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Performance Evaluation through CFD Simulation and Field Measurement on a Bio-Cleanroom for Vaccine Storage

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Abstract: Modern biomedical industries are increasingly turning to cleanroom technology for the environmental control or the development of new products. It is vital to provide thermo-stabilized environment and cost-effective operation conditions for bio-tech industries as well as for influenza vaccine plants. In this study, field measurement and numerical simulation of a full-scale bio-cleanroom has been carried out at a vaccine plant in Taiwan. Computational Fluid Dynamics (CFD) simulation were also conducted to investigate the temperature and airflow distribution as well as the energy saving potential of the bio-cleanroom. Validation of bio-cleanroom for egg-grown vaccine production was performed to meet the specification set at design stage. The results from computer simulation revealed that the improvement of energy consumption could be achieved satisfactorily by reduction of supply airflow rate and increase of supply air temperature. Different velocity and temperature of supply air could be assessed extensively not only by airflow and temperature distribution but also by transient simulation to achieve the design specification of 4°C for vaccine storage. It was also expected that CFD aided simulation could identify strategies for best practice at design stage as well as reduce running cost at full operation.

Key words: Bio-cleanroom, computational fluid dynamics, field measurement, performance analysis

INTRODUCTION

Recent advances in bio-medical technology and vaccine production necessitate regular reevaluation of the Heating, Ventilating and Air-Conditioning (HVAC) needs for biomedical cleanroom facilities. The purpose of the HVAC system for a bio-cleanroom is not only to achieve thermo-stabilized environment but also to remove airborne contamination. It is vital to perform the vaccine production in a particle-free and thermo-stabilized environment as well as maintain the minimization of energy consumption. However, little knowledge or quantitative information about energy-efficient HVAC system is available on how to control the environmental parameter in the bio-cleanroom for vaccine storage effectively. With cost of rising, value of conservation grows. Since, HVAC systems of bio-cleanroom operate continuously, it is vital and significant to consider energy-efficient strategies as well as to achieve an acceptable performance for environmental parameter contaminations control.

Thermo-stability is a critical biophysical property of viruses that has direct applicability to the delivery of live viral vaccines. The more thermostable a live viral vaccine, the easier it is to maintain infectivity under the conditions of clinical was (Ikizler and Wright, 2002). It is vital to keep the thermo-stabilization of egg grown influenza viruses during the production process. Influenza stocks usually have to be held at 4°C for a couple of hours for stability storage. Besides, the licensed influenza vaccines in the U.S. are currently produced in embrocated chicken eggs. However, Lu *et al*. (2006) investigated another option for H3N2 vaccine production to increase virus growth in embrocated chicken eggs. It is essential to provide a cold room at 4°C for vaccine production and storage. Furthermore, the experiment and modeling of airflow pattern as well as the diffusion of contaminants in an operating room was performed by Woloszyn *et al*. (2004). Computational Fluid Dynamics (CFD) simulation technique is a well-known and widely-accepted scientific technique that allows improvement of airflow distribution for cleanroom configuration (Wang *et al*., 2009). They

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also identified some option under a limited budget, as well as reduced trial-and-error effort when modifications of cleanrooms have to be conducted. Besides, Wang *et al*. (2008) also evaluated thermal comfort and contamination control for a cleanroom by CFD simulation technique and field measurement data as well. Moreover, the CFD codes were successfully used to simulate the air distribution and contamination decay as well as comparison of indoor particle concentration in different rooms by Zhao *et al*. (2004). Besides, the biological contaminant control strategies under different ventilation models in the hospital operating room have been proposed by using CFD simulation (Zhang *et al*., 2008). Results showed that improving air flow distribution could reduce particle deposition on certain critical surface. Furthermore, the effect of diffuser discharge velocity on ventilation performance in a cleanroom has been investigated by Chow *et al*. (2006) through CFD analysis as well.

Field-measurement is essential to assure the cleanroom performs correctly and achieves the contamination standards. The biological contamination control strategies under different models in operating room has been simulated and then compared with filed measurement to check the acceptable level of consistency (Zhang *et al*., 2008). Besides, bioaerosol characteristics related to human dispersion were evaluated extensively based on field tests data in bio-cleanroom with different class levels (Li and Hou, 2003). Some valuable information describing cleanroom measurement to evaluate the overall performance of cleanroom can be found in literature (IEST, 1993). General principles and methods on bio-contamination control of cleanroom are described extensively in the standard of ISO 14698 (2003). Besides, the essential information on design consideration, equipments and comprehensive procedures for certified testing of cleanrooms were reported in NEBB (1996).

Although, some research has been done on CFD simulation as well as for field measurement for cleanroom, little quantitative information is available on compromise of contamination control and energy saving potential. In this study, the strategic approach on performance improvement of the HVAC system for an bio-cleanroom for vaccine production will be investigated. Both numerical simulation and field measurement of a full-scale bio-cleanroom will be carried out in cold room of a bio-cleanroom for vaccine production in Taiwan. Different velocity and temperature of supply air could be assessed extensively not only by airflow and temperature distribution but also by transient simulation to achieve the design specification for vaccine storage.

SYSTEM DESCRIPTION AND FIELD MEASUREMENT

The investigated bio-cleanroom is part of a newly-constructed CGMP (current good manufacturing practice) level manufacturing plant for vaccine production. It provides the clean environment at 4°C for vaccine storage after virus growth in embrocated chicken eggs. The layout of HVAC system including the supply and return air arrangement for the investigated operating room is shown in Fig. 1. Supply air flow at 0°C (273 K) from air handling unit (with brine cooling coils) is provided to the bio-cleanroom through 6 pieces (1.5×0.75 m) of supply air grilles. Return air flow is recirculated through the return air grilles located at the opposite of the cleanroom to produce horizontal by laminar air flow and stable temperature at 4°C for vaccine storage. An inverter with variable frequency drives was installed to examine the performance variation and energy-saving potential under different supply air temperature and face velocity. The investigated bio-cleanroom for vaccine storage with the dimension of length 5.6 m, width 4.7 m and height 2.7 m, respectively.

