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A mathematical model for predicting the viability of airborne viruses

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A B S T R A C T

A mathematical model was developed to predict the viability of airborne viruses. The model uses water activity as the primary independent variable and an exponential decay function for the viability of the virus. This model was tested using published experimental data obtained by different investigators for influenza, Langat and polio viruses. The aerosolized media were modelled as a binary solution of water and sodium chloride. The water activity is related directly to the solute concentration in the binary solution. The minimum viability usually occurred just above the efflorescence point, which is the relative humidity at which the solution crystallizes. The relationship between water activity and relative humidity is based on the Köhler theory, whereby the Kelvin term was taken into account. Physical explanations are provided on the variation of viral viability at different relative humidity levels. The predictions obtained by the proposed mathematical model compare well with most of the published experimental data.

1. Introduction

Millions of people worldwide become infected with seasonal influenza virus every year. Recently, an influenza pandemic (2009 H1N1) emerged which has caused nearly 6770 deaths and more than 526,060 confirmed cases as of November 15, 2009 (WHO, 2009). The Centers for Disease Control and Prevention (CDC) have identified a North American avian influenza A H7 virus strain that has partially adapted to infect humans (Belser et al., 2008) and together with the avian influenza A H5N1 virus circulating primarily in Asia, Europe and Africa, the potential exists for emergence of a highly pathogenic human influenza A virus. Although considerable attention is paid to predicting which strains of influenza will be circulating for vaccine development, the mechanisms and factors influencing the transmission of influenza are poorly understood.

Large droplets (>20 μm) and direct contact with viral-laden secretions are presumed to be the primary routes of transmission of influenza virus (Tellier, 2006). Although controversial, there is evidence suggesting that small droplets (<5 μm), including droplet nuclei, may also play an important role in the transmission of influenza by the airborne route (Tellier, 2009). Unlike large droplets, small droplets remain airborne for prolonged periods, are easily respired, and have the potential to cause lower respiratory tract infections. Tellier (2006) supports the view that small droplets can reach easily the lower respiratory tract upon inhalation, and that the epithelial cells of the lower respiratory tract have certain receptors that bind influenza A virus. Research by Shinya et al. (2006) has shown that expression levels of the preferred α-2,3 linked sialic acid receptor for H5N1 attachment are primarily located in the lower respiratory tract. Likewise, attachment of the H5N1 virus to type II pneumocytes in the terminal bronchioles (van Riel et al., 2006) further validates that aerosol transmission of influenza indeed takes place.

Tellier (2006) cites many examples of airborne transmission, such as the Alaska airlines outbreak, which involved an unusually high infection rate of influenza (72%) on an aeroplane which was attributed to effective aerosol transmission of the virus due to an inoperative ventilation system (Moser et al., 1979). Lowen et al. (2006) assessed the droplet and/or aerosol transmission of influenza A/Panama/2007/99 (H3N2) between guinea pigs. An open, wire-top cage containing two uninfected animals was placed 91 cm (three foot rule) downstream of a cage containing two infected guinea pigs. The uninfected animals became infected between days 4 and 6. Transmission was not observed when the relative positions of the cages were reversed, suggesting that transmission depends on the airflow direction. In a later study, Mubareka et al. (2009) found more evidence of airborne long-range influenza transmission between guinea pigs separated vertically by 107 cm. However, one interesting difference between humans and guinea pigs regarding influenza transmission is that influenza virus-infected guinea pigs do not display expulsion events, such as coughing or sneezing (Mubareka et al., 2009). In two other separate studies on droplet dispersion in indoor environments and aerosol transmission of virus particles, Morawska (2006) and Tang et al. (2006) agree that airborne transmission is a significant mechanism

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for the spread of influenza virus. In a recent study, looking at the prevalence of airborne influenza virus in a hospital emergency room, Blachere et al. (2009) detected a large number of particles within the respirable aerosol fraction.

