國立交通大學

生醫工程研究所

碩士論文

人工密閉環境中二氧化碳對人類生理反應之研究

Research of Physiological Responses to Carbon Dioxide Concentration in an Airtight Room

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中華民國 一百年六月

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國 立 交 通 大 學

生 醫 工 程 研 究 所

碩 士 論 文

A Thesis

Submitted to Institute of Biomedical Engineering

College of Computer Science

National Chiao Tung University

in partial Fulfillment of the Requirements

for the Degree of

Master

in

Computer Science

June 2011

Hsinchu, Taiwan, Republic of China

中華民國一百年六

摘要

根據布朗運動定律與室內空氣品質標準，通風不良將造成環境二氧化碳濃度與溫度升高，而人體呼吸與代謝是室內環境二氧化碳的主要來源，為了探討環境二氧化碳濃度對於人體的影響，本研究模擬一間通風不良的環境，藉此觀察與分析其效應。受測者部分，徵求 10 位自願受測者參與，在連續 1 小時的實驗過程，監測環境訊號為二氧化碳濃度與空間溫度，生理訊號之擷取則包含：臉部表面溫度、血氧濃度與心電圖。初步實驗結果顯示，二氧化碳濃度升高使血液中的血氧濃度下降，臉部表面溫度升高，心臟跳動加快，使得中樞化學反射器感受到血液中氧與二氧化碳分壓的變化，改變心、肺循環系統進呼吸，以達到體內平衡。綜合本研究之實驗結果，通風不良的室內環境將影響人類一般生理狀態。

Abstract

According to Brownian motion and indoor air quality (IAQ) standard, the carbon dioxide concentration (C_{CO2}) and air temperature (T_a) increase when ventilation is poor. The main source of CO_2 pollution indoor is human respiration. This study simulates an airtight condition and uses 10 volunteer subjects to study the physiological responses to three C_{CO2}. Facial temperature (T_f), saturation of peripheral oxygen (SpO_2), and electrocardiography were spontaneously acquired while subjects were inside an airtight room. Analytical results indicate that SpO_2 decreased as C_{CO2} increased. Those results further demonstrate a positive correlation between C_{CO2}/heart rate and C_{CO2}/T_f, implying that the central-chemoreflex can stimulate the respiratory system since SpO_2 variance and an increased heart rate can promote pulmonary gas exchange. Notably, differences in T_f and T_a increased under low C_{CO2} and then reversed and stabilized. The antagonistic pattern accelerated rapidly initially and decelerated finally stabilized. These findings also imply that the internal body responded to changes in the external environment rapidly, attempted to homeostasis, and reached equilibrium slowly. Results of this study demonstrate that IAQ affects physiological responses in the symbiotic relationship between the human body and surrounding environment.

致謝

碩士論文的完成第一位要感謝的是我的指導老師 蕭子健教授，在碩士期間非常細心與耐心的給予指導，使我在碩士階段有著扎實的學習，並且抱持著『跨領域』的夢想不斷往前躍進；從蕭老師身上學到『大膽假設，小心求證』之研究精神，在老師的包容下開創出自己的小題目，逐步完成碩士論文，以至現在有著成熟穩健的學習態度。蕭老師的鼓勵是我這一路走來最大的動力，使我從醫事放射科學領域踏入資訊工程領域的懵懂無知，不斷自我挑戰，參與各項論文發表以及學習計劃與專利的撰寫，使我的碩士生涯更加充實。

感謝 江惠華教授在醫學工程領域專精與見證下，使我能在醫學工程領域之下勇敢與盡情的學習研究，並且給予我的碩士論文許多醫學工程面向的建議與支持；感謝 鍾崇斌所長在交大生醫工程研究所的用心與貢獻，使我能在交大具有濃烈的工程領域色彩環境之下從事生理相關研究，並且於碩士論文階段給予我許多正面的鼓勵與指導；感謝台大 葉德銘教授在環境工程領域的知識指導，使我的碩士論文在環境調控的知識更加廣泛；感謝 曲在雯教授奠定我扎實的生理學知識，並且於碩士口試階段給予我許多實驗設計的建議，引領我想像出更多的實驗架構。感謝所有口試委員的支持，有您們的肯定是我在研究階段繼續前進的動力。

感謝碩士階段幫助過我的朋友以及 VBM Lab 成員們，有您們的支持與陪伴使我的研究生涯不孤單。尤其感謝柏明學長與岱凌學姐的帶領，使我初踏入交大生醫工程研究所能夠很快地進入狀況，在您們的細心呵護與照料之下，專心的作研究；感謝朱朔嘉學長的引領，使我得以順利架設實驗儀器。最後則是要特別感謝我的父母與家人，有您們的支持使我無後顧之憂。

Contents

Lists of figures

Lists of tables

Chapter 1. Introduction

1.1 Background and Motivation

Indoor environmental quality simply refers to indoor air quality (IAQ) in confined spaces. Individuals generally spend 90% of their time inside buildings. Maintaining suitable IAQ is vital to human health. The US Center for Disease Control and Prevention announced many introductions and definitions for indoor air pollution and respiratory health. The most common indoor pollutants are suspended particles, organic matter, formaldehyde, carbon dioxide (CO_2), carbon monoxide, and ozone. The main factors associated with maintaining a suitable IAQ in confined space are temperature, humidity, and ventilation. If an individual remains inside a room with poor ventilation for a prolonged period, for example, 69 days underground in Chile's San Jose mine at 2010 or classroom window keeping closed with cold outside, the CO_2 concentration (C_{CO2}) increases over time.

The American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAEs) has recommended limiting indoor C_{CO2} to 1000 ppm for long-term sustainability [1]. Researchers have also established that a 10000 ppm C_{CO2} level absolutely causes breathing dysfunction [2], and a 1000 ppm indoor C_{CO2} level in office reduces employee productivity, and increase suffering dizziness, sweating, restlessness, disorientation, and visual distortion symptoms [3-4]. Other studies indicated that classroom without sufficient ventilation (i.e. 25 L s^{-1} per person) can reduce students learning ability, attention, and memory [5-9]. Hence, C_{CO2} can be treated as an IAQ index. For instance, this index can be applied to identify comfortable indoor conditions and reduce the amount of energy used by air-conditioning systems [10].

1.2 Indoor Air Quality

IAQ was defined in 1960s as a term referring to the air quality within and around buildings and structures, especially as it relates to the health and comfort of building occupants. The indoor air pollution sources that release gases or partials into air are the air quality problems in indoor. Poor ventilation can increase indoor pollutant levels by not bringing in enough outdoor air and by not carrying out indoor air pollutants. If too little outdoor air enters indoor room, pollutants can accumulate to levels that can pose health and comfort problems. Sick building Syndrome (SBS) was defined in 1970s as one of the term referring to the health problems in individual's place of work, e.g., office building or residence. Indicators of SBS include the acute discomfort, e.g., headache, eye, nose, or throat irritation, dry cough, itchy skin, dizziness, difficulty in concentration, fatigue, etc. Solutions to SBS usually include combinations of pollutant source removal or modification, increasing ventilation rates, or air cleaning.

A 1984 World Health Organization Committee report suggested that up to 30% of new and remodeled buildings worldwide may be the subject of excessive complaints related to indoor air quality (IAQ). Often this condition is temporary, but some buildings have long-term problems. Frequently, problems result when a building is operated or maintained in a manner that is inconsistent with its original design or prescribed operating procedures. Sometimes indoor air problems are a result of poor building design or occupant activities.

In 1992, there was an international association founded about IAQ and named as International Society of Indoor Air Quality and Climate (ISIAQ). ISIAQ is an international, independent, multidisciplinary, scientific, organization whose purpose is to support the creation of healthy, comfortable and productive indoor environments. We strongly believe this is achievable by advancing the science and technology of indoor air quality and climate as it relates to indoor environmental design, construction, operation and maintenance, air quality measurement and health sciences. Additionally, there were many researches about the effect between indoor air conditions and human responses. Some researchers investigated human learning/ working ability, attention, or memory in the classes or offices [25-28]. Notably, physiological mechanisms are also the important issues from human responses, so that many scientists investigate physiological responses more detail than the performance of human activity responses.