This bio-cleanroom with cleanliness level class 10,000 (ISO class 7) is equipped with high efficiency particulate air (HEPA) filters at the filtration efficiency over 99.97% (above 0.5 μm) in the air handling unit. Specified design conditions are temperature 4±1°C, humidity 45±5 (%RH) and the pressurization of 10±2.5 Pa. The colony forming unit (cfu) for microbial counts less than 175 cfu m^{-3} is specified. To establish the exact geometrical model for simulation, 30 chicken eggs racks with 6 rows×5 columns for vaccine storage were evenly arranged in the bio-cleanroom. The cross-section geometric schematic diagram of the investigated bio-cleanroom with eggs racks is shown in Fig. 2. There are four spacing room at each egg rack and each layer are denoted as first (1st), second

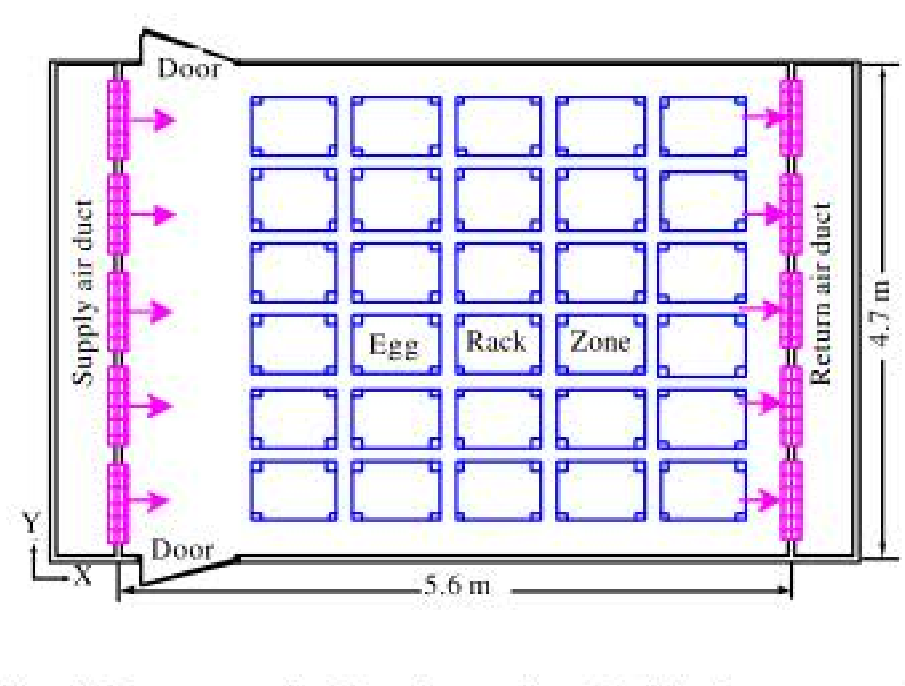

Fig. 1: Layout of the investigatal biocleanroom for vaccine production

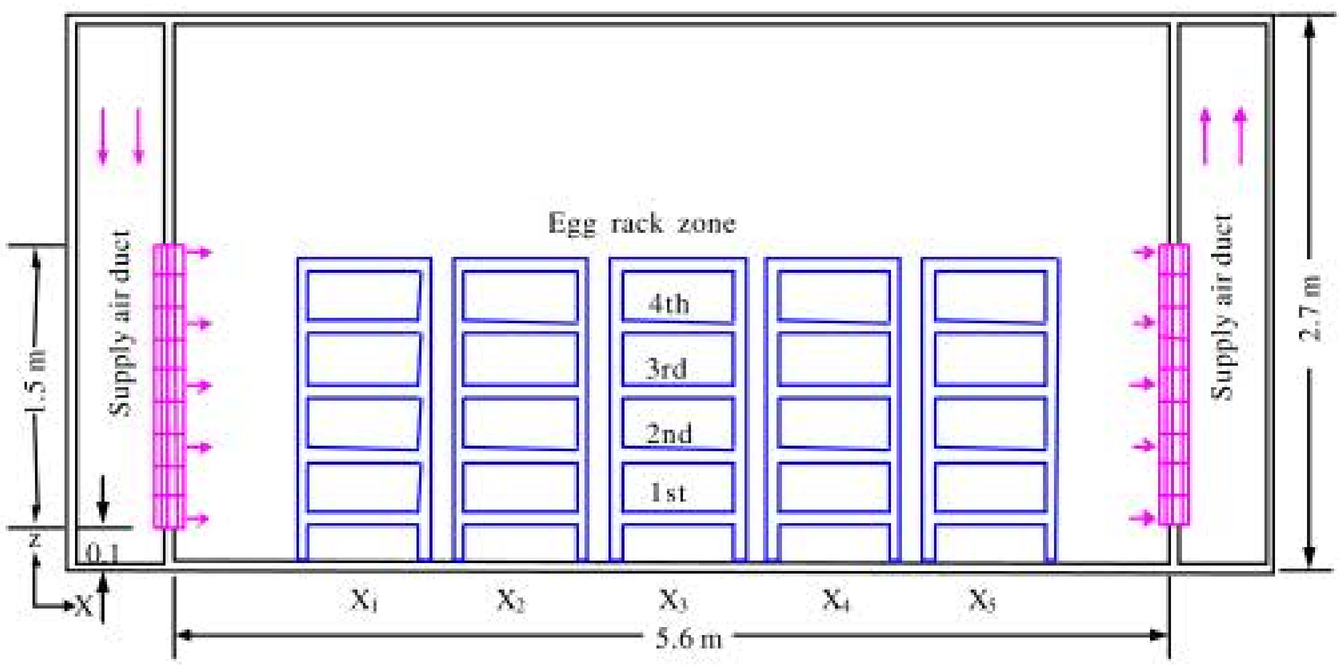

Fig. 2: Schematic diagram of the egg rack in the bio-cleanroom with supply and return grille

