Mechanism of Sulfoxidation in Artificial Cell System

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***Abstract*— Y. Suzuki and H. Tanaka have developed a molecular computing model, Artificial Cell System (ACS) with elementary membrane and hierarchically structurable membranes. A chemical analysis based on kinetic spectro photometric studies on the catalytic activities of iron (III) - salen ion for H_2O_2 oxidation of organic sulfides and sulfoxides was proposed by A.M.I. Jayaseeli and S. Rajagopal. In this present study a new membrane computing model on Kinetic ARMS is introduced and the mechanism on Artificial Cell system is proposed.**

Membrane structure, Abstract Rewriting System on Multiset, Artificial Cell System, Oxidation of Sulfides and Sulfoxides, Kinetic ARMS in ACS.

I. Introduction

Membrane is an important structure for living systems. It distinguishes "self" from its environment and composes hierarchical structures inside the system. Various ways of controlling the transfer of objects from a region to another one and of applying the rules, as well as possibilities to dissolve, divide, create, or move membranes were considered. [8, 9]. Y. Suzuki and H. Tanaka have introduced the multiset rewriting system, "Abstract rewriting System on multisets" (ARMS) [11]. Based on this system, they have developed a molecular computing model called Artificial Cell System which consists of a multiset of symbols, a set of rewriting rules and membranes [11]. These correspond to a class of P systems which is a parallel molecular computing model proposed by G. Paun and is based on the processing of multisets of objects in cell-like membrane structures.

In the past decades, biomimetic oxidation studies using model compounds has received attraction of the researchers [2, 7, 10]. The oxidation of sulfide moiety is important because of the central role of sulfides in living organisms and their ability to act as antioxidants [5]. Several metal ions $Fe^{III}, Ru^{IV}, Cr^{V}, Cr^{VI}, V^{V}, Mn^{V}, Re^{VII}$ and Ce^{IV} and others have been used as oxidants for the oxidation of organic sulfides. Metal - salen complexes are a valuable alternative to biomimetic heme -protein models [3, 4, 15]. They are extensively used as catalysts for epoxidation, sulfoxidation, ring opening and fixation of CO_2 in the form of carbonates [1, 13]. A. M. I. Jayaseeli and S. Rajagopal carried out kinetic spectro photometric studies on the catalytic activities of Iron (III) - salen ion for H_2O_2 oxidation of organic sulfides and sulfoxides. They have proposed possible mechanisms [6]. In this present study, the computational studies of the above mentioned work, based on membrane computing is proposed. Kinetic ARMS in Artificial Cell System with hierarchically structurable membrane (KACSH) is developed.

II. Preliminaries

A. $ARMS$ [11, 12, 14]

We recall the multiset rewriting system , "Abstract Rewriting System on Multisets". $ARMS$ is like a chemical solution in which molecules floating on it can interact with each other according to reaction rules. Technically a chemical solution is a finite multiset of elements denoted by $A^k = \{a, b, \cdots\}$; these elements corresponds to molecules. Reaction rules that act on the molecules are specified in ARMS by rewriting rules.

Let A be an alphabet (a finite set of abstract symbols). The set of all strings over A is denoted by A^*; the empty string is denoted by λ. The length of a string $w \in A^*$ is denoted by $|w|$. A rewriting rule over A is a pair of strings $(u, v), u, v \in A^*$. We write such a rule in the form $u \to v$, u and v can also be empty. A rewriting system is a pair (A, R), where A is an alphabet and R is a finite set of rewriting rules over A.

A multiset over a set of objects A is a mapping $M : A \to N$, where N is the set of natural numbers, $0, 1, 2, \cdots$. The number $M(a)$, for $a \in A$, is the multiplicity of object a in the multiset M. We do not accept here an infinite multiplicity. We denote by $A^{\#}$ the set of all multisets over A including the empty multiset, ϕ, defined by $\phi(a) = 0$, for all $a \in A$.