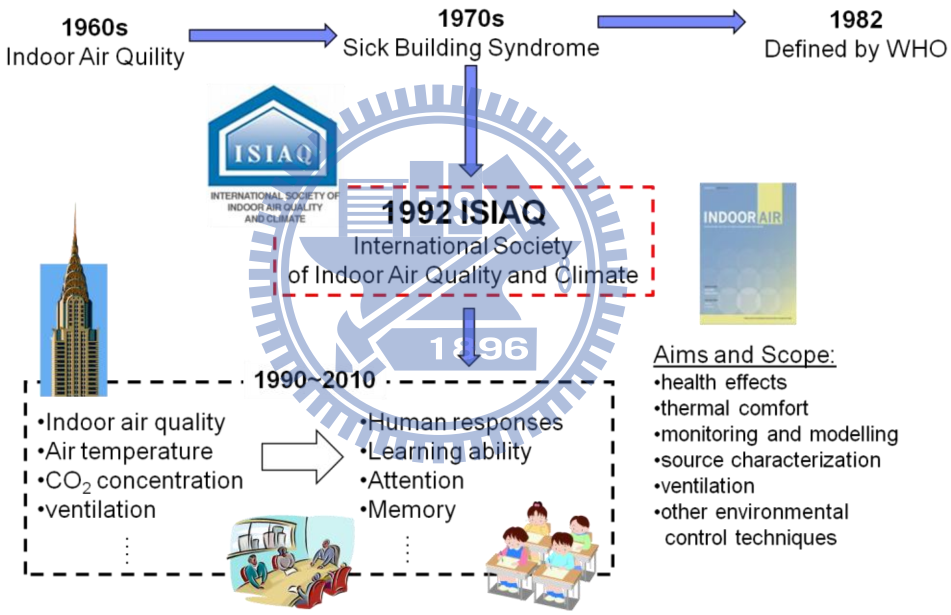

Fig. 1 The evolution of indoor air quality

1.3 Physiological issues for IAQ

In the medical field, physiologists have studied the relationships between ventilation rate and C_{CO2} and health, perception, and other human outcomes [4, 15, 18]. A high C_{CO2} level can adversely affect respiratory function and cause excitation, followed by depression of the central nervous system. Based on respiratory function, a high C_{CO2} level increases CO_2 partial pressure of alveolar CO_2 from respiratory tract [32] and may increase partial pressure of arterial CO_2 by alveolar ventilation [34]. Located on the ventral surface of the medulla, the central-chemoreflex can detect the changes in blood vessels and increase the respiratory rate. Additionally, the central-chemoreflex can also stimulate respiration and modulate body temperature to protect humans [2, 3, 6, 13]. Some animalistic experiments shown that the integrity of the serotonin (5-HT) system is essential to central nervous system and contributes to mechanisms of homeostatic control [31]. 5-HT neurons provide a major role to respiratory control network, most likely as CO_2/pH chemoreceptor. In thermoregulatory mechanism, 5-HT neurons also control for heat production and/or heat conservation [21-22]. Thus, respiratory and thermoregulation mechanism are linked closely to balance physiological circulation, defending the changes from external environment. If we want to discuss the interaction between environmental conditions (e.g., C_{CO2}) and human physiological responses, respiratory and thermoregulation mechanisms are all of important factor to be observed.

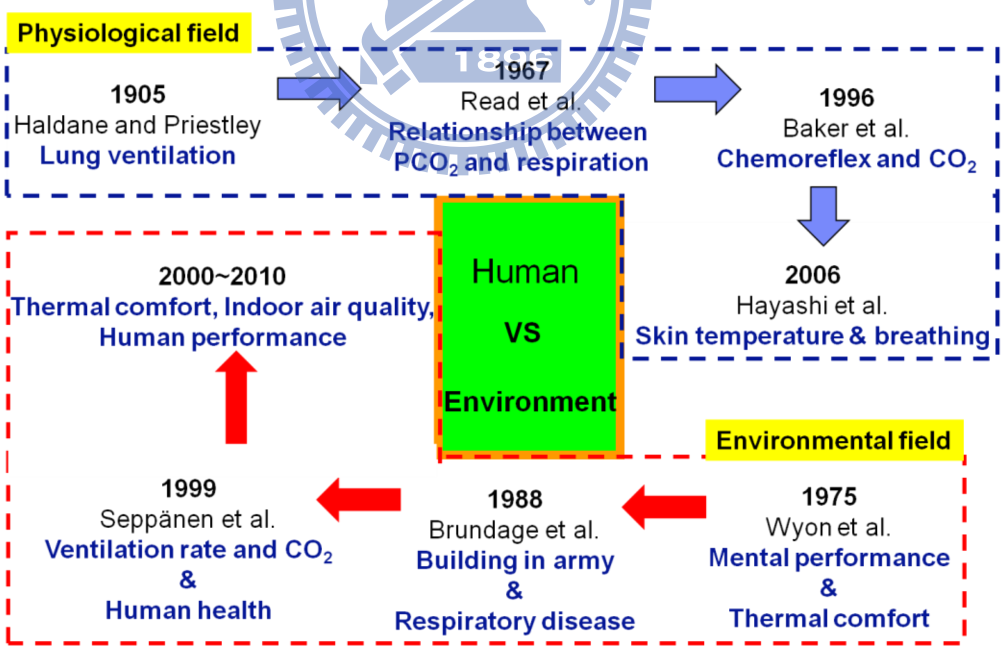

Fig. 2 The evolution of physiological issue for human health and environment

1.4 Proposed Hypothesis (Research Framework)

Although above studies demonstrated that environmental C_{CO2} induces physiological responses, an airtight environment has not been discussed thoroughly. Some physiologists have investigated how thermoregulation and environments are related, indicating that thermoregulation can be linked to race, gender, age, and perception. Additionally, different physiques respond differently to changes in air temperature (T_a). However, to our knowledge, exactly how C_{CO2} affects physiques respond has not been investigated experimentally [9, 11, 14, 19].

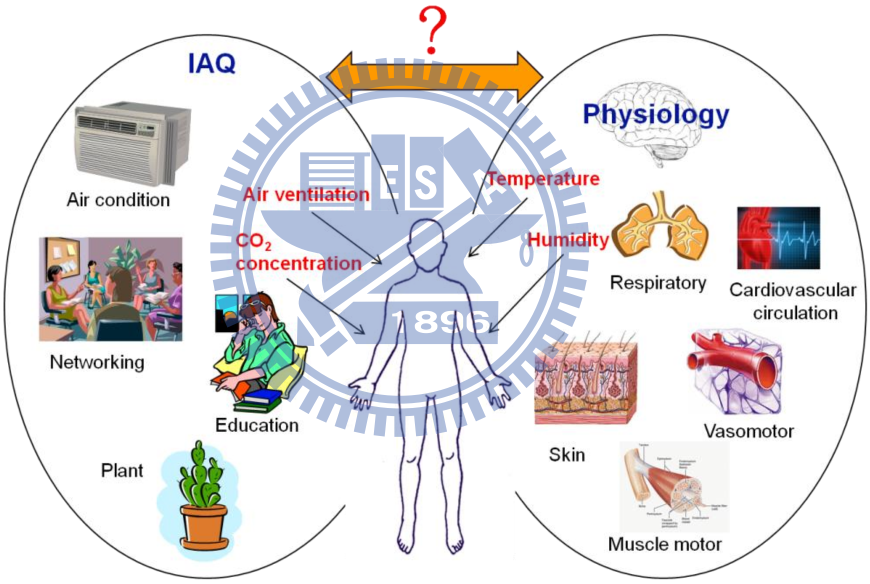

Fig. 3 The research proposed of interaction between IAQ and physiological responses

The proposed key point is shown above, which investigate how the environmental conditions influence physiological responses, how the physiological responses let environmental conditions changed, and the circulation between environment and human body. To verify these purposes, this thesis will hypothesize that C_{CO2} and T_a increased by un-controlled ventilation to lead negative influence of human physiological performance, and the variations of C_{CO2} or T_a will drive thermoregulation to inspirit protective mechanism in human body. The hypothesis in this study is human in the poor ventilation environment will lead to negative effect, and the variations of environmental conditions can be modeled by fundamental experiments.

1.5 Objectives and thesis Organization

The purpose of this study is to examine the interaction between IAQ and human physiology, as the fundamental study focused on the variations of environmental conditions and physiological responses. The main focus of this thesis is to develop equations of C_{CO2} and T_a, and examine the human electrocardiography (ECG), saturation of percentage oxygen (SpO_2), and facial temperature (T_f) based on increased C_{CO2} and T_a under fixed humidity.

This thesis is separated into five chapters. The first chapter introduces the background knowledge of IAQ and physiological research field, and proposes the hypothesis and object for this study. Chapter 2 introduces the material and method of experiments, and introduces the analysis method for this thesis. Chapter 3 is the main section, focusing on present the experimental results from environmental and physiological experiments. Chapter 4 is according to chapter 3 to discuss the results of experiments and demonstrate some findings in this thesis. The last chapter concludes this thesis according to above chapters, and describes the contributions and applications of this study works. The further and future works are also demonstrated finally.

Chapter 2. Materials and Methods

2.1 Structure of Research

In order to investigate the interactions between environment and human physiology, the variation of environmental conditions is important to be concerned. Hence, this study design a long term environmental experiment to study the variations of C_{CO2} and T_a, based on this fundamental experiment, it has enough understanding to occupied with human experiment. When human in poor ventilation environment, the C_{CO2} and T_a will be increased by human respiration, and physiological issues could be observed. Modeling, t-test, and analysis of variance (ANOVA) are applied to investigate the relationship between IAQ and human physiological responses.

