Mathematical Modeling of Infectious Diseases: Dynamics and Control

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Back-calculation and environmental modeling for the 2003 SARS epidemic and developing effective engineering control methods

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ABSTRACT

The 2003 severe acute respiratory syndrome (SARS) epidemic was characterized by the occurrence of large clusterings (i.e. super-spreading events) of infections. Environmental factors were suspected to play significant roles in some of these large outbreaks. For determining the environmental factors, it is important to estimate the time of infection. Estimating the time of infection, an unobservable event per se is also important in determining the other key transmission parameters and epidemiological characteristics of emerging infectious diseases. We first discuss a back-calculation method for estimating time of infection and the daily number of infected cases. We compare the estimated solutions from our proposed method to those obtained by the widely used expectation maximization method, for a simulated data set and two empirical SARS data sets from the 2003 Hong Kong SARS epidemic.

We then present a review of literature on the use of experimental and mathematical modelling of fluid mechanics in investigating the roles of building ventilation and air flow in some airborne diseases as well as developing new engineering control methods. The pros and cons of mathematical modelling in providing environmental investigations for large outbreaks of suspected airborne infectious diseases are discussed using the two example studies, i.e. the Amoy Gardens outbreak and the Prince of Wales Hospital 8A ward outbreak, and in studying ventilation systems in SARS isolation wards. A study of this nature needs an inter-disciplinary study with involvement of medical professionals, infection control experts, microbiologists, epidemiologists and engineers.

Note: These lecture notes are written based on both published and unpublished materials from my research at the University of Hong Kong, in collaboration with various organizations. Please do not cite these materials without permission.

1. BACK-CALCULATION METHOD

1.1 Introduction

The 2003 severe acute respiratory syndrome (SARS) epidemic was characterized by the occurrence of large clusterings (i.e. super-spreading events) of infections. Environmental factors were suspected to play significant roles in some of these large outbreaks. For determining the environmental factors, it is important to estimate the time of infection. Estimating the time of infection, an unobservable event per se is also important in determining the other key transmission parameters and epidemiological characteristics of emerging infectious diseases. We first discuss a new back-calculation method for estimating time of infection and the daily number of infected cases.

The actual time of infection was unobservable in the 2003 SARS epidemic, which is generally the case for all infectious diseases. The estimation of this parameter in the context of SSEs or a large cluster of infections is important for determining the exact environmental conditions at the time of infection, including meteorologic data, operation status of environmental systems such as mechanical ventilation and air-conditioning of buildings, in association with the activity and behavior of the occupants at the time of infection. Determination of environmental conditions is the first step for further epidemiologic investigations. Estimating infection time is also important for estimating key transmission parameters of an infectious agent and understanding other epidemiological characteristics related to the outbreak.

Different methods can be used to estimate the time of infection, such as the commonly used case-control design and contact tracing (Eames and Keeling 2003). However, these methods are not always optimally efficient, as detailed individual contact histories are often not available in real time and/or are unreliable (Chau and Yip 2003). Moreover, infected cases usually report multiple exposures, thus making any inference regarding a precise infection time difficult using traditional public health methodologies. Chau and Yip (2003) adopted a back-calculation method to estimate the unobserved daily number of infections for the 2003 Hong Kong SARS epidemic to evaluate the effectiveness of public health intervention and preventive measures. Walden and Kaplan (2004) previously presented a Bayesian approach for estimating the timing and size of a hypothetical bioterrorist attack, which is similar to the back-calculation methods mentioned above.

Back-calculation methods deduce the daily number of infections from the date of symptom onset and/or admission of incident cases in an epidemic. These methods have been developed for a number of diseases such as HIV/AIDS (Brookmeyer and Gail 1988; 1994; Brookmeyer 1991; Becker 1998), bovine spongiform encephalopathy (BSE) or "mad cow disease" (Anderson et al. 1996), hepatitis C (Deuffic et al. 1999) and anthrax (Brookmeyer and Blades 2003). For infectious conditions with a prolonged period of chronicity such as HIV/AIDS, back-calculation can provide assessment of historical incidence trends over time and an estimation of the current number of HIV-infected individuals, as well as project short-term HIV/AIDS trends.

Here, we introduce a new back-calculation method based on a normal distributional assumption for the measurement error. A penalty function is applied to rewrite the constrained least squares problem into a penalty optimization problem, which is then solved

by the trust region (TR) method. We first introduce the back-calculation problem, followed by three different back-calculation methods, i.e. the conjugate gradient (CG) method, the expectation maximization (EM) algorithm (Becker et al. 1991)and the new TR method. We compare the solutions obtained from these three methods for a number of simulated data sets. The advantages of the new proposed method are demonstrated. The recent 2003 SARS epidemic in Hong Kong is then analysed using the three methods. Each of the above methods gives one estimate among an infinite number of solutions for the back-calculation problem. We believe the most important criterion in choosing between alternative solutions for a particular disease or an outbreak such as SARS is the agreement between the predicted daily number of infections and the observed epidemiological data for which the infection time is known. The 2003 SARS epidemic has provided reasonably reliable epidemiological data that can be used for selecting the most appropriate solution, and thus the appropriate method in deriving that solution.

1.2 Back-calculation problem and methods

1.2.1 Problem Definition

As daily admission and onset data for the Hong Kong SARS epidemic is available, we adopt the day as the time unit. Let I_n , $1 \le n \le N$ be the daily number of individuals who were admitted to a hospital on day n for a duration of N continuous days; O_n , $1 - N_1 \le n \le N$ be the daily number of individuals with symptom onset (who were then assumed to become infectious) on day n, where N_1 is the longest incubation period, i.e. interval between infection and symptom onset (for SARS, $N_1 = 15$ (Farewell et al., in press)); and E_n , $1 - N_1 - N_2 \le n \le N$ be the daily number of newly infected individuals on day n, where N_2 is the longest infectious period, which was assumed to be from onset of symptom to admission (for SARS, $N_2 = 15$ (Leung et al. 2004a)). We consider the relation among the daily number of newly infected cases, the daily number of individuals with symptom onset and the daily number of admissions to a hospital using a simple statistical model:

$$O_n = \sum_{i=0}^{15} p_i E_{n-i}$$
(1)

$$I_n = \sum_{j=0}^{15} q_j O_{n-j}$$
(2)

where the incubation period distribution, p_j , was the probability of the onset of symptoms on the *j*th day after infection occurred. The daily admission distribution, q_j , was the probability of admission on the *j*th day after becoming symptomatic. Here it is assumed that the admission is predicated on presentation with symptoms. This is generally true, with the exception of nosocomial transmission, i.e. being infected while already in hospital for a different reason, such as in the initial Prince of Wales Hospital Ward 8A cluster (Lee et al. 2003). For the Hong Kong SARS data, we looked at the date of onset and the date of admission, and then omitted the ones with an admission date earlier than the onset date in the final data set before the back-calculation was carried out. The most reliable SARS data on the reported daily probability of symptom onset given infection, p_j , and the daily probability of admission given symptom onset, q_j , were those from Leung et al. (2004a), which were based on 81 well-defined cases in Hong Kong. Both the reported daily probability of symptom onset given infection and the reported daily probability of admission given symptom onset are smoothed using a gamma distribution (Donnelly et al. 2003) (see Figure 1). Substituting equation (1) into equation (2) we obtain:

$$I_n = \sum_{j=0}^{15} \sum_{i=0}^{15} q_j p_i E_{n-i-j}$$
(3)

The basic idea of back-calculation is to estimate the daily number of infected cases from either the daily number of admissions using both p_j and q_j , or the daily number of individuals with symptom onset using only p_j . The following description will be based on the first approach.