A multiset $M : A \to N$ for $A = a_1, a_2, \cdots, a_n$ can be naturally represented by the string $a_1^{M(a_1)} a_2^{M(a_2)} \cdots a_n^{M(a_n)}$ and by any other permutation of this string. Conversely, with any string w over A we can associate a multiset : denote by $|w|_{a_i}$ the number of occurances of a_i in $w, 1 \leq i \leq n$; then the multiset associated with w, denoted by $M_w(a_i) = |w|_{a_i}, 1 \leq i \leq n$.

The union of two multisets $M_1, M_2 : A \to N$ is the multiset $M_1 \cup M_2 : A \to N$ defined by $(M_1 \cup M_2)(a) = M_1(a) + M_2(a)$, for all $a \in A$. Then we say that the multiset M_1 is included in the multiset M_2 and we write $M_1 \subseteq M_2$. In such a case we define the multiset

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difference $M_1(a) - M_2(a)$, by $(M_2 - M_1)(a) = M_2(a) - M_1(a))$, for all $a \in A$. When M_1 is not included in M_2, the difference is not defined.

A multiset rewriting rule (evolution rule) over a set A of objects is a pair (M_1, M_2) of elements in $A^{\#}$ (which can be represented as a rewriting rule $w_1 \rightarrow w_2$, for two strings $w_1, w_2 \in A^*$ such that $M_{w_1} = M_1$ and $M_{w_2} = M_2$) We use to represent such a rule in the form $M_1 \rightarrow M_2$. An abstract rewriting system on multisets $(ARMS)$ is a pair

$$\Gamma = (A, (R, \rho))$$

where A is a set of objects, R is a finite set of multiset evolution rules over A, ρ is a partial order relation over R, specifying a priority relation among rules of R.

With respect to an $ARMS$ Γ, we can define over $A^{\#}$ a relation $(\Rightarrow)$: for $M, M^{'} \in A^{\#}$, we write $M \Rightarrow M^{'}$ iff $M^{'} = M - (M_1 \cup M_2 \cup \cdots \cup M_k)) \cup (M_1^{'} \cup M_2^{'} \cup \cdots \cup M_k^{'})$. For some $M_i \cup M_i^{'} \in R, 1 \leq i \leq k, k \geq 1$ and there is no rule $M_s \cup M_s^{'} \in R$ such that $M_s \subseteq (M - (M_1 \cup M_2 \cup \cdots M_k))$; at most one of the multisets $M_i, 1 \leq i \leq k$ may be empty.

With respect to $ARMS$ $\Gamma = (A, R)$ we can define various types of multisets: A multiset $M \in A^{\#}$ is dead if there is no $M^{'} \in A^{\#}$ such that $M \Rightarrow M^{'}$ (this is equivalent to the fact that there is no rule $M_1 \rightarrow M_2 \in R$, such that $M_1 \subseteq M$. A multiset $M \in A^{\#}$ is initial if there is no $M^{'} \in A^{\#}$ such that $M^{'} \Rightarrow M$.

B. Artificial Cell System [11]

Evolution of ACS

A transition ACS is a construct

$$\Gamma = (A, \mu, M_1, M_2, \cdots, M_n, (R, \rho), MC, \delta, \sigma),$$

where A is a set of objects, μ is a membrane structure (it can be changed throughout a computation) of degree $n, n \geq 1$, with the membranes labeled in a one to one manner, for instance, with the numbers from 1 to n. In this way also the regions of μ are identified by the numbers from 1 to n. $M_1, M_2, \cdots, M_n$, are multisets associated with the regions, R is a finite set of multiset evolution rules over A and ρ is a partial order relation over the rule set, it specifies a priority relation among the rules. MC is a set of membrane Compounds. δ is the threshold value of dissolving membrane σ is the threshold value of dividing membrane.

