Rhythms Emerge in a Collection of 'Blind' Chemicals by the Use of 'Genetic Switches'

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Abstract

This paper presents a new computational method in the modeling and simulation of gene expression by introducing the artificial chemical system. The artificial chemical system is specified by its four items: (1) components (five kinds of particles and DNA with Genetic Switches); (2) space (2-dimensional polar grids); (3) simple reaction rules (construction and destruction of molecules, etc.); (4) simple behavioral rules (stochastic movements and stochastic collisions, etc.). The simulation demonstrates the capability of the system to exhibit emergent behavior: that is, global order of the system (regular rhythms, i.e. regular oscillations in the amounts of some gene products, in this case) emerges out of the randomness (through stochastic movements and collisions) of the components.

1 Introduction

As is described in the following quotation, dynamic behavior is a very important property in artificial life as well as in natural life :

> ... Artificial Life involves the realization of lifelike behavior on the part of man-made systems consisting of populations of semi-autonomous entities whose local interactions with one another are governed by a set of simple rules. Such systems contain no rules for the behavior of the population at the global level, and the often complex, high-level **dynamics** and structures observed are emergent properties, which develop over **time** from out of all of the local interactions among low-level primitives by a process highly reminiscent of embryological development, in which local hierarchies of higher-order structures develop and compete with one another for support among the low-level entities.... (*Quoted from [6] preface xxii.*)

Then a question arises: what are the sources of dynamic behavior for natural organisms? 'Dynamics of the environment' would be one of the answers, but it is the 'external source'. Then what are the 'internal sources' for organisms that give rise to dynamic behavior? The answer would be their **genomes**, or more specifically, their **collections of 'Genetic Switches'** [7]. Without these switches, any organism cannot survive, just as an amoeba without nucleus cannot.

In fact, Genetic Switches are very nice contraptions. A Genetic Switch corresponds to an **if-then rule** [3, 4]. The then-part of a rule specifies **action(s) to be taken**, or more precisely, it specifies **gene product(s) to be produced**, whereas the if-part of the rule specifies **conditions** as to when the then-part of the rule should be activated. (See Fig. 1.) Now, suppose the environment of an organism changes, and the change is detected by one of the genetic switches of the organism. Then the organism is supposed to exhibit dynamic behavior via the change in the state of one of the genetic switches.

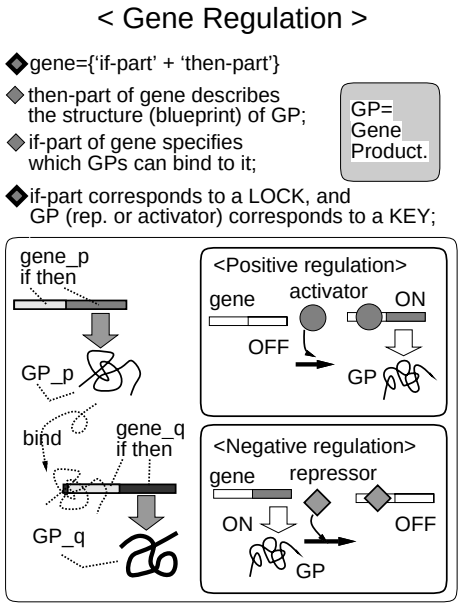

Figure 1: Regulation of gene expression

Since research that emphasizes the dynamic behavior of genetic switches does not seem to exist, this paper presents one step towards this direction[1]. As a simple example that uses genetic switches, the 'circadian rhythm' is chosen. Many lifeforms on earth exhibit circadian rhythms, in which processes the amounts of some gene products oscillate regularly. Genes contributing to circadian rhythms are found [1, 5] but details of circadian clocks are still unclear. Under these circumstances, we have designed the model of an artificial system and made some computer simulations, as will be described in the following sections.

2 The Model

Four items of the model, i.e. (1) components, (2) space, (3) reaction rules, (4) behavioral rules; are designed (see below). In this model, the **components** move around in the **space** following the **behavioral rules** and interact / react with one another according to the **reaction rules**.