Experimental evidence suggests strongly that airborne transmission of influenza exists, however, environmental conditions such as ventilation, humidity and temperature, can significantly affect the overall viability and transmission efficiency of influenza viruses. An in depth understanding of the factors that affect viral viability could provide the key to preventing its transmission. Influenza virus is an enveloped helical RNA virus with a diameter of approximately 120 nm (Morawska, 2006). The envelope is derived from the host cell membrane and is composed of phospholipids and proteins. Enveloped viruses generally survive better at low relative humidity levels and lower temperatures (Sobsey and Meschke, 2003). Consequently, the relative humidity and temperature of indoor environments are considered important seasonal factors in the epidemiology of influenza. Past research has associated the seasonality of influenza morbidity with the relatively low humidity levels that result from indoor heating during the cold winter months (Hemmes et al., 1960). In more recent studies, Lowen et al. (2007) found that cooler, dryer conditions enhanced the transmission efficiency of influenza virus and that a temperature of 30 °C blocks aerosol, but not contact, transmission of influenza virus (Lowen et al., 2008). Influenza virus exhibits an interesting trend of viability as a function of relative humidity; namely it is most viable at low humidity, least viable at intermediate humidity and moderately viable at higher humidity (Schaffer et al., 1976; Lester, 1948).

The variations in viability with humidity seem to be related directly to the type of tissue culture in which the virus was grown and the medium in which it was aerosolized (Sobsey and Meschke, 2003; Schaffer et al., 1976; Benbough, 1971). After performing experiments with two other enveloped viruses (Langat virus and SemLiki Forest virus), Benbough (1971) showed that the salt content of the suspending medium was the main cause of the low viability at intermediate humidity. This could be due to the hygroscopic properties of the salt. Schaffer et al. (1976) and Benbough (1971) also found that low protein content in the medium led to a sharp decrease in infectivity from mid to high humidity levels. Schaffer et al. (1976) reported that the minimum concentration of protein in the medium required for stability of the virus was 0.1 mg/mL. In both of these studies, it was observed that the addition of polyhydroxy compounds to the spraying medium improved viral stability at mid-range humidity. Inositol was shown to have a harmful effect at higher humidity levels, unlike sucrose and glucose (sucrose being more effective than glucose at the same concentration). A few other factors, such as exposure to ultraviolet light, open air factor and aerosol particle size, were reported by Sobsey and Meschke (2003) to have an effect on aerosolized viruses. Ultraviolet light is known to inactivate influenza virus, however, the open air factor is poorly defined and it is uncertain what effects this, and the aerosol particle size, have on the viability of influenza virus. Hogan et al. (2005) indicated that larger particles from the MS2 phage suspension have a higher probability of containing a viable virus. This seems logical because the number of viruses inside a droplet should be proportional to its volume. On the other hand considering the viability of a single virus, this should not be affected by the droplet size. Stallknecht et al. (1990) studied the effects of pH, salinity and temperature on avian influenza virus in water. At both 17 °C and 28 °C, the salinity and pH levels for optimum viability of the virus were inversely related, i.e., viability was highest at zero salt/high pH and was also high at high salt/low pH, whereas it was lowest at high salt/high pH and low salt/low pH. Collectively, these findings strongly suggest that the composition of the aerosol containing the virus may affect its viability.

The aim of the current study was to establish a simple, yet general, physics-based mathematical model which allows for the prediction of the viability of influenza, Langat, and polio viruses; taking into account the composition of the suspending (aerosol) medium, the hygroscopic properties of the solutes within the medium, and the relative humidity of the surrounding air. These factors seem to be the primary variables that determine the ability of a virus to remain viable in the airborne state (Benbough, 1971).

2. Brief description of experiments considered

Four primary sets of experiments were used to validate the proposed mathematical model, namely: Schaffer et al. (1976) on influenza virus, Benbough (1971) on Langat and polio viruses and Ijaz et al. (1987) on poliovirus.