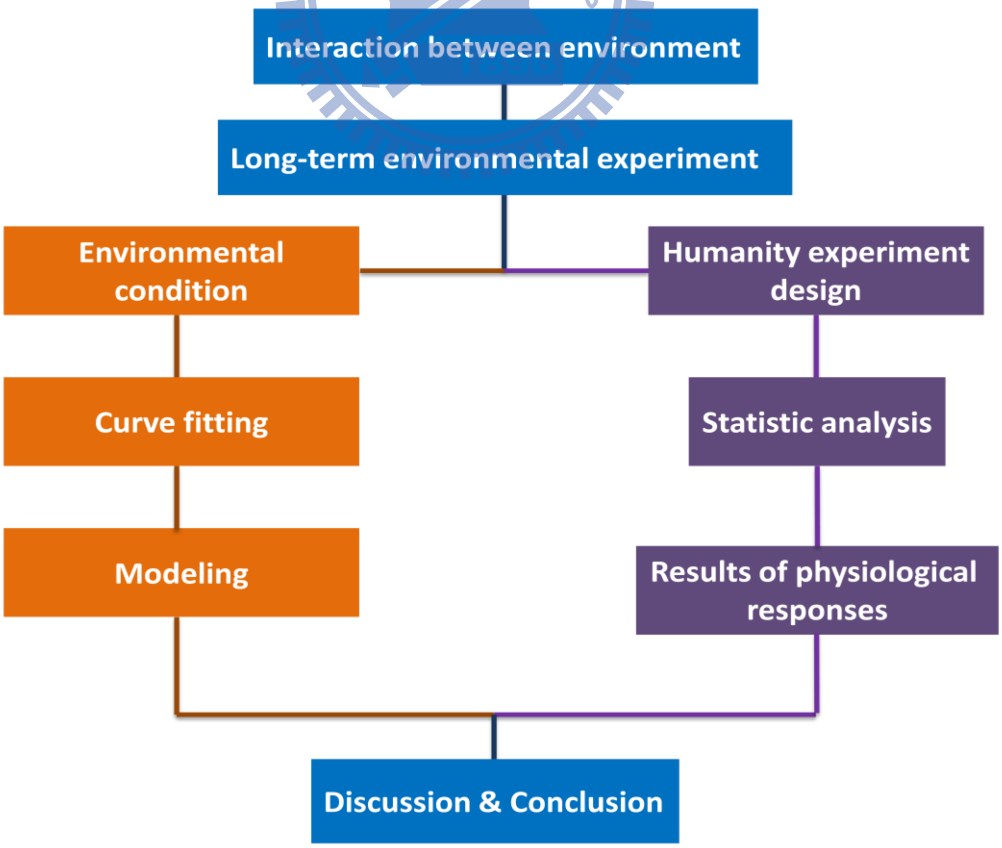

Fig. 4 The overview of experiment setting and applied methods

2.2 Experimental instruments and procedure

Figure 5 is the experimental environment. In order to having stabilization for subjects and indoor environment, the experiment was conducted in an Electromagnetic Interference (EMI) shielding room (Acoustic Systems, Inc., Austin, USA) isolating subjects without any external stimulus and eliminating unexpected signal interference and electrical noise (shielding effectiveness per IEEE-299: 100 dB, 10 kHz–40 GHz). Structure of room (2.13 m long × 2.74 m wide × 2.42 m high) is sealed off completely, and just has single air outlet to control airflow passing. The hermetic character and single air outlet can be treated as a poor ventilation environment under fixed indoor gas exchange rate. Although some research indicated that indoor ventilation rates which is up to about 25 L s^{-1} per person, is associated with reduced prevalence of sick building syndrome (SBS) [20], but the room ventilation rate is controlled to be lower than 12.5 L s^{-1} for simulating a poor ventilation environment. Indoor T_a and C_{CO2} were monitored by a commercial hand-held computerized CO_2 monitor (ZG-106; Radiant Innovation, Inc., Hsinchu, Taiwan) and located at air entrance, air exit, and indoor instrument placement. The T_f was captured non-contactly by an infrared camera (IR FlexCam; Everett, USA). The ECG and SpO_2 were acquired simultaneously by ECG recorder and digital pulse oximeter respectively (OSTAR Meditech Corp., Taipei, Taiwan).

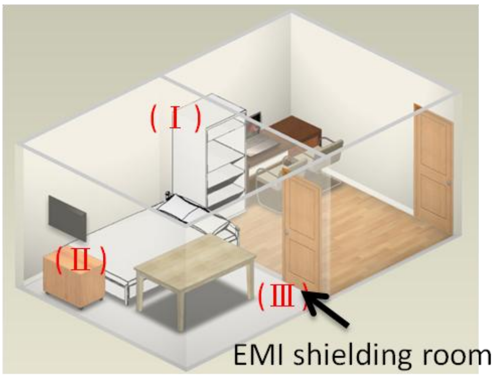

Fig. 5 Monitoring environmental conditions, three commercial hand-held computerized C_{CO2} monitors were used. Monitor I, II, and III were located at air exit, indoor instrument placement, and air entrance respectively.

This thesis was submitted to the Institutional Review Board, National Taiwan University Hospital, Hsinchu Branch. To investigate the interaction between IAQ index (especially T_a and C_{CO2}) and humans, the experimental procedure was divided into two phases for long-term environmental monitoring and humanity experiment. At first phase, indoor T_a and indoor C_{CO2} were monitored every 7 seconds without/with humans during 12- and 2-hour experiment periods. The purpose of 14-hour environmental monitoring is to discriminate the variation of environmental conditions without/with human, and to become the references for humanity experiment.

Fig. 6 Two experimental procedures. The first managed the environmental index for 14 hours in an airtight room 251.5 cm long × 191 cm wide × 196 cm high. The second procedure monitored physiological signals of subjects for 1 hour.

The second phase was to simultaneously record physiological signals. In total, 6 males and 4 females healthy volunteers were used in this phase. All subjects were selected randomly with no history or evidence of cardiac or pulmonary diseases, whose age ranged between 20 and 35 years (mean ± one standard deviation (SD) is 26±5 years), height was 168.2±6.8 cm, and weight was 64.0±16.2 kg. Before experiment, subjects gave written informed consent for the experimental protocol, which included an individual physiological baseline test. The experiment implemented 1 hour in afternoon at about 14:00-16:00. One subject stays in this room and plays puzzle game per trial for 1 hour in each trial. The T_a, C_{CO2}, electrocardiography (ECG), SpO_2, and T_f were acquired continuously during each trial.

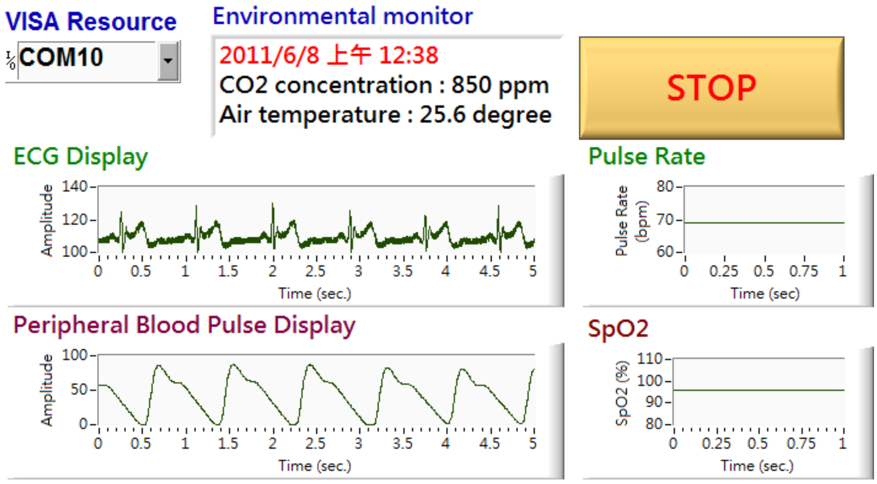

Fig. 7 The user interface of the recording system

2. 3 Analysis methods

The analysis methods which include modeling, ANOVA, and t-test were applied to examine the relationship between different C_{CO2} and human physiological responses. To investigate how the different C_{CO2} affect in cardiovascular system, R peaks to R peaks interval (RRI) were calculated from ECG signals. All values are given as mean ± SD. Comparison between groups was analyzed using a one-way ANOVA to analyze RRI variation from low (600-800 ppm) to high (800-1200 ppm) C_{CO2}, selecting half of time in the experimental period to separate low and high C_{CO2} in this stage. This study also used one sample t-test to examine whether the means of two groups are statistically different from each other. Significance was established at $P < 0.05$. According to the variation of SpO_2 depends on C_{CO2} changes over time, SpO_2 observes to different C_{CO2} and estimated to 0.01%. The variations of T_f also be concerned, the regression method which denotes as $\hat{y}_i = f(x_i)$ can find the trend about the interaction between C_{CO2} and T_f.