Figure 1. The daily probability of symptom onset given infection (Leung et al. 2004a) and the daily probability of admission given symptom onset for four different periods during the 2003 Hong Kong SARS epidemic. The curves for the daily probability of admission are smoothed from the reported data (Leung et al. 2004a) using a gamma distribution.

Rewriting equations (1)–(3) in matrix form, we have:

$$\mathbf{O} = \mathbf{PE}$$
Here $\mathbf{O} = (O_{-14}, O_{-13}, \dots, O_N)^T$; $\mathbf{E} = (E_{-29}, E_{-28}, \dots, E_N)^T$; and (4)

$$\mathbf{P} = \begin{pmatrix} p_{N_1} & p_{N_1-1} & \cdots & 0 & \cdots & 0 \\ 0 & p_{N_1} & \cdots & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & p_{N_1} & \cdots & p_1 \end{pmatrix}$$

is a $(N + 15) \times (N + 30)$ matrix.

$$I = QO$$

Here **I** = $(I_1, I_2, ..., E_N)^T$; and

(5)

$$\mathbf{Q} = \begin{pmatrix} q_{N_2} & q_{N_2-1} & \cdots & 0 & \cdots & 0 \\ 0 & q_{N_2} & \cdots & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & q_{N_2} & \cdots & q_1 \end{pmatrix}$$

is a $N \times (N + 15)$ matrix.

Finally:

$$\mathbf{I} = \mathbf{T}\mathbf{E} \tag{6}$$

Here
$$\mathbf{T} = \mathbf{QP}$$
, which is a $N \times (N + 30)$ matrix.

Hence the back-calculation problem considered here can be defined as follows.

Problem 1: To estimate the unknown vector **E** using the known vector **I** and the known matrix **T**, such that:

$$\mathbf{I} = \mathbf{T}\mathbf{E} \tag{7}$$

$$\mathbf{E} \ge \mathbf{0} \tag{8}$$

$$\sum_{n=1}^{N} I_n = \sum_{n=-29}^{N} E_n$$
(9)

Equation (8) states that all entries in the vector **E** are non-negative, while equation (9) states that the total number of infected cases should equal the total number of admissions. The latter is supported by the findings of Leung et al. (2004b) that SARS almost always presents as a florid clinical syndrome requiring in-patient treatment, with very few instances of asymptomatic presentations (<0.2% among close contacts of SARS cases, which is likely to be even lower for the general population).

The back-calculation problem as described by equations (7)–(9) is ill-posed, because there are $N + N_1 + N_2$ or N + 30 unknown variables, and there are only N + 1 equations. This means that the back-calculation problem, as defined by equations (7)–(9), has an infinite number of solutions. In order to obtain a sensible solution, some prior information must be given or assumed. For instance, certain smoothing conditions are usually assumed for a back-calculation problem (Becker et al. 1991). The smoothing conditions include the types of linear spline, quadric spline and cubic spline etc. Among them, the quadric spline is perhaps the most popular for estimating the infection curves. In this method, we assume that the daily number of infection satisfies a quadric smoothing condition, as in Becker et al. (1991):

$$E_{i-1} - 2E_i + E_{i+1} = 0, -28 \le i \le N - 1 \tag{10}$$

Rewriting equation (10) in a matrix form:

$$0 = \mathbf{B}\mathbf{E} \tag{11}$$

Here:

 $\mathbf{B} = \begin{bmatrix} 1 & -2 & 1 & \cdots & 0 \\ 0 & 1 & -2 & \cdots & 0 \\ 0 & 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & 1 \end{bmatrix}$

where **B** is a $(N + 28) \times (N + 30)$ matrix.

With this smoothing condition (equation (11)), Problem 1 can be rewritten into Problem 2 as follows.

Problem 2: To estimate the unknown vector **E** by using the known vector **I**, matrix **T** and matrix **B** such that:

$$\begin{bmatrix} \mathbf{I} \\ \mathbf{0} \end{bmatrix} = \begin{bmatrix} \mathbf{T} \\ \mu \mathbf{B} \end{bmatrix} \mathbf{E}$$
(12)

(13)

 $\mathbf{E} \ge 0$

$$\sum_{n=1}^{N} I_n = \sum_{n=-29}^{N} E_n$$
(14)

Here μ is a specified smoothing coefficient.

In Problem 2, there are $N + N_1 + N_2$ or N + 30 unknown variables and also $2N + N_1 + N_2 - 1$ or 2N + 29 equations. There are 2N + 28 equations in (12). The additional N + 28 equations given by the smoothing condition (10) provide additional constraining conditions for optimization. It should be noted that our objective is not to solve equations (12)–(14), but to find a solution that satisfies a particular target optimization function. The quality of the identified optimization solution depends on the choice of the optimum smoothing coefficient μ and/or the smoothing matrix **B**.

1.2.2 Back-Calculation Methods

Three different back-calculation methods are implemented. Two of the methods (CG and TR) are based on the assumption of a normal distribution, although the assumption is not used in the estimation process; and the third method (EM) is based on the assumption of a non-homogeneous Poisson process. Detailed methods are described elsewhere (to be published).

1.3 Application of the back-calculation method

1.3.1 Simulated Data Set

In order to test and compare the three methods, we first constructed a simulated data set with both the known daily number of newly infected cases and the daily number of admissions. For this artificial data set, a few SSEs comprising of pulse waves and sine waves were added to a constant infection curve for a duration of 200 days, with the first wave being the width of 10 days between day 44 and day 54, the second wave being two repeated waves, each with a width of 6 days, the third wave being a sine wave with a width of 20 days between day 85 and day 105, and finally the fourth being a peak wave with a width of 9 days between

day 123 and day 132. Spikes of varying widths (or periods) were created to test the ability of the numerical methods to deal with temporal resolution.

The daily number of admissions based on equations (2) and (1) was constructed from this assumed artificial infection data set by using two gamma distributions, i.e. the incubation period distribution, p_j , and the daily admission distribution, q_j . We re-predicted the daily infection data by the three back-calculation methods. We then compared the predicted daily number of new infections against the known infection data so that the accuracy of the three back-calculation methods.

1.3.2 SARS Data from the 2003 Hong Kong Epidemic

We applied the three back-calculation methods to estimate infection time for the 2003 SARS epidemic in Hong Kong. Distributions of the daily admission of SARS cases in Hong Kong as well as for the Amoy Gardens outbreak were extracted from the SARS Integrated Database (SARSID) compiled by the Department of Community Medicine, University of Hong Kong (Leung et al. 2004a). We excluded cases that were infected as a result of nosocomial transmission, i.e. individuals who were already in hospital for other reasons, but who were subsequently infected with SARS while in hospital, so as to satisfy the underlying assumption of equation (2) (i.e. admission was predicated on presentation with symptoms). There were a total of 1755 infected individuals, 133 of whom were excluded from the analysis because of nosocomial infection. Thus, we analyzed a data set of 1622 infected individuals, including those from the Amoy Gardens outbreak. We also obtained from SARSID the distribution of the daily number of cases with symptom onset. A total of 331 infected individuals were included in the analysis of the Amoy Gardens outbreak. We compared the dates of the predicted peaks and the dates of the reported SSEs.

