35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

An Implantable Neural Activity Monitor with Nonlinear Gain-Controlled Amplifier

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***Abstract*—An implantable neural spike monitor with nonlinear amplifier was proposed for robust measurement against noise. In embedded electrophysiological signal processing systems, detection performance depends on signal to noise ratio (SNR), however, it is getting worth after implantation because of neoformation surrounding the electrodes and so on. We proposed a spike enhancer in this study. It has two remarkable function; automatic gain optimization with feedback loop and SNR improvement by nonlinear amplifier. In this report, the system performance was evaluated without feedback loop. A prototype circuit is prepared with small number of parts and tested on input-output characteristics. For the final evaluation, neural spike signal from somatosensory cortex of a rat was applied to the circuit. The test results show that system can expand SNR on neural spike signal from rat. It indicates that the spike enhancer can improve total performance of neural activity processing system.**

I. Introduction

Real time neural activity measurement can be applicable for neural interface system such as neural prosthetics and brain machine interfaces. A realistic implementation may be an implantable electrophysiological signal detector with wireless transmitter. It is generally composed with electrodes, amplifiers with filters, analog to digital converter (ADC), microprocessor and power supply [1]-[3]. In recent studies on processing algorithms, most of challenges aimed to achieve high detection accuracy under severe signal to noise ratio (SNR) [4]-[7]. Highly complicated algorithms can be allowed owing to remarkable progress on digital processing device. New algorithms are proposed day by day, however, a generalized system structure has been still used.

In this study, analog part ahead of digital section was focused on. Especially, SNR improvement at the amplifier stage which is indispensable to the electrophysiological system is proposed. It will be achieved by a nonlinear amplifier. It is expected that improved SNR can make following circuits and algorithms simpler and smaller.

II. Proposed System

A. Neural Activity Monitor

Outline of the total embedded system is shown in fig.1. It has a similar structure with other previous systems however major signal processing is finished before a digital processing section. Especially, spike enhancing amplifier is the most important part in the system. It has two main functions; expanding SNR by using nonlinear circuit and maintain the signal level automatically by using feedback loop. A simple activity detection method can be used such like comparator because the spike enhancer continuously maintains SNR and amplitude of spikes at the input of the activity detector. This can also makes the digital processing simpler. If a spike frequency at the output of the comparator should only be transmitted, data counter and data converting function for transmitter are only required for the digital processor. ADC, which is one of major power consumers in the system, can also be excluded.

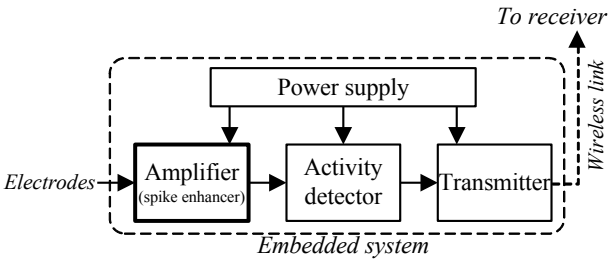

Figure 1. Neural activity monitor with spike enhancer.

B. Spike Enhancer

A simplified functional diagram of the proposed spike enhancer is shown in fig. 2. A characteristic feature is the nonlinear stage. At lower input amplitude than a threshold V_{th}, the gain is zero or far lower than the gain in exceeding V_{th}. The previous gain-controllable amplifier keeps the signal amplitude so that noise level in the signal should be lower than V_{th} as shown in fig.3. Higher SNR than input signal is obtained and kept automatically through the process. A conventional amplifier stage can be replaced to the enhancer.

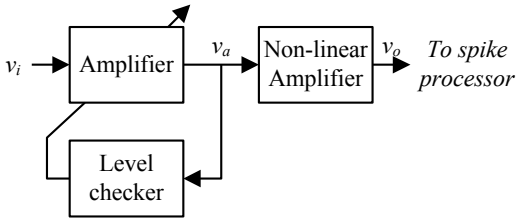

Figure 2. Spike enhancer.

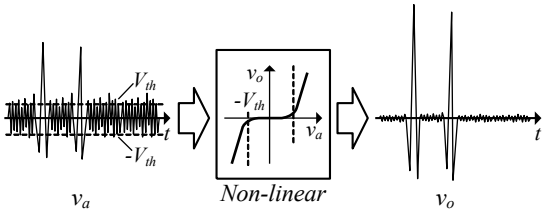

Figure 3. SNR expansion by nonlinear amplifier.

