Available online at www.sciencedirect.com
ScienceDirect
BioSystems 88 (2007) 191–201
BioSystems
www.elsevier.com/locate/biosystems

# Spontaneous activity of living cells

Fumio Oosawa*
*Aichi Institute of Technology, 2-17-1 Haruoka, Chigusa-ku, Nagoya 464-0848, Japan*
Received 22 May 2006; accepted 22 May 2006

**Abstract**

The purpose of this article is to give a theoretical framework to describe the mechanism of internal signal generation and discuss the physiological significance of spontaneous activities of certain living cells [Oosawa, F., 2001. Spontaneous signal generation in living cells. Bull. Math. Biol. 63, 643].


*Keywords:* Spontaneous activity; Paramecium; Potential fluctuation; Circular current; Sensory response; Memory; Population

## 1. Introduction

In living cells, there are three types of responses to the external stimulus or the environmental change, as illustrated in Fig. 1. One is the reflective response: to a specific stimulus, the cell always immediately shows a definite response. The stimulus and the response have a deterministic one-to-one correspondence. The input and the output are tightly coupled. The second case is the autonomic response. The same stimulus does not always produce the same response. The stimulus and the response do not have a deterministic relation. The response to a given stimulus changes depending on the state of the cell. The coupling between input and output is loose. In the third case, even without any specific stimulus from the environment, the cell shows spontaneously some behaviors. The cell responds to a signal generated in itself. In the second and third case, the behavior of the cell is not directly determined by the external stimulus.

* Tel.: +81 52 7516208.
*E-mail address:* foosawa@aitech.ac.jp.

## 2. Behaviors of single-cell organisms

The following story is based on the swimming behaviors of single-cell organisms such as paramecium (Nakaoka and Oosawa, 1977). Paramecium cells swim in water by beating a number of short cilia on the cell surface. The cell swims straight and occasionally changes the swimming direction in the absence of any external stimuli. The directional change is caused by transient reversal of the beating direction of cilia in a limited area of the cell surface. If all cilia were reversed, the cell swims backwards.

In the ordinary condition, the swimming speed of a paramecium cell is about 2–3 mm/s, which is 10 times larger than the cell length. The frequency of the direction change is about 0.1–0.2 $s^{-1}$; the time interval of successive directional changes is about 5–10 s on the average. The angle of the directional change has a uniform distribution and the time interval has approximately an exponential distribution. Therefore, it is likely that a stochastic process in the cell is involved in the process to induce the spontaneous change of swimming direction. A paramecium cell living in pond water has an inside-negative electric potential of about 20–30 mV (Majima, 1980). It was attempted to follow the electric potential in

0303-2647/$ – see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.biosystems.2006.05.006