1.4. Results and discussion

1.4.1 Better Accuracy in Resolving "Narrow" Peaks and Less CPU Required by TR Method

All three methods efficiently predicted the first and the last two peaks (SSEs) in the infection data from the simulated data set (see Figure 2). All three peaks had a width of close to or larger than the incubation period and admission period, both of which were 15 days. The predicted daily number of newly infected cases for the third peak with a 20-day width between day 85 and day 105 matches the actual (simulated) data well. However, there are some discrepancies between the predicted data and the actual (simulated) data for the first wave with a 10-day width between day 44 and day 54, and the fourth peak wave with a 9-day width between day 123 and day 132. This is expected as the width of the two peaks is less than the incubation period and admission period (i.e. 15 days). The agreement between the predicted and the observed data for the EM and TR methods are better than that with the CG method.



Figure 2. Comparison of the predicted and actual (simulated) daily number of infected cases for an artificial data set of hospital admission data. A convergence criterion of 0.01 was used for the EM predictions (B). In the notation MMS, MM represents the method (CG, EM or TR), S represents that smoothing was applied and C is the smoothing coefficient.

In Figure 2, the superiority of the TR method over the EM method can be seen in the predicted daily number of infected cases for the second wave, with two repeated "narrow"

waves each with a width of 6 days, which is much less than the incubation period and admission period of 15 days. The two repeated peaks are nearly smoothed out by the EM method, and are not seen in the predicted data when the EM method with two smoothing coefficients of 0.01 and 0.1 is used. The TR method predicts the two peaks in the second wave well, and the two peaks no longer appear in the predicted data when a much larger smoothing coefficient of 0.25 is used (TRS0.25).

We assumed a data set of daily number of infected cases from day 1 to day 200, and we then constructed a data set of the daily number of admission cases for 173 days from day 28 to day 200. The daily number of admission cases beyond day 200 could not be estimated as the assumed daily number of infections was unknown beyond day 200. From the daily number of admission cases from day 28 to day 200, we back-estimated the daily number of infected cases from day 28 to day 172. The estimated daily number of infected cases beyond day 172 or before day 28 was not accurate. However, due to the rapid decay (nearly zero) of the gamma function values for both the probability function of the incubation period and the period from onset of symptom to admission after 8–10 days, the duration of the estimated daily number of infected cases can be extended to between day 20 and day 190.

Figure 2 illustrates this "truncated" feature, i.e. the daily numbers of infected cases before day 20 and after day 190 are not predicted. Figure 2 shows that both boundaries of the back-calculated daily infection curve do not agree with the exact data. When there is no smoothing, the predicted daily infections by EM and TR exhibit strong overshooting for both the first and last peaks.

The CG method with and without smoothing performed the worst among the three methods for the artificial data set (Figure 2). The second wave with two repeated peaks was completely smoothed out by the CG method. The magnitude of the predicted trends failed to demonstrate the underlying dynamic range. This is analogous to the numerical diffusion in computational fluid dynamics (Li 1997). However, the predicted times of infection peaks were synchronous with the actual (simulated) peak times for all three methods.

Excluding the overshooting at the boundaries, our simulations for the artificial data set demonstrate that the TR method enables better prediction than the CG method, and also better prediction than the EM method for the daily predicted number of infected individuals. For the second wave of repeated peaks or SSEs with a width of 6 days, the TR method without smoothing captured the peak values better than the EM method, while both methods successfully predicted other SSEs in the artificial data set.

The effect of smoothing and the associated smoothing coefficient are also shown in Figure 2. Excluding the overshooting at the boundaries, the actual (simulated) daily numbers of infected cases for all five peaks (the second wave has two repeated peaks) were captured well by the TR method without smoothing, however when the smoothing was introduced, the five peaks were under-estimated, in particular for the two repeated peaks in the second wave. In the literature, it has been suggested that smoothing should always used, as in the well-known EMS method (Becker et al., 1991). It seems that either the smoothing method we used here was not perfect or that smoothing was unnecessary in the TR method. The lack of a need to use a smoothing method with the TR method for the present application warrants further investigation, but it can be considered as an advantage of this new back-calculation method for the applications presented here.

The TR method also required less computational time than the EM method, as compared to the analysis of the entire Hong Kong SARS epidemic data (see Table 1). A typical prediction using EM (convergence criteria 0.1) without smoothing required more than 1160 times more

CPU time than a typical prediction using the TR method. For the EM method, as the convergence criteria were further reduced to 0.01 and 0.001, the required CPU time increased greatly to 4300 times and nearly 16,000 times of that required by the TR method, as shown in Table 1.

The empirical superiority of the TR method, as we have demonstrated here, we believe, is probably due to its focus on $\min(||\mathbf{I} - \mathbf{TE}||^2)$ together with a balanced consideration of the additional constraints, i.e. considering them as a penalty. The CG method did not perform well because additional constraints were considered to be compulsory requirements, which have to be satisfied, even though CG also considers $\min(||\mathbf{I} - \mathbf{TE}||^2)$.

Method	CPU time (1 unit = 0.1406 s on a PC)	Standard derivation (persons)
TR	1.0	2.04
TRS0.1	1.1	2.16
TRS0.25	1.1	2.24
EM	1165.4	1.92
EMS0.01	190.3	2.08
EMS0.1	50.2	2.21
CG	30.9	2.21
CGS0.1	46.5	2.26
CGS0.01	18.3	2.39
EM_C0.1	1165.4	1.92
EM_C0.01	4309.7	1.91
EM_C0.001	15984.4	1.91

Table 1. Summary of CPU Time Required for Each Simulation With the TR Method and the EM Method for the Hong Kong SARS Data of 1622 Infected Individuals, as Well as the Standard Error of the Residuals Between the Predicted and Observed Daily Numbers of Cases With Symptom Onset. All Methods Were Implemented Using MatLab7.0

1.4.2 A Method for Minimizing "Overshooting" at the Boundaries

One disturbing feature in the predicted daily number of infection cases was the occurrence of overshooting at the boundaries, as shown in Figure 2. Various tests using the artificial data sets showed that the overshooting phenomenon occurred at the two boundaries of the data for all three methods, albeit to different degrees. Numerical experiments showed that overshooting occurred wherever there was a sudden change in the solution at the boundaries. The use of smoothing helped in eliminating overshooting, as shown in Figure 2, but at the expense of producing more "numerical diffusion" – a trade-off that is well known in

computational fluid dynamics (Li 1997). The use of smoothing to remove overshooting may be very important in HIV/AIDS applications, as the last period prediction is crucial for any short-term projection into the near future. We also found that overshooting became worse when the sharp gradient at the two ends in the original data became greater. This prompted us to artificially add zeros to both ends of the data (when both ends have zero admission cases) or smooth out the data, as shown in Figure 3. When a sufficient number of zeros or smoothing periods (for 30 days at both ends, i.e. the total duration of the incubation period plus the interval between symptom onset and hospital admission) were added, the overshooting phenomenon was virtually eliminated (see Figure 3).





