Pattern formation in a chain of logical elements

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Abstract

Mechanisms of pattern formation have been studied in great details using continuous models, such as FitzHugh-Nagumo system [1]. However, many features of patterns observed in developmental biology suggest that they arise due to interactions of non-continuous nature between biological cells [2]. Here we present a model represented by a chain of logical elements and develop a formalism to consider pattern formation in this model. Different sets of operations reflecting interactions between logical elements can lead to formation of stationary, propagating and oscillating patterns similar to those observed in continuous dynamical systems.

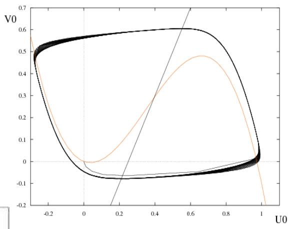
Patterns in continuous systems

Nonlinear systems can exhibit phenomena which are hard to anticipate on the bases of common sense. One of the simplest models to describe such phenomena is represented by FitzHugh-Nagumo equations. By varying model parameters one can get various solutions representing stationary and oscillating patterns as well as propagating waves.

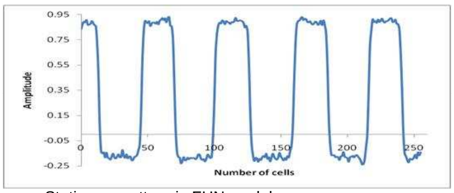
$$\frac{\partial u}{\partial t} = \Delta u + f(u,v),$$

$$\frac{\partial v}{\partial t} = D_v \Delta v + \varepsilon g(u,v)$$

Modified FitzHugh-Nagumo system [1].
f (u, v) and *g (u, v)* for reaction kinetics.
Δu and $D\ \Delta v$ for diffusion.



Phase diagram for FitzHugh-Nagumo equations. Nullclines are represented by the straight and the cubic lines. The intersection of the nullclines is an equilibrium point. In the presented case the equilibrium point is unstable (the dynamic is oscillatory).



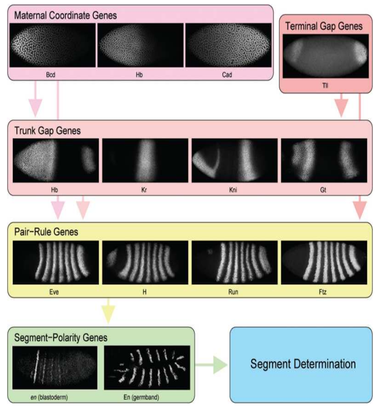
Stationary pattern in FHN model
(concentration profile of variable *u* is shown)

Segmentation pattern in the fly embryo

The body of a fly embryo is made up of a repeated structure called segments which are arranged along the head to tail axis. These segments form at early stages of embryogenesis and associated with mechanisms of identifying the position and identity of differentiating cells [3].

The patterning takes place in four levels:

1. Nonuniform distribution of maternity genes (bicoid, caudal). These control the spatial patterns of transcription of the gap genes (i.e. hunchback. Krüppel, knirps, etc.).
2. Spatial patterns of transcription of the gap genes (Hb, Kr, etc). The gap genes regulate each other and the next set of genes in the hierarchy, the pair-rule genes (even-skipped, hairy, etc.).
3. Pair-rule genes- form seven stripes of transcription around each embryo. Pair-rule genes determines the initial expression of segment polarity genes.
4. Segment polarity genes- form fourteen stripes of transcription around each embryo. First expressed at cellular blastoderm.



Chain of interacting logical elements (two-state model)

To investigate patterning due to cell-to-cell contact interactions we have developed a discrete model

- We consider number (say 64) of cells.
- Each cell can be in two states (defined by 0, as black, and 1, as white).
- Cells form a chain (one dimensional system).
- Cells interact with (two) closest neighbours.
- Depending on the states of neighbours and its own state the cell can change its state.
- Therefore set of 8 rules describe the dynamics of the system.
- There are 256 possible sets of rules.
- We analyse these sets of rules in order to distinguish those which result into nontrivial patterns.
- Nontrivial patterns include stationary, oscillating and propagating patterns.
- To be on safe side with the observed patterns we add a noise (say 1 %).

Example of stationary pattern forming in the chain

Illustration of the two-state Model

Time step *n*:	S_{i-1}^{n}	S_{i}^{n}	S_{i+1}^{n}
Time step *n+1*:	S_{i-1}^{n+1}	S_{i}^{n+1}	S_{i+1}^{n+1}

The Transition is given by a set of 8 rules:

Rule 0 (000)→(0$S_0$0)
Rule 1 (001)→(0$S_1$1)
Rule 2 (010)→(0$S_2$0)
Rule 3 (011)→(0$S_3$1)
Rule 4 (100)→(1$S_4$0)
Rule 5 (101)→(1$S_5$1)
Rule 6 (110)→(1$S_6$0)
Rule 7 (111)→(1$S_7$1)

Therefore each transition set can be described by a binary number $S_7S_6S_5S_4S_3S_2S_1S_0$ which varies from 0 to 255 (2^8).

