M-sequence family from cultured neural circuits

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We have already shown its feasibility by computer simulations that show a loop circuit can be copied to another area by back-propagation leaning algorithm; this is a key function of brain intelligence, which includes functions such as memory, association, reasoning, and abstraction. We also have found M-sequences in spike trains of cultured neuronal networks. In this paper, we report that we found family or fragment of M-sequence responses also in the instantaneous firing rates (PSTH's) from cultured neural networks of published data and our own data, which suggest the existence of loop circuits with a feedback link composed of 3 to 5 neuron cells or equivalent circuits.

Index Terms— biological neural networks, communication in brain, M-sequence, neural spike train

1. INTRODUCTION

Fig. 1 shows a time-shift diagram of 10.2 Hz MEG data that we obtained [1, 2], which represents a snap shot of communication occurring in the human brain. We note that each part of the brain can communicate with another part similar to that seen in a human society that utilizes multi-access communication tools. A typical multi-access communication tool is a CDMA mobile phone, where Gold sequence is used as a pseudo-random sequence to discriminate the target station in asynchronous communication mode [3-5]. The most representative and effective pseudo-random sequence in synchronous mode under common clock signal is the M-sequence, that is used, for example, to measure the distance in GPS.

In circuit theory it is well known that loop circuit with a feedback link generates a pseudo-random sequence including an M-sequence with maximum period length. On the other hand, it remains unclear how memory is stored in neural circuits of the human brain. We propose that M-sequence composes temporal independent basis functions in brain neural network for communication and memory storage.

A. Spatial independent component coding

It has been shown that directional receptive fields as seen in mammal simple-cells emerge by minimum information criterion [6] and independent component analysis (ICA) [7] for natural and facial images. That is, spatially independent basis functions are derived by self-organization. In the receptive fields of visual system, independent components are obtained by self-organization in the neural circuit with well known mutual inhibition [8]. We therefore expect to find the existence of temporal independent basis functions, which cooperatively work with the spatial independent basis functions.

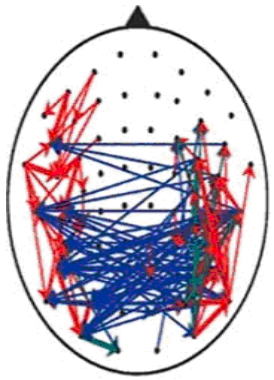

Fig.1. Time-shift diagram of 10.2Hz MEG, for a number counting task. Red: lag time < 5ms within each hemisphere, Blue: >10ms across the callosum. Green: 5-10 ms.

B. Loop circuit and temporal independent basis function

It has long been proposed that memory is realized by loops of the neural circuit in the cerebral cortex. For example, Lecerf [9] proposed a double loop and a chain to filter and process signals in the central nervous system (CNS), and Choe [10] analyzed and proposed a functionality of thalamo-cortical loop; however, no one could develop a reasonable and feasible circuit representation for memory and association in an algorithmically describable form with this self-organization function.

It is well known in circuit theory that a loop circuit with a feedback link generates a pseudo-random sequence such as the

M-sequence with maximum period length. We propose that M-sequences compose temporal independent basis functions in brain's neural networks for communication and memory storage [8]. We have already shown its feasibility through computer simulations in which a loop circuit can be copied to another area by a leaning algorithm; this is a key function of brain intelligence which includes functions such as memory, association, reasoning, and abstraction [11].

We have already found M-sequences in spike trains from cultured neuronal tissues [12]. In addition to this in this paper, we show M-sequence responses including its family and fragments are also detected in PSTH (poststimulus time histogram, or equivalently IFR; instantaneous firing rate) of published data and our own collected data.

II. LOOP CIRCUIT

Considering that a neuron has at least hundreds of synapses and that neural circuits have temporal storage functions of the order of 100 ms, we assumed that human memory includes many loop circuits. Given this, we showed through computer simulation that such neural circuits can be copied to another area by applying back-propagation algorithm [11]. An electrical loop circuit with a feedback link (i.e., a Linear Feedback Shift Register; LFSR) can generate a pseudo-random sequence, in particular an M-sequence such as the one shown in Fig.2 using exclusive OR logical elements.