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III. EXPERIMENT

Two experimental circuits were prepared and tested for feasibility study. In this report, experiments were performed with gain-controlled amplifier, nonlinear circuit in Fig.2. For the first evaluation, each circuit was tested separately. In later experiment with biological signal, these were combined to a manually-controlled spike enhancer.

A. Voltage Controlled Amplifier

A simple voltage controlled amplifier (VCA) was prepared with operational amplifier as shown in fig.4. It is based on non-inverting amplifier. A simple gain controller was realized by replacing a register to a junction type FET. The gain can be controlled by the voltage V_G applied to the gate because the resistance between source and drain is controlled by the voltage between gate and source.

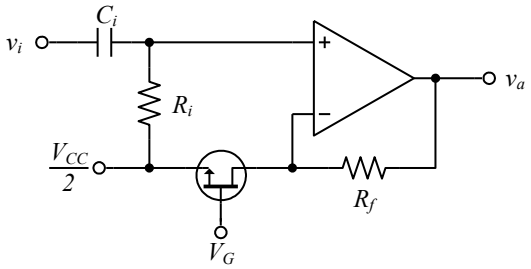

Figure 4. Voltage controlled amplifier.

B. Nonlinear Circuit

A nonlinear amplifier used in this experiment is unbiased common emitter amplifier with bipolar transistor as in fig.5. Only for positive input voltage, an inverting output is obtained at v_o. An operating voltage at v_o is V_{CC} when v_a=0. A junction FET is placed at the input to obtain high input impedance and lower V_{th} than the bipolar transistor.

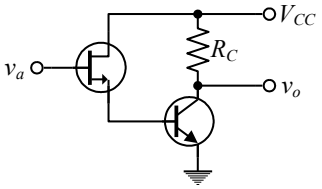

Figure 5. Nonlinear amplifier

C. Input-output Characteristics

Input-output characteristic for each block was tested. For the VCA, 1 kHz, 10 mV_{pp} of sinusoidal wave was applied as v_i. A relationship between V_G and gain was measured and evaluated. For the nonlinear amplifier, v_o was measured in changing dc voltage at v_a. Supply voltage V_{CC} in fig. 4 and fig. 5 was 5 V for all the experiments.

D. Test with Stored Biological Waveform

For the first evaluation with electrophysiological signal, electrocardiogram (ECG) previously recorded from a healthy adult was used. The signal was measured under noisy environment as shown in fig.6 by an analog to digital converter (ADC) with 16 bit of resolution at 240Hz of sampling frequency. Total length of a dataset is 80 s. The ECG data converted to analog signal was applied to the circuit. v_a and v_o were measured in changing V_G. V_G was switched to 2.30 V, 2.33 V, 2.35 V and 2.38 V every 20 s in the listed order.

SNR calculated with the data on v_a and v_o. It defined as a ratio between averaged peak amplitude and root mean square value of the signal during no action potential.

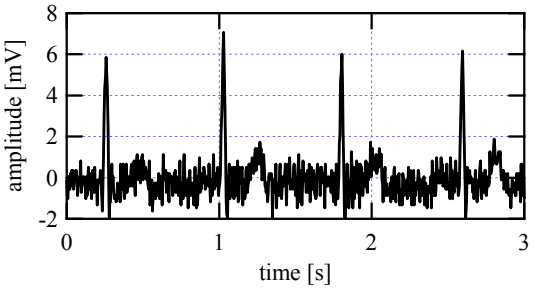

Figure 6. A previously stored ECG data for evaluation.

E. Evaluation with Signal from Rat

For the final evaluation, neural signal from a rat was recorded with the circuits. The same electrodes were shared with conventional linear amplifier and the circuit combined with the circuits in fig. 4 and 5. The output signals from two amplifiers were sampled simultaneously by 16 bit resolution ADC at 10 kHz of sampling frequency. A configuration of the experimental system is shown in fig. 7.

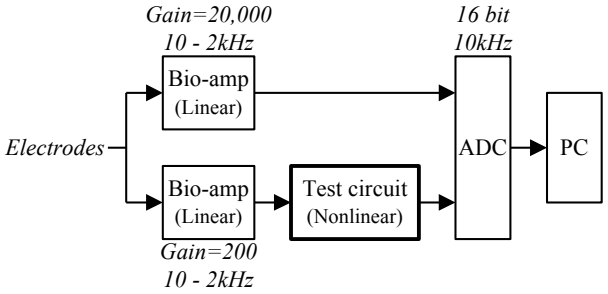

Figure 7. Neural signal experimental system.