Schaffer et al. (1976) studied the effects of the propagating host, relative humidity and the composition of spray fluids on the viability of airborne influenza A virus, strain WSN_H. The cell culture medium (minimum essential medium, MEM) was aerosolized in a Wells refluxing atomizer at 21 °C into a 208-L stirred settling chamber. Samples were taken at 1 min, 15 min, 30 min, and 60 min post-aerosolization with AGI-30 impingers.

In an earlier study on the viability of airborne viruses, Benbough (1971) removed defined components from the suspending medium of Langat virus, in order to measure their individual effects on the viability of this virus. The culture fluid contained approximately 10^9 plaque forming units (p.f.u.) in 199 medium containing 10% calf serum. Polydisperse aerosols were generated by a 3-jet collison Spray, which produced a droplet size distribution with a mean diameter of 2.5 μm (Benbough and Bennett, 1990; May, 1973). The total volume of the spray fluid was about 10 mL, containing 10^9 p.f.u./mL. The aerosol was stored in a 120 L rotating drum containing air at a controlled relative humidity. The aerosols were collected by Porton-raised impingers using phosphate-buffered saline, pH 7.4, containing 10% calf serum as the collecting fluid.

Benbough (1971) also conducted experiments with the standard Sabin attenuated type I (LSc2ab) strain of poliovirus. The viruses were grown in a 30 mL suspension of HeLa cells containing 1×10^7 cells/mL in 199 medium. The clarified culture fluid contained approximately 5×10^8 p.f.u./mL. Aerosol generation and storage of the poliovirus was similar to that of Langat virus described above.

As an independent test case, the experiments carried out by Ijaz et al. (1987) on poliovirus were used. Ijaz et al. used the MA-104 cell line for the cultivation and quantification of the Sabin strain of poliovirus type I. Virus-containing aerosols with aerodynamic sizes of less than 5 μm were generated using a 6-jet Collison nebulizer (BGI Inc., Waltham, MA, USA) and were stored in a 300 L stainless steel drum rotating at 4 rpm and kept at 20 °C. Experiments were carried out at three relative humidity levels: low (30%), medium (50%) and high (80%).

3. Mathematical model

3.1. Physical basis for the model

From the experiments described above, Benbough (1971) concluded that the susceptibility of airborne viruses to environmental conditions must be related to the partition of bound and unbound water between the virus, other constituents of the droplet and the surrounding atmosphere. Benbough suggested that there is a period of stabilization after the aerosolization of the solution. During this initial period, the concentration of certain solutes in the droplet increases to levels which may be toxic to the virus. This observation indicates that the viability of airborne viruses may

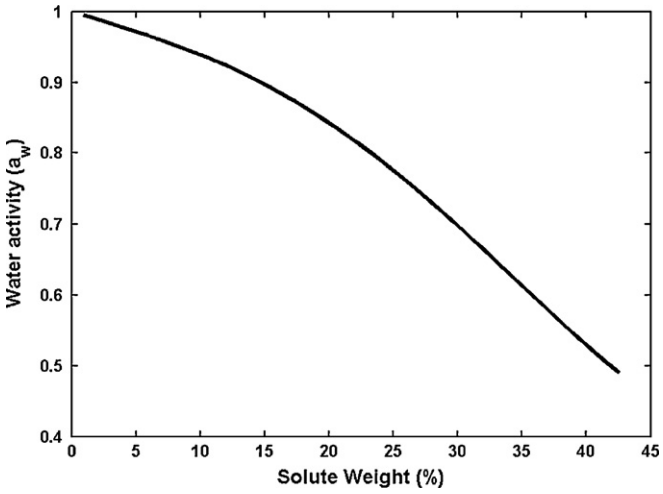

Fig. 1. Water activity as a function of the solute weight (%) for sea salt solutions, taken from Tang et al. (1997). Copyright 1997, American Geophysical Union, reprinted with permission from the American Geophysical Union.

