Evaluation of instantaneous causality among inspiratory neurons

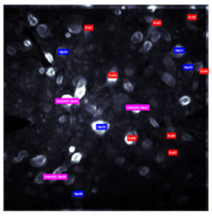
みわけいち
三分一 史和 モデリング研究系 准教授

1 Introduction

Respiration is an essential activity for life support in mammals, and it is known that the respiratory rhythm is generated by the self-excited activity of respiratory neurons in the brainstem. Our group has been studying the estimation of the network structure to maintain the self-excited activity by using a dynamical approach based on time series analysis. So far, we have used the standard Vector Autoregressive (VA) model to estimate the causality between neurons. However, when we examined the time lag of the waveforms among neurons using a more basic method, cross-correlation analysis, we found the highest correlation at lag=0[s]. This finding indicates that instantaneous causality should be taken into account. The Structural VA (SVA) model can estimate instantaneous causality, but the order of the variables (channels) must be fixed a priori due to the parameter identification problem. Since it is difficult to determine the causality a priori in the case of neurons, the SVAR model cannot be applied directly. Therefore, we used a reduced form of the SVAR model to evaluate whether generalized impulse response analysis, which can be computed through a reduced form of SVAR model and does not require a priori assumptions, can estimate instantaneous causality.

2 Time-lagged cross correlation analysis

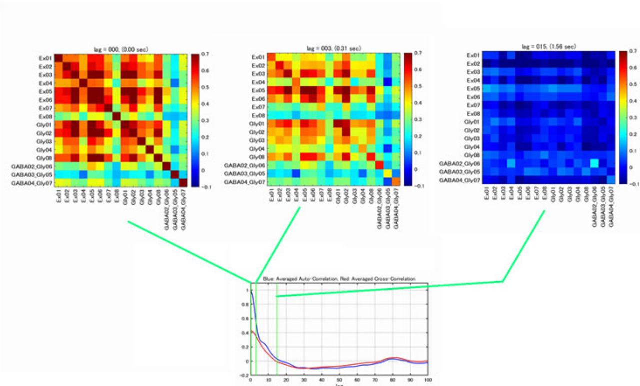
Spatial distribution of inspiratory neurons in the pre-Bötzinger complex



Blue: Glycinergic inhibitory neuron
Red: GABAergic inhibitory neuron
Magenta: GABA/glycinergic dual-transmitting neurons
Green: Excitatory neuron

$$R^{\nu}(\tau) = \eta^{\nu}(t)\varphi(t-\tau)/\sqrt{(\eta^{\nu})^2}\sqrt{\varphi^2}$$

$\eta^{\nu}(t)$: ν index of inspiratory neuron
$\varphi(t)$: reference neuron



More than 80% of the inspiratory neurons have the highest cross-correlation coefficient at lag=0[s].

3 Methods

SVAR(p) model $\quad A_0 Y_t = \sum_{i=1}^{p} A_i Y_{t-i} + E_t$

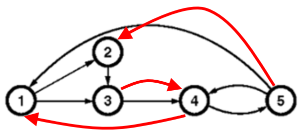
Reduced form $\quad Y_t = \sum_{i=1}^{p} A_0^{-1} A_i Y_{t-i} + A_0^{-1} E_t = \sum_{i=1}^{p} A_0^{-1} A_i Y_{t-i} + A_0^{-1} E_t = \underbrace{\sum_{i=1}^{p} B_i Y_{t-i} + U_t}_{\text{VAR}(p)\text{ model}}$

Impulse response function

$$\begin{aligned}
\Delta y(1) &= \text{Impact} \\
\Delta y(2) &= B_1 \Delta y(1) \\
\Delta y(3) &= B_1 \Delta y(2) + B_2 \Delta y(1) \\
&\vdots \\
\Delta y(p) &= B_1 \Delta y(p-1) + B_2 \Delta y(p-2) + \cdots + B_{p-1} \Delta y(1) \\
\Delta y(p+1) &= B_1 \Delta y(p) + B_2 \Delta y(p-1) + \cdots + B_p \Delta y(1) \\
&\vdots \\
\Delta y(h) &= B_1 \Delta y(h-1) + B_2 \Delta y(h-2) + \cdots + B_p \Delta y(h-p)
\end{aligned}$$

- Generalized IRF (gIRF) $\quad \text{Impact} = \frac{\Sigma_u e_j}{\sqrt{(\sigma_{jj})}}$

4 Simulation study



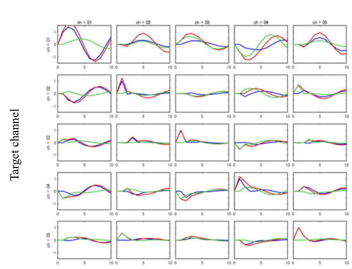
Red: instantaneous connectivity

SVAR parameters

$$A(0) = \begin{pmatrix} 1 & 0 & 0 & 0.5145 & 0 \\ 0 & 1 & 0 & 0 & -0.6604 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0.6356 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

$$A(1) = \begin{pmatrix} 1.3435 & 0 & 0 & 0 & 0 \\ -0.5000 & 0 & 0 & 0 & 0 \\ 0.2000 & 0 & 0 & 0 & 0 \\ 0 & 0 & -0.5000 & 0.3536 & 0.3536 \\ 0 & 0 & 0 & -0.3536 & 0.3536 \end{pmatrix}$$

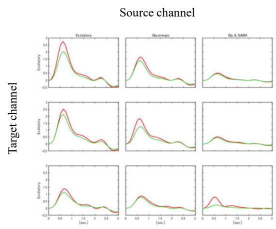
$$A(2) = \begin{pmatrix} -0.9025 & 0 & 0 & 0 & 0.5000 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0.4000 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$



Red: Generalized Impulse response function (sIRF)
Blue: Simple Impulse response function (gIRF)
Grenn: Generalized Impulse response function with non-diagonal component of Σu (ndgIRF)

4 Conclusions and further research

Through this simulation study, we found that sIRF can estimate causality considering only past values, gIRF can estimate causality considering both current and past values, and ndgIRF can estimate causality considering only current values. Thus, it may be possible to identify the time and spatial direction in which causality occurs by combining these impulse response functions.



Here is a short description of the results of the actual data analysis we are currently doing. This figure shows the average values for each type of impulse response function for each type of neuron. Currently, our research group is discussing physiological interpretations and investigating methodologies for more precise network structure estimation.