2. 3. 1 Statistic analysis

One-way ANOVA is a method of testing the equality of three or more population means by analyzing sample variances. It is the method for testing hypothesis that three or more population means are equal, so a typical null hypothesis will be H_0 and the alternative hypothesis (H_1) will be the statement that at least one means is different from the others. Based on sample means, ANOVA is also one of method to discuss the variance between and within samples.

$$H_0: \mu_1 = \mu_2 = \mu_3$$
$$H_1\text{:at least one means is different}$$

The ANOVA method is based on F distribution, which is a continuous probability distribution. The F distribution arises frequently as the null distribution of a test statistic, most notably in the ANOVA. Although the details of the calculations are complicated, the easy way to interpret results is based on P-value. If P-value is small, such as 0.05 or lower, reject equality of means. Otherwise, fail to reject equality of meas.

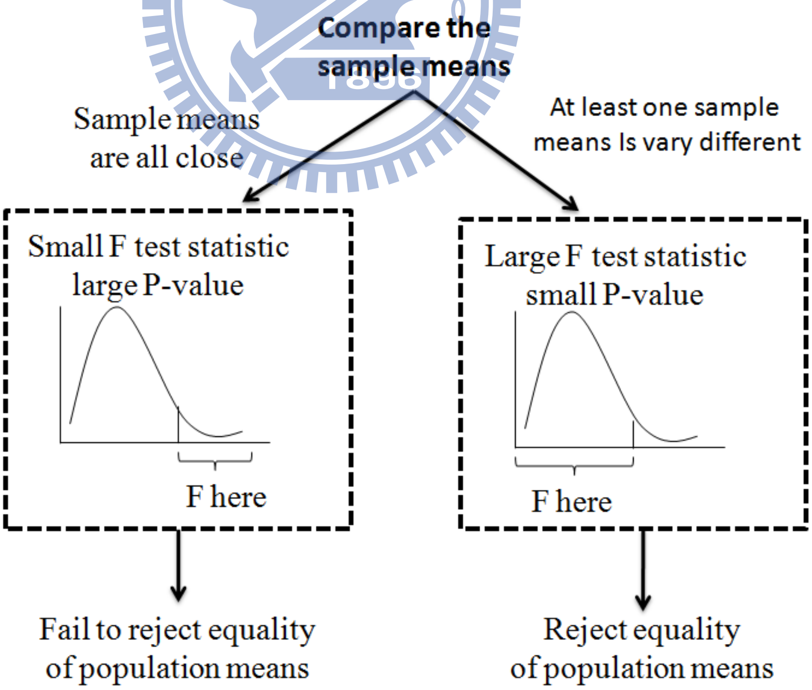

Fig. 8 Relationship between F test and P-value

2. 3. 2 Curve fitting & Correlation

The main object of curve fitting is to describe the association between C_{CO2} samples by finding the graph and equation of the straight line that represents the association. This straight line is called the regression line (or best fit, or least-squares line), and its equation is called the regression equation. The simple regression equation is show as equation (2) [23].

$$\hat{y} = f(t) = b_0 + b_1 t \tag{1}$$

Where b_0 is y-intercept and b_1 is slope.

Regression equations are often useful for predicting and modeling the value of one variable, given some particular value of the other variable. If the regression line fits the data well, then it makes sense to use its equation for predictions, provided that we don't go beyond the scope of the available values [23].

The correlation is to analyze a collection of paired sample data and determine whether there appears to be an association between the two variables. A correlation exists between two variables when one of them is related to the other in some way. The linear correlation coefficient R measures the strength of the linear association between the paired x- and y-quantitative values in a sample. Its value is computed by using equation (1). The linear correlation coefficient is sometimes referred to as Pearson product moment correlation coefficient in honor of Karl Pearson (1857-1936), who originally developed it.

$$R = \frac{n\sum xy - (\sum x)(\sum y)}{\sqrt{n(\sum x^2) - (\sum x)^2}\sqrt{n(\sum y^2) - (\sum y)^2}} \tag{2}$$

Where n represents the number of pairs of data present, x is x-values, y is y-values, and R is the linear correlation coefficient for a sample. The value of R is always between -1 and +1 inclusive. Additionally, the value of R^2 is the proportion of the variation in y that is explained by the linear association between x and y.

This research used conception of regression to model environmental condition, and used correlation coefficient to verify the accuracy between samples and modeling regression. The following equation demonstrates the correlation coefficient (R) between samples and modeling regression,

$$R = \frac{n\sum \hat{y}_i y_i - (\sum \hat{y}_i)(\sum y_i)}{\sqrt{n(\sum \hat{y}_i{}^2) - (\sum \hat{y}_i)^2}\sqrt{n(\sum y_i{}^2) - (\sum y_i)^2}} \quad (3)$$

where y_i is samples value, and $\hat{y}_i$ is the modeling value.

Chapter 3. Results

3. 1 Environmental conditions

3. 1. 1 Measurement

According to the kinetic theory of gases, molecules with diameters less than 0.04×10^{-2} m are subject to classical Brownian motion [16]. Gas collision in the room and the collision rate was determined by room volume, pressure, and temperature. The mass of gas molecules also affects the collision rate. Generally, root mean square velocity (V_{rms}) can be used to determine the collision rate for gas particles. The gas diffusion rate is derived as

$$V_{rms} = \sqrt{\frac{3kT}{m}} = \sqrt{\frac{3RT}{M}} \tag{4}$$

where *k* is a Boltzmann constant (1.38×10^{-23} J K^{-1}), *R* is an Idea Gas constant (8.31 J mol^{-1} K^{-1}), *T* is air temperature (K) in room, *m* is the mass of gas molecules, and *M* is standard molar mass (44×10^{-3} g for CO_2 molecules). Since air consists of nitrogen (78%), oxygen (21%), and CO_2 (0.03%), the V_{rms} of CO_2 is 412.3 (m s^{-1}) in a 23℃ environment and 415 (m s^{-1}) in a 31℃ environment (Fig. 9), indicating that CO_2 diffuses rapidly. The collision rate was roughly 100 times per second. Therefore, we infer that this experimental environment can reach equilibrium on the scale of human response. Additionally, the humanity experiment was driven by 23 - 31℃, and subjects can feel normal as daily life.

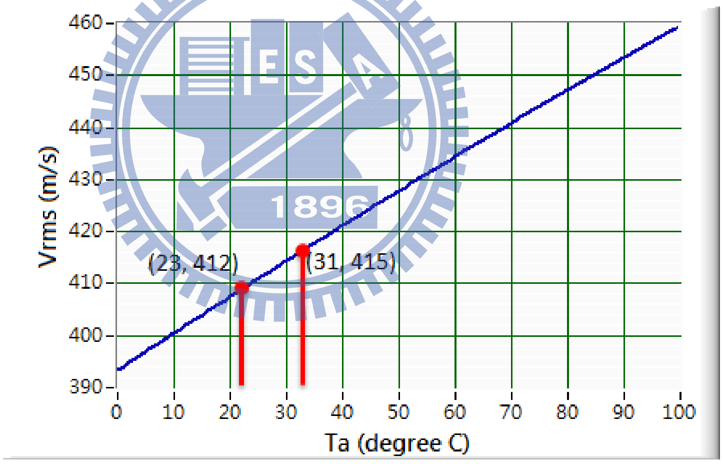

Fig. 9 Collision rate for gas particles between 0-100 ℃. This thesis drive 23-31 ℃ to do humanity experiment.

The entrance and exit of air and indoor instruments placement were considered the variations of C_{CO2} and monitors were placed at these locations (Fig. 5). Figure 10 shown the C_{CO2} time series of three monitors at first phase for long-term environmental monitoring. The C_{CO2} of environmental condition were monitored without human for 12-hour period (t_0-t_1) and with human 2-hour period (t_1-t_2). The mean ± SD of C_{CO2} started from 616±23 ppm (t_0 represented the time after finishing instruments setup), decreased to 428±25 ppm (t_1

represented the time before human inside), and increased to 712±25 ppm (t_2). Table 1 summarized the results of C_{CO2}, T_a, and ventilation rate at different indoor conditions. The results showed that C_{CO2} decreased to steady state (about 400 ppm) without human and increased when human inside. Human respiration is one of most important factors affecting C_{CO2} in the room (IAQ) if it's without any other pollution source.

Table 1 Indoor conditions include C_{CO2}, T_a, and Ventilation rate in different status.