Reaction rules are applied in the following manner. The same rules are applied to every membrane. There are no rules specific to a membrane. All the rules are applied in parallel. In every step, all the rules are applied to all objects in every membrane that can be applied. If there are more than one rules that can apply to an object then one rule is selected randomly. If a membrane dissolves then all the objects in its region are left free in the region immediately above or below it. All objects and membranes not specified in a rule and which do not evolve are passed unchanged to the next step. There are two types of ACS as follows. ACS with elementary membrane $(ACSE)$; in this system every membrane is elementary membrane. ACS with hierarchically structure-able membrane$(ACSH)$; In this system other membranes can appear inside a membrane.

C. Kinetic Studies

Kinetic studies are carried out using iron $(III)-$ salen complex as catalyst for H_2O_2 oxidation of aryl methyl sulfide and aryl methyl sulfoxide in $100\% CH_3CN$ at $298K$ under pseudo first order conditions. Analytic Jena specord S 100 diode array spectrophotometer was used to follow the decay of absorbance of iron $(III)-$salen complex with time.

This redox reactions proceed through Michaelis-Menten kinetics and the kinetics are analysed in terms of the following reaction.

$$Oxidant + Substrate \rightleftharpoons complex$$
$$Complex \xrightarrow{k} Product$$

where k is rate constant for the product formation.

D. Mechanism for Selective Oxidation of Sulfides

Spectral evidence and product analysis of iron $(III)-$salen catalysed H_2O_2 oxidation of aryl methyl sulfide selectively oxidized to aryl methyl sulfoxide and two possible mechanisms (oxygen atom transfer and electron transfer) were proposed.

E. Mechanism for Selective Oxidation of Sulfoxides

The kinetic studies of iron $(III)-$ salen catalysed H_2O_2 oxidation of aryl methyl sulfoxide under similar conditions selectively oxidized to sulfone. The oxidant - adduct formation followed by oxygen atom transfer mechanism was proposed.

III. Mechanisms on Artificial Cell System

The above proposed mechanisms for sulfoxidation reactions were analysed by theory of computation. The following conventional notation is used to deal the mechanism on Artificial Cell System.
$XF3X = Iron(III)salen, F3 = Fe^{III}, Z = H_2O_2, F4 = Fe^{IV}, R = C_6H_4, R' = CH_3$
The scheme is outlined as follows.

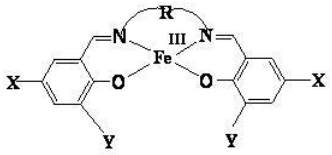

Fig. 1. Iron(III)-salen complex, $R = CH_2 - CH_2$

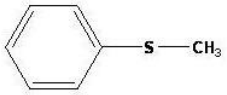

Fig. 2. aryl methyl sulfide

A. Mechanism for Sulfides Oxidation in ACS

Process A

$(a)\, Z + X(F3)X \rightarrow X(F4O)X;$
$X(F4O)X + RSR' \rightarrow X(F3)X + RSOR'$

A simple abstract reaction scheme is followed. Following convention is used to do the computation. When $X = H = L, X = Cl = M, X = Br = N, X = CH_3 = P$ and $X = OCH_3 = Q, (a)$ will have the following reaction rules

1. $Z + L(F3)L \rightarrow L(F4O)L;$
   $L(F4O)L + RSR' \rightarrow L(F3)L + RSOR'$
2. $M(F3)M + Z \rightarrow M(F4O)M;$
   $M(F4O)M + RSR' \rightarrow M(F3)M + RSOR'$
3. $N(F3)N + Z \rightarrow N(F4O)N;$
   $N(F4O)N + RSR' \rightarrow N(F3)N + RSOR'$
4. $P(F3)P + Z \rightarrow P(F4O)P;$
   $P(F4O)P + RSR' \rightarrow P(F3)P + RSOR'$
5. $Q(F3)Q + Z \rightarrow Q(F4O)Q;$
   $Q(F4O)Q + RSR' \rightarrow Q(F3)Q + RSOR'$

$(b)\, Z + XY(F3)XY \rightarrow XY(F4O)XY;$
$XY(F4O)XY + RSR' \rightarrow XY(F3)XY + RSOR'$

Following convention is used to do the computation.When $X = Y = Cl = M$ and $X = Y = t - Butyl = T$, (b) will have the following reaction rules