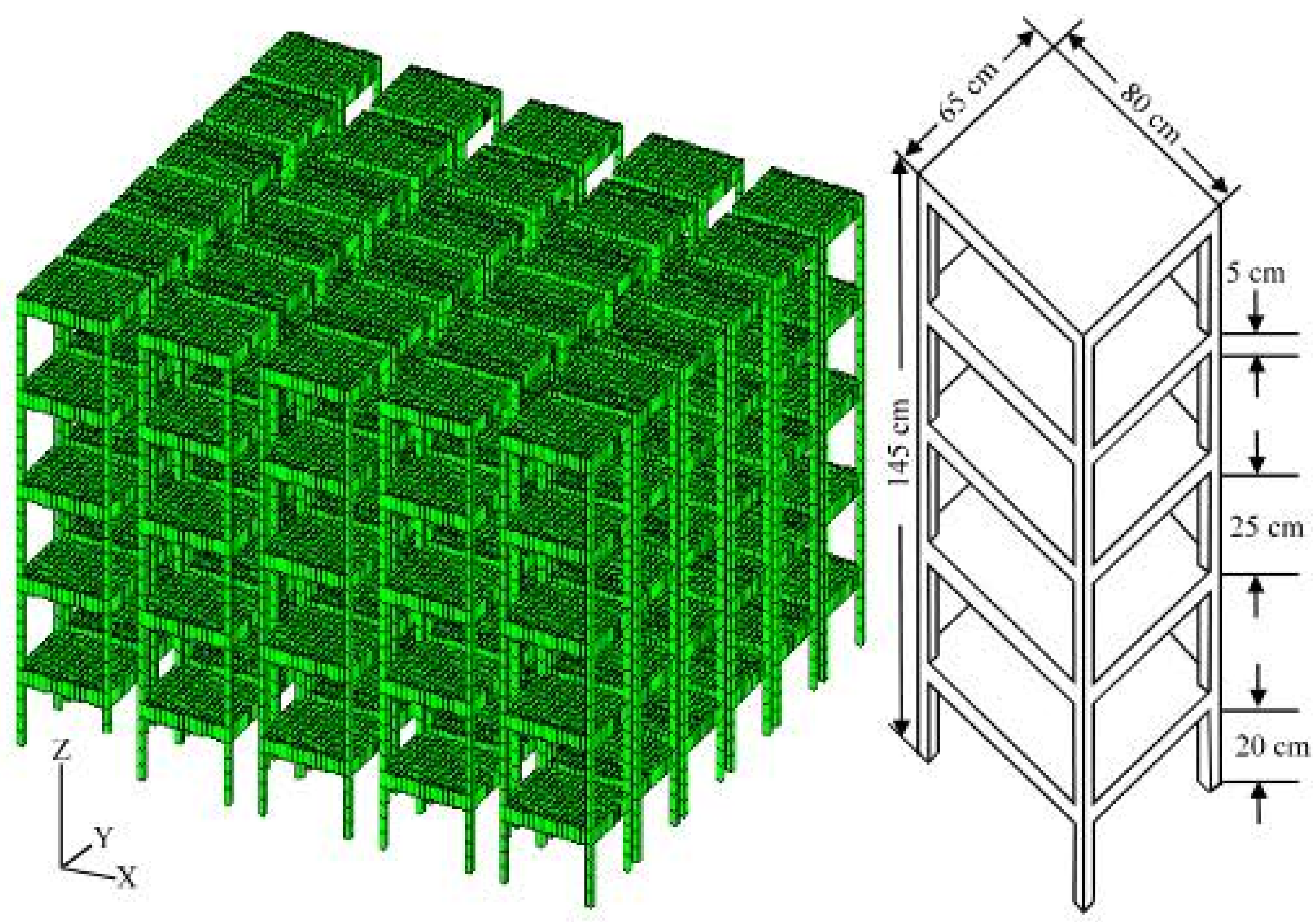

Fig. 3: Dimension of chicken eggs racks in the bio-cleanroom

(2nd) third (3rd) and fourth (4th), respectively along the z-axis. The schematic diagram with detail dimension of the chicken eggs racks for vaccine growth and storage is displayed in Fig. 3. Each egg rack is arranged side by side along x-axis and y-axis of the cold storage room to have a maximum production for vaccine. There are four spacing room (25 cm) for chicken egg holder at each egg rack. Dimension of the egg rack is adopted from the actual measurement. The full-scale geometric model along with all of the eggs racks is assumed to investigate the performance improvement of air flow and temperature distribution.

Field tests were conducted not only to provide reliable data for simulation but also to verify the simulation results for assessment of performance improvement of the bio-cleanroom. The particle counts of ten sampling locations were carried out at specified position of the operating room. Quantities tests of airborne particle counts were performed with a Met-One Model 3313 particle counter, sensitive to particles larger then 0.5 µm. Three times of measuring at each sampling location were conducted for accuracy and repeatability. The sampling flow rate for particle counter operates at 28.3 l min^{-1} (1 ft^3 min^{-1}) with sampling period of 1 min. Furthermore, to provide reliable data as the boundary condition of CFD simulation, the temperature and face velocity of each Fan-Filter Unit (FFU) were tested with an ALNOR Model 8585 hot-wired anemometer. A TSI Model 8386A digital manometer was employed to monitor the pressure difference of the cleanroom closure for contamination control concern during reducing the face velocity. The variation of temperature and humidity at return air grille were recorded by a multi-channel data logger (YOKOGAWA, Model MV100) with several temperature and humidity transmitters. Tests of temperature at accuracy of 0.2°C and humidity at accuracy of 2% RH were performed continuously for at least three hours under different measurement case. All instruments used in this study were calibrated regularly according to the manufacture's instructions.

