

# Practical Issues in Bispectral Analysis of Electroencephalographic Signals

Satoshi Hagihira, MD, PhD\*, Masaki Takashina, MD†, Takahiko Mori, MD§, Takashi Mashimo, MD, PhD||, and Ikuto Yoshiya, MD, PhD‡

\*Surgical Center, Osaka Prefectural Habikino Hospital; †Surgical Center and ‡Department of General Medicine, Osaka University Hospital; §Department of Anesthesiology, Osaka Prefectural General Hospital; and ||Department of Anesthesiology, Osaka University Graduate School of Medicine, Osaka, Japan

**B**ispectral analysis is an advanced signal processing technique that quantifies quadratic nonlinearities (phase-coupling) among the components of a signal. There are only a few reports concerning the bispectrum of electroencephalogram (EEG). Barnett et al. (1) first reported the Bispectral analysis of EEG in 1971. Sigl and Chamoun (2) introduced the detailed principle and concept of bispectral analysis in 1994. Ning and Bronzino (3) reported the changes of bispectrum of the rat EEG during various vigilance states, and Muthuswamy et al. (4) reported the bispectral analysis of burst patterns in EEG. This analytic technique is also known as a core technology of the Bispectral Index System (BIS) monitor (Aspect Medical Systems, Natick, MA).

Although bispectral analysis involves complicated mathematics, today's computers are powerful enough for real-time Bispectral analysis of EEG data. Nevertheless, at the time of this writing, there were no reports accurately showing the relationship between the "depth of anesthesia" and bispectrum and bicoherence, normalized variable of bispectrum, of EEG. To investigate such relationship, we developed a software application that runs under Microsoft Windows 95/98® (Microsoft Corp., Redmond, WA). While developing the software, we discovered several theoretical and practical problems with the bispectral analysis of EEG.

The aim of this report was to confirm the methodology of bispectral analysis of EEG.

## Materials and Methods

We custom built an application software named BSA (Bispectrum Analyzer), which analyzes EEG waveform

and calculates its bispectrum. Developed with C++ Builder Version 5® (Borland Japan Co., Tokyo, Japan), BSA runs under Microsoft Windows 95/98. Details of the application are described in the following section.

After securing institutional approval and informed consent from participants, we applied the software to analyze the EEG data of patients ( $n = 20$ ) who underwent elective abdominal surgery under general anesthesia combined with epidural anesthesia. EEG (FP<sub>1</sub>-A<sub>1</sub> lead) was monitored by using the 514X-2 EEG telemetry system (GE Marquette, Tokyo, Japan). FP<sub>z</sub> is used for body ground. The EEG high-cut filter was set at 60 Hz and the time-constant was set to 0.3 s. The low-cut filter was not equipped with our EEG monitor.

### *How Many Epochs Are Required?*

In computing the bispectrum, the EEG signal is first divided into a series of epochs. Because it is impossible to tell from a single epoch whether a signal is phase coupled, we have to examine multiple epochs to analyze phase coupling.

Sigl and Chamoun (2) used 60-s EEG segments for bispectrum calculation. According to the A-10x0 Serial Port Technical Specification, provided by Aspect Inc. and the review by Rampil (5), the BIS monitor (A-1050) calculates bispectral data from 61.5-s EEG segments (120 epochs). No evidence, however, has been reported to confirm whether 120 epochs are sufficient to produce reliable bispectral estimation.

Consequently, we compared bicoherence values calculated from different numbers of epochs.

### *Length of Epochs and Extent of Overlapping*

Sigl and Chamoun (2) used 4-s epochs, whereas the BIS monitor (A-1050) used 2-s epochs (5). Both methods use subsequent epochs that overlap the previous one by 75%. The power spectrum can be calculated from any length of epoch, but a longer epoch would be

Accepted for publication June 15, 2001.

Address correspondence and reprint requests to Satoshi Hagihira, Department of Anesthesiology and Surgical Center, Osaka Prefectural Habikino Hospital, 3-7-1, Habikino, Habikino City, Osaka, Japan 583-8588. Address e-mail to hagihira@masui.med.osaka-u.ac.jp.

more likely to be affected by artifacts. According to Niekas and Raghuvier (6), an overlapping method is effective in increasing the total number of epochs in the restricted sampling records. Therefore, we adopted length and overlapping of epochs identical to those of BIS.