Figure 3. Comparison of the predicted and actual (simulated) daily number of infected cases (mixed-sine curve) for an artificial data set of hospital admission data with the "overshooting" at both boundaries removed. A convergence criterion of 0.01 was used for the EM predictions (B). In the notation MMS, MM represents the method (CG, EM or TR), S represents that smoothing was applied and C is the smoothing coefficient.

In Figure 3, the actual (simulated) SSEs in the original infection data was well captured by both the EM and TR methods. They both yielded accurate predictions when the width of the infection peak was large. As discussed, the superiority of the TR method became evident when the period of infection data was small. The key question here is whether the back-calculation method introduced artificial peaks or SSEs. We have considered a wide range of artificial data sets when testing our new method. In all the test data sets, we did not find an example where the SSEs were an artifact of the back-calculation process. The SSEs were not introduced by the back-calculation method that we used.

1.4.3 Infection Time for the Amoy Gardens Outbreak in Hong Kong

The Amoy Gardens outbreak provided a good test case for our model as there were only two probable infection seeding times based on epidemiological investigations. More than 300 residents in this high-rise multi-block housing estate were infected with SARS during late March and early April 2003. The index patient who seeded the entire outbreak at Amoy Gardens visited a flat in one of the apartment blocks (Block E) on 14 March and again on 19 March, and used the toilet during both visits. Subsequent epidemiological and environmental investigations suggested a possible airborne transmission route in that outbreak (Yu et al. 2004). Transmission through other routes was also suggested (Department of Health 2003; WHO 2003b). The suggested airborne transmission hypothesis has been the only one so far to explain almost all features of the outbreak. The infection was caused by a number of unfortunate events. The virus-laden bio-aerosols were generated in the vertical drainage stack of Flats 7 in Block E after the identified index patient used and flushed the toilet. The bio-aerosols re-entered the flat through the dried-out water seal trap of the floor drain and then entered the re-entrant space by means of suction created by an exhaust fan. The bioaerosols moved upward within the re-entrant space due to the combined action of buoyancy force and wind, and entered the flats on the upper floors which bordered the re-entrant space. Air movement between flats through leakage areas in doors caused the horizontal spread of infection to other flats in the same block (Li et al. 2005a). After the plume reached the top of

the re-entrant space in Block E, the action of a predominant north–easterly wind caused the virus to spread to other flats at certain heights in Blocks B, C and D – three blocks with a concentration of infected cases out of a total of 18 other blocks in the Amoy Gardens housing estate (Yu et al. 2004).

The question arises as to which visit of the two or whether both visits caused this large SSE in the housing estate. Figure 4 shows the predicted daily number of newly infected cases for Amoy Gardens. A single peak stood out around 19 March, with another aggregate of infected cases around 3 April (predicted by EM). Thus, our predicted infection peak was 19 March. This agreed with the fact that the index patient stayed only one night on 19 March. No infection should have occurred before 19 March if the theory of airborne transmission, as suggested by Yu et al. (2004), were true. It is interesting that both EM and TR without smoothing predicted that the majority of the infection occurred on 19 March, while the predicted number of infected cases on 19 March using the EM method was higher than that using the TR method. However, when smoothing was applied, both predictions by EM and TR suggested that a significant number of infections occurred between 14 and 23 March. Nonetheless, both scenarios are plausible and consistent with the epidemiologic contact-tracing information.

The predicted curve of new infections using the EM algorithm was tighter than that predicted by the TR method. Although the TR method gave the best prediction for various artificial SSEs, as shown in Figure 3, we do not necessarily have more confidence in the results predicted by the TR method. The comparison of the predicted curve of cases with symptom onset shown in Figures 4(D)-4(F) also indicates that both methods yielded a reasonable agreement with the observed data of onset of symptoms. The agreement is better for the daily number of onset cases after 24 March, but not as good for those before 24 March, due to the sudden sharp increase of daily number of onset cases on 24 March.

1.4.4 Infection Time for Other SSEs in Hong Kong

Results were also obtained for the population-based SARS data set in Hong Kong using the three back-calculation methods. The predicted daily number of new infections are presented in Figures 5(A)-5(C). The predicted daily number of cases with symptom onset using the predicted daily cases of new infection were also obtained, and the results are compared with the observed data in Figures 5(D)-5(F). The standard error of the residuals between the predicted and observed daily number of cases with symptom onset are summarized in Table 1 for the three different methods with and without smoothing. As shown in Figures 5(A)-5(C), all three methods consistently predicted the periodic occurrence of infection peaks or aggregate cases over time. Each of these peaks can be interpreted as reflecting one or more SSEs, as shown in the simulation of the artificial data set shown in Figure 3. The differences in the errors between the methods TR and EM are not significant, we may suggest that the two methods are equally good. However, TR has its superiority in resolving two peaks that are very close to each other. The ability of resolving two close peaks is important in terms of identifying the infection times. As discussed, TR is also a much faster algorithm than EM.

In Figure 5, there are five obvious peaks (SSEs) in the curve for newly infected cases predicted by the TR method for the Hong Kong epidemic, namely on 4–6 March, 11–12 March, 18–20 March, 30–31 March, 7–10 April and 19–20 April. Almost all peaks are also predicted well by the EM method. The two peaks on 4–6 March and 11–13 March predicted by the TR and EM methods (Figures 5(B) and 5(C)) are merged into one peak, i.e. 4–6 March in the predicted data using the EMS method (Figure 5(B)). This merging behavior of

the EMS method is also shown in Figure 3 for the artificial data set when the widths of the two neighboring peaks are very small.

The first two peaks (4–6 March and 11–12 March) correspond to the outbreak of SARS at the Prince of Wales Hospital (Lee et al. 2003). A 26-year-old Hong Kong resident contracted the infection in late February. He was admitted on 4 March to Ward 8A at the Prince of Wales Hospital with a diagnosis of community-acquired pneumonia, which subsequently led to a large SARS outbreak (Lee et al., 2003) from 11 to 25 March 2003, with 138 probable cases. The patients included 69 health-care workers, 16 medical students who were attending clinical teaching or examinations in the ward, and 53 patients/visitors who were either in the same ward or had visited patients there. The index patient's cough persisted from 4 to 13 March, and was most severe from 4 to 7 March. Detailed epidemiological studies on the spread of SARS among the three different groups of victims have been reported elsewhere (see Lee et al. (2003) for health-care workers, Wong et al. (2004) for medical students, Yu et al. (2005) for in-patients and Li et al. (2005b) for airflow studies). The probability of airborne transmission was also suggested in these studies. Yu et al. (2005) concluded that 6 and 10 March were probably the most infectious days, corresponding to the two peaks observed in the epidemic curve on 11 and 15 March. Interestingly, the present statistical analysis also suggested two infection peaks on 4-6 March and 11-12 March, as shown in Figure 5.

The second peak (19–21 March) corresponded to the outbreak of SARS at Amoy Gardens (Department of Health 2003; WHO 2003b; Yu et al. 2004). There were no reported SSEs corresponding to the third peak.