NUMERICAL SIMULATION

The Computational Fluid Dynamics (CFD) technique has been proven to be very powerful and efficient in parametric studies of airflow distribution and temperature profile. In this study, a commercial CFD code, STAR-CD (CD Adapoc Group, 2001), was used to simulate the temperature airflow distribution of the bio-cleanroom accordingly. It will examine the improvement of bio-cleanroom configuration and energy saving potential without interfering any normal processes. The governing equations solved by STAR-CD include the three-dimensional time-dependent incompressible Navier-Stokes equation, time dependent convection diffusion equation and k-å turbulence equations. They are the continuity equation and the Reynolds-averaged Navier-Stokes equations which can be expressed as:

$$\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x_j}\left(\rho u_j\right) = 0 \qquad (1)$$

$$\frac{\partial}{\partial t}\left(\rho u_j\right) + \frac{\partial}{\partial x_j}\left(\rho u_j u_i - \tau_{ij}\right) = \frac{\partial p}{\partial x_i} + s_i \qquad (2)$$

where, x is the coordinate, subscripts i and j are the index of Cartesian component, u is the fluid velocity, ρ is the mass density, τ_{ij} is the stress tensor, p is the static pressure and s_i is the momentum source. The well-known finite control volume method with a Pressure Implicit with Splitting of Operator (PISO) algorithm was adopted to solve all the governing equations simultaneously. After solving the velocity field, the transient simulation of concentration field was conducted and concentration decay method based on mass concentration equation accordingly. The comparison of grid test for 335,836 cells and 590,592 cells possesses the relative error at 0.279%. Therefore, a grid with approximately 335,836 cells was used for numerical simulation it this study. The increase of cell number will provide more favorable information; however, it will accompany by a significant increase of computation resources.

To evaluate the energy-saving potential under different air temperature and face velocity of supply air grille, the performance improvement strategies with reduction of face velocity and increase the supply air temperature were proposed and analyzed by numerical simulation. It was assumed that the air flow field is homogenous, isotropic and three-dimensional. The temperature and face velocity of the supply air grille have been measured through field tests using a multi-function hot-wired anemometer to provide reliable measurement data as the boundary conditions of CFD simulation. Furthermore, all of the boundary conditions for solution domain were clearly defined according to the actual field tests data to carry out the accurate solutions. The face velocities of supply air grille were kept at 1.5 m sec^{-1} initially and then reduce to 1.0 and 0.5 m sec^{-1} to examine the variation of environmental parameter of the bio-cleanroom. It could be achieved by on-site adjusting the frequency of inverter at field test stage. The supply air temperature was maintained at 273 K (0°C) initially and then increase to 274 K (1°C) and 275 K (2°C), respectively. Typically, the no-slip condition was applied on the solid walls since they were not permeable.

RESULTS AND DISCUSSION

Figure 4 shows the airborne particle counts of the 10 sampling locations in the bio-cleanroom for particle size larger than 0.5 and 0.3 μm, respectively. The bio-cleanroom meets the specified class 10,000 (ISO class 7) and it even reached a higher class of class 100 (ISO class 5). It reveals that the possibility for over design

