

Quantifying Cardio-Respiratory Coupling with an Empirical Oscillator Model



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1. Introduction

Cardio-respiratory coupling (CRC) is a known physiological phenomenon in which the heartbeat drives the rhythm respiration and vice versa. It is believed to play an integral role in the control of homeostasis involving gas exchange. Primarily, CRC is regulated by peripheral inputs, including the baroreceptors and the afferent vagus nerve. (Fig. 1) In our experiments, we perform respiratory EMG and EKG recordings on naive anesthetized Sprague-Dawley rats before, immediately after, and 30 minutes after performing vagotomy. The experiments were carried out by Yee-Hsee Hsieh in Thomas E. Dick's lab, Department of Medicine, whereas I focused on the analysis and modeling of their data in the Galán lab.

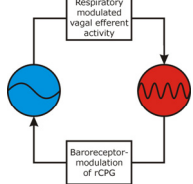


Figure 1: Schematic of CRC and believed pathways

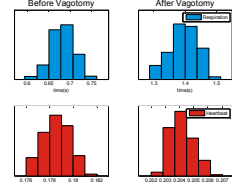


Figure 2: Distribution of inter-event intervals for respiration and heartbeat

In our study, we perform a similar type of analysis of coupled oscillators proposed by Rosenblum, *et. al.* That is, we first transform the EMG and ECG time series into phase time series. (Fig. 3,4) Then, under the assumption that both the heartbeat (H) and breathing (B) are well-described as phase oscillators (Fig. 2), we fit the data, in a least squares sense, to a mode of coupled generic phase oscillators given by the equations,

$$\begin{cases} \dot{\phi}_H = \omega_H + F_{B \rightarrow H}(\phi_B, \dot{\phi}_B) + \xi_H(t) \\ \dot{\phi}_B = \omega_B + F_{H \rightarrow B}(\phi_H, \dot{\phi}_H) + \xi_B(t) \end{cases} \quad \text{with} \quad \begin{cases} F_{B \rightarrow H} = \sum_{n,m} A_{n,m}^H e^{i(n\phi_B + m\dot{\phi}_B)} \\ F_{H \rightarrow B} = \sum_{n,m} A_{n,m}^B e^{i(n\phi_H + m\dot{\phi}_H)} \end{cases}$$

$\xi_H(t)$, $\xi_B(t)$ represent background noise and $A_{n,m}^H, A_{n,m}^B$ are the Fourier coefficients of the coupling functions $F_{H \rightarrow B}, F_{B \rightarrow H}$. By fitting $\phi_B(t), \dot{\phi}_B(t), \phi_H(t), \dot{\phi}_H(t)$, which are obtained from the data, to this oscillator model, we obtain the Fourier coefficients, and hence, the coupling functions. The coupling, c and directionality, d are then quantified as:

$$c_{H \rightarrow B} = \frac{\sum_{n,m \neq 0} |A_{n,m}^B|^2}{\omega_B^2}, \quad c_{B \rightarrow H} = \frac{\sum_{n,m \neq 0} |A_{n,m}^H|^2}{\omega_H^2}, \quad \text{and} \quad d = \frac{c_{H \rightarrow B} - c_{B \rightarrow H}}{c_{H \rightarrow B} + c_{B \rightarrow H}}$$

2. Computational Methods

In our analysis, we identify heartbeats and breaths from our ECG and EMG data, from which we define a phase time series, $\varphi(t)$, for each signal. $\varphi(t)$ takes values from 0 to 2π , between each successive event and is conceptually equivalent to traveling around the circle once from one event to the next. This mapping from our original time series into a point traveling on the unit circle (Fig. 3,4) allows us to utilize tools developed to study generic phase oscillators.

Figure 3: Mapping of ECG and EMG time series to the unit circle. Since the rate of heartbeat is faster than that of breathing, heartbeat always leads respiration.