Among the curves of newly infected cases predicted by the three different methods, the prediction by the CG method seems to be most diffused, represented by a flatter profile than those predicted by the TR and EM methods. The peaks predicted by EM and TR are both sharp and well-defined, among which the predicted peaks by the EM method without smoothing are the sharpest. We used the predicted curve of newly infected cases to predict the curve of onset of symptoms to evaluate the present methods. The predictions are compared with the observed data in Figures 5(D)-5(F). There seems to be good agreement for all three methods. Although there is general concordance between predicted onset and the observed data, it is difficult to judge which predicted curve of the infected cases in Figures 5(A)-5(C) is correct. As the TR method gave the best prediction for the Amoy Garden data as well as the artificial test data, we speculate that the predicted curve of infected curve of infected curves.

1.4.5 Dependence of EM-Predicted Infection Curve on the Convergence Criteria

It is well known that the EM algorithm has an inherent shortcoming, i.e. it is difficult to specify the convergence precision, since different precisions would lead to different solutions for certain data sets. Our simulation experience showed that the problematic data sets are those with an oscillation period of less than the incubation period. We demonstrated the dependence of EM-predicted infection curve on the convergence criteria using the Hong Kong SARS data. The results are shown in Figure 6 for three different convergence criteria. A converged numerical method should approach its "true" solution as the convergence criteria become very small. The solution obtained should be independent of the convergence criteria used when the convergence criteria become sufficiently small. Figure 6 shows that the predicted infection data by the three convergence criteria was fairly close for the peaks (waves) that were not close from each other. However, a difference occurred for the peak at

8–11 April, as predicted by the EM method with a convergence criterion of 0.1. As the convergence criteria became smaller, i.e. 0.01 and 0.001 respectively, the peak split into two peaks; however, the amplitudes of the two peaks were apparently different with the two convergence criteria. We believe that this difference is critical as it is not desirable to have a back-calculation method that is dependent on convergence thresholds. As shown in Table 1, the CPU time for the simulation with a convergence criterion of 0.001 is nearly 16,000 times that required by the TR method for the same problem.

2. ENVIRONMENTAL MODELLING

2.1 Introduction

Environmental modelling can supplement the epidemiological studies. The SARS virus was mostly spread by close personal contact and large droplet transmission (WHO, 2003b). Possible airborne transmission was documented for some super-spreading events in the SARS epidemics, for example, in the Amoy Gardens outbreak in Hong Kong (Yu et al., 2004). We have attempted various environmental modelling techniques have been useful to develop an understanding of the possible causes of airborne transmission in a number of SARS outbreak investigations.

It was known that many other respiratory viruses, such as those causing the common cold and flu, could spread from an infected person to a new host by airborne bio-aerosol inhalation, personal contact such as handshaking, and by touching contaminated surfaces. Past studies on transmission routes for communicable respiratory infection were reviewed by Barker et al. (2001) for community facilities and domestic homes, by Mendell et al. (2002) for work places such as offices, and by Cole and Cook (1998) for health-care facilities. Most studies on airborne transmission of various respiratory viruses were not as conclusive as for the person–person, or person–surface–person transmissions. A study by Duguid (1945) showed that sneezing and coughing could generate a million or so droplets up to 100 µm in diameter plus several thousand larger particles, while a recent study by Papineni and Rosenthal (1997) showed that for healthy individuals, the number of droplets generated during respiratory activities was much less. As droplets were humid, they started to evaporate after release and thus change their mass and size. Their size could be sufficiently small $(0.5-12 \,\mu\text{m})$ to be airborne (Cole and Cook, 1998). This also meant that if the large particles originally settled due to the effects of gravity, they could be resuspended as they evaporated and became smaller. The settling velocities for these small particles $(0.5-12 \mu m)$ were very low at between 0.05 and 0.3 mm/s. The rate of evaporation was dependent upon the ambient humidity. As the indoor relative humidity was generally controlled to be 50-60% in an air-conditioned room, the sizes of droplet in diameter of less than 100 µm reduced rapidly once released into the air; see Wells (1934) and Brundrett (1992). The airborne infectious particles were often considered to be droplet nuclei. Rudnick and Milton (2003) used CO2 as a marker for estimating the risk of indoor airborne infection.

Analysis of dispersion and transport of droplet nuclei and droplets in buildings can be done using the well developed mathematical modelling methods in buildings.

2.2 Basic theories

There are two basic sets of fluid dynamics equations that are primarily used to model the ventilation process; and these are:

- The Bernoulli's Equation for flow through an opening. In this equation, the effects of wind flows around buildings are generally included by using a wind pressure coefficient and the air flow in the room is assumed to be stagnant.
- The Navier–Stokes Equations. These equations apply to both laminar and turbulent flows. Reynolds-averaged or space-filtered equations are generally used to model turbulent flows. This approach allows for the movement of air within a room or zone to be represented.

Bernoulli-Equation approaches include simple analytical methods and network (multi-zone) methods. Navier–Stokers Equations are applied to computational fluid dynamics (CFD) methods. These techniques are considered in more detail in the following sections.

2.3 Simple analytical and empirical methods

Simple approaches vary from back-of-the-envelope computations and simple graphs to basic spreadsheet programs. Most analytical solutions are based on a conventional macroscopic approach that utilises the Bernoulli Equation. This equation, which is based on the conservation of energy, is used to calculate air velocities through openings. The Law of Mass Conservation is then applied to balance the mass flow rate of air into and out of the space (i.e. mass flow in equals mass flow out).

Li (2002a) has shown that analytical or direct solutions exist for calculating natural ventilation in a simple one-zone building with between two and four openings. No analytical solutions exist for natural ventilation problems with more than four openings. He also developed analytical solutions for single zone enclosures with up to three openings incorporating two simple mixed-mode ventilation systems. For a problem in which the temperature condition is defined (i.e. the inside and outdoor temperatures are given), the ventilation rate is expressed as a function of indoor/outdoor air temperature differences, wind pressure, flow rate from mechanical fans, and the size of ventilation openings. For a problem in which the heat production rate is defined (instead of the indoor temperature) the ventilation rate is expressed as a function of heat source strength, wind pressure, flow rate from mechanical fans, and so on.

Examples for which simple analytical or empirical models have been derived include:

- Single-sided ventilation, including both wind-driven and stack-driven flows (CIBSE, 1997);
- Single-zone buildings with two openings, including wind-driven, stack-driven and combined-driven flows (CIBSE, 1988; BSI, 1991), when the indoor air temperature is known. The model for simple stack-driven flows is often referred to as the "hot column" model in the literature. It has been very successfully applied to natural ventilation design (Bruce, 1978);
- Single-zone buildings with two openings, including wind-driven, stack-driven (Linden et al., 1990) and combined-driven flows (Li and Delsante, 1998), when the indoor air temperature is not known. Solar radiation and envelope heat conduction can also be considered in Li and Delsante's (1998) formulation. In some models, air temperature stratification can be considered (Andersen, 1995);
- Multi-zone buildings with effectively two openings in each zone (Li, 2002a).