Neural signal was measured from barrel field on the cerebral cortex of a rat. The field is one of the sensory fields related with whisker. In this experiment, a tip of a needle electrode was inserted in the area. A reference electrode was placed on the cortex where it had no relation with the activity. After checking signal level by a preliminary measurement, the gain at the VCA was set to an optimal level with V_G manually. The signal with and without stimulus to the whisker were measured. SNR was calculated with the data as the same way in the previous experiment.

All the experiments were approved by the Medical Ethics Committee of Tokyo City University. The experiments with human participant conform to the ethical principles provided by Declaration of Helsinki. We obtained informed consent from all the participants of the experiments, and ensured the protection of personal information.

IV. Results & Discussion

A. Input-output Characteristics

Fig. 8 shows a relationship between control voltage V_G and gain. The gain is controlled by V_G between 2.2 V and 2.5 V. V_G and gain have a logarithmic relationship within this range of V_G. It also shows that the gain for V_G less than 2.15 V is constant because pinch-off occurs at the FET.

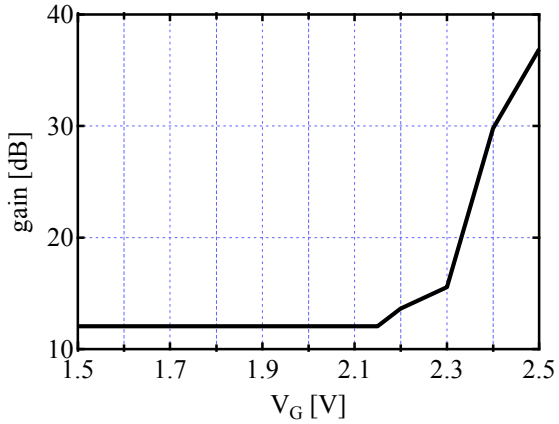

Figure 8. V_G and gain on voltage controlled amplifier.

Fig. 9 is an input-output characteristic of the nonlinear amplifier. This inverted amplifier responds to positive voltage of input signal. A gain was 0 dB with v_a less than 0.05 V and maximum gain was 33 dB at 0.25 V of v_a. Flection input voltage corresponding to V_{th} in fig.3 can be estimated to 0.15 V approximately. In order to suppress noise level at the output, V_G should be controlled so that noise level was kept under 0.15V. A better SNR improvement is expected by using the device which has sharper flection characteristic.

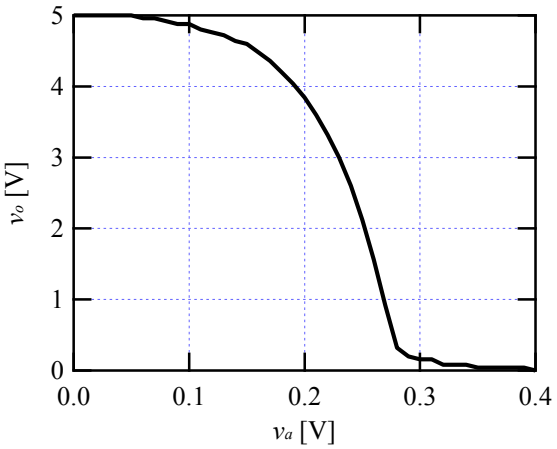

Figure 9. v_a and v_o on nonlinear amplifier.

B. Test with Stored Biological Waveform

Fig. 10 shows the waveforms at the output of the VCA and final output in increasing V_G. The upper half is an output waveform from a linear amplifier and the lower is an output waveform from the nonlinear circuit. Estimated gain at VCA is 15-30 dB from the applied V_Gs and fig.8.

At the first section from start to 20 s, desired signal, that is R wave, is not enhanced well on v_o because the peak amplitude does not exceed flection level V_{th} where the gain at the nonlinear circuit changes. An enhanced waveform and an improved SNR can be seen from 20 s. In later half of v_o, the signal peaks are trimmed to a saturation level. Such waveform is suitable for spike count because of the monotonous amplitude of spikes and low noise level. If V_G is larger than this case, SNR may be worse because noise level may exceed flection level at the nonlinear circuit. A V_G controller as a level checker in fig.1 should be designed to keep sufficient signal level and adequate SNR for accurate spike detection.