1 ⟨ the components ⟩ : The world consists of (1) five kinds of particles $\{g, e, f, d, b\}$ and (2) DNA containing two genes ('E' and 'F') and their Genetic Switches. (See Fig. 2.)
Particles are assumed to make **hierarchical structure**: { particle (**'P'**), molecule (**'M'**), complex (**'C'**) }. Namely, a complex is composed of molecules, and a molecule is composed of particles[2].

We assume three kinds of molecules $\{G, E, F\}$ and their component-parts to be 'g's, 'e's, 'f's, respectively. (See Fig. 2.) The particle 'd' (for **"destroyer"**) catalyzes the **dissociation** of

[1]Although the MFA (Movable Finite Automata) model [2, 8] captures one aspect of dynamic behavior (i.e. conformational changes), the model is unsatisfactory, because it seems to be "one-way". That is, the model does not seem to have the "room of choices in the chain of events". Therefore, one event always leads to the specific next event in the MFA model.

[2]Although 'atoms' are the building blocks of molecules in the real world, the term 'particles' is used to describe the building blocks of molecules in this model. The reason for this is that the building blocks in this model are remniscent of 'amino acids' rather than 'atoms'.

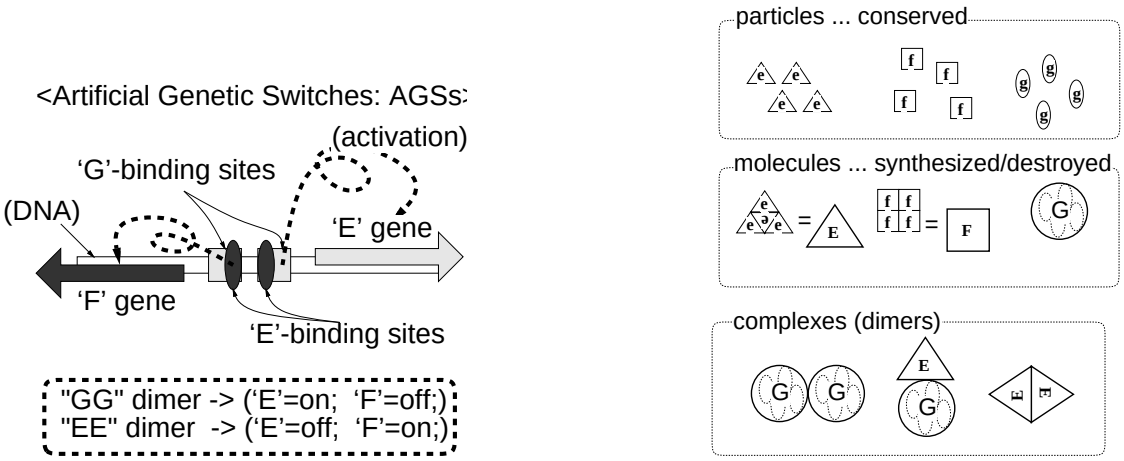

Figure 2: (Left) Artificial Genetic Switches, (Right) Hierarchical Structure: from particles to complexes

'E's and 'F's, whereas the particle 'b' (for **"builder"**) catalyzes the **synthesis** of 'E's and 'F's, as follows:

$$E \xrightarrow{d} \alpha e; \quad F \xrightarrow{d} \beta f; \qquad \alpha e \xrightarrow{b(e)} E; \quad \beta f \xrightarrow{b(f)} F;$$

(α and β are integer parameters)

Note(1): The particle 'b' takes one of the three states: $\{\, b(), b(e), b(f)\,\}$, and this state determines its catalytic capability[3].