Further recent examples of analytical solutions are presented by Li (2002a) and include:

- Single-zone building with two openings and a fan incorporating:
 - Combined stack and supply-fan driven flows with fully mixed conditions;
 - Combined stack and exhaust-fan driven flows with fully mixed conditions.
- Single-zone building with three openings incorporating:
 - Stack-driven flow with fully mixed conditions.

The solutions for the above situations are quite simple, however, analytical solutions for building incorporating four openings can be very complex. If a simple analytical solution can be found for a particular problem, then the solution can be very useful in providing an in-depth understanding of the governing parameters. It also often provides a test case for more complicated numerical methods such as the multi-zone method. Simple analytical solutions can also be used for basic vent sizing. Simple non-dimensional methods developed by Etheridge (2002) are good examples. Such sizing techniques were compared with experimental studies by Fracastoro et al (2002) who showed a reasonable agreement.

2.4 Network (multi-zone) methods

In the case of multi-zone coupled thermal and airflow analyses (Liddament, 1986), the building is divided into N_Z zones in which, in general, each room is treated as a separate zone. The total number of openings is N_O . From classical network theory, there are $N_L = N_O$ - N_Z independent closed loops. This relationship is well established in the hydraulics literature, e.g. Larock et al (2000). Zones are interconnected by flow paths, such as cracks, windows, doors and shafts, to form a flow network. In situations when all the internal openings are sufficiently large to assume that they do not significantly inhibit the movement of air, a building might be approximated by a single-zone. Network methods may be used to predict the overall ventilation rate for the entire building, the ventilation rate of each zone and the individual air flow rate and direction through each opening. Network methods are able to take into account the effects of outdoor climate, the location and size of each opening, and stack, wind and mechanically driven ventilation. There are two main types of multi-zone methods, these being:

- The zonal pressure-based approach;
- The loop pressure equation-based approach, see Li (2002c). Nitta (1994) presented a detailed implementation of this method for coupled air flow and thermal analyses. The loop pressure equation-based approach is widely used in pipeline network analyses and design; see Larock et al (2000). However, apart from the work by Nitta (1994), the authors are not aware of other multi-zone models, which have adopted the loop pressure equation-based approach. Axley (1998) proposed to use a loop equation method for natural ventilation design.

The network method is based on the application of the Bernoulli Equation to determine the pressure difference and hence flow rate across each opening in the flow network. Indoor air velocities are assumed to be negligible, however Axley (2002) and Graca et al, (2002) show that this assumption is not valid when ventilation openings are relatively large and there is a strong wind effect. The flow rate through each opening is generally expressed as a simple function of the pressure difference, such as the power law relationship. This pressure

difference can be a result of wind pressure, stack pressure, fan-induced pressure, or a combination of all of these. In a zonal pressure-based approach, we apply a mass balance to each zone. This leads to a set of simultaneous non-linear equations, the solution of which gives the internal zonal pressures.

Direct solution of these equations is not possible and, instead, an iterative approach is required. This is commonly based on the Newton–Raphson method. To speed convergence, relaxation techniques are used. Axley (2002) has found that this assumption implicitly demands that all changes in kinetic energy be dissipated and may, therefore, introduce significant errors. Axley (2002) has introduced the generalized Bernoulli equation that does not have this shortcoming.

A literature review undertaken in 1992 (Feustel and Dieris, 1992) identified 50 different multi-zone models which have been developed since 1970. Despite the large number of existing programs, the development of multi-zone infiltration and ventilation models shows a relatively slow evolution. Since the late eighties, a number of other multi-zone programs have been developed, most of which consider large openings. This facility is essential for most practical natural ventilation studies. Examples of these programs include BREEZE (BRE, 1994), COMIS (Feustel and Rayner–Hooson, 1990; Feustel and Smith, 1998), AIRNET (Walton, 1989), MIX and CHEMIX (Li, 1993; Li and Delsante, 1997), ESP-air (Clarke *et al.*, 1990), AIOLOS (Dascalaki and Santamouris, 1998), and Tas-Flows (EDSL, 1996).

Most existing network models assume that the air temperature in each zone is uniformly constant however, in reality, this assumption is not valid in most buoyancy-driven natural ventilation and displacement mechanical ventilation situations. In theory, multi-zone methods can also accommodate other known temperature profiles in a room, such as linear stratification. Li (2002b) has shown that the effect of thermal stratification on air flow can be very significant and lead to significant underestimation of the neutral level in a building, see. He has also identified the conditions under which thermal stratification is important and how it should be considered in natural ventilation analysis.

A further issue is the simulation of air flow through large openings such as doorways in which flow can take place in both directions at the same time. A model for simulating doorway flows was developed in the COMIS project (see Feustel and Smith, 1998). In addition Li (2002b) also developed a new method.

It is important to remember that natural ventilation is driven by wind and indoor/outdoor temperature difference. These parameters are introduced to zonal models via the boundary conditions. However the ventilation flow itself will often alter the thermal boundary condition (e.g. incoming air heating or cooling the space). For this reason there is often a strong need to integrate ventilation models with thermal models so that the temperature and hence ventilation condition can be solved simultaneously. Rousseau and Mathews, (1996) show that this is particularly important for the prediction of the yearly performance of hybrid ventilation systems in terms of thermal performance and ventilation flow rates. Kendrick (1993) has reviewed various approaches to combined airflow and thermal modelling. In order to evaluate how well such combined tools model hybrid ventilation systems and control strategies, a test simulation of ventilation in a typical single-zone classroom using four different tools was performed by Annex 35 experts (Delsante and Aggerholm 2002). The results show that the different tools used were quite consistent with respect to IAQ performance and fan energy. However, there were some deviations with respect to heating energy, possibly because of quite different implementations of the heating controller. This study underlines the importance of

modelling control strategies in the simulation of buildings with the performance of hybrid ventilation systems. Other recent application of multi-zone methods for hybrid ventilation can be found in Heikkinen et al (2002) and Seifert et al (2002).

The ability to simulate flows in buildings with a large number of zones or rooms, and their compatibility with most zonal-based thermal modelling programs is the most significant feature of multi-zone methods. As well as being used in their own right, multi-zone integrated airflow and thermal models can be used to provide boundary conditions for CFD applications.

2.5 Computational fluid dynamics methods

Computational fluid dynamics (CFD) methods provide numerical solutions of the partial differential equations governing airflow and related physical processes. CFD techniques are particularly suitable for air movement analysis in and around buildings, and they allow the airflow patterns and contaminant distribution inside a ventilated space to be analysed in great detail.

With CFD techniques, the geometrical domain (e.g. room or zone) under analysis is subdivided into a large number of small cells over which the equations of conservation of mass, energy and momentum are discretised and solved. Finite volume methods are probably the mostly successfully used in engineering flow simulations including building ventilation. Many CFD codes use unstructured grids and can handle very complex geometries.