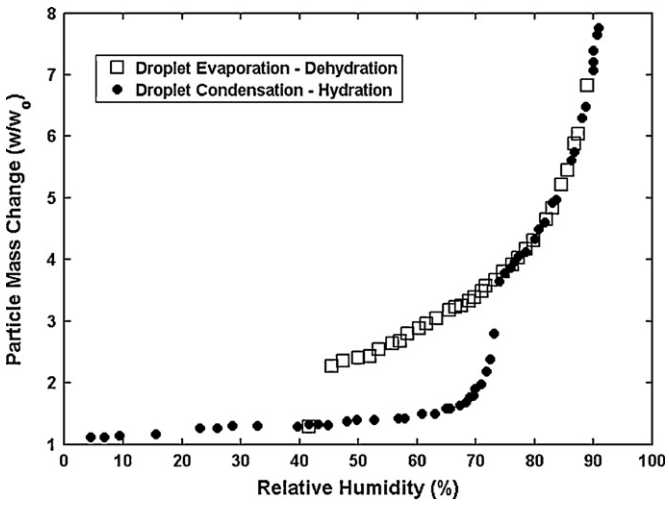

Fig. 2. Phase transformation, growth and evaporation of a sea salt particle as a function of relative humidity, taken from Tang et al. (1997). Copyright 1997, American Geophysical Union, reprinted with permission from the American Geophysical Union.

depend on the water activities of saturated solutions of the solutes in the aerosolized fluid (Bateman, 1968). De Jong et al. (1973) identified two mechanisms which might be largely responsible for the inactivation of viruses in aerosols: dehydration and surface inactivation. De Jong et al. also highlighted the protein coat as the target of aerosol decay and stated that water molecules are essential for the stability of this protein coat. Based on these observations, it is proposed in the current study that water activity (a_w) is the primary independent variable which controls the viability of airborne viruses. Water activity is a measure of the availability of the water in a solution, and it is a function of temperature and pressure.

The culture fluid used by Schaffer et al. (1976) and Benbough (1971) consisted mainly of water (99%) and sodium chloride (1%), hence a simple binary solution containing only these two constituents is also assumed for the current model. Another reason for this assumption is that there is little information in the literature about how other elements in the media affect the water activity and the efflorescence relative humidity. The change in the water activity as a function of the percentage weight of solute (NaCl) for sea salt solutions can be seen in Fig. 1.

Fig. 2 shows the phase transformation, growth and evaporation of a sea salt particle as a function of relative humidity (Tang et al., 1997). Upon increasing relative humidity (filled circles), a solid (dry) NaCl particle remains unchanged until it deliquesces at 75.3% relative humidity, where it rapidly acquires more water to become a homogeneous solution droplet. The droplet then grows continuously and smoothly as relative humidity is further increased. As relative humidity decreases (open squares), the droplet gradually loses mass by water evaporation, but remains a supersaturated metastable solution beyond the deliquescence (saturation) point, until efflorescence occurs at about 45–48% relative humidity. At this point, the NaCl particle suddenly sheds all of its water and crystallizes, while the sea salt particle does not return to its initial weight immediately (Tang et al., 1997).

3.2. Proposed empirical equations

Since numerous physico-chemical processes exhibit an exponential decay rate, the time variation of viability, S, of infective airborne viruses is modelled as an exponential decay function:

$$S = \alpha \exp(-\beta t^n) \quad (1)$$

where α and β are model coefficients, and t is the aerosol exposure time. The coefficient α is the viability at the initial time