Factor of IAQ / Status	C_{CO2} (ppm)	T_a (℃)	Ventilation rate (L s^{-1} per person)
t_0	616±23	30.55±0.83	~12.50
t_1	428±25	27.01±0.49	~25.00
t_2	712±25	30.78±0.92	~12.50

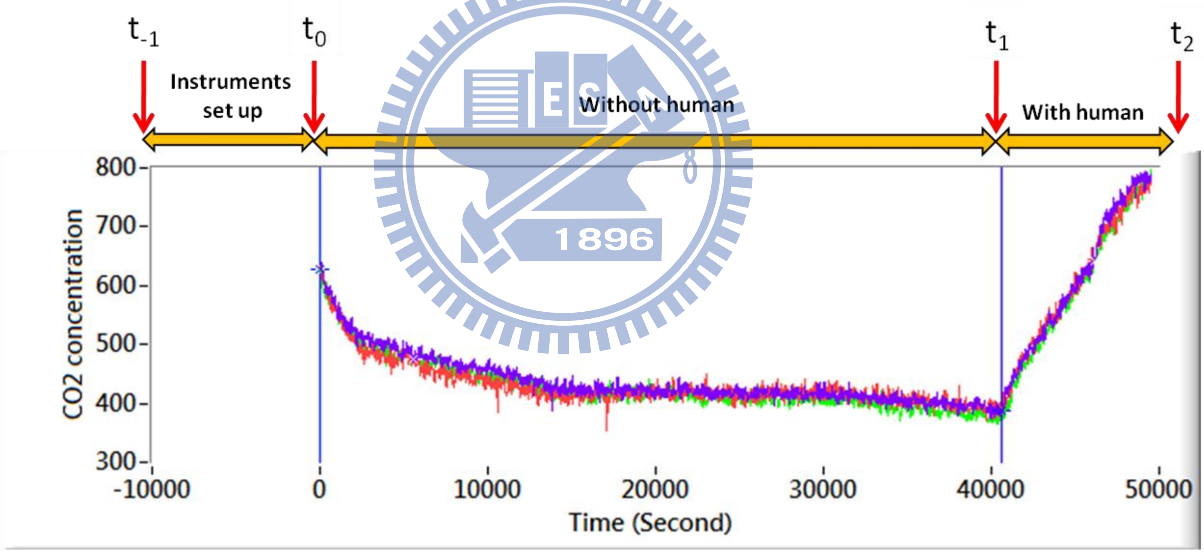

Fig. 10 The C_{CO2} variations of different environmental conditions for 14 hours. The x-axis represents time and the y-axis represents the CO_2 concentration. Instruments set up are from t_{-1} to t_0, monitors start to measure from t_0, and human entrances to stay at airtight environment from t_1 to t_2.

This study calculated the SD of three monitors' results to study on the confidence in three different areas. SD is a widely used measurement of variability or diversity used in statistics and probability theory. It shows how much variation or dispersion there is from the average (mean, or expected value). In addition to expressing the variability of a population, standard deviation is commonly used to measure confidence in statistical conclusions. In environmental experience result indicated that the SD distribute Gaussian distribution, and the mean of SD is 9.34, the variations presented the uniform distribution, and have the stable environment (Fig. 11).

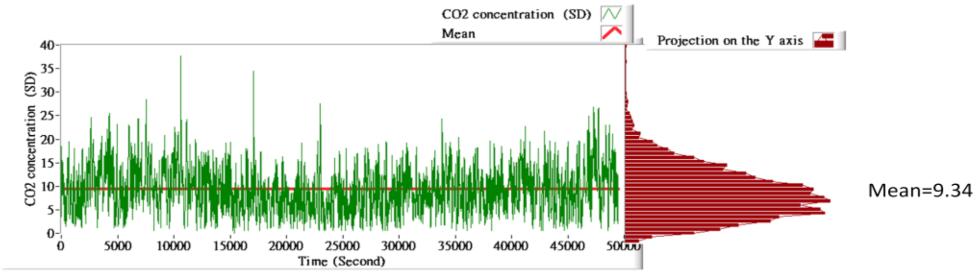

Fig. 11 The standard deviation (SD) of three C_{CO2} monitors.

3. 1. 2 Modeling

Notably, the fluctuation of C_{CO2} in environment is exponentially increasing and decreasing. It is individual difference, since the C_{CO2} increased to a steady state when indoor with human and the extent of increasing depends on population, human activity, and metabolism rate in the environment [33]. Additionally, when indoor environment is without human, the C_{CO2} in indoor and outdoor environment is equal to 428 ppm (Fig. 9(b)). Based on above conditions, this study modeled the exponential growth and decay (Eq. (5)) to fitted the C_{CO2} fluctuation when one human stay in the environment or without any human (Fig. 12). Where value of a_0 is Where value of a_0 is amplitude (+ is down, - is up), b_0 is power index (0.0001), and c_0 is extreme value.

$$y = f(t) = a_0 e^{-b_0 t} + c_0 \tag{5}$$

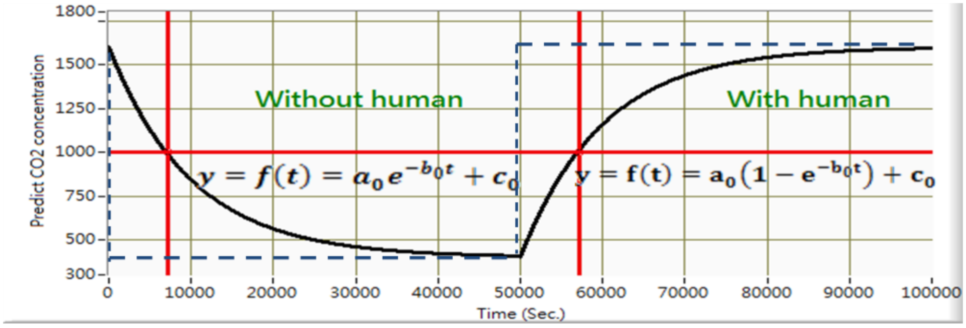

Fig. 12 Exponentially increasing and decay of C_{CO2}. The C_{CO2} increased to a steady state when environment with human and decay to 400 ppm when environment without human.

Table 2 indicates the performance of modeling by using minimizing root mean square error (RMSE) which was created according to the result of Fig. 10, and three critical parameters (a_0, b_0, and c_o) are similar each other, and indicate highly correlated between model and measurement ($R > 0.92$).

Table 2 The performance of modeling is correlated between model and measurement ($R > 0.9$).

Critical value / monitor	**Without human**				**With human**			
	a_0	b_0	c_o	R	a_0	b_0	c_o	R
I	243.13	-0.00011	399.61	0.92	-356.29	-0.00023	795.58	0.99
II	282.42	-0.00010	398.78	0.97	-397.83	-0.00023	814.33	0.96
III	263.57	-0.00011	391.83	0.97	-330.07	-0.00032	738.30	0.99
(I+II+III)/3	248.09	-0.00015	404.17	0.97	-332.57	-0.00031	752.65	0.97

The performance of model is show as Fig. 13 and is confidence to predict the variations of environmental conditions and can be referenced to design humanity experiment. According to above model, the half period of C_{CO2} growth is the stage C_{CO2} increase intensely and this period need one hour approximately. Hence, this study designed one hour to do humanity experiment to investigate the interaction between environment and human responses.

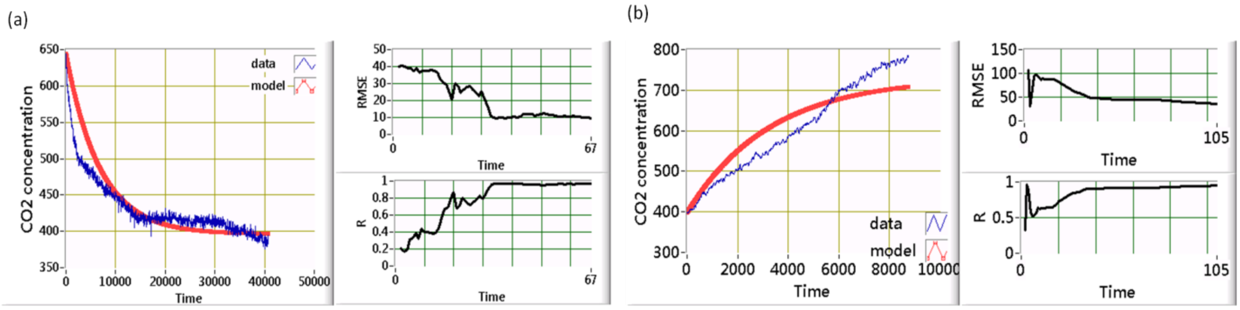

Fig. 13 The performance of model is based on root mean square error (RMSE) and indicates the highly correlated between model and measurement (R > 0.9).

According to above model, the half period of C_{CO2} growth is the stage C_{CO2} increase intensely and this period need one hour approximately. Hence, this study designed one hour to do humanity experiment to investigate the interaction between environment and human responses (Fig. 14) . And the appropriate initial C_{CO2} sated in 600 to 700 ppm for humanity experiment.