The incompressible, time-averaged continuity, the Navier–Stokes and the energy equations can be written as:

$$\frac{\partial \overline{U}_i}{\partial x_i} = 0 \tag{15}$$

$$\frac{\partial \overline{U}_i}{\partial t} + \frac{\partial}{\partial x_j} (\overline{U}_j \overline{U}_i) = -\frac{1}{\rho} \frac{\partial \overline{P}}{\partial x_i} + \frac{\partial}{\partial x_i} [\upsilon(\frac{\partial \overline{U}_i}{\partial x_j} + \frac{\partial \overline{U}_j}{\partial x_i}) - \overline{u_i u_j}] + \beta g \delta_{i2} (\Theta - \Theta_{ref})$$
(16)

$$\frac{\partial \overline{\Theta}}{\partial t} + \frac{\partial}{\partial x_j} (\overline{U}_j \overline{\Theta}) = \frac{\partial}{\partial x_i} [\frac{\upsilon}{\Pr} \frac{\partial \overline{\Theta}}{\partial x_j} - \overline{u_i \theta}]$$
(17)

where the overbar indicates the time-averaged values and the small letters, u, p and θ are the fluctuating velocity, pressure and temperature respectively. Turbulent stresses and turbulent heat fluxes act as additional diffusion terms due to correlations between the fluctuating velocities and temperature, which are unknown and can be modelled by different turbulent closures such as the simple eddy-viscosity models and the Reynolds stress models. An alternative modelling approach is large eddy simulation (LES) where small eddies are modelled, while larger eddies are predicted. Large eddy simulation is a time dependent method and generally more expansive than most time-averaged models in terms of computer power requirement. In most ventilation problems, it is often sufficient to use the eddy-viscosity models, in which the turbulent stresses and the turbulent heat fluxes are replaced by introducing turbulent viscosities. For a detailed description of various numerical methods

and turbulence models in CFD, reference must be made to available textbooks and some other introductory publications, e.g. Patankar (1980), Heiselberg *et al.* (1998) and Awbi (1989).

CFD simulations are more time-consuming to establish and execute than multi-zone methods. Because of limitations in computer power, it may not be possible to use CFD to simulate a complex building with a large number of rooms. However, the application of CFD to mechanical ventilation has been very successful. There is a wide range of investigations and evaluations available (see for example Nielsen (1974), Borchiellini *et al.* (1994), Li and Fuchs (1993) and Chen (1996)). A number of useful air distribution indicators such as age of air have also been successfully analysed by CFD, e.g. Davidson and Olsson (1987).

The application of CFD to examine the effect of air infiltration on indoor airflow was first studied by Wang *et al.* (1991). However, the literature on CFD applications in natural ventilation is still relatively limited (see Clifford *et al.*, 1997; El Telbay *et al.*, 1985a; 1985b; FLOMERICS, 1998). Chikamoto *et al.* (1998) and Kato *et al.* (1999) presented a CFD analysis of a building ventilated by a hybrid system. The hybrid air-conditioning system studied in the paper is based on the concept of task/ambient air-conditioning. The task zone is conditioned with the aid of a mechanical air-conditioning system and the remaining ambient zone is conditioned by cross-wind ventilation.

Choosing a computational domain is one of the first steps in a CFD simulation. Natural ventilation is linked to the outdoor flow and thermal environments.

It is believed that the large eddy simulation (LES) approach has significant potential for natural ventilation flows. With LES, much more information is obtained about the flow regime than is possible when using traditional time-averaged turbulence models since most of the turbulence is resolved. Information about the nature of turbulent fluctuations can be obtained which can be important for thermal comfort. Flows in a mechanically ventilated room was simulated using LES by Davidson and Nielsen (1996), Davidson (1997), Jiang and Chen (2001, 2002) and cross-ventilation through open windows were studied using LES by Kato *et al.* (1992).

2.6 Probabilistic methods

All models need input parameters. A deterministic approach implies that all input parameters and model coefficients are 100% certain; see Haghighat et al (1988). In practice, this is not the case, for instance occupant behaviour and internal heat loads may vary significantly. Also external conditions such as wind velocity, external temperature and solar radiation are obviously stochastic in nature. In the case of mechanically ventilated buildings, this randomness may usually be neglected. This is because that such buildings are often highly "damped" (e.g. high thermal mass and well insulated) and are also well shielded t from external conditions. Variations in both indoor and outdoor conditions may normally be smoothed out by means of the building energy management system and the HVAC system. However, naturally or hybrid ventilated buildings, with lighter construction, can be very sensitive to stochastic load variations. As part of the Annex 35 project, probabilistic methods were applied to thermal building simulation, single zone models, multizone models and CFD, see Brohus (2002a-c).

When using probabilistic methods, some or all of the input parameters are modelled either as random variables or stochastic processes. Various statistical parameters are applied such as mean values, standard deviations, auto-correlation functions, etc. and the results are presented in the form of probabilities of occurrences. A stochastic method is thus a formulation of a physical problem, where the randomness of the parameters is taken into account. In principle, any of the above-mentioned analysis methods can be applied stochastically. The advantage of probabilistic methods is the possibility of not only designing for peak load and estimating annual energy consumption based on a reference year, but also to examine the range of variation and to quantify the uncertainty. For instance, a building designer can prescribe the probabilistic modelling can also be used to gain further knowledge and develop simple easy-to-use deterministic models. Probabilistic modelling can be very useful in considering the effect of occupant behaviour.

2.7 Application to SARS outbreak investigations

For the 8A ward investigations, to assist the epidemiological studies of the Ward 8A outbreak carried out by Wong et al. (2004) and Yu et al. (2004), we carried out ventilation and air distribution studies in Ward 8A. Retrospective on-site inspections and measurements of the ventilation and air distribution system were carried out three months after the outbreak. Limited on-site measurement of bio-aerosol dispersion was carried out in Ward 8A on 22 July. Computational fluid dynamic (CFD) simulations were performed to analyze the bio-aerosol dispersion in the hospital ward. We attempted to predict the air flow distribution in Ward 8A at the time of exposure in March 2003 and at the time of measurement in July 2003. The latter provided an opportunity to evaluate our predictions and also to study the effects on bio-aerosol dispersion of the number of beds in the ward. Possible improvements to air distribution in the hospital ward were also considered.

For the Amoy Gardens outbreak, we used a combination of multi-zone air flow modelling, simple fluid mechanics analysis, and computational fluid dynamics (Figure 7). Multi-zone methods (Axley, 1989) allow us to calculate hourly airflow rates between flats, and the concentrations of virus-laden bio-aerosols within each flat (Sandberg, 1984 and Awbi, 1991) in a building. In these methods, each flat or room is considered as a zone. Zones are interconnected by flow paths, such as cracks, windows, doors and shafts, to form a flow network. For closed windows and doors, the effective leakage area is calculated based on the data from Orme et al. (1998). Flow rates through doorways and windows are assumed to be driven by pressure differences. Air temperature difference, winds and exhaust fans introduce driving pressures. Multi-zone methods are able to take into account the effects of outdoor climate, the location and size of each opening, and stack-, wind- and mechanically driven ventilation. We used the computer program MIX, which was developed and evaluated by one of the authors (Li et al., 2000).

