

Autonomous system including an observer, illustrating dynamic instability of individual microtubules.

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ABSTRACT. A model system including an observer is constructed by reentrant form using Brownian algebra. It is connected with a universe through the observer's motivations which are formalized as modulator and oscillator functions. Due to the interaction between them the systems behave autonomously. The instability of microtubule in vitro is explained as an example of this model.

INTRODUCTION

In the present paper, we succeed the concept of autonomy in the form of self-reference (i.e. reentry, self-identity), and point out the weakpoint taken after Spencer-Brown (1961) and Varela (1979). They established the descriptive perspective from the viewpoint of an observer. Strictly speaking, observed systems can be behaved as the autopoiesis through observer's brain. However Varela's motivation is the formalization of the system including an observer, observer's language is not observer himself. Hence, it is bound on a universe. The concept of the autopoiesis is originated from the openness and/or connection with a universe, and any formal language is closed. With respect to living or autopoietic systems, we have to appreciate the connection between language and a universe.

In this perspective for living systems, results of simulations do

not refer to organisms, but probably approximate organisms in vitro. We contend with this restriction, because reentrant form extended semantically is regarded as autonomous unit illustrating the property of microtubules. It is the first step to show what the living or autopoietic system is.

It has previously been shown that only microtubules in vitro is in self-organizing process (Mitchison & Kirschner, 1984a,b; Horio & Hotani, 1986; Walker et al. 1988). Horio & Hotani demonstrated that growing and shortening populations of microtubules coexisted in steady-state condition, by visualization of the dynamic behaviour of individual microtubules in vitro by dark-field microscopy. It was reported that both ends of a microtubule existed in either the growing or the shortening phase and alternate quite frequently between the two phases in a stochastic manner. This phenomenon is regarded as the basic property of self-organizing and/or autonomous unit, and we emphasize that the mechanism of the microtubule assembly can be a minimal model of autonomy in the extended sense of Varela (1979).

The previous models of microtubule are constituted where this biological phenomenon is recognized as critical one. Therefore, the phase transition itself is thought to be resulted from the thermal fluctuation. In the present paper, what is regarded as fluctuation is included in deterministic system, called reentrant forms. We explain reentrant forms by Brownian algebra at first, and its theoretical extension especially the interpretation as modulators. At last we show the behaviour of this system, illustrating dynamic instability of microtubules.

OSCILLATOR-MODULATOR COMPLEMENTARY

Using Brownian algebra (Spencer-Brwon, 1969), I have proposed a few models on morphogenesis (Gunji, 1989a,b,c). Here, I extend the same type of models based on Brownian algebra in a broad sense, and construct biological space and time, illustrating autonomous behaviour

of microtubules in vitro.

Gunji (1989a) interpreted self-referential forms as the form of observation itself including both an observer and an object. Hence, we can invent an intrinsic observer within an object (e.g. living system). As long as we hold this perspective, namely, we construct the stance that an object involves an observer (subject). We can behave as if we observed from the inside of the object.

Even though we describe organisms taking the stance of the intrinsic observer, the subject is arbitrarily constructed or invented. In other words, the relationship between the observer and the object in the form of Brownian algebra contributes to axioms. The self-referential form in the form with an intrinsic observer is not opened to a universe, and is nothing but a specific language. We would consider the way to overcome this limit, turning back to the principle of the self-reference.

Self-referential Forms as Intrinsic Observers

Spencer-Brown's algebra (Spencer-Brown, 1969), which is called Primary algebra by Varela (1979) is basically a dual valued logic, and can be compared to Boolean algebra (see Appendix). We find the following two significant arguments in Spencer-Brown's algebra suggesting to biology and/or cognitive science. The first is indistinction between operand and observer. It represents that what we indicate, names or values are nothing but our indications themselves. Hence we can interpret an object as what we observe. Anything do not exist till they are indicated.

The second point is the emplacement of self-reference. Logical contradiction is generally regarded as impropriety. However, Spencer-Brown suggested the logic that positively includes contradiction. Actually there might be many ways and logics in order to include contradiction. On the one hand Spencer-Brown constructed the concept of time for this purpose, on the other hand Varela (1979)

constituted extended algebra with the introduction of the third value newly invented.

Gunji (1989a,c) extended Spencer-Brown's notion that every perception is dependent on self-reference, originated from the concept that content is also operational. Where Spencer-Brown interpreted tautological proposition $\underline{a}=\underline{a}$ as $\underline{a}=\overline{\underline{a}}$, which involves two reflections between observer and object, Gunji adds a symbol of subject in this form, and constructed the self-referential forms that object =subject sees an object.