### *The BSA Application*

Currently, for real-time processing, BSA supports the REX5054B analog-to-digital converter (PCMCIA card, 12 bit 4 channel; Ratoc Co., Osaka, Japan) and collects EEG wave data via this converter. Normally, because bispectrum comprises two wave components, bispectrum values are usually plotted three-dimensionally. However, three-dimensional plotting is too complex and time-consuming for real-time processing with available computing resources. Therefore, we opted for two-dimensional plotting, which displays calculated values in color-spectral scale (topographical plotting in Figure 1.)

BSA requires an EEG monitor, which gathers 0.5–47.5 Hz of EEG and is equipped with an analog output. BSA also has an offline mode to allow more detailed analysis of acquired data. Further development, BSA for BIS, allows the use of a BIS monitor (A-1050) as the EEG source.

### *Algorithm for Data Processing*

EEG wave data were sampled at 512 Hz and digitized data were used for analysis. After artifact detection, wave data were down sampled at 128 Hz by averaging every four samples. This over-sampling technique can improve the accuracy of data sampling.

After applying a Blackman window function, the Fourier transform of each epoch is computed. The power spectrum of each epoch is calculated by Cooley and Tukey's fast Fourier transformation algorithm (7), and the 0.5–47.5 Hz (0.5 Hz step) power spectrum components are used for bispectral analysis. Bispectrum values and bicoherence values are calculated according to the equations shown in the Appendix.

### *Data Sampling and Statistics*

We compared the values of bicoherence calculated from 120, 240, 360, 480, 600, and 720 epochs. (End-tidal concentration of isoflurane was reached at 0.7% 30 min before data sampling and was maintained for >1 h.) We calculated bicoherence at two pairs of frequencies, BIC\_8 (8.0 Hz, 8.0 Hz) and BIC\_20 (20.0 Hz, 20.0 Hz). Seven bicoherence values were calculated and averaged in each of the six groups. Each bicoherence value is calculated from randomly selected artifact-free periods. Initially, we checked the difference of variance values by F-test. Mean values were compared by using the Scheffé multiple comparison

test;  $P$  values <0.05 were considered significant. To confirm the steady state, we also calculated spectral edge frequency 90% (SEF90) every minute.

We also compared the changes of bicoherence values calculated from 120 epochs and 360 epochs in the transient state.

## **Results**

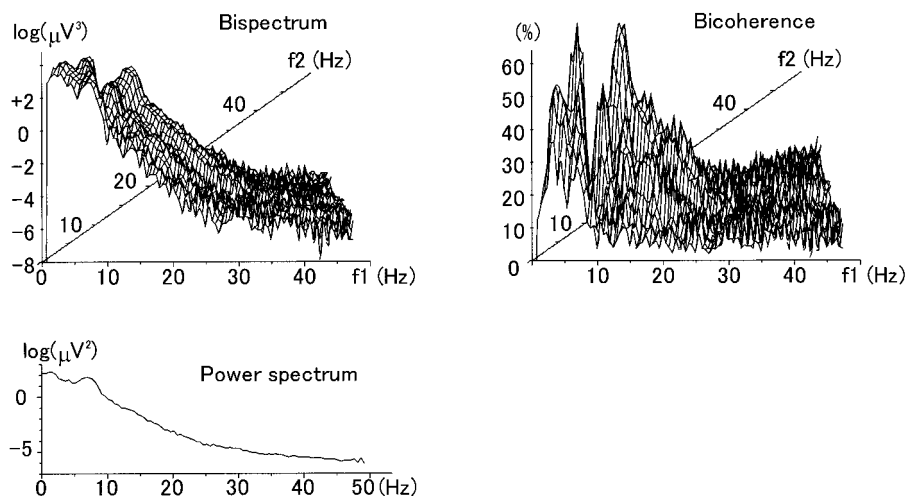
Figure 1 shows typical bispectrum, bicoherence, and power spectrum of EEG in a 53-yr-old woman undergoing distal gastrectomy with isoflurane anesthesia. The end-tidal isoflurane concentration was kept at 0.9% for 30 min before EEG sampling. As the figure shows, bispectrum values were generally high in the lower frequency area and bicoherence values were significantly higher in the  $\theta$  range and  $\alpha$  range around the diagonal line ( $f_1 = f_2$ ). In other regions, however, bicoherence values were quite small.

