamma \vdash b : Noraml\ \Gamma \vdash P : Ok}{\Gamma \vdash P\{b/x\} : Ok}\textit{T-Sub} \qquad \frac{\Gamma \vdash P : Ok\ Q \equiv P}{\Gamma \vdash Q : Ok}\textit{T-stc}$$

5 Secrecy of Signals by Typing

As mentioned in the section 2, an important principle in the modelling signal transduction is to guarantee that category of signals can not be detected. In this section, we show that a signal-receiver can not distinguish the difference of signal using our typing system. The original idea is from [7]. In that paper, Martín Abadi applies the similar typing system to *Spi calculus*, and uses it to analyzes security protocols. Our main result says that if only variables of level $Unknown$ and only names of level $Normal$ are in the domain of the environment E, if σ and σ' are two substitutions of values for the variables in E, and if P typechecks, then $P\sigma$ and $P\sigma'$ are testing equivalence.

We write $E \vdash \sigma$ when $\sigma(x)$ is a closed term such that $fn(\sigma(x)) \subseteq dom(E)$ for every $x \in dom(E)$.

Lemma 2. *Suppose that E is an environment which all variables in $dom(E)$ are of level $Unknown$, $E \vdash P : ok$ and $E \vdash \sigma$. Then we have*

(1) *if* $P\sigma \xrightarrow{\tau} Q'$*, then there exists a process* Q *such that*
- $Q' = Q\sigma$
- $E \vdash Q : ok$
- $P\sigma' \xrightarrow{\tau} Q\sigma'$ *whenever* $E \vdash \sigma'$

(2) *if* $P\sigma \xrightarrow{\beta} A'$*, there exists a process* A *such that*
- $A' = A\sigma$
- $E \vdash A : ok$
- $P\sigma' \xrightarrow{\beta} A\sigma'$ *whenever* $E \vdash \sigma'$

Theorem 1. *Given an environment* E*, suppose that all the variables in* $dom(E)$ *are of level* $Unknown$*. Suppose further that* $E \vdash \sigma$ *and* $E \vdash \sigma'$*. Then the relation*

$$\{(P\sigma, P\sigma') \mid E \vdash P : ok\}$$

is a strict barbed bisimulation.

This conclusion means that a signal-receiver can not distinguish $P\sigma$ and $P\sigma'$, so it can not detect the difference of signals.

6 An Example in Signal Transduction

In order to illustrate the use of our typing rules, we consider as an example of aberrance of *Ras* protein. *Ras* protein is an important protein in the well-studied *RTK-MAPK* pathway.

Fig.1 gives an example of *Ras* Activation of the ST pathway, *RTK-MAPK*. At the normal state, the protein-to-protein interactions bring the *SOS* protein close to the membrane, where *Ras* can be activated. *SOS* activates *Ras* by exchanging *Ras*'s *GDP* with *GTP*. Active *Ras* interacts with the first kinase in the *MAPK* cascade, *Raf*. *GAP* inactivates it by the reverse reaction. When *Ras* mutates aberrantly, it does not have any effect on the *Ras*'s binding with *GTP* but will reduce the activity of the *GTP* hydrolase of *Ras* and lower its hydrolysis of *GTP* greatly; in the meantime *Ras* will be kept in an active state; it keeps activating the molecule, inducing the continual effect of signal transduction, which result in cell proliferation and tumor malignancy. Aviv Regev and his colleagues have given the representation of normal *RTK-MAPK* using the *pi* calculus [4]. We had given the representation of the aberrant *Ras* protein using $I\pi$-*calculus*.[8].

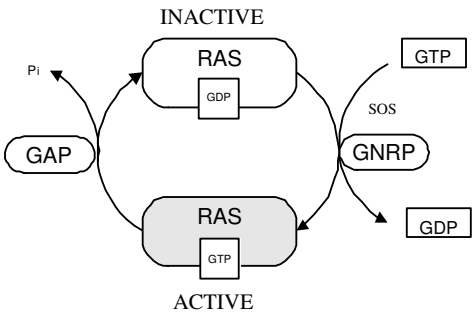

Fig.1. *Ras* Activation

The interpretation of *Ras* in the *Iπ-calculus* can be done in the following manner: The system defined in (1) is a collection of concurrently operating molecules, seen as processes with potential behavior. Here the operator | is the concurrent combinator. In biological models, all the names are bounded, for simplicity, we here only list the aberrant names for restriction :

$$\begin{aligned} SYSTEM ::= & (\nu s_{ACTSWI_I})(\nu bbone_{ACTSWI_I})(\nu sg_{ACTSWI_II}) \\ & (RAS \mid SOS \mid GAP \mid RAF) \end{aligned} \tag{1}$$

A protein molecule is composed of several domains, each of which is modelled as a process as well. In (2) through (5) the detailed *Iπ-calculus* programs for the proteins *Ras*, *SOS*, *Raf* and *GAP* are given:

$$RAS ::= INASWI_I \mid INASWI_II \tag{2}$$

$$SOS ::= S_SH3_BS \mid S_GNEF \tag{3}$$

$$\begin{aligned} RAF ::= & R_Nt \mid R_ACT_BS \mid R_M_BS \\ & \mid INA_R_Ct \mid R_ATP_BS \end{aligned} \tag{4}$$

$$GAP ::= sg(x).\overline{x}(gdp).GAP \tag{5}$$

The molecules (or domains) interact with each other based on their structural and chemical complementarity. Interaction is accomplished by the motifs and residues that constitute a domain. These are viewed as channels or communication ports of the molecule:

$$INASWI_I ::= \overline{bbone}.ACTSWI_I \tag{6}$$

$$INASWI_II ::= \overline{sg}(rs_1).rs_1(y).bbone.ACTSWI_II \tag{7}$$

$$S_GNEF ::= bbone.S_GNEF + sg(z).\overline{z}(gtp).S_GNEF \tag{8}$$

$$S_SH3_BS ::= \overline{bbone}.S_SH3_BS \tag{9}$$

The following interactions are possible:

$$INASWI_I \mid S_GNEF \longrightarrow ACTSWI_I \mid S_GNEF \tag{10}$$

$$INASWI_II \mid S_GNEF \longrightarrow^{*} bbone.ACTSWI_II \mid S_GNEF \tag{11}$$

$$bbone.ACTSWI_II \mid S_SH3_BS \longrightarrow ACTSWI_II \mid S_SH3_BS \tag{12}$$

