Designing a chemical program using chemical organization theory

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Summary

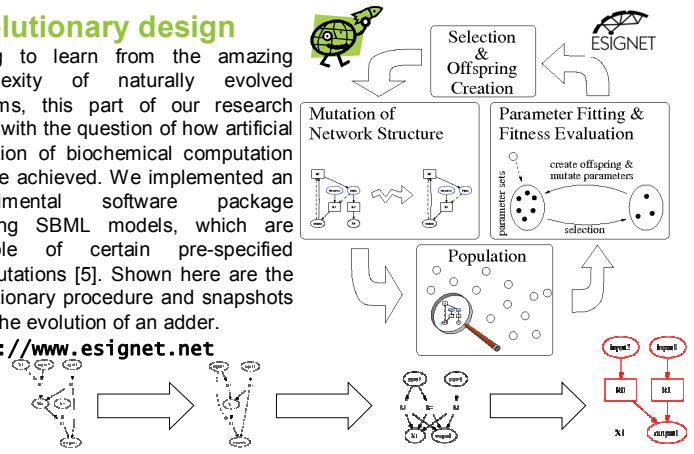
Behaviors of biological organisms are results of complex but orchestrated biochemical reactions. The complexity of the reaction network is a source of robustness and adaptability of biological systems. To harness the complexity for computation, following two design methodologies are considered here: evolutionary design and constructive design. While evolutionary design is focused on heuristically achieving approximate solutions, constructive design aims at exact solutions.

When engineering reaction systems, their complexity hinders users to program and control as desired. A small modification to the reactions may cause the system to enter unexpected behavioural regimes. A major alternation may exhibit little change in the global level. The gap between micro level (e.g., reaction rules) and macro level (e.g., chemotaxis behavior) has to be bridged. As a method to link these two levels, chemical organization theory has been introduced. We show below through two concrete examples how chemical organization theory benefits chemical programming.

Evolutionary design

Trying to learn from the amazing complexity of naturally evolved systems, this part of our research deals with the question of how artificial evolution of biochemical computation can be achieved. We implemented an experimental software package creating SBML models, which are capable of certain pre-specified computations [5]. Shown here are the evolutionary procedure and snapshots from the evolution of an adder.

http://www.esignet.net



Organization-oriented programming

Maximal Independent Set Problem: Given an undirected graph $\langle V,E\rangle$ with $N=|V|$ vertexes and $M=|E|$ edges, a chemical program is designed as a chemical reaction network with $2N=|\mathcal{M}|$ molecular species and $2(M+N)=|\mathcal{R}|$ reactions. Focusing on the organizations constituted of N species, the configuration of the species in any of these organizations corresponds to a maximal independent set (MIS). This correspondence can be mathematically proven.

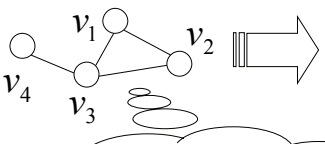
Species Name: S_i^{bin} — bin: Membership to the independent set; i: Vertex ID

$$(\forall n\in \text{Neigh}(v), n.Ind == False) \mapsto (v.Ind := True)$$
$$(\exists n\in \text{Neigh}(v), n.Ind == True) \mapsto (v.Ind := False)$$

Predicates for distributed system from [3]

$$\mathcal{R}=\bigcup_{i=1}^{N}\mathcal{R}^i \begin{cases} \underbrace{s_j^0+s_k^0+\cdots+s_l^0}_{n_i:\text{number of neighbors}} \to n_i s_i^1 \\ \{s_j^1\to s_i^0 \mid (v_i,v_j)\in E\} \\ s_i^0+s_i^1\to\phi \quad (\phi:\text{empty set}) \end{cases}$$
$$\mathcal{M}=\{s_i^0, s_i^1 \mid i=1,\cdots,N\}$$

$N=4, M=4$



Algebraic Chemistry

$$\mathcal{M}=\{s_1^0, s_1^1, s_2^0, s_2^1, s_3^0, s_3^1, s_4^0, s_4^1\}$$
$$\mathcal{R}=\bigcup_{i=1}^{4}\mathcal{R}^i: \text{(16 reactions total)}$$

MIS: $\{v_1,v_4\}$, $\{v_3\}$, $\{v_2,v_4\}$

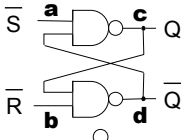
Organisations with 4 species:

$\{s_1^1,s_2^0,s_3^0,s_4^1\}$, $\{s_1^0,s_2^0,s_3^1,s_4^0\}$, $\{s_1^0,s_2^1,s_3^0,s_4^1\}$

correspond to MIS.

Logic circuit: RS flip-flop: Organization-oriented programming for a chemical logic circuit is discussed in [4]. A NAND-based RS flip-flop is shown as an example.