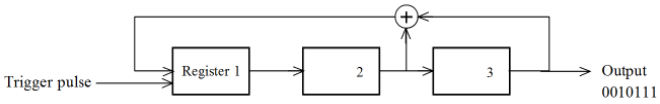

Fig. 2. Electrical Linear-feedback-shift-register with 3 logical elements (registers) outputting M sequence of length 7.

A binary counter with n-bit logical elements (registers) can count up to 2^n-1. With an adequate feedback link, the loop circuit becomes equivalent to a binary counter, whose output becomes an M-sequence with length 2^n-1 called the period, where the "M" stands for maximum length. If we use this resulting M-sequence as an intrinsic code of its own loop, we can discriminate 2^n-1 loops under synchronous mode. List of M-sequences for n=3-5 is shown in Table 1.

The existence of exclusive OR neuron cell has already been reported [13]. Equivalently, however, it can also be generated by four threshold element circuit with connection matrix

$$C=\begin{pmatrix} 0 & -1 & 0 & 1 \\ 1 & 0 & 1 & -1 \\ 1 & 1 & -1 & 0 \\ 1 & 1 & -1 & 1 \end{pmatrix},$$

where each element outputs "1" when sum of inputs is 1 or more and 0 otherwise.

Table 1. List of reversal M-sequences. Rotationally shifted and inverse ordered are also in this family.

No. of elements n	Reversal M-sequence
3	1101000
4	011101100101000
5	010100010011100000110010110111 010010101110001000011011001111 001010110111010000100110001111

III. M-SEQUENCE IN PUBLISHED BALJON'S DATA

We found M-sequence-like response IFR from cultured neural network in a literature [14], where M-sequence of length 7 generated from a 3-element LFSR, although "0" and "1" are reversed from the conventional representation.

IV. IFR OF OUR DATA

We used IFR data of hippocampal neurons isolated from a Wister rat (embryonic day 18) and cultured for 37 days (first data) and 22 days (second data) on a multi-electrode arrays dish as described in our previous work [12,15].

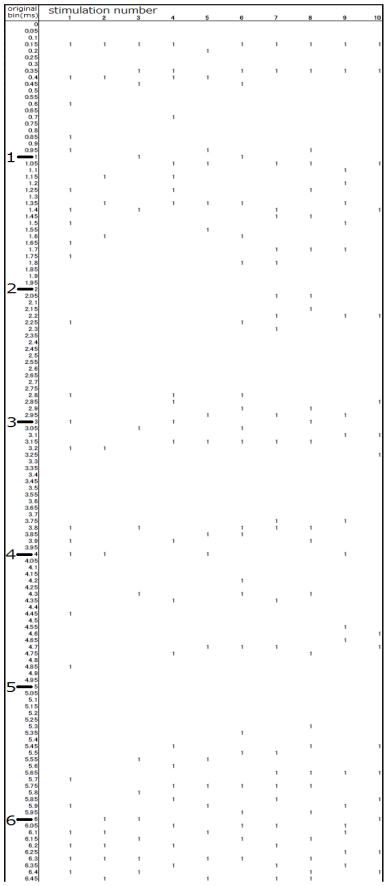

Fig.3. A part of spikes detected at each original bin of 0.05 ms for 10 trials of our first data. Horizontal axis is trial number (stimulation number), and vertical axis is original bin (ms).

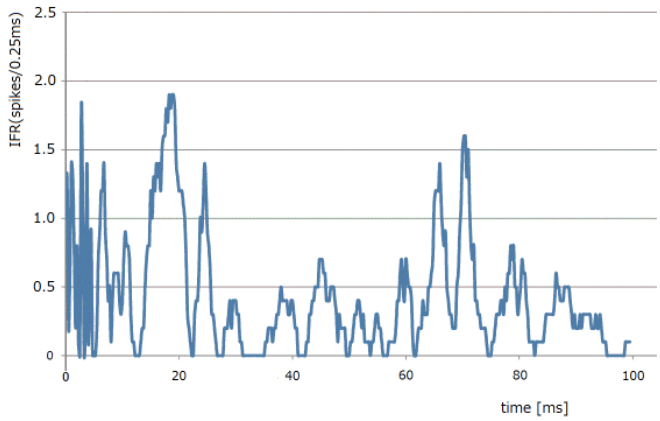

Fig. 4. IFR of our first data up to 100 ms..