Signal levels and SNRs were calculated from the data in

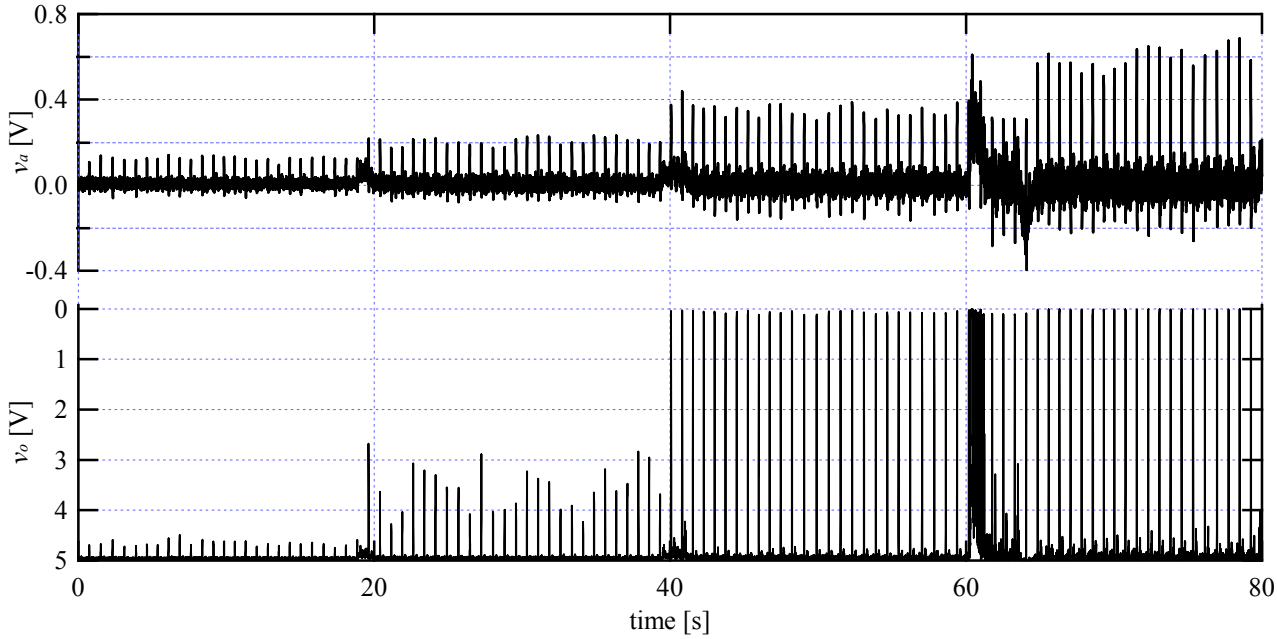

Figure 10. ECG signal at v_a and v_o in changing V_G.

fig. 10 for each V_G. Those are summarized to table I. Noise level and peak amplitude of R wave on v_a increase following to increase of V_G. This simply means gain difference. A slight improvement of SNR on v_a by larger V_G comes from a noise floor of the experimental system. SNR on v_o shows a major improvement from v_a. The best SNR improvement with the nonlinear amplifier is 25 dB in this experiment. SN ratio with the largest V_G is worse than SNR at V_G=2.35 V because R peaks were saturated at V_G=2.35 V as shown in fig.10.

TABLE I. SNRS ON ECG

V_G [V]	v_a			v_o		
	RMS noise [mVrms]	*Mean peak amp. [V]*	*SNR [dB]*	*RMS noise [mVrms]*	*Mean peak amp. [V]*	*SNR [dB]*
2.30	12.5	0.118	19.5	8.24	0.29	31.1
2.33	18.2	0.197	20.7	12.3	1.35	40.9
2.35	27.7	0.337	21.7	21.9	4.75	46.7
2.38	42.0	0.589	22.9	38.2	4.75	41.9

C. Evaluation with Spike Signal from Rat

Fig.11 shows a spike signal from a barrel field on the cortex of a rat. The upper is a measured signal at the output of the linear, conventional amplifier and the lower is from the nonlinear amplifier. The whiskers of the rat had been brushed between 0-4 s. V_G at the nonlinear amplifier was set to 2.40 V where noise level could be adequately suppressed.