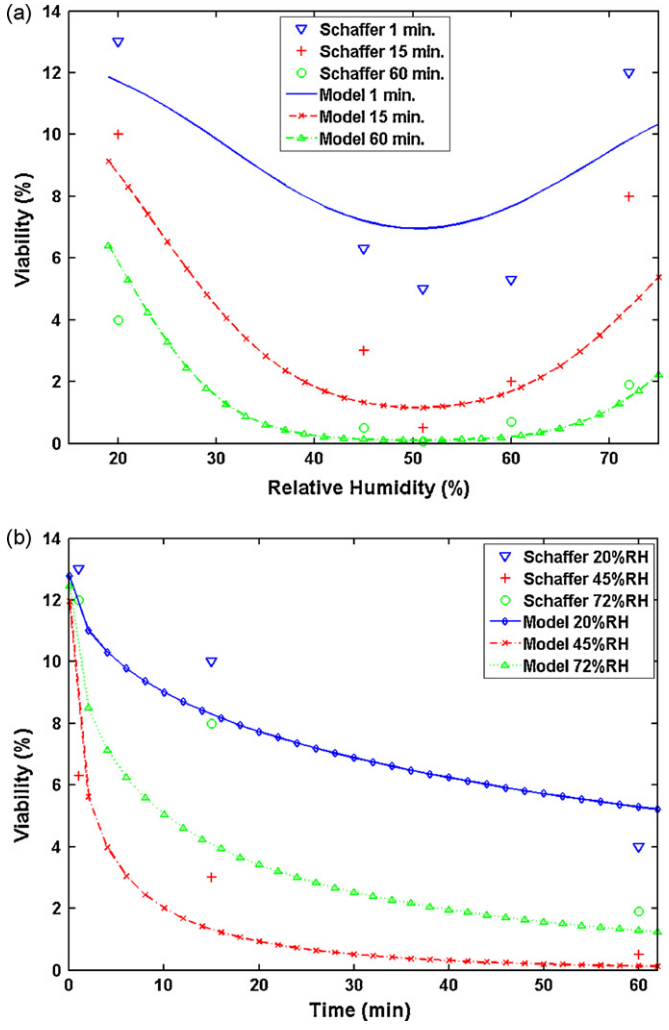

Fig. 3. Comparison between the experimental data from Schaffer et al. (1976) and the proposed model for viability of influenza virus in aerosols sprayed from culture fluid. (a) Viability versus relative humidity, and (b) viability versus time; RH = relative humidity.

Table 1
Model parameters used to predict the viability of airborne viruses*.

Case	Virus	α	c_1	c_2	c_3	a_{cr}	q	n
1	Influenza	0.13	0.6	20	0.1	0.5	2	0.5
2	Langat	1.00	0.6	20	0.1	0.5	2	0.5
3	Poliovirus	1.00	2.0	20	0.1	0.3	2	0.5

α, initial viability; c_1, minimum viability when $a_w = a_{cr}$; c_2, c_3 and q are model coefficients; a_{cr}, critical water activity; and n, viability decay rate. All these are model parameters used in Eqs. (1) and (2).

($t = 0$). The exponent n controls the viability decay rate. The β coefficient for the binary aqueous solution should be determined through Eq. (2):

$$\beta = c_1 \exp[-c_2(a_w - a_{cr})^2] + c_3 a_w^q \quad (2)$$

where c_1, c_2, c_3 and q are model coefficients which need to be determined empirically; a_{cr} is the critical water activity in the solution where crystallization (efflorescence) occurs; and a_w is the water activity in the solution defined as the vapour pressure of water in a solution ($p_{v,sol}$) divided by the saturation vapour pressure of pure water ($p_{v,sat}$) under the same conditions. The relative humidity is the ratio between water vapour pressure (p_v) and the saturation vapour pressure of pure water ($p_{v,sat}$) in the ambient air surrounding the droplet.

Table 1 lists the values of the parameters used in our model to predict the viability of the influenza, Langat and polio viruses. These values were determined as discussed in section 4. The parameters needed from experiments to predict the viability of one of these viruses are the critical water activity (a_{cr}), the minimum viability (c_1) and the viability at time zero (α).

In theory, the viability (or the survival rate) at time zero should be equal to 100%, since all the viruses are assumed to be viable (infective) at the beginning of the experiment. Hence, $\alpha = 1.0$ and an additional model parameter does not need to be determined. This parameter needs to be adjusted only when experimental circumstances, such as inactivation of some viruses due to shear stress during aerosolization, may cause the initial conditions to be less than ideal (Ijaz et al., 1987). Collection methods and other experimental factors may also lead to a lower value for α. Therefore, in laboratory experiments, the value of α may depend on how the actual experiments are conducted.