In his context, the subject (observer) is represented by an alphabet, and the object is described as the relationship between the object and the observer. For example, let \underline{b} and \underline{a} be the subject and the object, respectively. Indeed, supposing that \underline{a} is explicitly distinguished from \underline{b} (i.e. there is a cross between \underline{a} and \underline{b}). Hence, we describe \underline{a} as the relationship of \underline{a} -cross- \underline{b} -cross (cross represents the distinction between two);

$$\underline{a} = \overline{\underline{a} | \underline{b}} . \quad (1)$$

Actually this form represents the infinite reentries like regressus in infinitum. Even when you circulate along the observational circle (Fig. 1) twice, you obtain,

$$\overline{\overline{\underline{a} | \underline{b} | \underline{a}} | \underline{b}} = \overline{\underline{a} | \underline{b} | \underline{a} | \underline{b}} | \underline{a} | \underline{b} . \quad (2)$$

Hence, the circulation at infinite times is written as the same form as eq(1). The simplest relationship between \underline{a} and \underline{b} is classified to three types, namely explicit distinction, $\underline{a}=\overline{\underline{a} | \underline{b}}$, implicit one, $\underline{a}=\overline{\underline{a} \underline{b}}$, and fusion, $\underline{a}=\underline{b}$ (Gunji in preparation). Hence, generally speaking, the relationship between \underline{a} and \underline{b} is written in the canonical form as,

$$\underline{a} = \overline{\underline{a} | A} | \underline{a} | \underline{B} | \underline{C}$$

$$b_i = \overline{b_i} \underline{A_i} \overline{b_i} \underline{B_i} \underline{C_i} \quad (3)$$

where b_i ($i \in \{1, \dots, N\}$, N is natural number) represents a component which constitutes the observer b . Symbols \underline{A} , \underline{B} and \underline{C} represent any expressions involving any symbols in $\{b_1, \dots, b_N\}$, $\underline{A_i}$, $\underline{B_i}$ and $\underline{C_i}$ are expressions \underline{a} and $\{b_1, \dots, b_N\}$, excluding b_i . In the sense of Primary algebra, the forms (3) generally involve self-contradiction. We can arbitrarily construct another axiom, and can invent another algebra to resolve the self-contradiction. The simplest method to resolve the self-contradiction is the distinction \underline{a} in right hand from \underline{a} in the left hand, denoting \underline{a}' and \underline{a} . This is the primary form generating time (Spencer-Brown 1969).

In the discussions mentioned above, there are two essential problems. (1) Time is originated from the reentrant form, why space is generated in the same manner? (2) Spencer-Brown positively allowed the modification of the meaning of the equational symbol. Then the reentrant forms are arbitrarily constructed and modified through observation. In this sense there are double observers; the one is included in the reentrant form itself and the other appear at the moment of the construction of the form, strictly in the appearance of equational symbol. Does it take any time for observation itself?

We think that these two points are dependent on the connection between observer and a universe, and would extend the reentrant forms to improve them.

The Motivation of Language; Modulator and Oscillator

There are many models that realize the distinction in order to resolve self-contradiction in self-referential forms, and the kind of model depends on the motivation of the user of this language. Essentially this motivation exists out of logic. Let consider addition, $1+1=2$. What is the substance of symbol 1 ? What is indicated

by symbol l is dependent on referent, and what determines the referent is nothing but user's motivation. The number l might represent an apple or a pen. The way of resolution in reentrant forms, which is illustrated by the way of labeling suffices is understood on a similar interpretation. For example, in the formulas,

$$\begin{aligned} \underline{a'} &= \underline{f(a, b)} \\ \underline{b'} &= \underline{g(a, b)}, \end{aligned} \quad (4)$$

we can interpret them as

$$\begin{aligned} \underline{a^{t+1}} &= \underline{f(a^t, b^t)} \\ \underline{b^{t+1}} &= \underline{g(a^t, b^t)}, \end{aligned} \quad (5)$$

and also as,

$$\begin{aligned} \underline{a^{t+1}_k} &= \underline{f(a^t_k, b^t_k)} \\ \underline{b^{t+1}_k} &= \underline{g(a^t_k, b^t_k)}. \end{aligned} \quad (6)$$

This kind of interpretation (model, mapping) is arbitrarily selected by user's motivation, and comes out of the language. We can give other explanations using suffices l, m, \dots . Let us consider the difference between (5) and (6). Here we call the form (5) oscillator and the form (6) modulator.