Note(2): All particles are assumed to be **conserved**. Denotating $N(X)$ as the amount of the particle (or molecule) X, and $\dot{N}(X)$ as $(d/dt)N(X)$, $\dot{N}(g) = \dot{N}(e) = \dot{N}(f) = \dot{N}(d) = \dot{N}(b) = 0$. We also assume $\dot{N}(G) = 0$; but $\dot{N}(E) \neq 0$; $\dot{N}(F) \neq 0$;

2 $\langle$ the (grid) space $\rangle$: Each of 'P's or 'M's or 'C's exists in one of the grids. (The current version of the space is the 2-dimensional polar grids: see Fig. 3.) These 'P's or 'M's or 'C's move

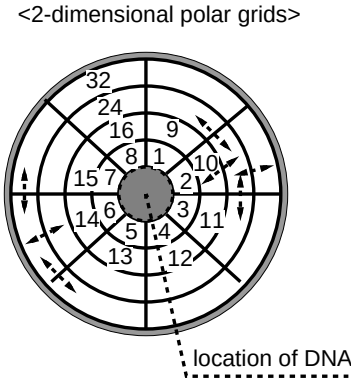

Figure 3: 2D polar grids

around and/or collide one another (according to the behavioral rules) and react (according to the reaction rules) after collision. DNA is assumed to stay in the center of the polar space.

[3]Each of particle 'b' performs the functions which correspond to the functions of both **ribosome and mRNA**.

3 ⟨ the reaction rules ⟩ :
◇◇ Dimers formations ◇◇ :
Molecules 'G's and 'E's react in the following way, when they collide:

$$G + G \rightarrow GG;$$

$$G + E \rightarrow GE;$$

$$E + E \rightarrow EE;$$

Dimer 'GE' is assumed to be more stable than dimers 'GG' or 'EE'. Therefore, the following reaction occurs, after the collision of each combination:

$$G + EE \rightarrow GE + E;$$

$$GG + E \rightarrow GE + G;$$

$$GG + EE \rightarrow 2GE;$$

◇◇ Reaction with DNA ◇◇ :
Only one dimer, either 'GG' or 'EE', is assumed to be bindable to DNA. (See Figs. 2, 4.) Other entities except for 'b's, (i.e. 'G's, 'E's, 'F's, 'g's,'e's, 'f's, and 'd's) do not interact with DNA. When one dimer (either 'GG' or 'EE') is binding to DNA, other dimers cannot bind to DNA. The binding dimer can react in the same way as the 'free' dimers when other molecules or dimers collide to it. (By this rule, DNA can get free from the binding dimer, providing chances for free dimers to bind to DNA.)

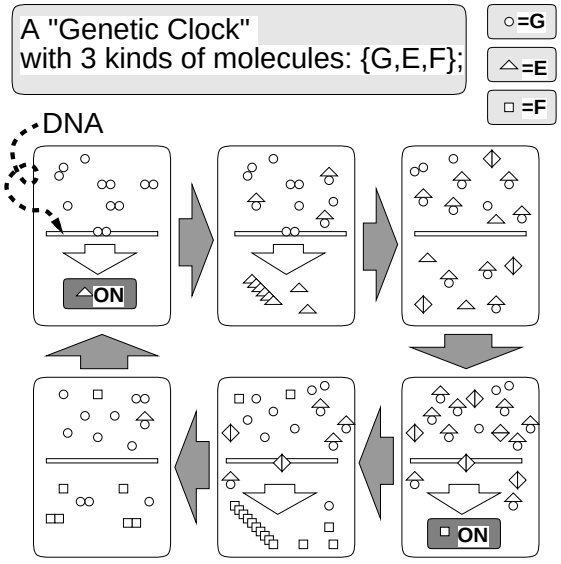

Figure 4: Clock cycle with {G,E,F}s

When a particle 'b' collides with DNA, the state of 'b' changes as follows:
(1) If a dimer 'GG' is binding to DNA, then $b(*)$ [4] $\rightarrow b(e)$;
(2) If a dimer 'EE' is binding to DNA, then $b(*) \rightarrow b(f)$;

[4] $(b(*) \in \{b(), b(e), b(f)\})$

Otherwise, the state of 'b' does not change. (See Fig. 2.) [5]

◇◇ Synthesis of 'E's/'F's by $b(e)/b(f)$ ◇◇ :
Partcle $b(e)$ or $b(f)$ accumulates 'e's or 'f's, respectively, to synthesize molecule E or F, respectively as follows: [6]

$$b(e) + e \rightarrow b(e)[1]$$

$$b(e)[1] + e \rightarrow b(e)[2]$$

$$b(e)[i] + e \rightarrow b(e)[i+1]$$

$$b(e)[\alpha - 1] + e \rightarrow b(e) + E$$

(... A molecule 'E' is synthesized.)

$$b(f) + f \rightarrow b(f)[1]$$

$$b(f)[1] + f \rightarrow b(f)[2]$$

$$b(f)[i] + f \rightarrow b(f)[i+1]$$

$$b(f)[\beta - 1] + f \rightarrow b(f) + F$$

(... A molecule 'F' is synthesized.)