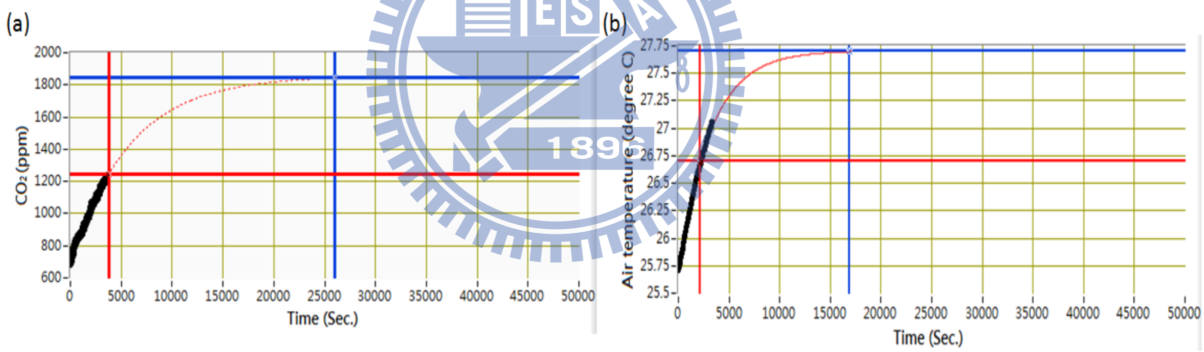

Fig. 14 The half of growth to steady state need one hour approximately so that this study designed one hour to do humanity experiment. (a) C_{CO2} and (b) T_a.

3.2 Physiological responses

The appropriate initial C_{CO2} sated from 600 to 700 ppm for humanity experiment. 10 subjects but only three subjects were successfully to analysis. The C_{CO2} is 700–1200 ppm and T_a is 25-27 ℃ in the humanity experiment. The C_{CO2} was divided into the following three levels: low, medium, and high, according to the variation of T_f in three subjects are distributed especially into three stages, increased rapidly, steady-state, and increased slightly (Fig. 15(b)).

Physiological responses in this section demonstrate the study on C_{CO2} and SpO_2, heart rate, and T_f separately.

3.2.1 CO_2 and SpO_2

Different C_{CO2} phase changes in SpO_2 (%) were compared. Table 3 demonstrates more detail results about three different C_{CO2} phase changes in SpO_2 analyzed by one –way ANOVA. The p-value is smaller than α (0.05), it is significant difference in three different subject. The C_{CO2} and SpO_2 had an inverse relationship, the environmental C_{CO2} increased but SpO_2 decreased in peripheral body. The response is typically in hypercapnia. Hypercapnia is the condition in which dissolved oxygen is below the level necessary, and the oxygen in blood is insufficient. The ventilatory response to carbon dioxide is mediated by central and peripheral chemoreflexes. The term chemoreflex consists of the chemoreceptors, their afferent connections to the respiratory neurons in the medulla, medullary processing, the descending output to the respiratory motoneurons in the spinal cord, the efferent nerve connections to the respiratory muscles and the production of pulmonary ventilation [29].

Table 3 Results of three different C_{CO2} phase changes in SpO_2 (%).

C_{CO2}	Subjects	SpO_2 (ms) within subject	SpO_2 (ms) between Subject
Low CO_2 (<800 ppm)	A	96.37±3.84	97.74±1.20
	B	98.24±1.10	
	C	98.60±26.26	
Mid. CO_2 (800-1000 ppm)	A	97.23±3.97	97.20±0.13
	B	97.32±1.28	
	C	97.06±0.06	
High CO_2 (>1000 ppm)	A	97.23±2.95	96.99±0.29
	B	96.67±0.49	
	C	97.09±0.08	

3. 2. 2 CO_2 and Heart rate

The extent to which environmental changes impact the heart was also a key observation. Therefore, HR with RRI was subjected to a t-test to examine differences among the three C_{CO2}. Experimental results show that RRI for the high C_{CO2} was slightly shorter than that for low C_{CO2} (Table 3), indicating that subjects had a faster HR in the high C_{CO2} environment. Increased HR can increase cardiac output to improve blood circulation in the lungs for rapid gas exchange, such that the blood contains sufficient oxygen.

Table 4 The differences in R-R intervals for low and high CO_2 concentrations.

C_{CO2}	Subjects	RRI (ms) within subject	RRI (ms) between Subject
Low CO2 (<800 ppm)	A	13.55±1.42	15.27±3.23
	B	13.26±0.68	
	C	19.00±0.97	
Mid. CO2 (800-1000 ppm)	A	13.41±0.34	15.17±3.09
	B	13.35±0.98	
	C	18.74±0.96	
High CO2 (>1000 ppm)	A	13.51±1.15	15.04±3.01
	B	13.11±0.64	
	C	18.52±0.93	

3. 2. 3 CO_2 and Facial Temperature

Notably, T_f increased as C_{CO2} increased and were correlated ($R=0.953$; $R^2=0.908$) (Fig. 15(b)). The T_f results were significantly different for the low and high C_{CO2} ($p < 0.0005$) (Fig. 15(a)). Thus, C_{CO2} induced body temperature changes. Fig. 15(b) also shows the impact of C_{CO2} on subjects. One subject's T_f increased due to increased C_{CO2}. Additionally, T_f increased as C_{CO2} increased and stabilized at roughly 37℃. When C_{CO2} continued increasing, T_f also increased; however, no subject developed hyperthermia (>38℃). Maintaining a normal body temperature (36–37.5℃) is an internal protection mechanism.

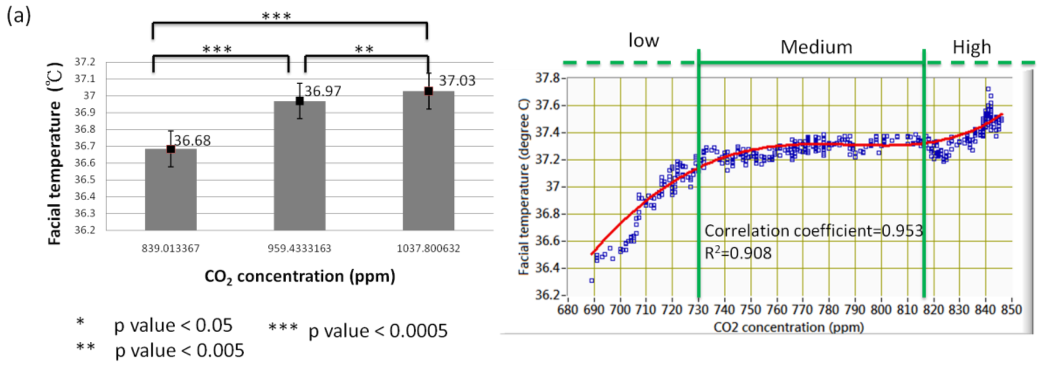

Fig. 15 The x-axis is C_{CO2} (ppm) and the y-axis is facial temperature (°C). (a) T_f increased as C_{CO2} increased. (b) One subject's T_f changed due to the C_{CO2} increase. The C_{CO2} was divided into the following three levels: low, medium, and high based on the T_f of subjects are distributed into three stages.

Differences between T_f and T_a increased under low C_{CO2}, and then reversed and stabilized with 1 hour (Fig. 16). The pattern of this change reveals that the antagonistic relationship between T_f and T_a is excited in the first stage and finally stabilizes. Above experimental results further suggest that the body responds the changes in the external environment and adapted to these changes, reaching an equilibrium state within a short time.

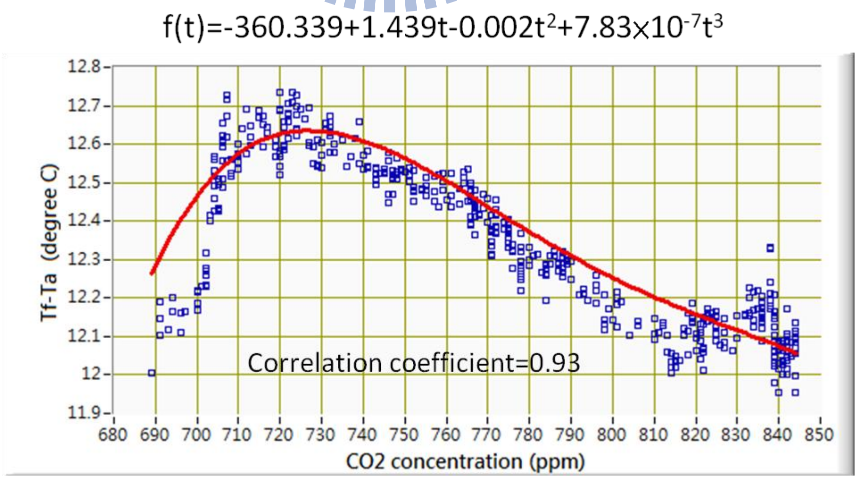

Fig. 16 Differences between T_f and T_a increased under low C_{CO2}, and then reversed and stabilized with 1 hour.

Chapter 4. Discussions

According to above results, there are many issues can be discussed. This section will separate into environmental conditions and physiological responses to discuss results of this thesis and infer the interaction between environment and human physiology.