On detailed examinations, Varela(1979) discussed the oscillator, and proved that we can construct it with solutions of any periodic sequence of values from $\{0, 1\}$. Because modulators have less frequently been discussed, we focus on their features.

In modulators, we can interpret that waveforms in k -direction is modulated in t -direction. Any reentrant forms are interpreted as modulators, using multi-dimensional suffices. To examine the properties of modulators, let us consider such a simple case as

$$\begin{aligned} f(a, b) &= \overline{a \ b} \ \overline{a \ b} \\ g(a, b) &= \overline{a \ b} \ \overline{a \ b} \end{aligned} \quad (7)$$

substituting for the equation (2-6). Patterns generated by this evolution equation are shown in Fig. 2. It is found that there are many white triangles whose apices are upward. This is invertible function for $a_{i,t+1} = (a_{i-1,t} + a_{i,t}) \bmod 2$. In cellular automata, the pattern represents the propagation of information by interactions. In modulators, it represents that there is spatial long-term correlation which looks as if there were a long-range of interactions.

In addition, we can construct fractal patterns by modulators. These modulators can articulate space by oscillators and interpret the articulated pattern step by step. For example, let us consider the case of Cantor set-type modulators. The Cantor set is defined as the following. The closed interval $[0,1]$ is divided into three equal parts, and open intervals $(1/3, 2/3)$ are omitted. Call remained intervals I_{11}, I_{12} ($n=1$). When similar procedure is repeated, we obtain,

$$C^{(n)} = \bigcup_{i=1}^{2^n} I_{ni}, \quad C = \bigcap_{n=1}^{\infty} C^{(n)}. \quad (8)$$

In modulators, we define the process that closed interval is divided into three parts and central subpart is omitted as the waveform $(\neg, _, \neg)$. Then, according to Varela (1979), we construct the self-referential form producing this waveform as,

$$\begin{aligned} a &= \overline{b} \\ b &= \overline{a \ b} \end{aligned} \quad (9)$$

Substituting these forms for the switching function (Gunji, 1989c), we obtain the modulator,

$$\begin{array}{l}
 \overline{a_k^{t+1} = b_k^t \overline{a_k^t}} \\
 \overline{b_k^{t+1} = \overline{a_{k-1}^t} \overline{a_k^t} \overline{b_k^t} \overline{c_k^t} \overline{a_{k-1}^t} \overline{a_k^t} \overline{b_k^t}} \\
 \overline{c_k^{t+1} = \overline{a_{k-1}^t} \overline{a_k^t} \overline{b_k^t} \overline{a_{k-1}^t} \overline{a_k^t} \overline{c_k^t}} \quad (10)
 \end{array}$$

Patterns generated by this form is shown in Fig. 3. Actually, we can construct any modulators which produce any fractal-like sequences by this procedure.

We emphasize the strong power of modulators, which can generate space through articulation and interpretation. The most important point of self-referential forms is not only the property of modulators (or oscillators) but the ambiguous which is regarded as diverse motivations. There is no problem in physical science when one specific motivation is fixed (implicitly). On the other hand in biology, diverse motivation is a central problem. Final cause in organisms comes from the outside of a language, however an observer provide a special language. Hence, an observer doubts that the present language is not enough to describe them, and turns back to the stance of observation (inerpretation). Because the interpretation is chosen due to the motivation of the observer, the language coupled with diverse motivations are effificent means to describe organisms.

OBSERVATION INCLUDING TIME

Here we would think about the construction of reentrant forms. As discussed above, the observer in the second sense appear in this attitude. The observational circle (Fig.1) is reconsidered. In the previous section, we regard that circulation in the circle once equals to twice circulation. However, it essentially depends on the usage of the equational symbol.

The observational circle is repeated by the sequence, juxtaposion of $\underline{a} \Rightarrow$ cross \Rightarrow juxtaposion of $\underline{b} \Rightarrow$ cross $\Rightarrow \dots$. When we complete the observation, constructed expression (Appendix) is connected with \underline{a} by the equational symbol. Because an observation here is represented by

expression, it does not include time. We cannot generate time except for reentrant form (the form). However, doubt for the stance or the motivation of an observer appear at the moment of the construction of the form. Therefore observations should be written as the form, and they include time. Now we have to take the equational symbol into the observational circle, in the sequence -juxtaposition of \underline{b} -cross = the construction of the form connecting " \underline{a} " = ...