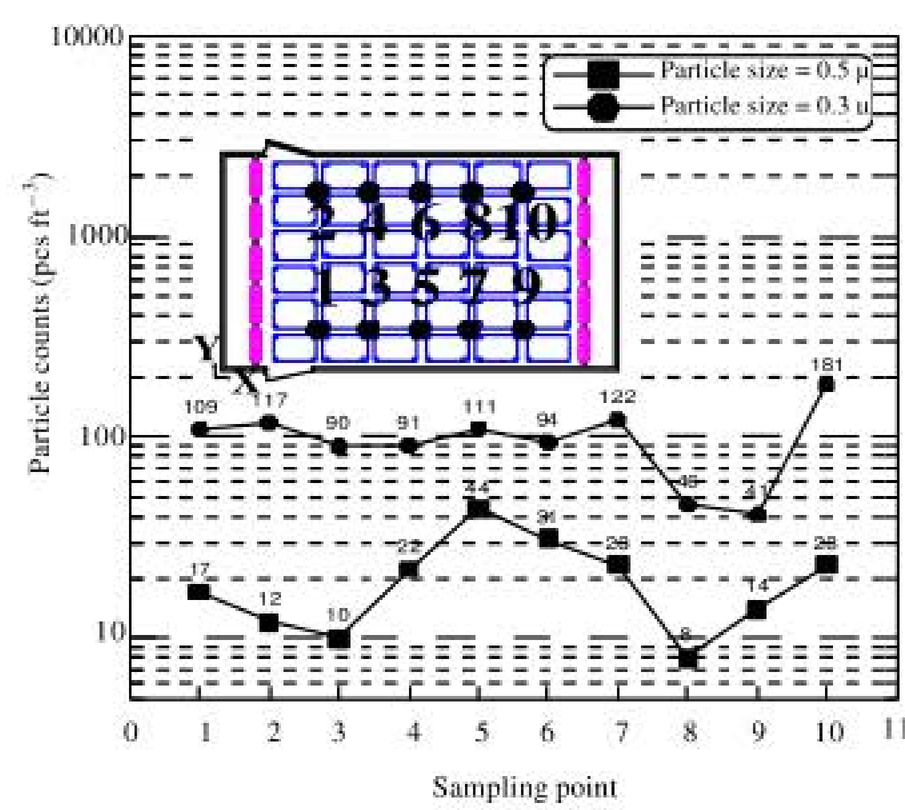

Fig. 4: Particle counts of sampling locations in the bio-cleanroom

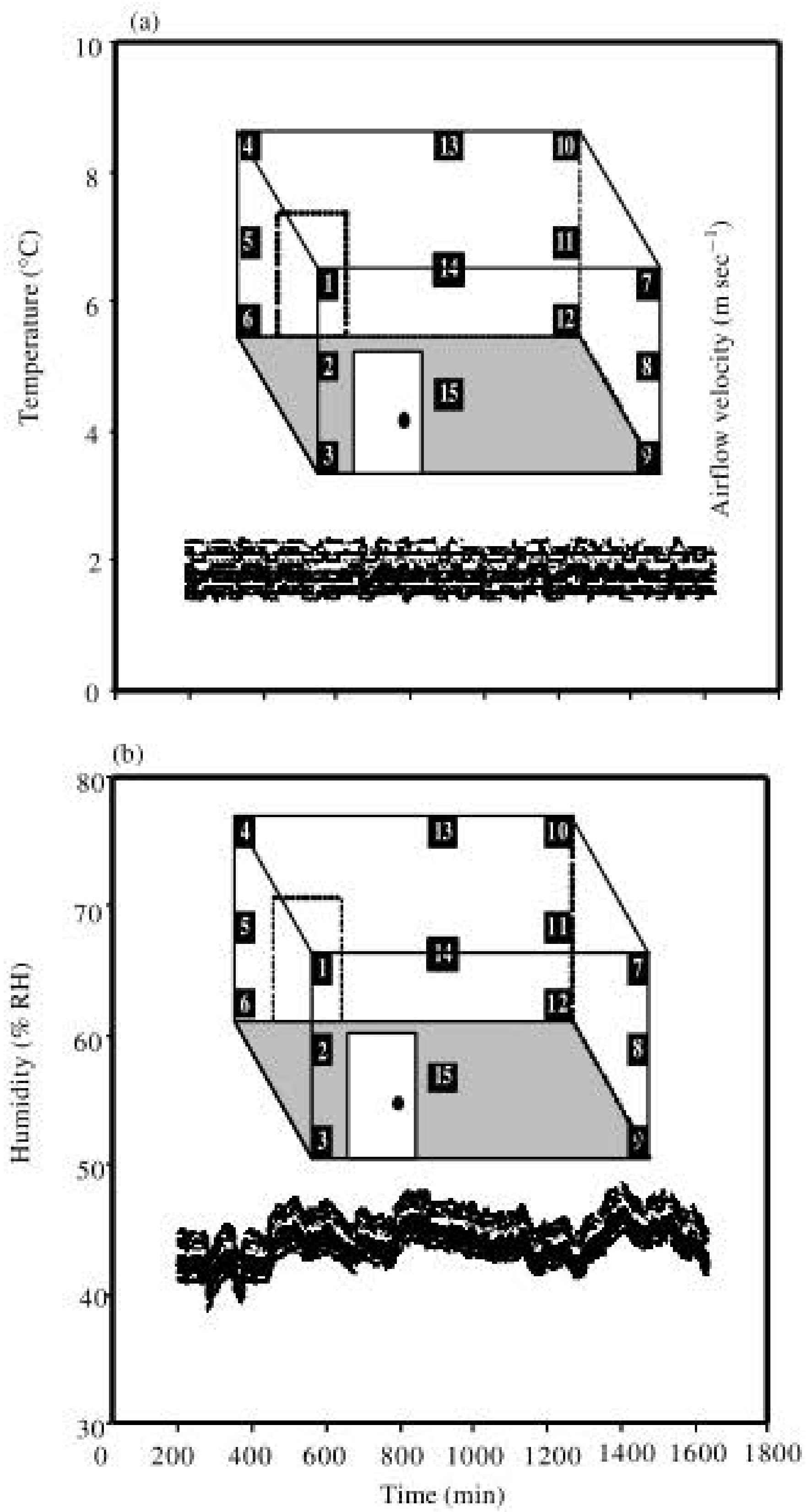

Fig. 5: Field tests of temperature and relative humidity, (a) temperature and (b) relative humidity