Figure 2 shows how varying the number of epochs affects the bicoherence calculation. During data sampling, SEF90 values were  $11.0 \pm 0.18$  (mean  $\pm$  SD), ranging from 10.8 to 11.5. At this anesthetic level, BIC\_8 was significantly high (phase-coupling exists), whereas BIC\_20 was low (phase-coupling is weak or absent). With 120- and 240-epoch data, the variance values for BIC\_8 were significantly larger than the value from 720-epoch data. But there was no significant difference among the mean values of BIC\_8. With 120-epoch data, the variance value for BIC\_20 was also significantly larger than the value from 720-epoch data. Although BIC\_20 showed a tendency to gradually decrease with the increase of epoch numbers, we found no statistically significant differences in mean values of BIC\_20. These results suggest that at least 360 epochs (3 min) are required to calculate reliable and reproducible bicoherence values. However, the longer the sampling period is, the more difficult the rapid detection of change may be.

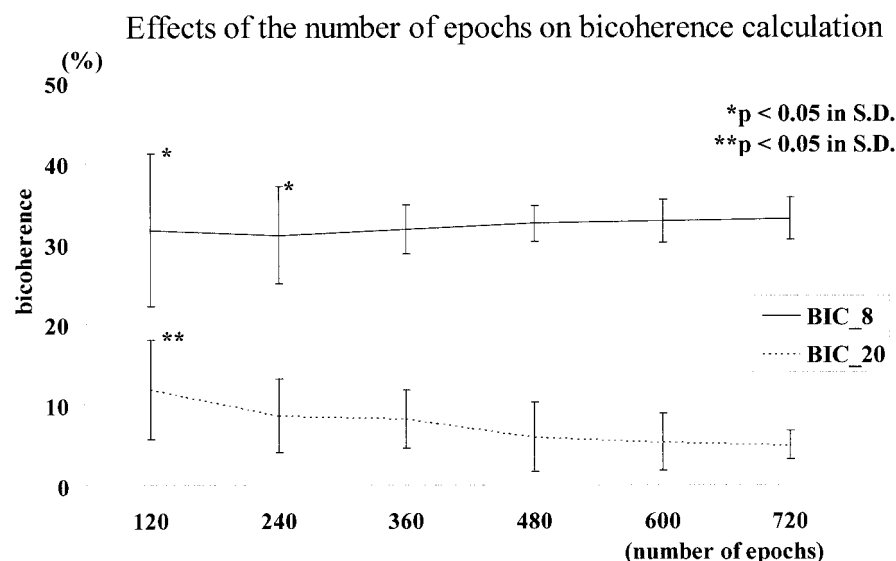
Figures 3 and 4 show the changes of bicoherence values at the consecutive 3 min (sampling period was 5 min) while the expired isoflurane concentration was changed from 1.1% to 0.5% in a 58-yr-old woman undergoing hysterectomy and bilateral salpingo-oophorectomy (Fig. 3 was calculated from 120 epochs and Fig. 4 from 360 epochs). As shown in Figure 3, bicoherence values calculated from 120 epochs had large variance, and it was difficult to know how they were changing. However, bicoherence values calculated from 360 epochs (Fig. 4) showed smaller variation and we could observe the peaks in the  $\theta$  and  $\alpha$  ranges becoming smaller minute by minute.

## **Discussion**

Because bispectral analysis is a statistical technique, we should clarify how many epochs are required to



**Figure 1.** Typical patterns of bispectrum, bicoherence, and power spectrum during isoflurane anesthesia (isoflurane = 0.9%) calculated from 360 epochs. Bispectrum values (in log scale) and bicoherence values are plotted topographically. The power spectrum is a plot of log values.