Now we have to deal with the equational symbol as the functional symbol in language. It is elegant to adopt the convention of indicating the point at which a form reenters by an extension of a cross that contains the whole expression: for example, the system $\underline{a}=\underline{a}\underline{b}$ with $\underline{b}=\underline{b}$ is written as,

$$\underline{a}=\underline{\underline{b}} \quad \text{and} \quad \underline{b}=\underline{\underline{\quad}} \quad (11)$$

then,

$$\underline{a}=\underline{\underline{\underline{\quad}}}. \quad (12)$$

It is noted that extended cross itself represents the form. In equation (12) inner extended cross represents the form involving \underline{b} . Therefore, the circulation of observational circle twice is expressed as (when $\underline{b}=\underline{\underline{\quad}}$),

$$\underline{a}=\underline{\underline{\underline{\underline{\quad}}}}. \quad (13)$$

Any forms expressed by extended cross equal to relational equations, whose number of variable is decided by the number of a reentering cross. Now as the observation proceeds, the observational form continues to be modified. The observation is expressed as the reentrant form reentering itself. This type of observation is illustrated as the form (14). $\underline{a}\nabla$ represents nested reentrant form, and \underline{n} in $\underline{a}\nabla(\underline{N})$ represents the number of nests (i.e. the number of observation, if $\underline{N}=\underline{t}$, the observation proceeds with the object

phenomenon of the microtubules. (1) There are two phases, growing and shrinking. (2) The velocity of growing or the accretion of tubule-unit at ends is much less slower than that of shrinking, and it is constant. (3) The time-sequence of the phase transition looks like random or chaotic. Plotting the length of a microtubule in time-length plane, we find irregular saw-like patterns.

We now adopt the self-referential form as rule, and construct both space and time by the rule owing to the property of modulator. At the same time self-exciting oscillator is constituted by the same rule due to the property of oscillator. We naturally illustrate the total images of constructing patterns of self-referential forms in a simple way. Remind that equation (5) represents the temporal oscillator or self-exciting oscillator and equation (6) represents modulator, multiplication and/or generation of space. We find the essence of self-referential forms in the diverse interpretations of them. To be generalized, we consider the case of modulators of the form of (2-2).

There are two states in tubulin units, namely GTP- (T) and GDP-tubulin (D) (Mitchison & Kirschner, 1984b; Carlier et al., 1984). However, the difference of this state may not be essential for the phase transition. At the ends, (T) only adds, but the tubulin-end soon hydrolyzes. Therefore, the most end of GTP-tubulin cap is either GTP or GDP in any phase (shrinking/growing). Supposing that shrinking/growing phase is dependent only on the state of end (Carlier et al.), we suspect that the state of GTP/GDP is independent of the phase transition. Let us then assume that the states of deeper interior tubulins influence the phase transition. In this case, we may think that the total length and the length of cap determine the phase. Even then we have the same problem that the temporal change of a tubulin falls into a limit cycle, or roughly monotonous increase (or decrease), because the number of sequence with binary value is finite as long as the process is a Markov process.

Hence, we have to introduce other variables and spatial and/or temporal memories. We assume that there is an other parameter with

binary values which influences the phase transition. On the phase transition we only take this parameter into account. In other words, we regard the state of a microtubule as a sequence of symbols which consists of binary values namely $_$ and $_$. This state is different from GTP/GDP. This assumption allows us to introduce the model with self-referential forms.

It is noted that whenever we interpret the self-referential forms as modulators, we can also interpret the forms as oscillators. In origin this interpretation is ambiguous, and hence, we can adopt the interpretation of some behaviour as oscillators at any sites in space which is generated by modulators. Details of the modulator-oscillator model is the following.

Model. (1) We construct any self-referential forms ($\underline{a}=\underline{h}(\underline{a})$) which does not generate local patterns. Here the eq(14) with $\underline{N}=1$ is chosen.

(2) We think that the site $\underline{k}=1$ only is interpreted as the self-exciting oscillator ($\underline{a}_1^{t+1}=\underline{h}(\underline{a}_1^t)$).