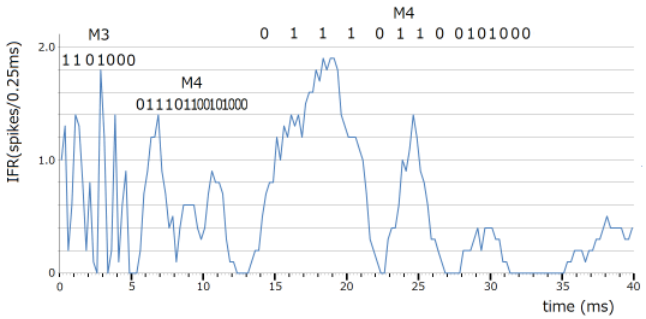

Fig.5. Detected M-sequences in the IFR of our first data. Top sequences M3 and M4 represent the expected response as reversed M sequence of 3 and 4 elements, respectively. In case of M3, it is interpreted as "0's" correspond valley of the curve.

The experimental procedures were performed in accordance with the accepted guidelines for animal care and used as specified by the National Institute of Advanced Industrial Science and Technology. We recorded 10 and 25 response sequences in the first and the second experiment, respectively, for 100 ms excepting the initial 0.3 ms under single stimulation by bipolar pulse (width:100 μ s$\times$2, current: $\pm$10 μ A) with original bin of 0.05 ms using spike-detecting threshold of 5-times of background noise level as shown in Fig. 3 for our first data. Stimulating and recording electrodes are separated by 300 μ m and 335 μ m in the first and the second experiment, respectively. After combining 5 original bins into new bin, we obtained IFR's as shown in Fig. 4.

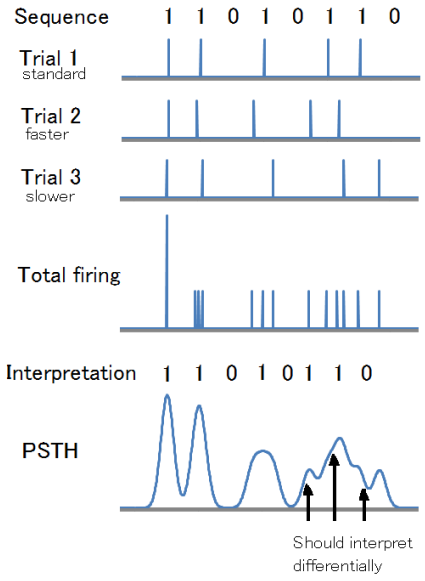

Fig.6 Interpretation of PSTH. Since the spike position varies trial to trial, PHTS should be interpreted differentially in the time elapsed area.

A. Interpretation of our first IFR data

For the interval 0-5 ms of our first IFR (equivalent to PSTH (post-stimulus time histogram)), although the spike intervals are shorter of the order of 0.5 ms, we observe almost the same response of M3 (i.e., reversal M-sequence of a 3-element loop) as observed in Baljon's data, as shown in Fig. 5. Please note

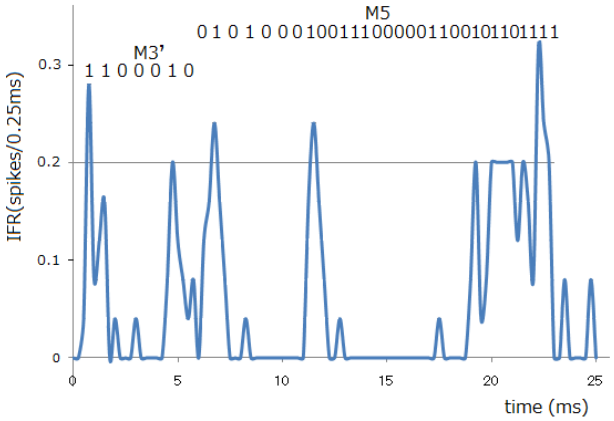

Fig.7. M-sequences in our second data.