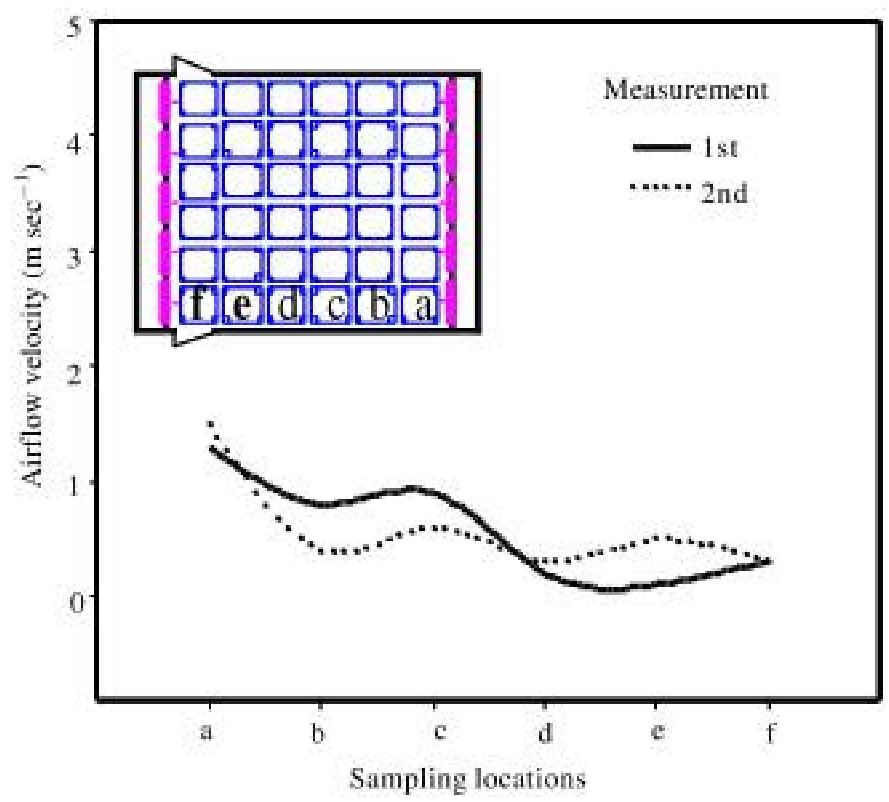

Fig. 6: Field measurement of air velocity at different rows of eggs

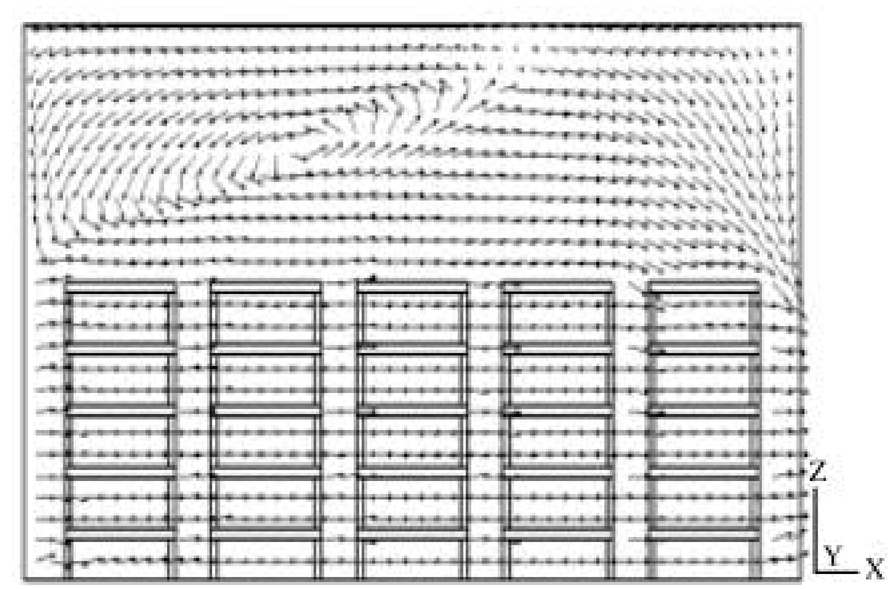

Fig. 7: Velocity in the bio-cleanroom at y = 1.975 m

and the energy saving potential is accessible for HVAC system of the bio-cleanroom. On the other hand, as shown in Fig. 5a, the field measurement data of temperature variation during 24 h for 15 sampling location specified in the cleanroom are about 2°C. It represents the cooling capacity of HVAC system can meet the temperature requirement for thermo-environment control of the cleanroom under the supply air temperature of 0°C and face velocity of 1.5 m sec^{-1}. Besides, as it depicts in Fig. 5b, the variation of relative humidity during 24 h of these 15 sampling locations also reveals that the HVAC system provides satisfactory compliance with the design specification of 45±5%(RH). Furthermore, Fig. 6 depicts the field measurement of air velocity at different rows of eggs racks. It also represents good agreement of the specification set at the design stage.

Although, the field data provide satisfactory compliance with the design specification of the bio-cleanroom, it is vital and significant to evaluate energy-efficient strategies, especially judging from the field measurement data of particle counts. The CFD simulation has been conducted to investigate the temperature and airflow distribution as well as the energy saving potential of the bio-cleanroom. Figure 7 shows the velocity vectors in the bio-cleanroom at the y = 1.975 m under the supply air temperature 0°C (273 K) and face velocity of 1.5 m sec^{-1}. The uniform and favorable velocity vectors can be obtained in the vicinity of eggs racks even though there are some vortices above the eggs rack.

Since, the HVAC systems of the bio-cleanroom operate continuously, different velocity and temperature of supply air can be assessed by the CFD simulation to identify the energy-saving strategies for the bio-