(3) This oscillator is supposed as the spot which fires pulse signals, propagating space generated by modulators. Note that \underline{a} can be expressed by several components. We choose two of them \underline{a}' and \underline{b} , and we interpret $\underline{a}=\underline{h}(\underline{a})$ as a modulator expressed by $\underline{a}'_{k^{t+1}}=\underline{f}(\underline{a}'_k^t, \underline{b}_k^t, \dots)$ and $\underline{b}_{k+1}^t=\underline{g}(\underline{a}_k^t, \underline{b}_k^t, \dots)$. A spatial pattern of waveform which consists of $_$ and $_$, as shown in Fig. 5, emerges from the modulator. The modulator is interpreted to play two roles. First, the tubulin end at $\underline{k}=\underline{n}$ grows at each time step, thus,

$$\underline{a}'_{n^{t+1}}=\underline{f}(\underline{a}'_n^t, \underline{b}_n^t, \dots). \quad (15)$$

Second, the signal fired by the oscillation at $\underline{k}=1$ propagates as a waveform with the speed of \underline{v} , thus

$$\underline{a}'_{k^{t+1}}=\underline{f}(\underline{a}'_k^t, \underline{b}_k^t, \dots) \quad (\underline{k}=\underline{p}, \dots, \underline{p}+\underline{v}), \quad \text{with } \underline{N}=2 \quad (16)$$

where \underline{p} is the propagation front of the wave. The reason of $\underline{N}=2$ is

resulted from finite time in observatin. In other positions of \underline{k} , $\underline{a}'_{k,t+1} = \underline{a}'_{k,t}$.

(4) When the signal reach the end ($\underline{k} = \underline{n}$), it works as a switch, that is,

$$\begin{aligned} & \text{tubulin starts shrinking, if } \underline{a}'_{n,t} = _ , \\ & \text{or} \\ & \text{tubulin continues to grow, if } \underline{a}'_{n,t} = _ \end{aligned} \quad (17)$$

(5) The tubulin end shrinks till it experiences $\underline{a}'_{k,t+1} = _$ for \underline{n} times. Site of $\underline{a}'_{k,t} = _$ are assumed to stabilize tubulines.

Patterns generated by this model are shown in Fig. 6. When site \underline{n} is interpreted as the tubulin end, \underline{n} represents the length of a microtubule. These patterns are similar to the patterns of temporal change of the length of a microtubule, observed by Horio & hotani (1986).

It should be noted that spatial and temporal memories are already taken into consideration in this model. Suffix \underline{t} does not indicate the specific point on time-axis, but it represents only relative discrimination in temporal direction. Consider the situation that after the length of tubulin reaches the value of $\underline{n} = \underline{s}$, the tubulin shrinks and then it grows again. While its length is less than \underline{s} , $\underline{a}'_{n,t}$, $\underline{b}_{n,t}$, ..of modulator (16) represent value of $(\underline{t}-1)$ -th step. However, when the tubulin grows longer than the length \underline{s} , $\underline{a}'_{n,t}$ may represent the value of much older \underline{a}' , when the length of tubulin was greater than \underline{s} . In this sense, the modulator holds temporal memories, dependent on the length of sequence. It goes without saying that spatial memories are taken into consideration because of the formulation of modulators.

The models of self-referential forms or modulator-oscillaor complemetary can be also regarded as holistic views of a system. They include the time/space perspective and arbitrarilly interpret it and generate time and/or space. We cannot find locality in this

formulation (interactions are not defined), but understand that locality is expressed in it. We emphasize that it is one of the serious solutions in description of biological time-space perspective, as long as we cannot describe the gap between the speed of external observer's observation and that of the propagation of biological interactions (Matsuno, 1989).

CONCLUSION

Extending the idea of reentrant forms, we propose the system including double observers in order to understand the behaviours of living systems and/or self-organization. The one observer constructs the reentrant form and interprets them (modulator/oscillator), and the other who is positively described in the form generates time and/or space according to the interpretation.

Oscillators are regarded as self-exciting oscillators and produce periodic sequences of binary value. Modulators generate space and also produce time in interpreting articulated space. Unexpectability can be generated in space/time perspective using both oscillators and modulators.

We illustrate the application of this method in the case of the instability of microtubule in vitro. However, behaviours of microtubule in a cell can be understood only with this method, fixed with the variety of interpretations on reentrant forms. The meaning of the time in observation will be more taken in the approach.

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APPENDIX

According to Spencer-Brown (1969), we give the following Brownian

language. The following symbols are given;

variable: a, b, c, \dots (Latin letters), constant symbol: \neg

functional symbol: \neg , juxtaposition (no symbol)

relational symbol: $=$

$$\text{axiom: } \overline{\overline{p \ r} \ \overline{q \ r}} = \overline{\overline{p \ q} \ r} \quad (\text{J-1})$$

$$\overline{\overline{a} \ a} = \quad (\text{J-2})$$

Let us describe the concept of a propositional formulas.