6. $Z + MM(F3)MM \rightarrow MM(F4O)MM;$
   $MM(F4O)MM + RSR' \rightarrow MM(F3)MM + RSOR'$
7. $Z + TT(F3)TT \rightarrow TT(F4O)TT;$
   $TT(F4O)TT + RSR' \rightarrow TT(F3)TT + RSOR'$

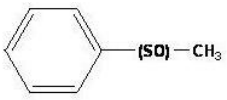

Fig. 3. aryl methyl sulfoxides

B. KARMS in ACS with Hierarchically Structurable Membrane (KACSH - A)

We introduce the Kinetic Abstract Rewriting System on multisets based on Artificial Cell System with Hierarchically structurable membrane to describe the complex formation between the oxidant and the substrate. Shortly we call the new system as $KACSH - A$

Behaviour of KACSH - A

Consider the KACSH

$$\Gamma = (A, \mu, M_1, M_2, M_3, (R, \rho), i_0)$$

where $A = (Z, S, A_i, B_i, P_i, i = 1 - 7)$
$\mu = [[[\,]_3]_2]_1$
M_1, M_2, M_3 are the multisets associated with the regions $1, 2, 3$ of μ
$M_1 = Z, A_i, i = 1\,to\,7, M_2 = S, M_3 = \phi$
$i_0 = 3$ is the output membrane and $\rho = \phi$
$R = R_1, R_2, R_3$ consists the following rewriting rules.

$$R_1 = \left\{ \begin{array}{l} Z + A_1 \rightarrow B_{1in}, \\ Z + A_2 \rightarrow B_{2in}, \\ Z + A_3 \rightarrow B_{3in}, \\ Z + A_4 \rightarrow B_{4in}, \\ Z + A_5 \rightarrow B_{5in}, \\ Z + A_6 \rightarrow B_{6in}, \\ Z + A_7 \rightarrow B_{7in} \end{array} \right\}$$

$$R_2 = \left\{ \begin{array}{l} B_1 + S \rightarrow A_{1out}, +P_{1in}, \\ B_2 + S \rightarrow A_{2out} + P_{2in}, \\ B_3 + S \rightarrow A_{3ou}t + P_{3in}, \\ B_4 + S \rightarrow A_{4out} + P_{4in}, \\ B_5 + S \rightarrow A_{5out} + P_{5in}, \\ B_6 + S \rightarrow A_{6out} + P_{6in}, \\ B_7 + S \rightarrow A_{7out} + P_{7in} \end{array} \right\}$$

$$R_3 = \phi$$

The rules R_1 and R_2 are applied to all the objects in all membranes. Initially, $Z \,\&\, A_i, i = 1$ to 7 will be in membrane 1. Applying the rule R_1, Z reacts with any one of A_i's. The output B_i is sent to membrane 2 . Now the rule R_2 can be applied in membrane 2 with the objects B_i and S and the resultant product P_i (methyl phenyl sulfoxides) will be sent to membrane 3 whereas the resultant A_i is sent out to membrane 1.

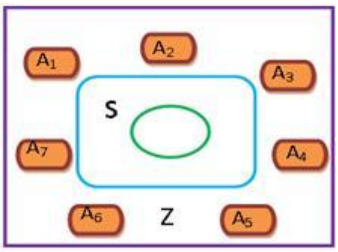

Fig. 4. KACSH - A

C. Mechanism for Sulfoxides Oxidation in ACS

Process B

$(a)\ Z + X(F3)X \rightarrow X(F4O)X;$
$X(F4O)X + RSOR' \rightarrow X(F3)X + RSO_2R'$

A simple abstract reaction scheme is followed. Following convention is used to do the computation. When $X = H = L, X = Cl = M, X = Br = N, X = CH_3 = P,$ and $X = OCH_3 = Q, (a)$ will have the following reaction rules.