Results for stationary and oscillating patterns

The transition given by the binary number **11001100** does not change the state of any cell and therefore we will call it identity transition and denote as T_e=204 (shown in the first column).

T_e=204	$(T_e)^{-1}$=51	T_s=77	$(T_s)^{-1}$=178
(000)→(000)	(000)→(010)	(000)→(010)	(000)→(000)
(001)→(001)	(001)→(011)	(001)→(001)	(001)→(011)
(010)→(010)	(010)→(000)	(010)→(010)	(010)→(000)
(011)→(011)	(011)→(001)	(011)→(011)	(011)→(001)
(100)→(100)	(100)→(110)	(100)→(100)	(100)→(110)
(101)→(101)	(101)→(111)	(101)→(101)	(101)→(111)
(110)→(110)	(110)→(100)	(110)→(110)	(110)→(100)
(111)→(111)	(111)→(101)	(111)→(101)	(111)→(111)

T_e results into formation of non-regular stationary pattern. The inverse of T_e ($(T_e)^{-1}$=51) makes the oscillating pattern (with no special periodicity). By changing the two endpoints, we obtain T_s =77=**01001101**—this set of rules results into formation of spatially regular stationary pattern (the special period is given by two cells). The inverse of T_s ($(T_s)^{-1}$=178) makes the oscillating pattern (with regular periodicity).

Other set of rules resulting in nontrivial patterns

The transition 15 (=**00001111**) results into fragmentation of triples (triple zero and triple one get an opposing symbol in the middle) and also when the states of two neighbours differ from each other the transition accepts the state of the right neighbour. As a result there appear waves moving to the left and causing a formation of a stationary pattern, which grow on the left side of the medium. Transition 85 is similar to the transition 15 except that it accepts the state of the left neighbour and therefore the waves propagate to the right. There are also other transitions resulting into combinations of stationary patterns with propagating waves. Two transitions 175 and 80 give left and right propagating waves respectively. There are many other transitions (84, 112, etc) resulting into formation of stationary patterns.

T_{srw}=15	T_{slw}=85	T_{lrpw}=175	T_{rlpw}=80
(000)→(010)	(000)→(010)	(000)→(010)	(000)→(000)
(001)→(011)	(001)→(001)	(001)→(001)	(001)→(001)
(010)→(010)	(010)→(010)	(010)→(010)	(010)→(000)
(011)→(011)	(011)→(001)	(011)→(011)	(011)→(001)
(100)→(100)	(100)→(110)	(100)→(110)	(100)→(110)
(101)→(101)	(101)→(101)	(101)→(101)	(101)→(101)
(110)→(100)	(110)→(110)	(110)→(100)	(110)→(110)
(111)→(101)	(111)→(101)	(111)→(111)	(111)→(101)

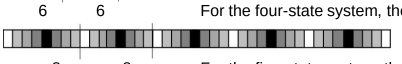
Model with three and more states per cell

The transition for logical element having three states are given by 27 rules: as each cell in the triple will have three possible states (3^3). The transition when logical elements have *n*-states thus would include n^3 rules. The analysis of two-state systems permits to make reasonable assumptions on "interesting" sets of rules for *n*-state systems and therefore to avoid consideration and simulation of all possible transition sets (total number of which is 3^3 for 3-state systems and 4^{64} for 4-state systems).
The regular stationary patterns in two-state system has special periodicity 2 (1 white + 1 black).

3 3 For the three-state system, the periodicity can be up to 3.

The 3-periodic stationary patterns can form under a number of transitions, for example:
T=111111111000000000222222222.

6 6 For the four-state system, the periodicity can be up to 6.

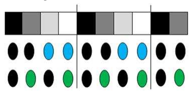


8 8 For the five-state system, the periodicity can be up to 8.

Biological implementation of the model

Here we presented our results in patterning due to local interactions of logical elements. Such interactions can represent contact (membrane-to-membrane) interactions between cells in biological tissues resulting into differentiation of cells. For example two-state model can represent chain of locally interacting cells, where cells in state "1" express some particular gene while in state "0" don't. Therefore the modelled interactions can be seen as regulating the differentiation of cells. The periodic stationary pattern forming in a two-state model represents a chain of cells where each second cell expresses the gene. These patterns can form under various interactions (transitions) from wide range of initial conditions. Three-state model doesn't have direct biological implementation, while the four-state model can be viewed as modelling cells whose differentiation is associated with expression of pair of genes. Four-periodic pattern (i.e. 0,1,2,3,0,1,2,3... or alternating **black, dark grey, light grey and white) can correspond to the following alternation of gene expression:**

Generation of four periodic pattern:
Gene 1 pattern
Gene 2 pattern



Formation of periodic stationary patterns in four-state model extremely sensitive to the initial conditions, i.e. these patterns form only when very special initial conditions met. This may explain the multi- (four-) level of segmentation in the fly embryo. Our model can account for interactions between segment polarity genes with specific initial conditions set by above three levels of patterning.

References:

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4. Vasiev, B. N., *Classification of patterns in excitable systems*, Elsevier, 2004.