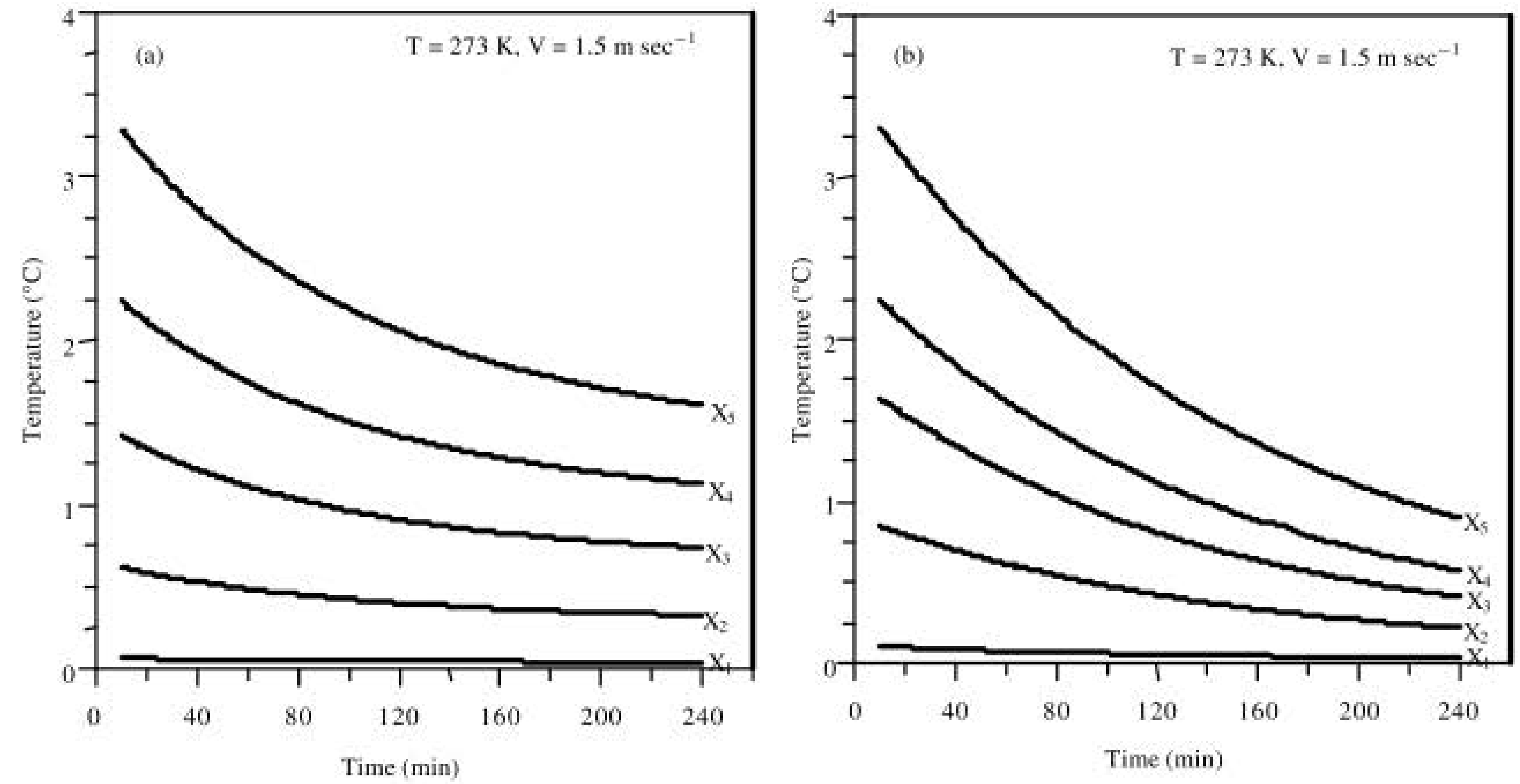

Fig. 8: Temperature distribution at different layers of eggs racks, (a) 1st layer and (b) 3rd layer

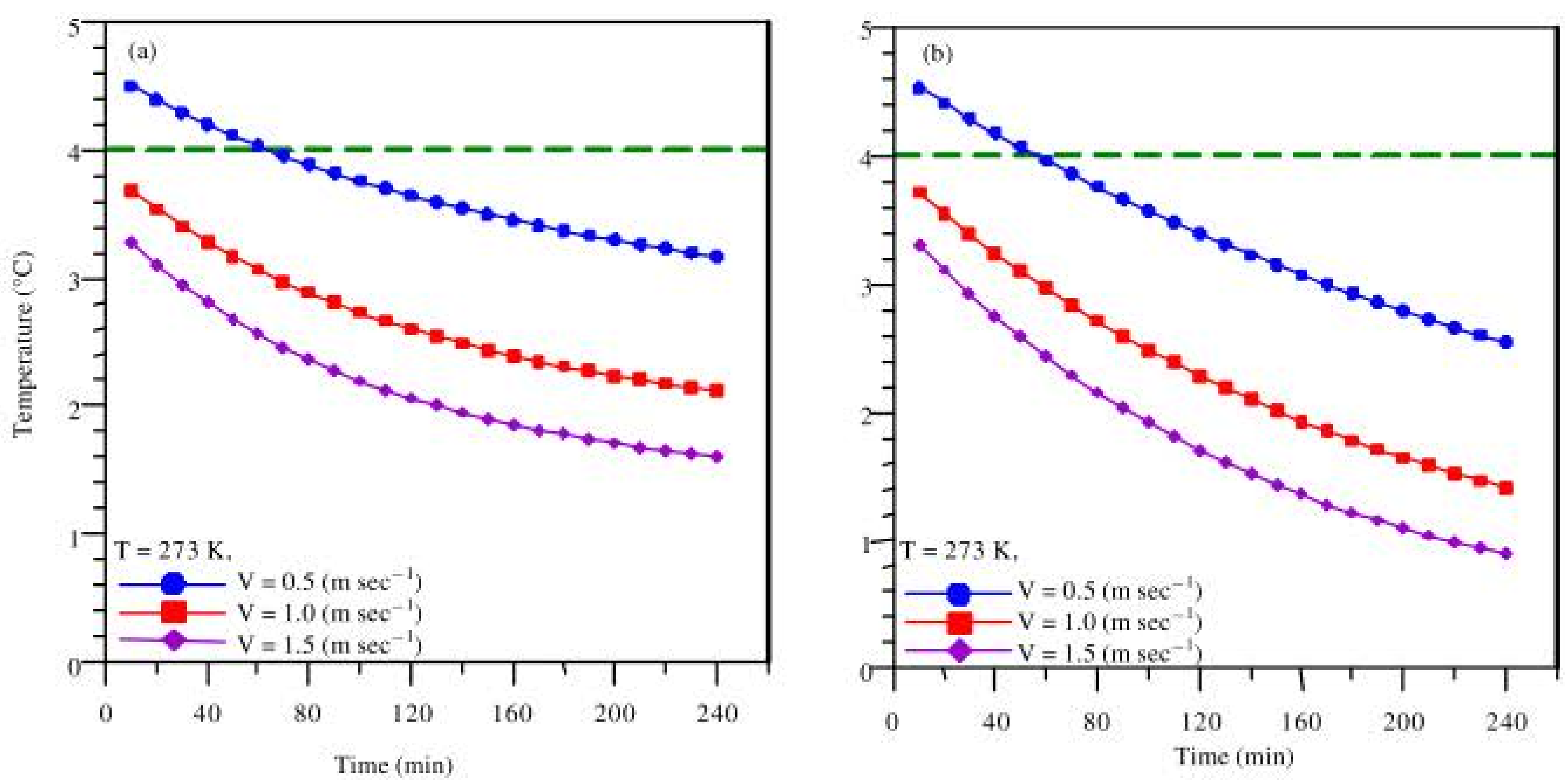

Fig. 9: Temperature distribution under different supply air velocity, (a) 1st layer and (b) 3rd layer

cleanroom. As shown in Fig. 8a and b, the temperature distribution at different layers (1st layer and 3rd layer) of eggs racks is presented by transient simulation for 4 h at supply air temperature of 273 K (0°C) and face velocity of 1.5 m sec^{-1}. It displays the favorable simulation results for temperature distribution at both eggs rocks during four hours. The first column (X_1) of eggs racks presents the lowest temperature because they are close to the low temperature supply air mostly. Besides, the fifth column(X_5) of eggs racks can achieve the design specification under 4°C easily as well. It also reveals the feasibility of energy saving strategies by increase the supply air temperature or reduction of face velocity.