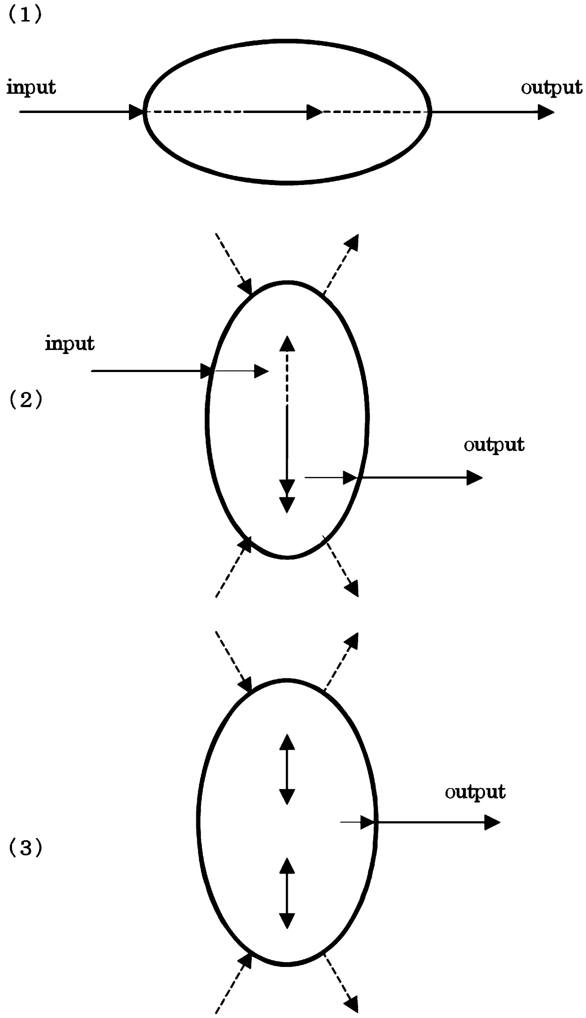


Fig. 1. Three types of the input–output or stimulus–response relations in living cells: (1) reflective, (2) autonomous, and (3) spontaneous.

the cell by inserting a microelectrode into the cell fixed on a glass plate. As shown in Fig. 2, even when the cell is kept in a constant environmental condition without any stimulus, the potential is not kept constant, but shows random fluctuation of average amplitudes of the order of a few mV. In addition, sharp spike-like fluctuations of the height of about 5–10 mV are sometimes observed. The potential fluctuation consists of two components; the basic fluctuation and the spike-like fluctuation. The cell fixed on the plate continues beating cilia and partial reversal of the beating direction, if it happened, is observable by the reversed flow of water around those cilia. The partial reversal is found to be associated with the spike-like potential change. The spike is regarded as the signal for the spontaneous change of the swimming direction.

## 3. The mechanism of generation of the electric potential fluctuation in the cell

In the living cell, the concentration of various kinds of salt ions is different between inside and outside of the cell. In most cases, the concentration of sodium ions is much higher outside than inside, whereas the concentration of potassium ions is higher inside than outside. In the whole volume of the cell, the electric neutrality is held. The concentration differences of each ion are produced by ion pumps composed of protein molecules and buried in the cell membrane. The pump is usually driven by the free energy released by the hydrolysis of ATP.

In addition, various kinds of ion channels also composed of protein molecules are distributed in the membrane. Each channel has a specific structure to make usually only one kind of ions permeable. For example, potassium ions can pass through only potassium ion channels.

Let us consider a channel for potassium ions in the membrane. Some potassium ions move through the channel, on the average from inside to outside according to the concentration gradient. Inside the cell, negative ions remain in excess, so that an inside-negative electric potential is produced. The flow of potassium ions is stopped when the mechanical force due to the electric field and the entropy change due to the concentration gradient are balanced. The potential inside is given by the equation:

$$V(\mathrm{K}) = \left(\frac{kT}{e}\right) \log\left(\frac{[\mathrm{K}]_\mathrm{o}}{[\mathrm{K}]_\mathrm{i}}\right)$$

where $k$ is the Boltzmann constant, $T$ the absolute temperature, $e$ the electronic charge; $[\mathrm{K}]_\mathrm{o}$ and $[\mathrm{K}]_\mathrm{i}$ are concentrations of potassium ions, outside and inside, respectively. The potential difference does not change when the number of potassium ion channels increases. The ion channel usually has a gating structure, which assumes two states, the open state and the closed state. In the above case, the open–close transition of one of the channels does not change the potential $V(\mathrm{K})$.

When there are only sodium ion channels in the membrane, the potential inside is given by the equation:

$$V(\mathrm{Na}) = \left(\frac{kT}{e}\right) \log\left(\frac{[\mathrm{Na}]_\mathrm{o}}{[\mathrm{Na}]_\mathrm{i}}\right)$$

which gives a positive value; $[\mathrm{Na}]_\mathrm{o}$ and $[\mathrm{Na}]_\mathrm{i}$ are concentrations of sodium ions outside and inside. This potential is also independent of the number of sodium channels in the open state.

If there are two kinds of channels, for potassium ions and sodium ions, respectively, then in the stationary state