1. $L(F3)L + Z \rightarrow L(F4O)L;$
   $L(F4O)L + RSOR' \rightarrow L(F3)L + RSO_2R'$
2. $M(F3)M + Z \rightarrow M(F4O)M;$
   $M(F4O)M + RSOR' \rightarrow M(F3)M + RSO_2R'$
3. $N(F3)N + Z \rightarrow N(F4O)N;$
   $N(F4O)N + RSOR' \rightarrow N(F3)N + RSO_2R'$
4. $P(F3)P + Z \rightarrow P(F4O)P;$
   $P(F4O)P + RSOR' \rightarrow P(F3)P + RSO_2R'$
5. $Q(F3)Q + Z \rightarrow Q(F4O)Q;$
   $Q(F4O)Q + RSOR' \rightarrow Q(F3)Q + RSO_2R'$

$(b)\ Z + XY(F3)XY \rightarrow XY(F4O)XY;$
$XY(F4O)XY + RSOR' \rightarrow XY(F3)XY + RSO_2R'$

Following convention is used to do the computation. When $X = Y = Cl = M$ and $X = Y = t - Butyl = T, (b)$ will have the following reaction rules

6. $Z + MM(F3)MM \rightarrow MM(F4O)MM;$
   $MM(F4O)MM + RSOR' \rightarrow \left\{ \begin{array}{l} MM(F3)MM + \\ RSO_2R' \end{array} \right\}$
7. $Z + TT(F3)TT \rightarrow TT(F4O)TT;$
   $TT(F4O)TT + RSOR' \rightarrow TT(F3)TT + RSO_2R'$

D. KARMS in ACS with Hierarchically Structurable Membrane (KACSH - B)

We introduce the Kinetic Abstract Rewriting System on multisets based on Artificial Cell System with Hierarchically structurable membrane to describe the complex formation between the oxidant and the substrate. Shortly we call the new system as $KACSH - B$

Behaviour of KACSH - B

Consider the KACSH

$$\Gamma = (A, \mu, M_1, M_2, M_3, (R, \rho), i_0)$$

where $A = (Z, SO, A_i, B_i, P_i, i = 1 - 7)$
$\mu = [[[\,]_3]_2]_1$
M_1, M_2, M_3 are the multisets associated with the regions $1, 2, 3$ of μ
$M_1 = Z, A_i, i = 1\,to\,7, M_2 = SO, M_3 = \phi$
$i_0 = 3$ is the output membrane and $\rho = \phi$.
$R = R_1, R_2, R_3$ consists the following rewriting rules.

$$R_1 = \left\{ \begin{array}{l} Z + A_1 \rightarrow B_{1in}, \\ Z + A_2 \rightarrow B_{2in}, \\ Z + A_3 \rightarrow B_{3in}, \\ Z + A_4 \rightarrow B_{4in}, \\ Z + A_5 \rightarrow B_{5in}, \\ Z + A_6 \rightarrow B_{6in}, \\ Z + A_7 \rightarrow B_{7in} \end{array} \right\}$$

$$R_2 = \left\{ \begin{array}{l} B_1 + SO \rightarrow A_{1out}, +P_{1in}, \\ B_2 + SO \rightarrow A_{2out} + P_{2in}, \\ B_3 + SO \rightarrow A_{3ou}t + P_{3in}, \\ B_4 + SO \rightarrow A_{4out} + P_{4in}, \\ B_5 + SO \rightarrow A_{5out} + P_{5in}, \\ B_6 + SO \rightarrow A_{6out} + P_{6in}, \\ B_7 + SO \rightarrow A_{7out} + P_{7in} \end{array} \right\}$$

$R_3 = \phi$

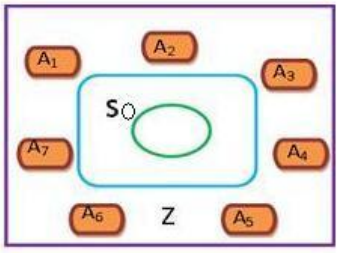

Fig. 5. KACSH -B

The rules R_1 and R_2 are applied to all the objects in all membranes. Initially, $Z \,\&\, A_i, i = 1$ to 7 will be in membrane 1. Applying the rule R_1, Z reacts with any one of A_i's. The

output B_i is sent to membrane 2 . Now the rule R_2 can be applied in membrane 2 with the objects B_i and SO and the resultant product P_i (methyl phenyl sulfones) will be sent to membrane 3 whereas the resultant A_i is sent out to membrane 1.