Computational fluid dynamics (CFD) allows detailed airflow pattern in the re-entrance and around the building blocks to be reasonably accurately predicted. Similar airflow models have been used for studying the foot-and-mouth disease and the Sverdlovsk anthrax outbreak of 1979. In applying such a modelling tool, turbulence models, numerical methods as well as the user's experience can introduce significant errors. Hence, proper evaluation of the results generated is essential. Two CFD software packages were used in our study. "Fluent" is a three-dimensional general-purpose CFD package for modeling fluid flows. We used the basic Renormalization Group (RNG) turbulence model and the Reynolds stress model for modeling turbulence effects on airflow and pollutant dispersion. The virus-laden water droplets generated from the flat where the index case stayed were found to evaporate

rapidly (within a few seconds in air) when we modeled the virus-laden plume in the reentrance. For most of the simulations, we approximated the droplet nuclei as passive scalars and thus the deposition effect was neglected. "Airpak" is a three-dimensional CFD package developed for modeling building ventilation flows. We used the RNG turbulence model in Airpak to carry out CFD simulations for both the plume flow in the re-entrance and the aerosol spread between blocks. Currently, both particles and droplet evaporation are included in our mathematical analysis.



Figure 7. Spatial distribution of infected flats in the Amoy Gardens SARS outbreak and the CFD prediction of wind-driven plume from the re-entrant between Flats 7 and 8. (Left figure from Yu et al (2004).

3. Developing Engineering Control Methods

3.1 Introduction

Engineers appear to be largely invisible in control of airborne infection in both non-hospital and hospital environments. However, in challenging crisis situations, the partnership and contribution of engineers is invaluable.

Viruses in emerging infection diseases might have jumped from animals (or birds) to human, but it is mostly in buildings that the infectious diseases such as severe acute respiratory syndrome (SARS) spread among us. The practical importance and frequency of airborne infections have been a matter of dispute for many years. To some degree, the barrier between the disciplines of medicine, infection control, occupational health and engineering has prevented a meaningful development in control of airborne infections in both hospitals and non-hospital environments.

There are a full range of issues to deal with on this topic, e.g.

- Generation mechanisms of bioaerosols in lung, mouth, nebulizers, toilet flushing...control
- Dispersion mechanisms of bioaerosols evaporation, turbulence, ventilation, components of bioaerosols...
- Surface deposition of bioaerosols mechanisms, control, resuspension, surface properties...
- Survival of microorganisms in air RH, droplet evaporation, particles/dusts...
- Detection of microorganisms in air CFU, microscope, DNA sequencing...
- Optimization of engineering control as compared to administrative control/PPE, or ventilation, ultraviolet germicidal irradiation (UVGI), photocatalytic oxidation (PCO), control of particle numbers, etc.

Here we focus on ventilation system design in general isolation rooms and hospital wards.

3.2 Evidences of the roles of building ventilation

First we report our recent literature review (InDiVent) of the literature between 1960 and March 2005 on the association of building ventilation/air flows and the transmission of infectious diseases.

We searched the following databases: MEDLINE, ISI web of knowledge, ScienceDirect, and PubMed using various combinations of the following key words, "ventilation", "air flow", "health", "airborne", "droplet", "droplet nuclei", "aerosol", "bioaerosol", "transmission", "survival", "infectivity", "nosocomial", "tuberculosis", "measles", "influenza", "chickenpox" "and "disease". References cited relevant articles, books as well the authors' archives are also included. Only peer-reviewed articles are selected.

More than 150 papers are gathered by searching the databases by March 2005 and after initial screening, a total of nearly 100 papers were selected including papers with evidences of airborne transmission. A final 46 papers (or 40 studies with some studies presented in more than 1 paper) are chosen, considering the scope of the InDiVent review, i.e. evidences of the impact of ventilation and/or air flow pattern on airborne transmission of infectious diseases.

The 40 studies were evaluated through both email communication (phase I) and face-to-face meeting (phase II). Finally, a total of 10 studies were considered to be conclusive on at least one of the following four questions.

- If author(s) investigated a disease outbreak, did the outbreak occur due to a lack of providing outdoor air into an enclosed space?
- If author(s) investigated a disease outbreak or carried out a population based study, was the rate of increase of new cases of airborne infection in a group of susceptible hosts inversely correlated with the ventilation flow rate per susceptible occupant?
- If author(s) investigated a disease outbreak in an enclosed space, did the outbreak occur due to the air transport of airborne particles and/or droplet nuclei containing the pathogen from one location to another location in space that is farther than 1 m that a large droplet can spread/spray, as demonstrated by tracer gas, smoke or any other experimental or computer simulation studies?

• If the authors carried out a population-based study, was the ventilation rate shown to be associated with the incidence of an airborne disease?

The following consensus was reached by the InDiVent assessment panel members.

1. There are strong and sufficient evidences that demonstrate the association of ventilation and control of air flow directions in buildings and the transmission and spread of infectious diseases such as measles, TB, chickenpox, anthrax, influenza, smallpox and SARS. These evidences support the use of negatively pressurized isolation rooms for patients with these diseases in hospitals, in addition to the use of other engineering control methods.

2. There are not sufficient evidences that support the specification and quantification of the minimum ventilation requirements in hospitals and isolation rooms in relation to spread of airborne infectious diseases. The knowledge gap is obvious.

3. There are also no evidences that support the specification and quantification of the minimum ventilation requirements in schools, offices and other non-hospital environments in relation to spread of airborne infectious diseases. The knowledge gap is obvious.

4. There is a strong need for inter-disciplinary study in investigating outbreaks of and impact of air environment on the spread of potentially airborne infectious diseases. Such an approach would allow the combined use of the available molecular biology test methods and the new computer modeling and experimental methods for investigation building ventilation.

The work is still on-going and the final results will be reported elsewhere.

3.3 Application of environmental modelling methods

Without going into details, we will give a few examples during the presentation, including

- Understanding the evaporation and dispersion of droplets in indoor environments
- Understanding survival of micro-organisms in droplets during evaporation process
- Understanding the interaction of breathing flows between people in hospital wards (Figure 8)
- Developing better and effective ventilation systems for isolation rooms



Figure 8. Penetration of exhaled flow of the source patient (left) into the breathing zone of the receiving patient (right) with smoke visualization in a full-scale test room .

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Figure 4. Comparison of the predicted daily number of newly infected SARS cases in the 2003 Amoy Gardens SARS outbreak in Hong Kong using three back-calculation methods ((A)–(C)), and comparison of the predicted and observed daily number of cases with symptom onset ((D)–(F)): (A) and (D) using the CG method (non-smoothed) and with two smoothing coefficients of 0.01 and 0.1; (B) and (E) using the EM algorithm (non-smoothed) and with two smoothing coefficients of 0.01 and 0.1; (B) and (C) and with smoothing coefficients of 0.1 and 0.25.





Figure 5. Comparison of the predicted daily number of newly infected cases in the 2003 Hong Kong SARS epidemic using three back-calculation methods ((A)-(C)), and comparison of the predicted and observed daily number of admissions ((D)-(F)): (A) and (D) using the CG method (non-smoothed) and with two smoothing coefficients of 0.01 and 0.1; (B) and (E) using the EM algorithm (non-smoothed) and with two smoothing coefficients of 0.01 and 0.1; (B) and (E) using the EM algorithm (non-smoothed) and with two smoothing coefficients of 0.01 and 0.25.



Figure 6. Comparison of the predicted daily number of newly infected cases in the 2003 Hong Kong SARS epidemic using the EM algorithm (nonsmoothed) with three convergence criteria of 0.1, 0.01 and 0.001.