**Figure 2.** Bicoherence values during isoflurane anesthesia (isoflurane = 0.7%). \*Indicates significant difference in variance values compared with the variance value of BIC\_8 from 720-epoch data. \*\*Indicates significant difference in variance values compared with the variance value of BIC\_20 from 720-epoch data.

obtain reliable bicoherence data. Our findings suggested that at least 360 epochs (3 minutes of monitoring) are required to get reliable bicoherence values in the steady state.

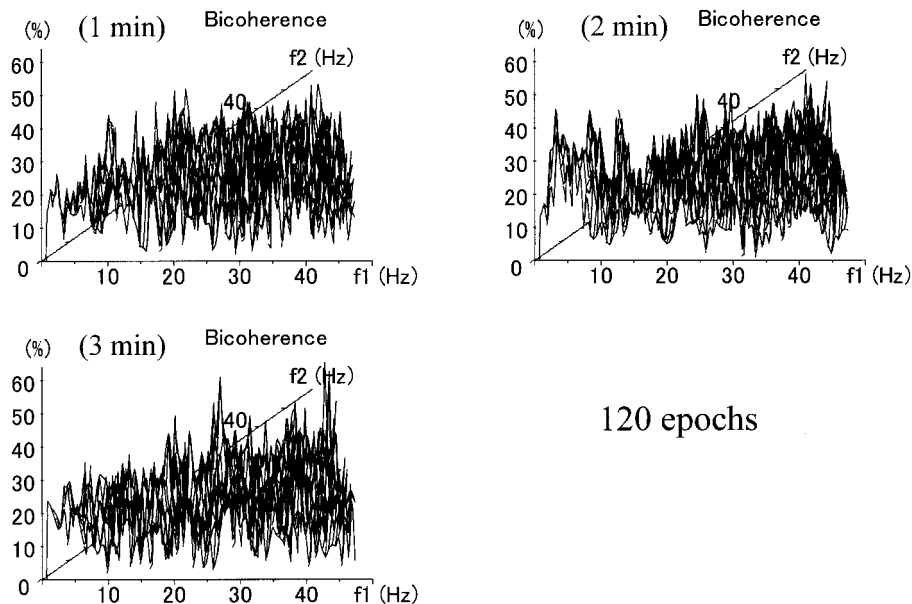
Furthermore, bicoherence values seemed to change in accordance with the changes of anesthetic level in the transient state, as shown in Figure 4. The latest changes in degree of phase coupling would also be reflected in the bicoherence values calculated from the latest 360 epochs. And smaller variation made it possible to detect even their small changes. As a result, by watching the changes of bicoherence values calculated from 360 epochs, we could detect their changes on time. Thus, bicoherence could be usable as a monitor in the transient state as well as in the steady state, as supported by Figures 3 and 4.

Nikias and Raghuveer (6) described that the variance in the bispectrum estimation is inversely proportional to the total amount of data. Although our observed variance values decreased when the number of

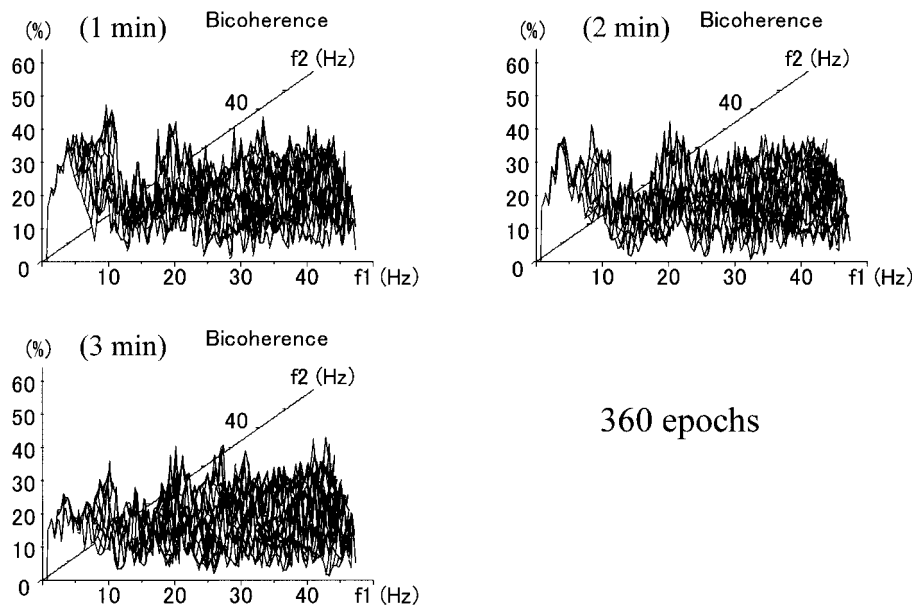
epochs used for calculation increased, they were not inversely proportional to the number of epochs. In the current study, we investigated the variance of bicoherence, not that of bispectrum, and bicoherence is a normalized value. This is why our result was not in accordance with that description.