Species Name: S_i^{bin} — bin: Binary state; i: Variable name



$\overline{S}$	$\overline{R}$	Q_{t+1}	
0	0	-	
0	1	1	set
1	0	0	reset
1	1	Q_t	hold

1. Each NAND gate is converted to 4 reactions.

NAND 1	a	d	c
	0	0	1
	0	1	1
	1	0	1
	1	1	0

$$s_{\mathbf{a}}^0+s_{\mathbf{d}}^0\to s_{\mathbf{c}}^1$$
$$s_{\mathbf{a}}^0+s_{\mathbf{d}}^1\to s_{\mathbf{c}}^1$$
$$s_{\mathbf{a}}^1+s_{\mathbf{d}}^0\to s_{\mathbf{c}}^1$$
$$s_{\mathbf{a}}^1+s_{\mathbf{d}}^1\to s_{\mathbf{c}}^0$$

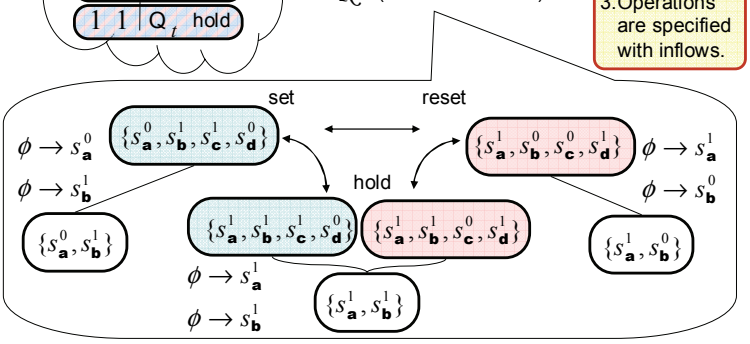
2. Species representing contradictory situations are defined to decay..

$$\bigcup_{i=\mathbf{a},\mathbf{b},\mathbf{c},\mathbf{d}}(s_i^0+s_i^1\to\phi) \quad (\phi:\text{empty set})$$

Algebraic Chemistry

$$\mathcal{M}=\{s_{\mathbf{a}}^0, s_{\mathbf{a}}^1, s_{\mathbf{b}}^0, s_{\mathbf{b}}^1, s_{\mathbf{c}}^0, s_{\mathbf{c}}^1, s_{\mathbf{d}}^0, s_{\mathbf{d}}^1\}$$
$\mathcal{R}$: (12 reactions total)

3. Operations are specified with inflows.



Theory of chemical organization

Chemical organization [1] is defined, given an algebraic chemistry, as a set of molecular species that is closed and self-maintaining. More precise definition is given below.

Algebraic Chemistry: pair $\langle\mathcal{M},\mathcal{R}\rangle$ of a set of elements (molecular species) $\mathcal{M}=\{s_i\}$ and a set of reaction rules $\mathcal{R}=\{A_j\to B_j \mid \forall j: A_j, B_j\in P_{Mul}(\mathcal{M})\}$

A set $C\subseteq\mathcal{M}$ is ***closed***, if for all reactions $(A\to B)\in\mathcal{R}$, with A a multiset of elements in C $(A\in P_{Mul}(C))$, B is also a multiset of elements in C $(B\in P_{Mul}(C))$.

Given an algebraic chemistry $\langle\mathcal{M},\mathcal{R}\rangle$ with $m=|\mathcal{M}|$ molecular species and $n=|\mathcal{R}|$ reactions, and let $\mathbf{M}$ be the $(m\times n)$ stoichiometric matrix implied by the reaction rules in $\mathcal{R}$. A set $S\subseteq\mathcal{M}$ of molecular species is ***self-maintaining***, if there exists a flux vector:

$$\vec{v}=(v_{(A_1\to B_1)},\cdots,v_{(A_n\to B_n)})^{\mathrm{T}}\in\Re^n$$

such that the following three conditions apply:

(1) $v_{(A_j\to B_j)}>0$ if $A_j\in P_{Mul}(S)$;

(2) $v_{(A_j\to B_j)}=0$ if $A_j\notin P_{Mul}(S)$;

(3) $(\forall i: s_i\in S \mid f_i\geq 0)$ where $\vec{f}=(f_1,\cdots,f_m)^{\mathrm{T}}=\mathbf{M}\vec{v}$

$P_{Mul}(*)$: powerset of all multisets consisting of the species in the set where a multiset allows multiple occurrences of an element.

References

1. Dittrich, P. and Speroni di Fenizio, P: **Chemical Organization Theory**. *Bull. Math. Biol.*, 2006, (in print).
2. Matsumaru, N. and Dittrich, P: **Organization-Oriented Chemical Programming for the Organic Design of Distributed Computing Systems.** *Proc. of Bionetics*, 2006.
3. Sukla, S. K., Rosenkrantz, D. J., and Ravi, S. S.: **Observaions on Self-Stabilizing Graph Algorithms for Anonymous Networks.** *In Proc. of 2nd Workshop on Self-Stabilizing Systems* 1995.
4. Matsumaru, N., Centler, F., Speroni di Fenizio, P., and Dittrich, P.: **Chemical Organization Theory as a Theoretical Base for Chemical Computing.** *IUUC* 2007, (in print).
5. Lenser, T., Hinze, T., Ibrahim, B., and Dittrich, P.: **Towards Evolutionary Network Reconstruction Tools for Systems Biology.** *In Proc. of EvoBIO* 2007 (in print)

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