◇◇ Destruction of E / F molecules ◇◇
When a particle 'd' collides with molecule E / F, the molecule dissociates into α 'e's / β 'f's, respectively. (Molecules 'G's are assumed to be never destroyed.)

$$E + d \rightarrow \alpha e + d;$$

$$F + d \rightarrow \beta f + d;$$

When molecules E and F collide, they react as follows:

$$E + F \rightarrow \alpha e + \beta f;$$

When dimers GE or EE collides with molecule F, the following reaction occurs:

$$GE + F \rightarrow \alpha e + \beta f + G;$$

$$EE + F \rightarrow \alpha e + \beta f + E;$$

4 ⟨ the simple behavioral rules ⟩ : (See Fig. 5.) Iterate the following eternally:

1 At each time step, pick up one particle X randomly. (If the particle chosen belongs to a molecule / dimer, then choose the whole molecule / dimer.)

2 If the {P/M/C} chosen is located in the center of the polar space, then react with DNA according to some probability and go to 5. Otherwise go to 3.

3 Move the {P/M/C} chosen to one of the adjacent grids according to some probability and go to 5. Otherwise go to 4.

[5] Transitions among $b(*)$ correspond to **transcription processes** in nature.
[6] This process corresponds to **translation process** in nature.

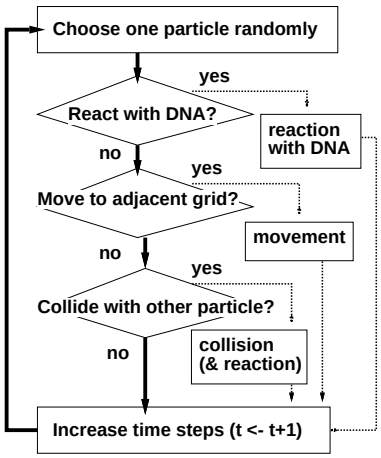

Figure 5: Behavioral flow chart

4 Select another particle Y which belongs to the same grid as X. (As before, Y may be M/C.) Then make collision (and reaction if possible) between X and Y.

5 Increase the time step.

As is observed in this rule and the previous (reaction) rule, the **'chemicals'** (i.e. particles, molecules, and complexes) are **'blind'**. That is, (1) they do not react **unless they collide**, and (2) they **cannot choose which chemicals to collide**.

3 Experiments and Results

Several experiments are done with various parameter settings. Graphs in Fig. 6 are obtained by the following settings, respectively. (In all cases, $\alpha = \beta = \gamma = 7$)

Table 1: Numbers of particles for Fig.6

	(top)	(middle)	(bottom)
$N(g)$	350	3500	14000
$N(e)$	700	7000	18000
$N(f)$	350	3500	14000
$N(d)$	100	100	100
$N(b)$	400	400	400
$N(total)$	1900	14500	56500

As is shown in Fig. 6 almost regular rhythms in the amount of dimers 'GE's emerged. The period of the oscilation is controlled mostly by the size of $N(g)/\gamma$ (i.e. the amount of 'G' molecules), since this amount determines the 'capacity of guard': as is seen in Fig. 4, a dimer 'EE' cannot bind to DNA, unless 'guarding Gs or GGs' are 'neutralized' to 'GE's.