(1) Latin letters a, b, c, \dots are called elementary formulas.

(2) If A and B are formulas, then expressions involving A and B connected by juxtaposition and/or \neg are also formula.

(3) The constants and \neg are formulas.

(4) If A is a formula, one can substitute any formula B and write $A=B$ if;

(i) this expression is a formula or an axiom of Brownian algebra (J-1) and (J-2),

(ii) there is a finite chain of such substitutions transferring A into B , and each substitute formula agrees with (i). We call this finite chain a proof sequence.

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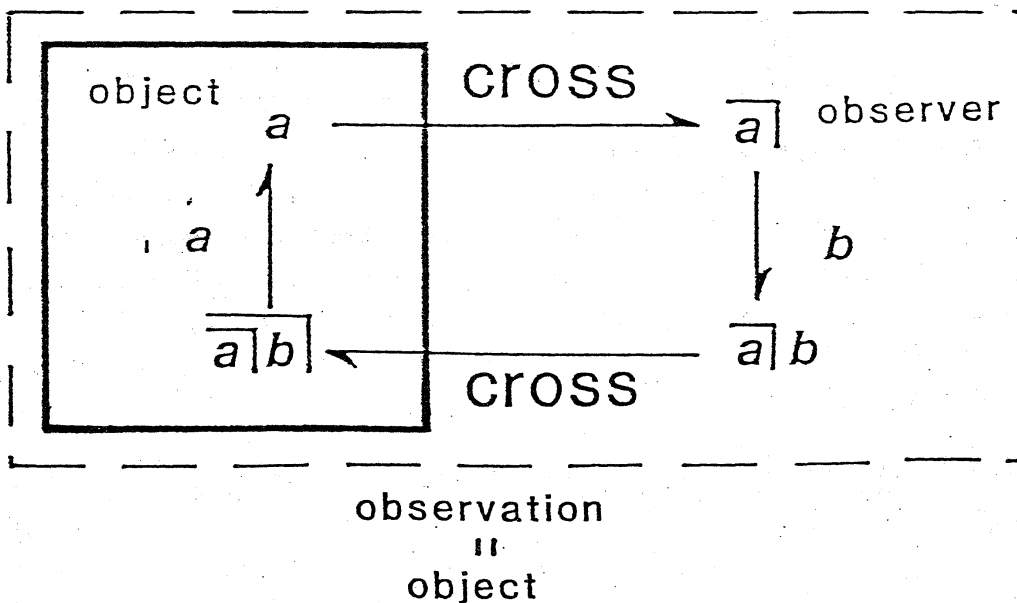


Fig. 1. The typical relationship between an observer (b) and an object (a). Symbols are here meaningless and a broad line (cross, \neg) represents explicit distinction between \underline{a} and \underline{b} . The formula (1) is constructed following the direction of arrow. An observation is written as the expression (Appendix), and "observation=object" is regarded as the form. Starting from non-mark in object side, \underline{a} appears by the juxtaposition of \underline{a} . Secondly, \underline{a} crosses the cross then $\underline{a|}$ is obtained. In observer side, $\underline{a|}$ is accompanied with \underline{b} by the juxtaposition of \underline{b} . After that, $\underline{a|b}$ crosses the cross again and enters the object side. The observation circle (this diagram) is completed in this scheme. It represents "an observer sees an object in which an observer an object in which ...".