The noise had kept an even level whether there was a spike or not. A spike amplitude variation can be seen in the upper waveform. This means that signals from two or more cells are mixed. The lower shows that this variation was enhanced at the nonlinear amplifier output. This can be pointed out as a fault in general point of view, however, detection is easier than the signal by linear amplifier because SNR was improved through the nonlinear amplifier as shown in table II. In this experiment, SNR was improved by 10 dB.

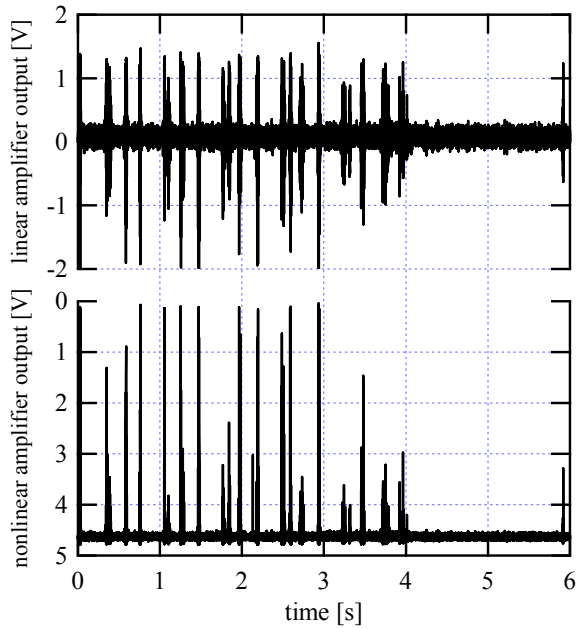

Figure 11. Comparison between linear and nonlinear amplifier with neural spike from a rat.

TABLE II. SNR ON RAT SPIKE SIGNAL

Linear amplifier			*Nonlinear amplifier*		
RMS noise [mVrms]	*Mean peak amplitude [V]*	*SNR [dB]*	*RMS noise [Vrms]*	*Mean peak amplitude [V]*	*SNR [dB]*
70.9	1.00	23.0	28.9	3.38	33.6

V. CONCLUSION

In order to improve signal quality for embedded neural activity monitor, we proposed a spike enhancer with analog nonlinear circuit. We prepared two prototype circuits and evaluated them with biological signal and neural spike from a rat. The results shows that proposed signal enhancer can expand SNR with properly controlled V_G.

For the next step, total performance of the proposed system as in fig.2 should be evaluated. A closed loop feedback circuit should be prepared and tested with VCA and level checker. A level checker in fig.2 can be either analog circuit or microprocessor controlled one. The best structure should be selected by comparative experiments. After evaluation of individual block, we will try to integrate them into an implantable system as shown in fig.1. In this step, the system should be realized by integrated circuit to evaluate total performance, size, and power consumption.

REFERENCES

[1] T. Akin, K. Najafi and R. M. Bradley, "A Wireless Implantable Multichannel Digital Neural Recording System for a Micromachined Sieve Electrode," IEEE J. Solid-State Circuits, vol. 33, no. 1, pp. 109-118, Jan. 1998.

[2] M. A. L. Nicolelis, "Actions from Thoughts," Nature, vol. 409, pp. 403-407, Jan. 2001.

[3] A. M. Sodagar, K. D. Wise and K. Najafi, "A Fully Integrated Mixed-Signal Neural Processor for Implantable Multichannel Cortical Recording," IEEE Trans. Biomed. Eng., vol. 54, no. 6, pp. 1075-1088, Jun. 2007.

[4] S. B. Wilson and R. Emerson, "Spike detection: a review and comparison of algorithms," *Clinical Neurophysiology*, vol. 113, no. 12, pp. 1873-1881, 2002.

[5] I. Obeid and P. D. Wolf, "Evaluation of Spike-Detection Algorithms for a Brain-Machine Interface Application," *IEEE Trans. Biomed. Eng.*, vol. 51, no. 6, pp. 905-911, JUNE 2004

[6] J. H. Choi, H. K. Jung and T. Kim, A New Action Potential Detector Using the MTEO and Its Effects on Spike Sorting Systems at Low Signal-to-Noise Ratios," *IEEE Trans. Biomed. Eng.*, vol. 53, no. 4, pp. 738-746, Apr. 2006.

[7] S. Shahid, J. Walker and L. S. Smith, "A New Spike Detection Algorithm for Extracellular Neural Recordings," *IEEE Trans. Biomed. Eng.*, vol. 57, no. 4, pp.853-866, Apr. 2010.