Our result would not directly indicate the fault of the BIS monitor. According to the review by Rampil (5), the BIS monitor uses bispectrum values (not bicoherence values) which are calculated from the latest 61.5 seconds (120 epochs). As shown in our result, the variances of bicoherence values calculated from 120 epochs were significantly larger than those calculated from 360 epochs. The variances of bispectrum values also became larger. In a single frequency pair, it is true. But the BIS monitor uses SynchFastSlow (5) as a bispectrum-derived variable, which is the logarithm of ratio of 2 sums of bispectral activities in the different regions. SynchFastSlow is calculated from >1000 bispectrum values and is a logarized value, which

**Figure 3.** Changing of bicoherence values in transient state of consecutive 3 min (isoflurane concentration was changed from 1.1% to 0.5%). The changes of bicoherence values calculated from the latest 120 epochs.



**Figure 4.** Changing of bicoherence values in transient state of consecutive 3 min (isoflurane concentration was changed from 1.1% to 0.5%). The changes of bicoherence values calculated from the latest 360 epochs.



makes the variance much smaller. Furthermore, the BIS monitor used other variables such as the relative  $\beta$  ratio from power spectral analysis and the burst suppression ratio from time domain analysis. During induction of, or recovery from, anesthesia, BIS readings rapidly change, but the relative  $\beta$  ratio, which is derived from power spectrum, is most heavily weighed on BIS values at the anesthetic level, as reported by Sleight et al. (8).

We used bicoherence instead of bispectrum in this report. Bispectrum values are influenced by the amplitude of signals as well as the degree of phase coupling, whereas bicoherence values directly indicate

the degree of phase coupling. Thus, bicoherence is most important in bispectral analysis.

It is still necessary to observe and evaluate how bicoherence changes with levels of anesthesia. Our rather small number of clinical trials has indicated it may be possible to assess the precise depth of anesthesia by monitoring bicoherence. However, additional studies are needed to evaluate its clinical relevance and applicability. We conclude that bicoherence calculated from 360 2-second epochs is appropriate for clinical monitoring as well as for research purposes.

To encourage scientific investigation and analysis of EEG during anesthesia, we are distributing BSA

and BSA for BIS software for scientific research. Upon request, we will provide any information concerning the application algorithms. Downloads are available via the Internet from: <http://www.med.osaka-u.ac.jp/pub/anes/www/software/software.E.html>.

## Appendix

### Calculating Method of Bispectrum

Each bispectrum value is calculated as follows:

$$TP_j(f_1, f_2) = X_j(f_1) \cdot X_j(f_2) \cdot X_j^*(f_1 + f_2) \quad (1)$$

$$B(f_1, f_2) = \left| \sum_j TP_j(f_1, f_2) \right| \quad (2)$$

Complex numbers,  $X(f_1)$ ,  $X(f_2)$  and  $X(f_1 + f_2)$ , are power spectrum components by FFT.  $X^*(f)$  is the conjugate of  $X(f)$ .  $TP_j$  is called triple product. The summation in Equation (2) is the heart of the bispectral analysis.