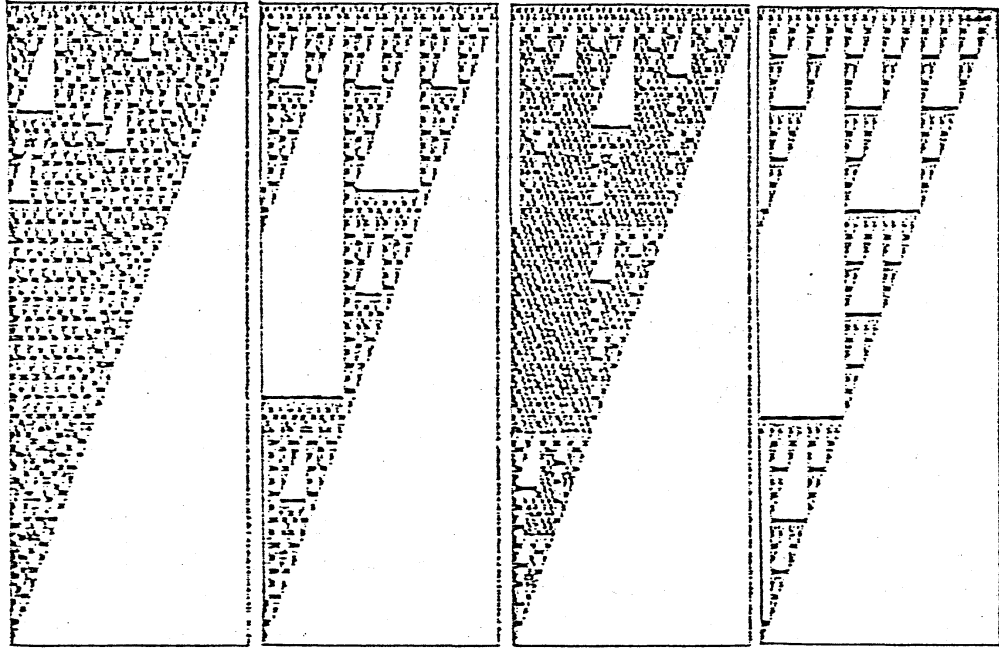


Fig. 2. Patterns generated by the form (7) which is substituted in the form (5). Dot represents \uparrow , and space represents \downarrow . Vertical axis or horizontal one represents time and space respectively. Initial and/or boundary condition is not in principle defined, however we can also say that initial one is that all sites are \uparrow , and periodic boundary. It shows time-reversal pattern of Sierpinsky Gasket.

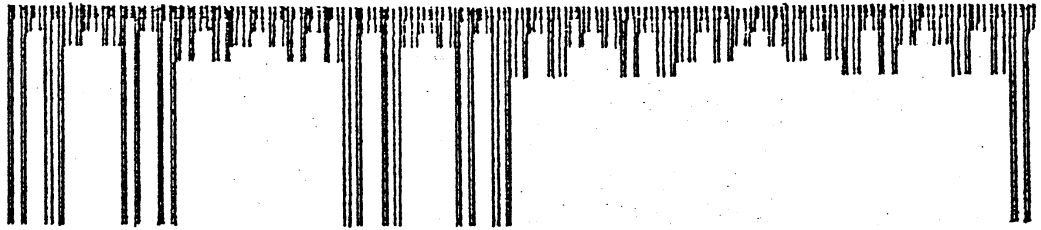


Fig. 3. Patterns generated by fractal-like modulator (10). Using an adequate normalization, we can obtain Cantor set where $t \rightarrow x$. Dot represents \uparrow , and space represents \downarrow . Vertical axis or horizontal one represents time and space, respectively.

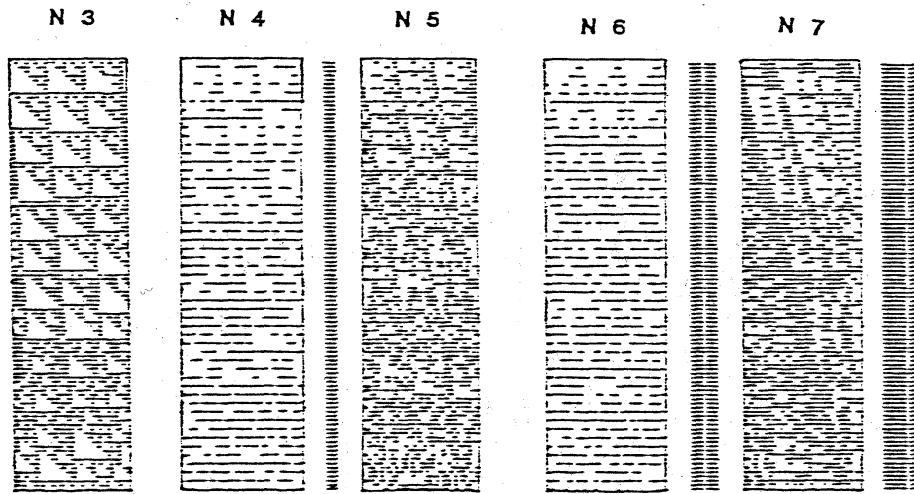


Fig. 4. Patterns generated by reentrant form (14) including the time taken in observation. The value of N represents the number of nested reentrant forms in the form (14). Dot represents γ , and space represents \cdot . Vertical axis or horizontal one represents time and space respectively.