4. 1 Effect in environmental conditions

This thesis simulated the un-controlled environment to model the variation of C_{CO2} and verify some humanity experiments (ventilation rate is 50 cfm=1.415×10^6 ml/min.). In the section 3.1.2 demonstrates the model of C_{CO2}, and Eq. (5) result the variation of C_{CO2} when environment with human. To investigate increased situation of C_{CO2}, this thesis demonstrate the increase rapidly period when half of C_{CO2} growth to steady state, and there are following three statuses to be discussed the required time of increase to steady state. The driving equation and discussion is according to Eq. (5).

$$y = f(t) = a_0 \times \left(e^{-b_0 t}\right) + c_0$$

$$\text{when } y = \frac{1}{2}(a_0 + c_0) \rightarrow t_{\frac{1}{2}}$$

$$\frac{1}{2}(a_0 + c_0) = a_0 \times e^{-b_0 t_{\frac{1}{2}}} + c_0 \rightarrow e^{-b_0 t_{\frac{1}{2}}} = \frac{-c_0}{2a_0}$$

$$\text{when a<0} \quad \rightarrow \quad e^{-b_0 t_{\frac{1}{2}}} = \frac{c_0}{2a_0}$$

$$-b_0 t_{\frac{1}{2}} = \ln c_0 - \ln 2a_0$$

$$\rightarrow t_{\frac{1}{2}} \propto \ln 2a_0 \propto \frac{1}{b_0} \propto ln c_0 \tag{6}$$

In the normal condition, this study set the a_0 is 1200 ppm, b_0 is 0.0001, and c_0 is 400 ppm, and change these critical values (a_0, b_0, and c_0) to discuss different status. Firstly, when a_0 is increased to 2000 ppm and b_0, c_0 fixed. Since the difference between initial C_{CO2} and maxima C_{CO2} is increased by different human metabolic rate, C_{CO2} need more time to increase to steady state (Fig. 17 (a)). Secondly, when b_0 is increased to 0.001 and a_0, c_0 fixed. Exponential character lead C_{CO2} need more time to reach steady state (Fig. 17 (b)). The third status is c_0 increased to 800 ppm and a_0, b_0 fixed. C_{CO2} need less time to steady state, since initial C_{CO2} is high enough and close to steady state.

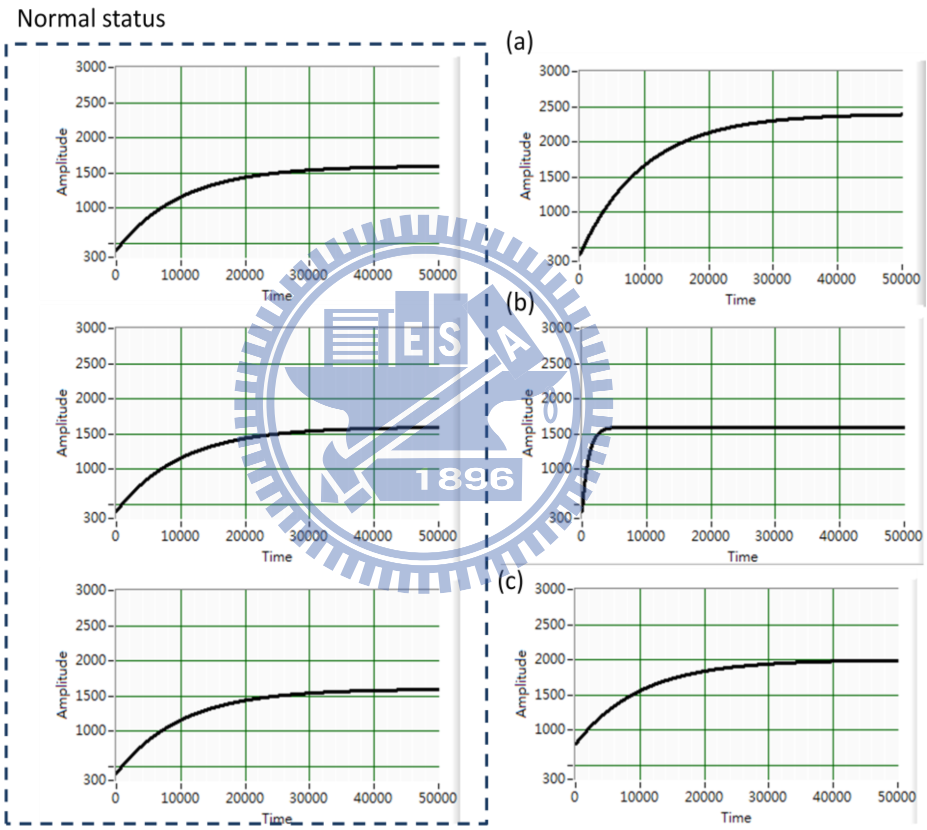

Fig. 17 Three statuses to be discussed the required time of increase to steady state. (a) a_0 is increased to 2000 ppm and b_0, c_0 fixed, (b) when b_0 is increased to 0.001 and a_0, c_0 fixed, and (c) c_0 increased to 800 ppm and a_0, b_0 fixed.

These discussed results can be used to predict different conditions in the environment clearly. Additionally, the variations of environmental conditions are affected by human metabolism in the room, and it is necessary to verify the performance of predict model by more humanity experiments.

4. 2 Physiological issues

4. 2. 1 Essential conditions for choice physiological parameters

If environmental conditions changed, hot flashes can be observed easily. Since face is located in the vicinity of central nervous system, the facial features can response endogenetic variation faithfully. Additionally, the option of monitoring a subject's physiological signals via a remote, noncontact means for improving and enhancing the delivery of primary healthcare. Currently, proposed solutions for noncontact measurement of vital signs such as using infrared camera or webcam to monitor latent variation from facial regions is one of a simple, low-cost method for measuring multiple physiological parameters [24]. Based on above reasons, this study chose facial temperature to monitor the variation of temperature on human body, and expected this method can mimic daily life.

This thesis still lack of respiratory results to discuss the respiratory responses when environmental conditions changed. End Tidal CO_2 ($ETCO_2$) is one of choice to monitor the variations of respiration. $ETCO_2$ is the partial pressure or maximal concentration of carbon dioxide (CO_2) at the end of an exhaled breath, which is expressed as a percentage of CO_2 or mmHg. The normal values are 5% to 6% CO_2, which is equivalent to 35-45 mmHg. But $ETCO_2$ was not used in this stage, since mask method let subjects feel uncomfortable, and simultaneously affect experimental results. But respiratory issues are important in this research, it is necessary in next stage to consider respiratory signals and not disrupt normal activities. Additionally, the local variation between environment and human respiration is one of novel issue, finding the influence fact of the human respiration could have positive influence for this study.

4. 2. 2 Physiological mechanisms

Figure 16 shows the systemic mechanism of the human body under poor indoor ventilation. Generally, gas exchange is rapid and based on Brownian motion and kinetic theory. Poor ventilation affects human physiological responses. In environments with high C_{CO2}, responses are manifested in breathing, metabolism, and cardiovascular system. If a human stays in an environment with high C_{CO2}, the blood SpO_2 will decrease. The chemoreceptor in blood vessels responds to environmental changes and transport information to the chemoreflex in the central medulla. The central-chemoreflex is important to responding to pH changes in blood and thermoregulation. This reflex also accelerates breathing to maintain fluid balance. As breathing can increase body temperature [20], T_f was increased indirectly. A rapid HR improves blood volume in the cardiovascular system. The effect of this acceleration of gas exchange increases in the alveolar microvasculature. The main purpose of physiological response is to supply the blood with sufficient oxygen for normal organs function. Therefore, this mechanism is an internal protective mechanism for maintaining homeostasis.

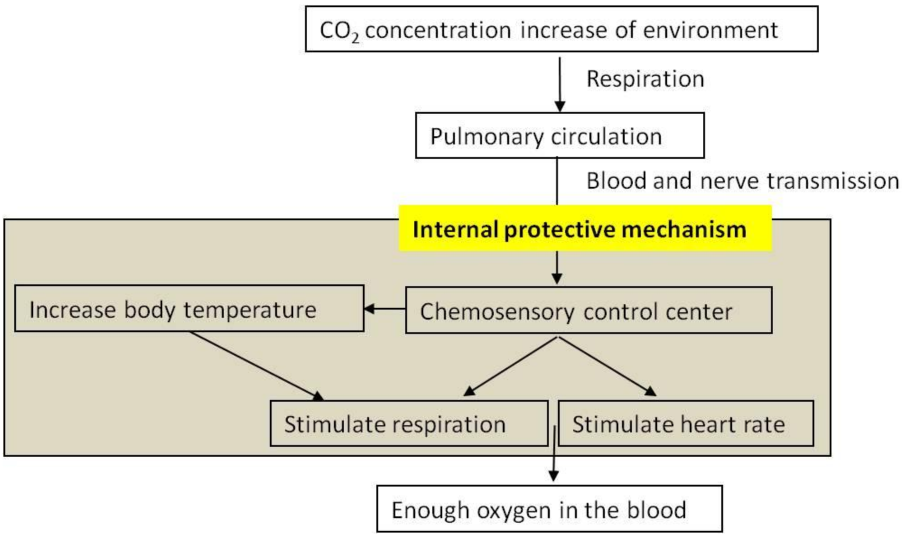

Fig. 18 The systemic mechanism of humans staying inside the poorly ventilated room

4. 2. 3 Quantity of Subjects issues

Virtually, the quantity of subject in this thesis is insufficient, doing more humanity experiments to verify the interaction between environment and human is necessary. However, doing humanity experiments need the permission from institutional review board (IRB) and observe the medical rules. IRB is a committee that has been formally designated to approve, monitor, and review biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the research subjects. In the United States, the Food and Drug Administration (FDA) and Department of Health and Human Services (specifically Office for Human Research Protections) regulations have empowered IRB to approve, require modifications in planned research prior to approval, or disapprove research. And in Taiwan, organizations of IRB locate in public or teaching hospitals, integrating doctors' professional knowledge to manage these societies.