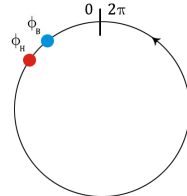
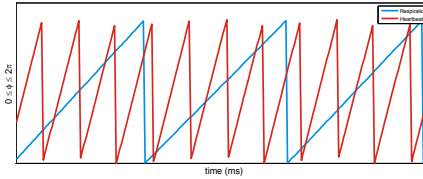


Figure 4: Phase time series definition. Each cycle between subsequent events are used to define a phase that is bounded between 0 and 2π .



3. Results

Our preliminary analysis with this dataset shows that CRC is strongest in the direction from heartbeat to breathing. In all experiments, the dominant coupling function was $F_{H \rightarrow B}$, before performing the vagotomy, (Fig. 7) whereas in most experiments, coupling in the other direction, $F_{B \rightarrow H}$, is essentially zero. After vagotomy, the coupling functions for both heartbeat and respiration go to zero, which means that coupling vanishes after the vagus nerve is severed; however for a small subset of our dataset, our method shows that coupling weakly returns even after the vagus is cut.

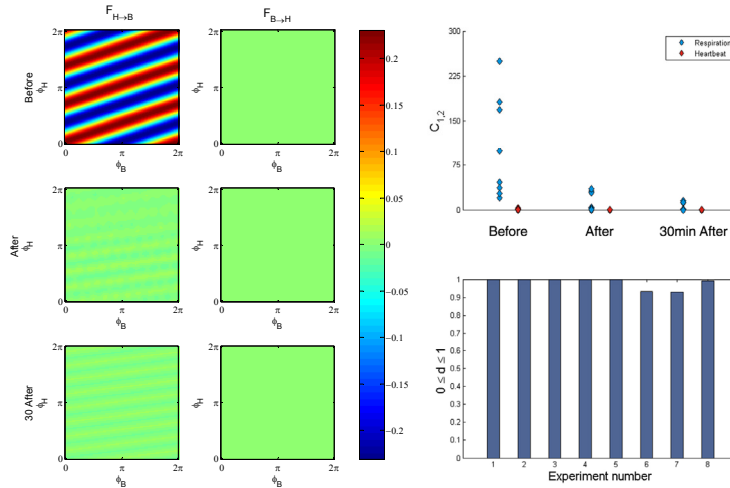


Figure 6: Coupling functions for respiration and heartbeat at baseline and different states after vagotomy.

Figure 7: Population view of coupling function magnitudes ($c_{1,2}$) and directionality constants (d) for baseline state.

4. Experimental Methods

Experiments were conducted on anesthetized Male Sprague-Dawley rats that were previously anesthetized with urethane. ECG (electrocardiogram) and respiratory EMG (electromyogram from the diaphragm) were performed on this preparation in the naive state and after surgery was performed to sever the vagus nerve. (vagusotomy)

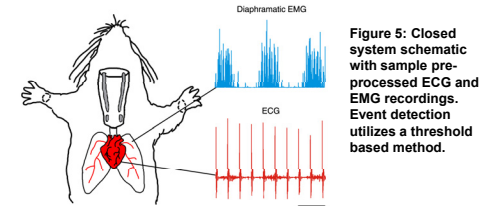


Figure 5: Closed system schematic with sample pre-processed ECG and EMG recordings. Event detection utilizes a threshold based method.

5. Conclusions

Thus far we have developed tools which improves upon current methods used to study coupled generic phase oscillators. Using these tools, we have begun the characterization of CRC in the naive and vagotomized state of an anesthetized Sprague-Dawley rat. In general, our results are consistent with current knowledge in physiology. From the analysis of our analysis we conclude that the interaction between the heartbeat and respiration is dependent mostly on the vagus nerve pathway, at least in anesthetized rats. This method shows promise in its ability to detect and quantify the presence of coupling from the non-invasive EMG and ECG recordings. The results of this research could aid in the development of tools that may be used to study CRC-related respiratory pathologies in human patients, and assist in their proper diagnosis.

References

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