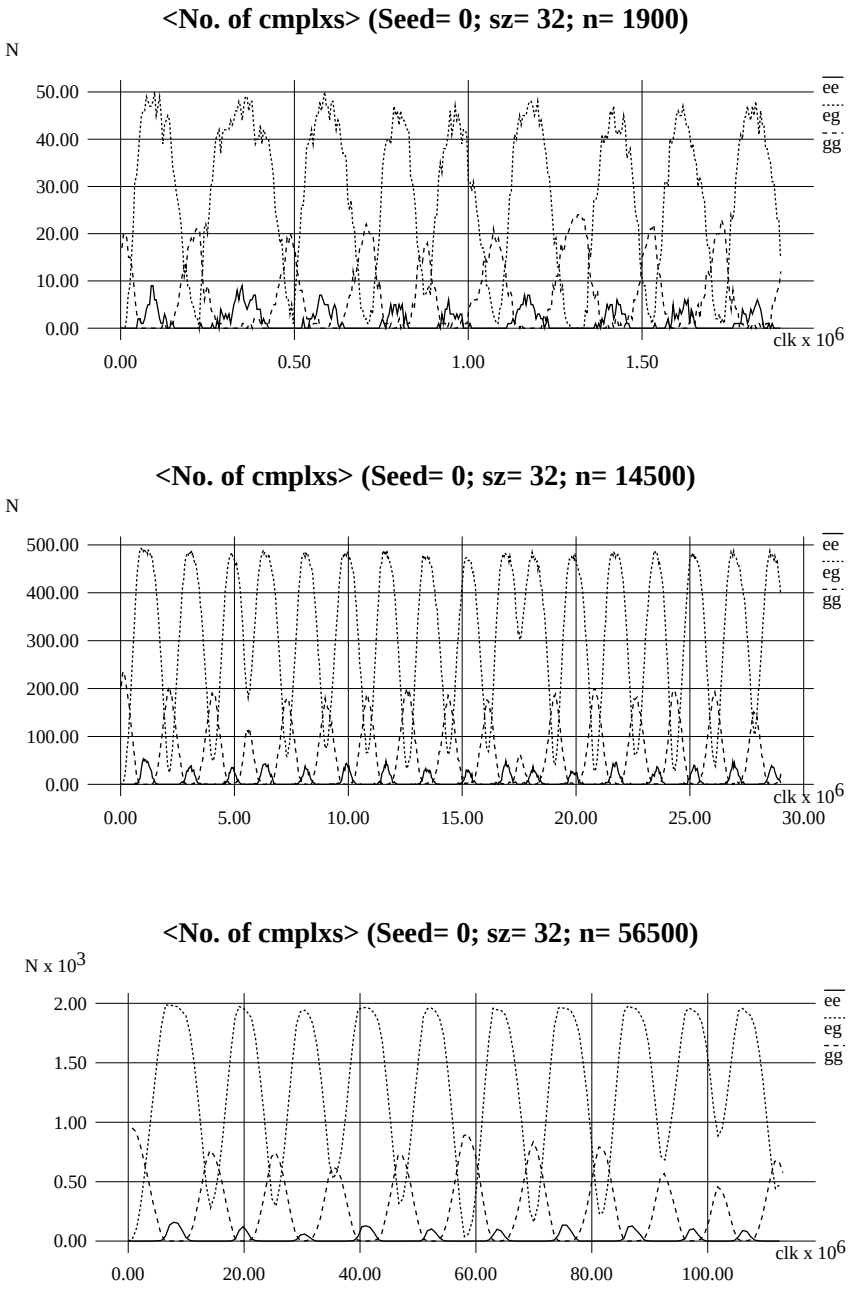

Figure 6: Examples of the simulation; time vs. amounts of dimers

4 Discussion

In the current model, DNA takes one of the three states: { (0) nothing is binding to it; (1) a dimer 'GG' is binding; (2) a dimer 'EE' is binding; }. (See Figs. 4, 2.) Transitions occur between these states.

We are now analysing these transitions. Fig. 7 shows some examples. From this figure, we can see that

- transition of "(1)→(0)→(2)" , or "g→e" is faster than that of "(2)→(0)→(1)", or "e→g";
- The "g→e" transition seems to have smaller variance than the "e→g" transition.

More detailed analysis is in progress.

