Artificial Chemistry

Hideaki Suzuki*,**
National Institute of Information and Communications Technology (NICT)

Peter Dittrich†
Friedrich Schiller University Jena, Institute of Computer Science, and Jena Centre for Bioinformatics

During the long history of science, theory and experimentation have often worked together like the two wheels of a bicycle. In the last century, the most representative examples can be found in physics. Today, this is also true of modern biology, as in the case of brain science and artificial neural networks or of biochemistry and systems biology. Theoreticians in neuroscience construct artificial neural networks with a computer, and through simulations, they try to understand the mechanisms of the brain, whose elementary units—neurons—and their switching properties are already known by modern neurophysiology but whose entire functions, such as thought processes and consciousness, have not yet been clarified. Models of artificial neural networks are useful not only for understanding the design principles of the brain, but also for constructing powerful engineering/computational systems that have desirable features in common with living things.

The same has happened to the recent relationship between systems biology and biochemistry—two modern biosciences that study cells at a molecular level. Systems biology's researchers construct fine models of molecular activities and try to simulate the biological cell system as a whole. Unlike artificial neural network research, however, systems biology research is currently contributing only to biology. A biological cell is such a huge system that the computational cost to simulate the entire cell on a molecular level is enormous. When we try to examine the origin and evolution of biological cell systems or when we want to engineer a bio-inspired computational system imitating molecular activities, we have to design more abstract models than those currently used by systems biology.

The theme of this special issue, artificial chemistry (AChem), is a research field that complements systems biology from this point of view. In a typical AChem study, we construct a model of a biological system at a molecular level, but we minimize the computational cost by dramatically simplifying the model in order to make self-organizing phenomena or functional emergence happen on a computer. The biomolecular system is one of the few systems whose elementary processes (molecular reactions) are well known and that exhibit such phenomena as self-organization or self-assembly. AChem facilitates one of the most promising approaches toward the design of computational systems with emergent characteristics.

Although the term "artificial chemistry" itself was coined by Rasmussen [4], Fontana [1], and others around 1990, the methodology of AChem (i.e., abstracting biomolecular processes computationally) has some other roots. Approaches like Turing patterns [6], typogenetics [2], and Laing's molecular machines [3] should capture fundamental properties of (bio)chemistry without trying to model specific chemical processes in detail. In Tierra [5]—as another, more recent example—two self-replicating programs can interact with one other by complementary nop matching, which we can now regard as a typical example of an invention for AChem.

* Contact author.
** National Institute of Information and Communications Technology (NICT), Kobe Advanced ICT Research Center (KARC), 588-2, Iwaoka, Iwaokaka-cho, Nishi-ku, Kobe, 651-2492 Japan. E-mail: hsuzuki@nict.go.jp
† Friedrich Schiller University Jena, Institute of Computer Science, and Jena Centre for Bioinformatics, D-07743 Jena, Germany. E-mail: dittrich@cs.uni-jena.de

Since the time of the above-mentioned studies, quite a few articles on AChem have been published in this journal and the proceedings of the major ALife conferences in the past fifteen years. These are roughly classified into two categories in terms of their purpose: works that focus on finding some insight into biological systems, and works aiming to contribute to engineering. The articles collected in this issue are well balanced from this point of view: the articles by Benkö et al., Lenaerts and Bersini, Oohashi et al., and Suzuki and Ikegami are in the first category, and those by Buisman et al., Hutton, Oohashi et al., Sayama, and Tominaga et al. are in the second, with the exception of the article by Oohashi et al., which presents results for both. In what follows, we discuss the articles one by one, providing an overview.

In "Computing Algebraic Functions with Biochemical Reaction Networks," H.J. Buisman, H.M.M. ten Eikelder, P.A.J. Hilbers, and A.M.L. Liekens propose a novel chemical model that utilizes chemical reactions for computational purposes. They show how to implement addition, subtraction, multiplication, division, and square roots. By coupling these elements, a general approach is developed that allows one to build arbitrary polynomials. Of course, this does not provide a method to replace the silicon computers we use today, but the article is valuable in that it presents the possibility of new analog calculators that work in a totally different environment than silicon devices.

In "The Organic Builder: A Public Experiment in Artificial Chemistries and Self-Replication," Tim J. Hutton presents a two-dimensional AChem model in which a cell made up of a genetic chain and a closed membrane chain divides itself. This is a direct extension of the author's previous works that try to bring about cell-like behavior by preparing a set of man-made symbolic reaction rules, but the result is unique in that the reaction rules were not designed by the author himself, but by participants of a public game the author established on the Internet. Usually, in AChem studies, we not only mimic biomolecular reactions but also devise man-made reaction rules. This article suggests that by preparing an arena in which a number of players take part, we are able to devote much more time and energy than that available to us as individuals, and as a result, we might obtain a better design than we expect.