that tail "000" corresponds to the valley of the curve. For the interval 5-13 ms we observe an M4 sequence. We also observe the second M4 in the interval 13-33 ms, which is longer than the first M4, which may reflect the structure including hierarchy of the network to be investigated in future. In each sequence, there is also a tendency that the latter part becomes faster (i.e., shortened in time). For the interval 35-59ms, there seems exist sequence of M5 (0101000100111000001100101101111) with interpreting incremental and decremental change as "1" and "0", respectively, since sequence timings are diverged because they lapsed long time. The above sequence M5 is one generated from LFSR with only one feedback link among three shapes as shown in Table 1 where two others are with three feedback links. It is impossible, however, to show it clearly from our first data of 10 spike trains. Fig.6 shows a computer simulation when there are speed differences in trials. PSTH is obtained from total firing with Gaussian weight. We can see that we should interpret PSTH differentially, but it is apt to interpret shorter in the tail.

It is noted that the sequence is well arbitrated so that just after ending one M-sequence, the next M-sequence appears, and they do not overlap. It seems that their traffic is controlled like Ethernet connected via hub-neuron [16] (I/O specialized neuron).

B. Interpretation of our second IFR data

In our second data, we observe M3' for the interval 0-6ms as shown in Fig. 7. Though the sequence is different from Baljon's and our first data, it is equivalent to these with inverse order and half phase shifted, which is generated from circuit of Fig. 2 with feedback from the 1st register instead of the 2nd register. We observe M5, the same sequence as estimated in our first data, directly after M3'.

C. Automatic detection of fragmental M-sequences from PSTH in our data

Above data are by manual inspection and lack objectivity. To confirm the presence of M-sequences, its family, or fragments, we performed their automatic detection from PSTH patterns.

Fig.8 shows an example of PSTH patterns displayed on 8×8 electrode array. The bin is set 0.1 ms, and frequency of spikes falling into each bin for 9-48 trials is counted and filtered with Gaussian weight of $\sigma = 2$. Then, top ten (or less) peaks with high PSTH value among 1.3 times protruding from background are picked up to make peak train for each electrode. Several interval-shuffled peak sequences are also generated simultaneously for comparison. Then, the peak sequence is decoded/ interpreted into one (or more when overlapped decoding) of 120 kinds of "1" "0" sequence (code sequence) with more than 3 "1" and length is less than 8. However, in this paper since "0" is not simple to detect, we compared mainly for three kinds of sequence of Sq1=111, Sq2=1011, and Sq3=1101. We took data for 5 cultured tissue samples.

Automatic detection of code from peak sequence

First we took two peaks in the peak sequence of PSTH. Then, we checked between them do the peaks exist according to the code sequence arrangement with time error allowance (margin) of 0.01-0.3.

Fig.8 shows an PSTH's calculated from 9 trials of sample No.2 and arranged according to the 8×8 electrode array, each of whose horizontal full time range is 19ms from the stimulation and vertical axis full range is 0.25 [spikes/0.1ms]. Over range parts are shown cut. Many sequences "1101" are detected for 1% time margin as shown by red ellipses. In practice, there are no time errors in the present time bin setting. Though totally 37 sequences are detected, there was two misdetection of peaks, and so only 35 ellipses are shown in Fig.8. Some of them show possibility of tailing "000" for perfect reversal M-sequence "1101000", which is shown by prolonged ellipse to the right hand. Fig.9 shows number of fragmental reversal M-sequence "1101" detected in PSTH in Fig.8 from 64 electrodes for 20ms after electrical stimulation compared with 6 shuffled peak sequences. We can say the sequence "1101" is significant both for margin=0.01 ($p=0.035$) and for margin=0.1 ($p=0.076$). That is, genuine sequence "1101" in PSTH generated by neural circuits is disturbed by shuffling, which is other than by chance.

From another sample, we found also the sequence "1011" which is reverse of "1101" and also a fragment of reversal M-sequence "1101000." That is, cores of reversal M-sequences are detected from the original peak sequence more than that of from the shuffled. These findings may reflect the circuit structure around the electrode.