5 Concluding remarks

This paper described the Artificial Chemical System in which **order at the global level emerges out of local interactions** (i.e. random collisions / reactions) among the components of the system. In the natural organisms, order at the global level emerges despite of the blindness and randomness of their components (i.e. molecules / molecular complexes). Therefore, our task now is to find a set of simple local (molecular) rules that gives rise to dynamic behavior / order of the natural organisms. This paper presented one step towards this direction.

Acknowledgments

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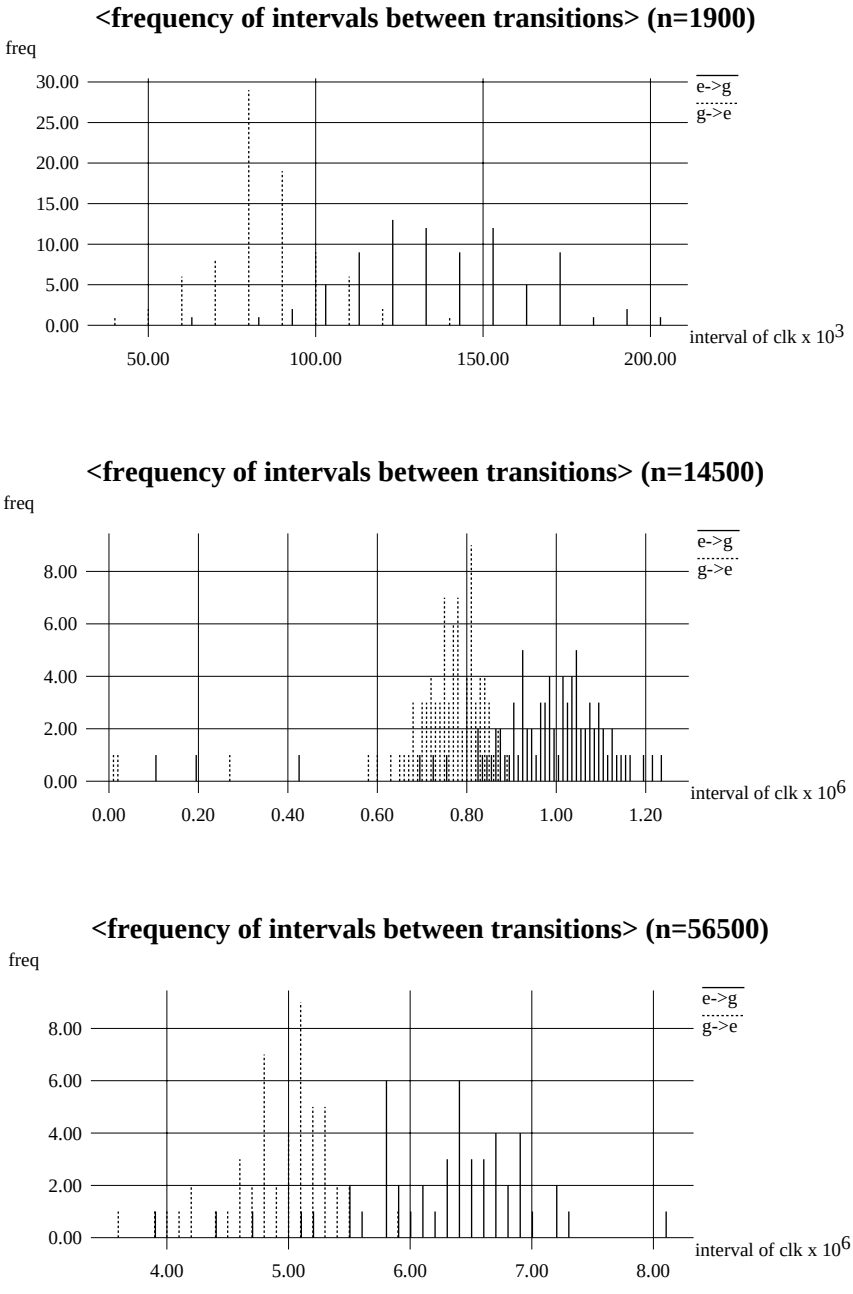

Figure 7: Analysis of intervals between transitions