IV. Conclusion

In this paper a new membrane computing model on Kinetic ARMS is introduced and the mechanism on Artificial Cell system is proposed. This is only a preliminary research work. It is decided to extend the work to investigate the correlation between ACS and P System. It is worth to find out the power of this computing system and the characteristics of the concentration of chemical compounds. Further application and properties of the proposed system could be studied.

V. References

1. B. Bahram, M. Valiollah, T. Shahram, M. Majid, Catalytic epoxidation of olefins and hydroxylation of alkanes with sodium periodate by water-soluble manganese(III)salen , J. Mol. Catal. A. Chem, 2006, 244, 139.
2. A. Bassan, M.R.A. Bloniberg, P.E.M. Siegbalm, L. Que, Jr., Two faces of a biomimetic non-heme HO-Fe(v)=O oxidant: olefin epoxidation versus cis-dihydroxylation, Angew Chem. Int. Ed. 2005, 44, 2939.
3. K.P. Brylaiakov, E.P. Talsi, Iron-Catalyzed Oxidation of Thioethers by Iodosylarenes: Stereoselectivity and Reaction Mechanism Chem. Eur. J., 2007, 13, 8045.(5)
4. H. Egami, T. Katsuki, Fe(salan)-catalyzed asymmetric oxidation of sulfides with hydrogen peroxide in water. J. Am. Chem. Soc., 2007, 129, 8940.(6)
5. C. Jacob, A scent of therapy: pharmacological implications of natural products containing redox-active sulfur atoms Nat. Prod. Rep. 2006, 23, 851.(4)
6. A.M.I. Jayaseeli, S. Rajagopal, [Iron(III)-salen] ion catalyzed H_2O_2 oxidation of organic sulfides and sulfoxides. J.Mol.Catal, A:Chem, 2009,309,103(10)
7. W. Nam, High-Valent Iron(IV)-Oxo Complexes of Heme and Non-Heme Ligands in Oxygenation Reactions Acc. Chem. Res., 2007, 40, 522.(2)
8. Gh. Paun, Computing with membranes, Journal of Computer and System Sciences, 61, 1 (2000), 108-143
9. Gh.Paun , Membrane Computing. An Introduction,Springer, Berlin, 2002.
10. V.K. Sivasubramanian, M. Ganesan, S. Rajagopal, R. Ramaraj, Iron(III) [bond] Salen complexes as enzyme models: mechanistic study of oxo(salen)iron complexes oxygenation of organic sulfides, J. Org. Chem.2002, 67, 1506. (1)
11. Y. Suzuki, H. Tanaka, A New molecular Computing Model Artificial Cell System, 2000;http://www.cs.bham.ac.uk/ wbl/biblio/gecco 2000/AA218.pdf
12. Y. Suzuki, H. Tanaka, Abstract Rewriting Systems on Multisets and Their Application to Modelling Complex Behaviours,Rovira i virgili Univ. Tech. Rep.26, (M. Caveliere, C. Martin Vide, G. Paun , Eds.)Brain storming week on Membrane Computing, Tarragona, 2003, 313 - 331
13. L. Tatiana, S. Wladimir, H. Diana, K. Laf, Pitelment,J. Mol. Calal. A. Chem, 2007, 261, 16.(9)
14. M.Umeki, Y. Suzuki, A simple Membrane Computing Method for simulating biochemical reactions, Computing and Informatics, 27, 2008,529-550
15. N.S. Venkataraman, S. Premsigh, S. Rajagapal, K. Pitchumani, . Electronic and steric effects on the oxygenation of organic sulfides and sulfoxides with oxo(salen)chromium(V) complexes J. Org.Chem., 2003, 68, 7460.(7)