Figure 9a and b show the temperature distribution of the bio-cleanroom with fixed supply air temperature at 0°C (273 K) under different supply air velocity of 1.5, 1.0 and 0.5 m sec^{-1}. The results present the feasibility of reducing the supply air velocity from 1.5 to 1.0 m sec^{-1}. It will be possible to reduce the face velocity to 0.5 m sec^{-1} even though there exists about 50-60 min of risk for over the

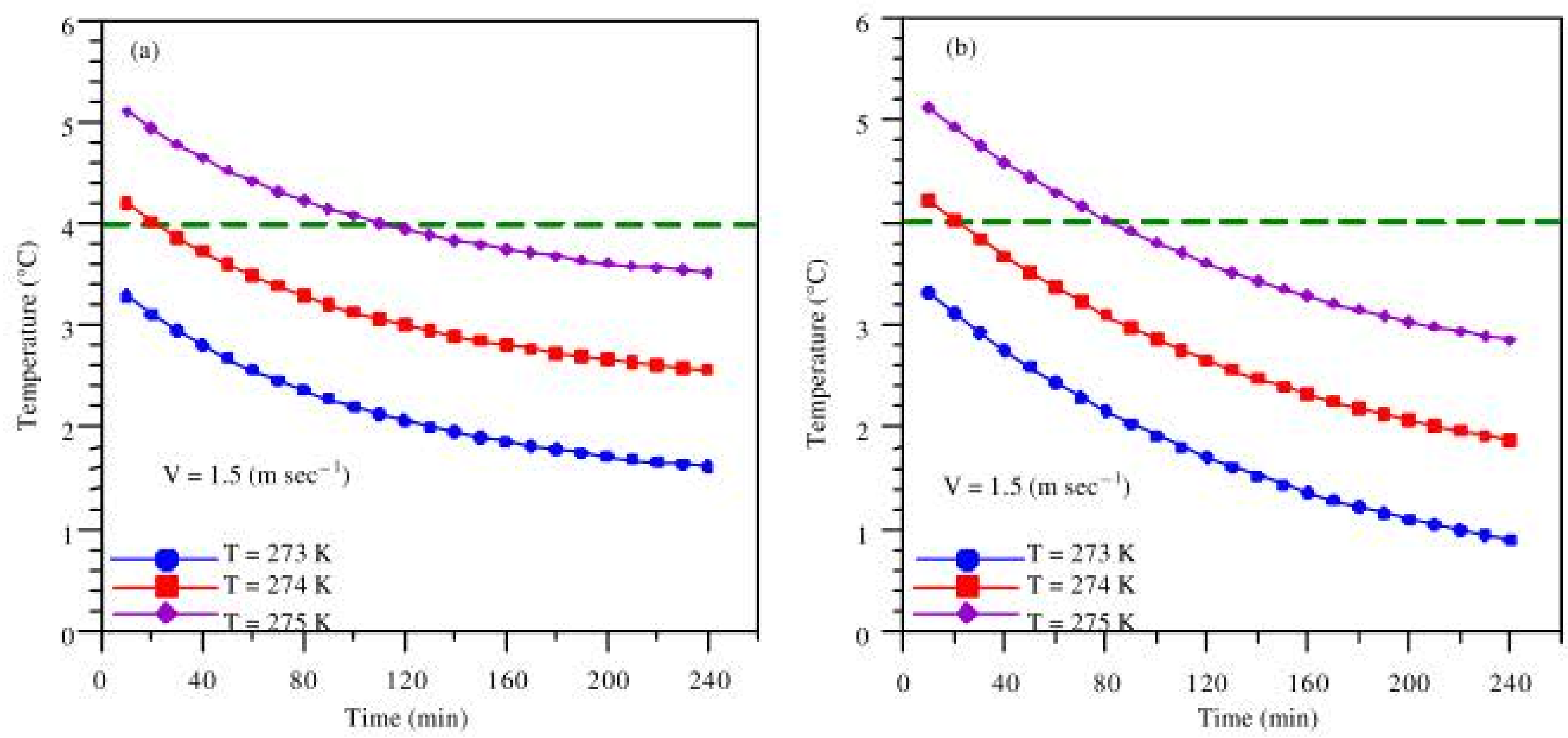

Fig. 10: Temperature distribution under different supply air temperature, (a) 1st layer and (b) 3rd layer

design specification at 4°C. Another scheme for energy saving potential is to increase the supply air temperature. Figure 10a and b show the temperature distribution of the bio-cleanroom with fixed supply air velocity at 1.5 m sec^{-1} under different supply air temperature of 273, 274 and 275 K. The simulation results for temperature distribution are similar for first layer and third layer of eggs racks under different supply air temperature. It is feasible to increase the supply air temperature from 273 to 274 K to reduce energy consumption for HVAC system. However, it may be inappropriate to raise the supply air temperature from 274 K to 275 K because it will take more time (over 1.5 h) to cool down the airflow in the vicinity of eggs racks for the bio-cleanroom.

CONCLUSION

It is essential to provide clean and thermo-stabilized environment and cost-effective operation conditions for bio-tech industries as well as for vaccine production and storage field measurement and numerical simulation of a full-scale bio-cleanroom has carried out an vaccine plant in Taiwan. The CFD simulation has been conducted extensively to investigate the temperature and airflow distribution as well as the energy saving potential of the bio-cleanroom. Different velocity and temperature of supply air could be assessed extensively not only by airflow and temperature distribution but also by transient simulation to achieve the design specification of 4°C for vaccine storage. The results from computer simulation revealed that the improvement of energy consumption could be achieved satisfactorily by reduction of supply airflow rate and increase of supply air temperature. Results in this study should provide valuable information to the facility engineer facing the compromise between energy saving strategy and environmental control consideration in the bio-cleanroom. It was also expected that CFD aided simulation could identify strategies for best practice at design stage as well as reduce running cost at full operation.

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