This study will cooperate with department of internal neurology from Hsin Chu General Hospital, and the IRB project is in application. Department of internal neurology can supply and guide the knowledge of CNS, and have positive effect to help design experiments in this research topic. If it is possible, this study will design more fundamental experiments including respiratory responses, cardiovascular system, and thermoregulation to verify humanity mechanism, and expect 30 subjects in this study work.

Chapter 5. Conclusions and future work

5.1 Conclusions of environment and physiological responses

This study is the first time to use the un-controlled ventilation environment to investigate the interaction between an airtight indoor environment and human physiological responses. The most contribution in this thesis is to develop the variations model of C_{CO2} and T_a, realizing the changes of environmental conditions easily and can be used to predict the environment status. The results demonstrate the highly correlated ($R > 0.9$) between prediction and real measurement, the results is useful to design experimental environment in next stage.

In the physiological results show that SpO_2 decreased under high C_{CO2}, and the central-chemoreflex accelerated breathing in response to the pH of blood in vessels. Notably, T_f was strongly correlated ($R = 0.953$) with C_{CO2} and could be thought it is stimulated indirectly by breathing. Moreover, rapid HR improves blood volume in the cardiovascular system. Additionally, the effect of HR acceleration on gas exchange increased pulmonary circulation. All physiological responses were to achieve homeostasis and protect the body.

Based on the introduction of this thesis had disused about in vivo biomarker: 5-HT system. 5-HT system is essential to CNS and contributes to mechanisms of respiratory and thermoregulatory. But measurement of 5-HT neurons is invasively, and still in the animal experiment stage. This thesis demonstrates the method to investigate the interaction between an airtight indoor environment and human physiological responses and measure these parameters non-invasive. The proposals of physiological metabolisms and the variations in environmental conditions can be built as the important parameters in the interaction between human and environment in the future. Efforts are underway to investigate the control mechanisms of humans in an airtight or non-airtight environment. This human homeostasis study significantly contributes to apply thermoregulation systems and/or develop environmental control based on the human central-chemoreflex mechanism.

5. 2 Next research works

This thesis had finished preliminary study to proposed physiological mechanism and establishes equations to model the environmental conditions and human responses. These model parameters can be used to understand the interaction between environment and human, and it is also useful to predict how humanity affects environment and the physiological variations. However, this study still immature to verify the interaction between environment and human, it is needs much verification and experimental evidences to demonstrate the complete predict mechanisms. Therefore, the further works in the airtight environment should be controlled strictly, and detail develops equation to investigate the human physiological responses between increased and decreased C_{CO2} in the controlled environment. In the physiological experiments, responses within human body are also the interested issue in this study, so that the experiments will focus on respiratory and thermoregulation responses and local variations between environment and human. Expecting the fundamental experiments can validate this research clearly.

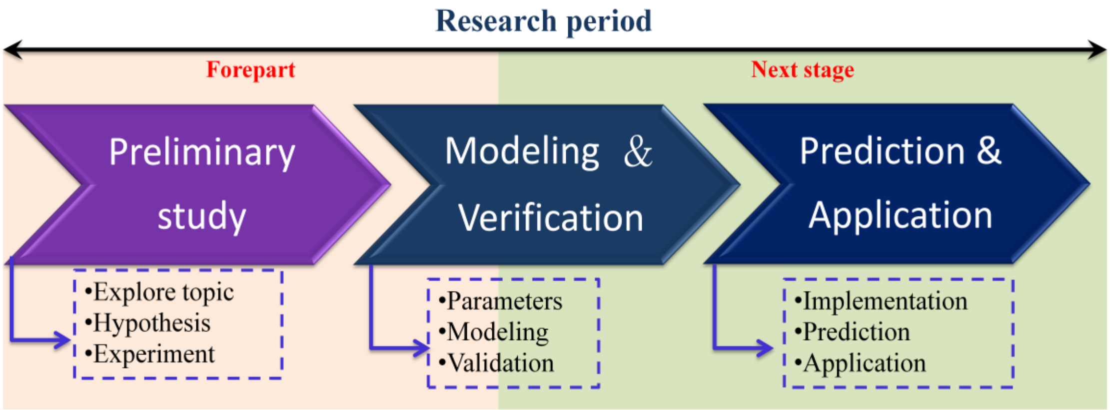

Fig. 19 The research works for forepart and next stage.

5. 3 Applications

For the physiological research, based on respiratory response and thermoregulation, it could be discussed as the fundamental physiology as the relationship and protect mechanism by non-invasive measurements. Integrating the physiological responses could be used to find the biomarker in vitro, and predict the most comfortable conditions for human body. These results also could be thought of the reference for the special occupational field such as mine for miner or the operator working in airtight environment. Additionally, the applications of respiratory responses and human mental performance affect human activity including learning, memory, decision making, etc. is also the interested issues in environmental science field.

The equations in this research could be used to develop the Heating, ventilation and air condition (HVAC) system. The main purposes of a HVAC system are to help maintain good indoor air quality through adequate ventilation with filtration and provide thermal comfort. HVAC systems are among the largest energy consumers in schools, hospitals, transportations, and other public fields. If these equations could help to understand the requirement of human body successfully, it is could easier control and maintain the appropriate air quality in indoor. Additionally, the physiological responses in this study could be considered to establish the standard for IAQ. With HVAC system and standard of IAQ, it would be technically feasibility to apply the living-care in daily life.

On the other hand, indoor plants as air filter can keep air clean. Another way to have cleaning indoor air, we can place plants, because plants can absorb CO_2 and release oxygen. We can place like india rubber tree, gerbera, dot plant, nephrolepis exaltata, or African violets to reduce indoor CO_2. Recommended planting density is each 9 square meters of floor that at least place a 6-inch size plants to improve indoor air quality. It is one of the nature ways to achieve air purification function.

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Appendix 1.   Agreement for the prior study

國立交通大學 VBM 實驗室分析量測實驗

Physiological Responses to Carbon Dioxide Concentration Test Agreement

【受測者同意書】 **編號：______________**

敬啟者：

為「二氧化碳濃度個體生理狀態影響」的試驗，邀請您同意作為本研究之主要受測對象，這是一項個體生理資訊感測紀錄分析的研究，只有同意參加者才需接受此實驗測試。若您對本試驗進行的方法與步驟有任何疑問，我們願意盡可能提供進一步的解說，以其您能充分了解。

內容：

二氧化碳濃度的升高會影響人類健康，無論是血壓、心跳、體溫都受到一定程度的影響，本研究藉由封閉示環境，使環境中二氧化碳濃度增高，同時量測生理訊號，探討二氧化碳對於生理狀態的影響。

Along the path of research, excessive carbon dioxide concentrations will affect human respiration, body fluid, body temperature and other physiological responses, but the mechanism of changes in body temperature, blood pressure and heart rate have never been examined. This study provided a way to estimate underlying mechanisms of bio-regulatory states influence on carbon dioxide concentrations in an environment by utilizing information contained in body temperature and skin conductance.

試驗流程：

1. 填寫受測前問卷與同意書。
2. 採坐臥姿勢，靜待於封閉環境內，進行生理訊號擷取紀錄 60 分鐘。

確認：

☐ 此研究牽涉的範圍為個人生理資訊隱私，但作為純研究探討用，會對受測者資訊做保密，研究結果會公開。

☐ 將會對單一受試者進行長時間生理資訊量測紀錄，探討不同二氧化碳濃度的差異性與對個人生理狀態的影響。若受測者想中途停止實驗，可隨時終止。

(測試途中若深感不適，請直接推開門走出，以示終止實驗。)

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其他		

本人已詳閱上述表格及注意事項，同意受測資料紀錄分析使用與成果公開。

(簽名) ______________________________

Appendix 2. Test recording for the prior study

國立交通大學 VBM 實驗室分析量測實驗

Physiological Responses to Carbon Dioxide Concentration
Test Record

【受測紀錄】編號 ___________

日期__________________　　時間_________________

一、 受測者基本資料：

姓名		年齡	
身高		體重	
嗜好	☐ 抽煙　☐ 咖啡 ☐ 喝酒　☐ 茶類	疾病	

二、 受試前狀態(前兩小時內，可複選)

☐用餐；□工作；□睡覺；□休閒娛樂；□運動；□疲累想睡；

☐ 喝茶、咖啡；□其他_______________。

三、 受試者實驗狀態

最初二氧化碳濃度		最初溫度	
最終二氧化碳濃度		最終溫度	

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五、 其他