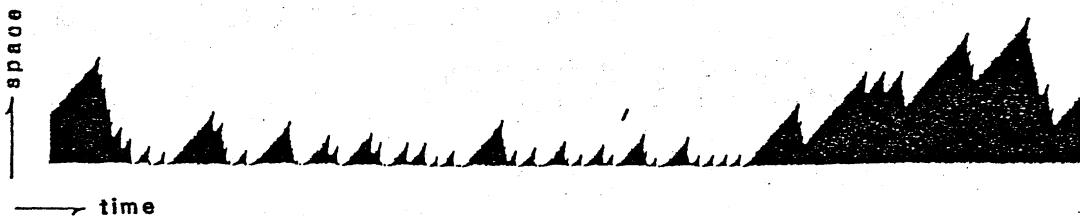


Fig. 6. Patterns generated by the model for instability of microtubule. Parameters are set $\gamma=5$ and $N=3$. Dot represents γ , and space represents \cdot . Vertical axis and horizontal one corresponds to external observer's time and the length of microtubule, respectively. See text for further discussions.

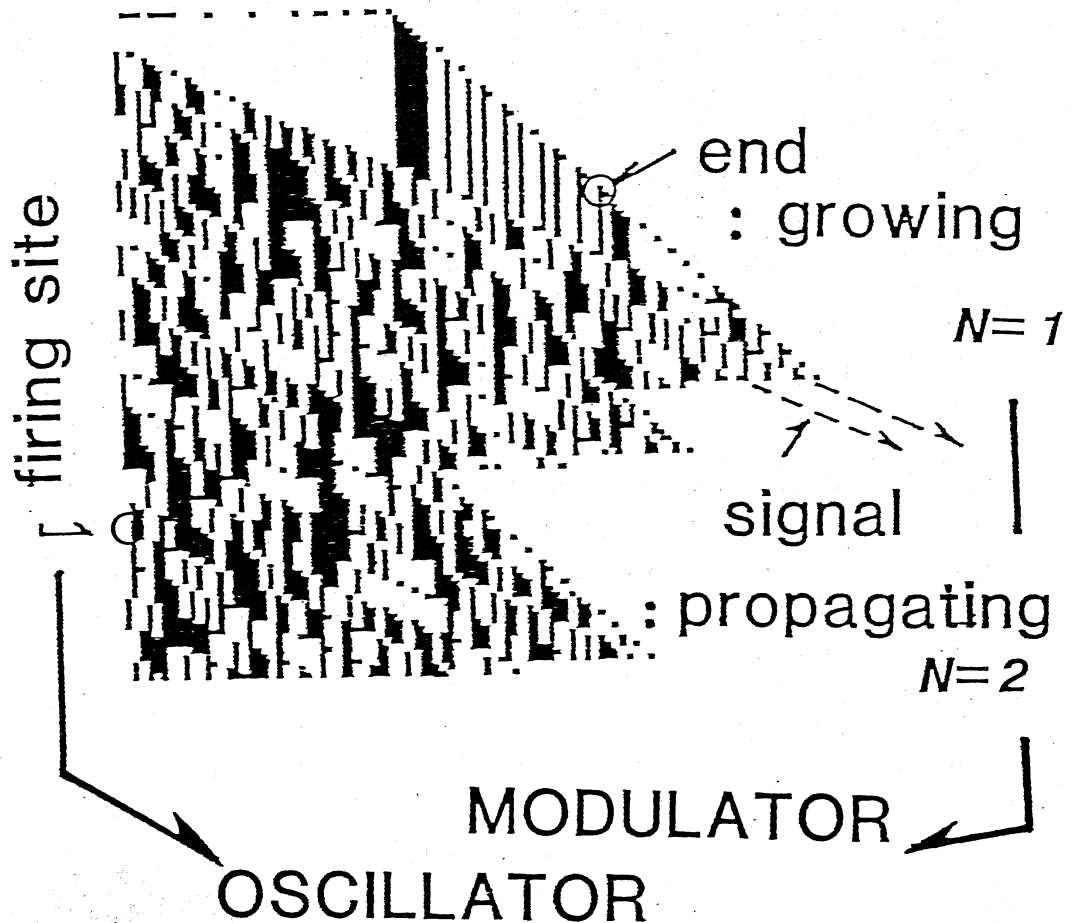


Fig. 5. Schematic diagram of the model for the instability of microtubule. It is based on modulator-oscillator complementarity. Modulators are used for both the growth at the end and the propagation of signals which are fired by an self-exciting oscillator at the origin. The value of N represents the number of nested reentrant forms in the form (14).