The interaction (10) shows that the domain $INASWI_I$ of *Ras* is activated by the domain of S_GNEF of *SOS*. The interaction (11) and (12) show that the domain $INASWI_II$ of *Ras* is activated by the domain S_GNEF and S_SH3_BS of *SOS*.

The detailed *Iπ-calculus* programs for activated domains, $ACTSWI_I$ (Aberrant), $ACTSWI_II$ (Aberrant) of the protein *Ras* and the domain R_Nt of *Raf*

are defined in (13) through (15):

$$
\begin{aligned}
ACTSWI_I^* ::= {} & (\nu s)[i_s = 0]\sharp(\overline{s}(rs_2).\overline{rs_2}).INACTSWI_I + \\
& (\nu bbone)[i_{bbone} = 0]\S(\overline{bbone}).INASWI_I && (13)\\
ACTSWI_II^* ::= {} & (\nu sg)[i_{sg} = 0]\S(\overline{sg}(r_swi_1)).r_swi_1(h).\overline{bbone}. \\
& INACTSWI_II && (14)\\
R_Nt ::= {} & s(i).i.ACTR_Nt && (15)
\end{aligned}
$$

The processes so defined have the following interactions:

$$
\begin{aligned}
ACTSWI_I^* \mid R_Nt \longrightarrow^* {} & (\nu s)[i_s = 0]\sharp(\overline{s}(rs_2).\overline{rs_2}).INACTSWI_I \\
& \mid ACTR_Nt && (16)\\
ACTSWI_II^* \longrightarrow {} & 0 && (17)
\end{aligned}
$$

The interaction (16) shows that the active domain $ACTSWI_I$ of *Ras* interacts with the domain R_Nt of *Raf*, but it can not be inactivated any more. (17) shows that the domain $ACTSWI_II$ of *Ras* can not inactivated by *GAP*.

In order to indicate how the process $SYSTEM$ typecheks, we annotate its bound names and variables with there levels, as they are introduced.

Let E be an environment, where the variables are $Unknown$ levels:

$$x : Unknown,\ z : Unknown, h : Unknown\ i : Unknown.$$

The bound names with their $Normal$ levels:

$$
\begin{aligned}
& sg_{GAP} : Normal,\ bbone_{INASWI_I} : Normal,\ sg_{INASWI_II} : Normal, \\
& rs_1_{INASWI_II} : Normal, bbone_{INASWI_II} : Normal, bbone_{S_GNEF} : Normal, \\
& sg_{S_GNEF} : Normal,\ bbone_{S_SH3_BS} : Normal,\ rs_2_{ASWI_I} : Normal, \\
& r_swi_1_{ACTSWI_II} : Normal,\ \ bbone_{ASWI_II} : Normal,\ \ s_{R_Nt} : Normal.
\end{aligned}
$$

The bound names with there *Aberrant* levels:

$$s_{ACTSWI_I} : Aberrant, bbone_{ACTSWI_I} : Aberrant, sg_{ACTSWI_II} : Aberrant.$$

We define:

$$
\begin{aligned}
Ras \triangleq {} & (\overline{bbone} : Normal)[(\overline{s} : Aberrant)(rs_2).(\overline{rs_2} : Normal).INACTSWI_I + \\
& (\overline{bbone} : Aberrant).INASWI_I] \mid (\overline{sg} : Normal)(rs_1).(rs_1 : Normal)(y) \\
& .(bbone : Normal).(\overline{sg} : Aberrant)(r_swi_1).(r_sw_1 : Normal) \\
& (h).(\overline{bbone} : Normal).INACTSWI_II \\
SOS \triangleq {} & (\overline{bbone} : Normal).S_SH3_BS \mid [(bbone : Normal).S_GNEF + (sg : \\
& Normal)(z).(z : Unknown)(gtp).S_GNEF] \\
RAF \triangleq {} & (s : Normal)(i).(i : Unknown).ACTR_Nt \mid ... \\
GAP \triangleq {} & (sg : Normal)(x).(\overline{x} : Unknown)(gdp).GAP
\end{aligned}
$$

Finally, in the given environment E, we set

$$SYSTEM \triangleq (\nu s_{ACTSWI_I} : Aberrant)(\nu bbone_{ACTSWI_I} : Aberrant)$$
$$(\nu sg_{ACTSWI_II} : Aberrant)(RAS \mid SOS \mid GAP \mid RAF) \quad (18)$$

It is easy to find $E \vdash SYSTEM : Ok$. By Theorem 1, as a consequence of the typechecking, we obtain that $SYSTEM$ does not reveal the aberrance of *Ras* protein.

7 Future Prospects

The typing system we introduced is very simple but strong. It can applied not only into analyzing security protocols but also in the study of signal transduction with exception, which is also opening up new possibilities in modelling of biochemical systems.

To make quantitative analysis is another important step for studying biochemical systems. So far, our *$I\pi$-calculus* is concerned about qualitative analysis. Could it do some quantitative analysis? Two functions ρ and σ which are used to describe some quantitative properties of proteins will be found its value in future work.

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