V. DISCUSSION

Spike trains from neural network reflects the network structure. Different from the cortex, structure of cultured neural network may be more simple and may be more directly interpreted from circuit theory. Based on this viewpoint, the followings are discussed.

A. Loop circuit

Given that neural loop circuits are composed of n=3, 4, and 5 neurons, we can also assume the presence of neural loop circuits with 6 or more neuron cells. These neural loop circuits can communicate with each other as long as they are the same type of loop circuits. Note that theoretically there exists only 1, only 1, 3, 3, 9, and 8 different kinds of M- sequences for LFSR with n = 3, 4, 5, 6, 7, and 8, respectively. We expect these loop circuits may work as access point or a part of memory.

Basically loop circuit composed of n neurons (n-neural loop) has a function of unit memory with n bit and communication element with code length 2^n-1 that can discriminate 2^n-1 loops under the synchronous communication/retrieval; however, if these cells have different mode, such as bank change of computer memory where different synapse weights appear, it may have more memory capacity. Neural loops with adequate length of M-sequence may work as parallel identifiers for retrieving larger memory contents to avoid long delays.

B. Transient signaling

The above discussions are based on stationary interpretation of the circuit behavior. However, almost signals are transmitted as transient signals. Since it is important, we have already begun to analyze spike trains as the transient signals as well as its modeling.

VI. CONCLUSIONS

We found M-sequences in IFRs of neural networks as expected from the necessity of communication within the brain. We estimated the existence of loop circuits from the fundamental circuit theory. We also provided a temporal version of independent component coding in the brain. Brain waves might support synchronous communication based on the corresponding M-sequence. For both Baljon's data and our own data, we showed its ability to detect characteristics of neural circuits with the help of circuit theory.

Our future work includes investigations into:

(1) how and which one is selected among the different M-sequences from neural loops;

(2) what is the relationship between outside cell recording and IFR (i.e., what kind of information of the loop circuits is recorded);

(3) how the hierarchical structure of the loops and memory structures are organized; and

(4) whether it is possible to "write" information in-to the brain's memory, although there might exist ethical problems to be considered.