When we design an AChem system, one of the most important issues is the choice of the elementary symbols. The smaller the elements we take, the more universal (reusable) they are, but the more computational power we need. An emergent system, whether natural or artificial, needs to have an appropriate number of elementary units for the efficient reconstruction of higher functions. In "An Effective Hierarchical Model for the Biomolecular Covalent Bond: An Approach Integrating Artificial Chemistry and an Actual Terrestrial Life System," Tsutomu Oohashi, Osamu Ueno, Tadao Maekawa, Norie Kawai, Emi Nishina, and Manabu Honda suggest the possibility that in living beings, this requirement is met by the hierarchical difference in the covalent bond energy of biomolecules. They examine this overlooked trait through both biological and computational experiments and obtain results supporting the model. This work is a wonderful example of how AChem works, wherein a computational model is checked with biological data.

In "Shapes and Self-Movement in Protocell Systems," Keisuke Suzuki and Takashi Ikegami deal with chemotaxis of a two-dimensional autopoietic cell. By revising local rules for the intracellular metabolism and membrane shape modification, the authors succeeded in making the cell movable in a grid space and observing chemotactic behavior of an artificial cell under a resource density gradient. The implemented cell has no explicit sensors on its membrane, and the result might constitute the first step toward constructing a theory that clarifies the origin and mechanisms of a long-term mystery in the biological sciences—chemotaxis.

Artificial chemistries have stimulated the development of novel theoretical concepts for dealing with complex chemical systems. In "A Topological Approach to Chemical Organizations," Gil Benkö, Florian Centler, Peter Dittrich, Christoph Flamm, Bärbel Stadler, and Peter Stadler review mathematical approaches operating on the reaction network's stoichiometric structure, while abstracting from more detailed kinetic laws. They present a novel interpretation in terms of set-valued set functions, which allows us to build a bridge to the field of generalized topology. They illustrate how topological concepts like connectedness can be applied to describe structural features of a chemical system.

In early AChem work, such as in [1] and [3], molecules and their reaction rules were defined in a rather abstract way, using concepts from computer science like the Turing machine or lambda

calculus. Today we can witness a progression of the field toward more realistic artificial chemistries. In "A Synthon Approach to Artificial Chemistry," Tom Lenaerts and Hugues Bersini present an approach that incorporates the logical structure of constitutional chemistry and its kinetics in order to define the space of possible molecules and their reaction rules. This approach allows us to study the topological evolution of the structure of the chemical reaction network under assumptions that are more realistic from a biochemical perspective, while at the same time being abstract enough to perform large-scale simulations.

In artificial chemistries, the set of possible molecules is usually defined explicitly by enumerating all molecular species or implicitly by a grammarlike formalism describing the structure of valid molecules. However, in "Swarm Chemistry," Hiroki Sayama proposes a novel approach in which molecules are emergent phenomena in an artificial swarm system. Consequently, the reactions also emerge in a dynamic pattern resulting from "colliding" different swarms, which represent the reacting molecules.

The complexity of biochemical reaction systems found in living organisms is enormous. Therefore, classical approaches applied by computational biology and systems biology in which the set of molecular species and their reactions is defined explicitly are limited to rather small systems and do not scale with the need to capture the combinatorial complexity we are facing in molecular biology. AChem research has a long tradition of representing chemical systems implicitly, nowadays also known as rule-based modeling. In "Modeling Biochemical Pathways Using an Artificial Chemistry," Kazuto Tominaga, Yoshikazu Suzuki, Keiji Kobayashi, Tooru Watanabe, Kazumasa Koizumi, and Koji Kishi present how an artificial chemistry based on string pattern matching and recombination can be applied to model and design biochemical systems. Moreover, this approach allows for reasoning and model checking.

References

1. Fontana, W. (1992). Algorithmic chemistry. In C. G. Langton, C. Taylor, J. D. Farmer, & S. Rasmussen (Eds.), *Artificial Life II: Proceedings of an interdisciplinary workshop on the synthesis and simulation of living systems* (pp. 159–209). Redwood City, CA: Addison-Wesley.
2. Hofstadter, D. R. (1979). *Gödel, Escher, Bach: An eternal golden braid*. New York: Basic Books.
3. Laing, R. (1972). Artificial organisms and autonomous cell rules. *Journal of Cybernetics*, *2*(1), 38–49.
4. Rasmussen, S., Knudsen, C., Feldberg, R., & Hindsholm, M. (1990). The coreworld: Emergence and evolution of cooperative structures in a computational chemistry. *Physica D*, *42*(1–3), 111–134.
5. Ray, T. S. (1992). An approach to the synthesis of life. In C. G. Langton, C. Taylor, J. D. Farmer, & S. Rasmussen (Eds.), *Artificial Life II: Proceedings of an interdisciplinary workshop on the synthesis and simulation of living systems* (pp. 371–408). Redwood City, CA: Addison-Wesley.
6. Turing, A. (1952). A chemical basis for morphogenesis. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, *237*, 37–72.