### Bispectrum and Bicoherence

Bicoherence is defined as the normalized degree of phase coupling (ranging from 0% to 100%). Several calculating methods of bicoherence have already been described in the literature (1-3,5,9). Mathematically, the following equation is most reasonable:

$$BIC(f_1, f_2) = \frac{B(f_1, f_2)}{\sum_j |TP_j(f_1, f_2)|} \cdot 100 \quad (3)$$

$$= \frac{B(f_1, f_2)}{\sum_j \sqrt{P_j(f_1) \cdot P_j(f_2) \cdot P_j(f_1 + f_2)}} \cdot 100 \quad (4)$$

Bispectrum is defined as the magnitude of the sum of complex numbers [equation (2)], so it should be scaled by the sum of the magnitude of each complex number. For example,

$$|z_1 + z_2| \leq |z_1| + |z_2|$$

If  $z_j \neq 0$ , then equal is only satisfied when the phase angles of  $z_1$  and  $z_2$  are equal. Applying this relation,

$$\begin{aligned} \left| \sum_j X_j(f_1) \cdot X_j(f_2) \cdot X_j^*(f_1 + f_2) \right| \\ \leq \sum_j |X_j(f_1) \cdot X_j(f_2) \cdot X_j^*(f_1 + f_2)| \end{aligned}$$

Incidentally, the magnitude of the product of complex numbers is equal to the product of each magnitude of complex number. Furthermore, conjugate is equal to the magnitude of its original complex number.

Then,

$$\begin{aligned} |X_j(f_1) \cdot X_j(f_2) \cdot X_j^*(f_1 + f_2)| \\ = |X_j(f_1)| \cdot |X_j(f_2)| \cdot |X_j^*(f_1 + f_2)| \\ = |X_j(f_1)| \cdot |X_j(f_2)| \cdot |X_j(f_1 + f_2)| \\ = \sqrt{|X_j(f_1)|^2 \cdot |X_j(f_2)|^2 \cdot |X_j(f_1 + f_2)|^2} \\ = \sqrt{P_j(f_1) \cdot P_j(f_2) \cdot P_j(f_1 + f_2)} \end{aligned}$$

Finally,

$$B(f_1, f_2) \leq \sum_j \sqrt{P_j(f_1) \cdot P_j(f_2) \cdot P_j(f_1 + f_2)} \quad (5)$$

(Equal is only satisfied when phase angles of all triple products are equal.) Thus bispectrum should be normalized by  $\sum_j \sqrt{P_j(f_1) \cdot P_j(f_2) \cdot P_j(f_1 + f_2)}$ .

## References

1. Barnett TP, Johnson LC, Naitoh P, et al. Bispectrum analysis of electroencephalogram signals during waking and sleeping. *Science* 1971;172:401-2.
2. Sigl JC, Chamoun NG. An introduction to bispectral analysis for the electroencephalogram. *J Clin Monit* 1994;10:392-404.
3. Ning T, Bronzino JD. Bispectral analysis of the rat EEG during various vigilance states. *IEEE Trans Biomed Eng* 1989;36:497-9.
4. Muthuswamy J, Sherman DL, Thakor NV. Higher-order spectral analysis of burst patterns in EEG. *IEEE Trans Biomed Eng* 1999;46:92-9.
5. Rampil IJ. A primer for EEG signal processing in anesthesia. *Anesthesiology* 1998;89:980-1002.
6. Nikias CL, Raghuveer MR. Bispectrum estimation: a digital signal processing framework. *Proc IEEE* 1987;75:869-91.
7. Cooley JW, Tukey JW. An algorithm for machine calculation of complex Fourier series. *Math Comput* 1965;19:297-301.
8. Sleight JW, Steyn-Ross DA, Steyn-Ross ML, et al. Comparison of changes in electroencephalographic measures during induction of general anesthesia: influence of the gamma frequency band and electromyogram signal. *Br J Anaesth* 2001;86:50-8.
9. Huber PJ, Kleiner B, Gasser T, Dumermuth G. Statistical methods for investigating phase relation in stationary stochastic processes. *IEEE Trans Audio Electroacoust* 1971;AU-19:78-86.