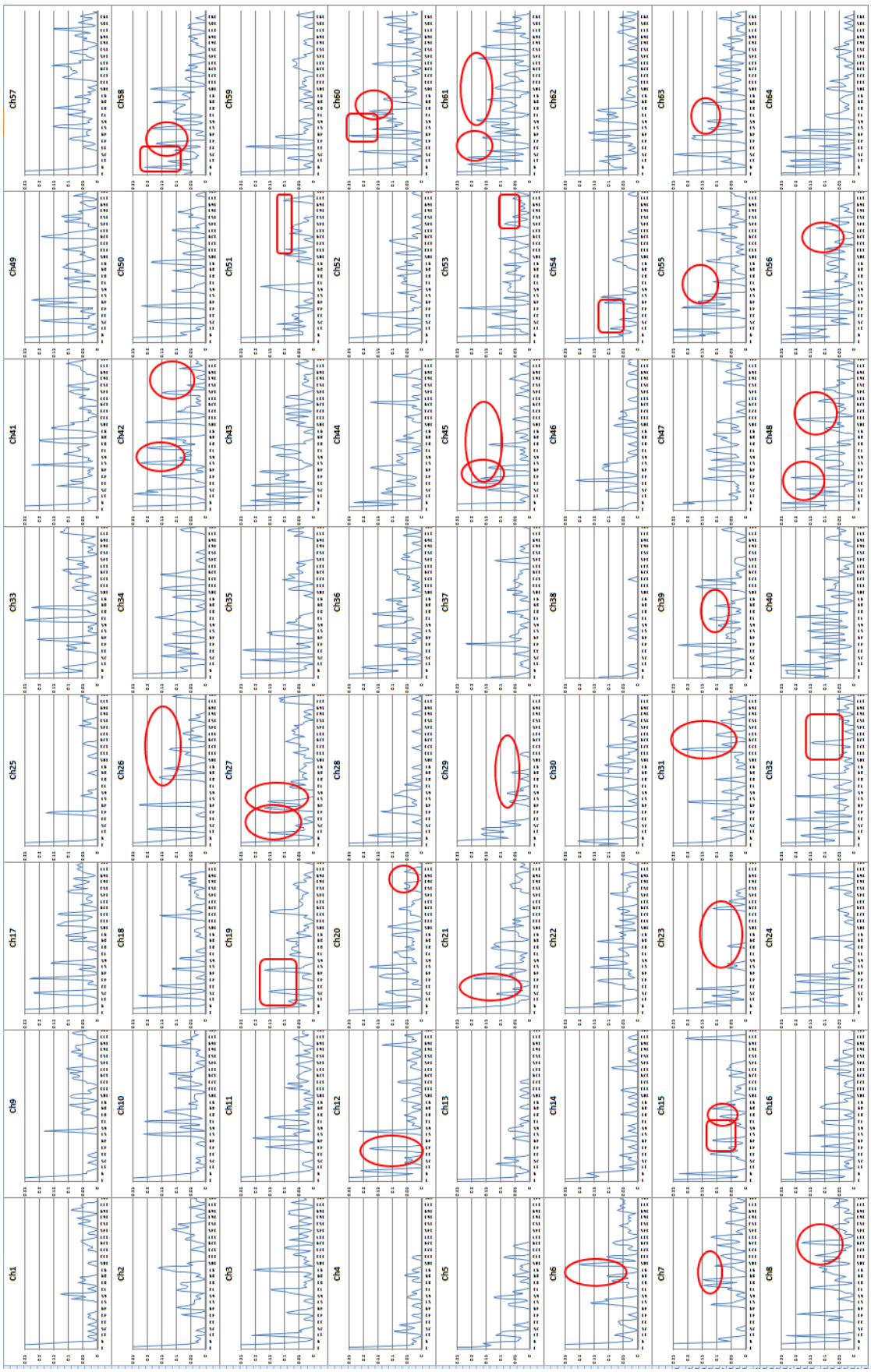

Fig.8 PSTH's of sample No.2 for 19ms after electrical stimulation arranged geometrically according to 8×8 electrode array. Vertical full range is 0.25 [spikes/0.1ms]. Stimulation electrode is No.38, near the center. Red ellipse shows automatically detected sequence "1101" with time margin of 1%. Some ellipses are prolonged to the right hand to show the possibility of "1101000".

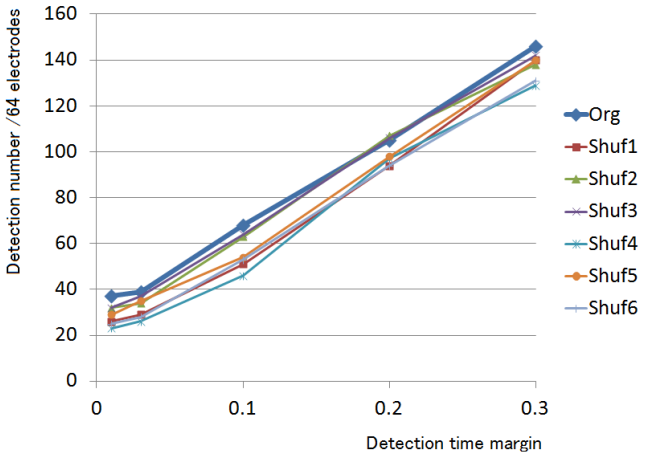

Fig.9 Number of fragmental reversal M-sequence "1101" detected in PSTH's of Fig.8 from 64 electrodes for 20ms after electrical stimulation

The present paper reports the existence of M-sequence by IFR. It matches well to our previous paper reporting directly the existence of M-sequence in spike sequence. Identifying network shape and structure within the brain is challenging; however, if successful, we will establish an important base for investigating the intelligent processing that occurs in the brain and opens a new field of "computational brain architecture.

Acknowledgement --- We thank T. Kamimura, K. Nakamura, Y. Kawaguchi, and K. Yoneda for supporting the experiments. We also thank T. Fujiwara for suggesting about the pseudo random sequence. This work was supported in part by the Grant-in-Aid for Scientific Research of Exploratory Research 21656100, and Scientific Research (A) 22246054 of Japan Society for the Promotion of Science.

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