The critical water activity, a_{cr}, is defined as the water activity at the crystallization relative humidity where the viability is minimal (Eq. (1)). The experimental data indicates that this corresponds roughly to the crystallization water activity and for the experiments considered in this paper it is usually in the range of 0.3–0.7, depending strongly on the composition of the droplet. It is possible to compute the value of a_{cr} from the properties of the constituents that are within the droplet, such as lipids, proteins, and salts. The authors are currently working on such a model for a multi-component droplet.

The toxic effect of NaCl on viability is greatest when a_w is near 0.5 (Bateman, 1968). As relative humidity decreases from a salt-water droplet (Fig. 2), the droplet gradually loses mass by evaporation but remains a metastable solution until efflorescence occurs at about

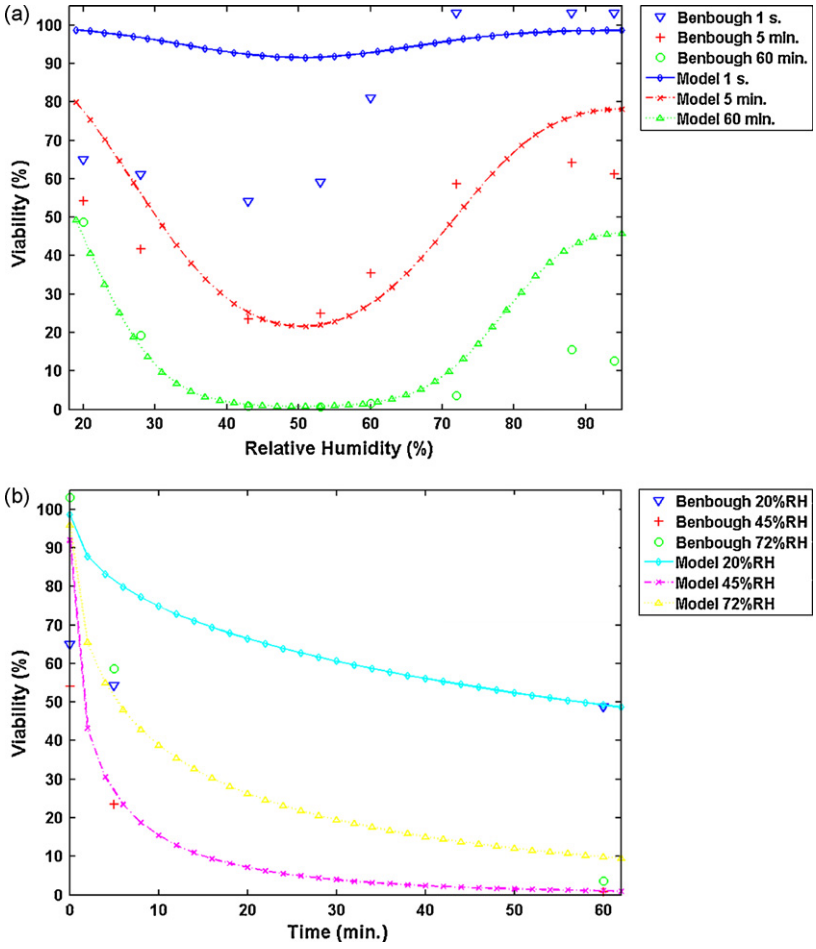

Fig. 4. Comparison between Benbough's (1971) experimental data and the proposed model for viability of Langat virus in aerosols sprayed from culture fluid. (a) Viability versus relative humidity, and (b) viability versus time; RH = relative humidity.

45–48% relative humidity (Tang et al., 1997). Thus the value of 0.5 is used as an approximate value for the critical water activity (a_{cr}) in the current model.

The proposed model is similar to that proposed by Ijaz et al. (1987) in that it also uses an exponential function to model the viability. However, Ijaz's model does not take into account the changes in infectivity with respect to the water activity. The proposed model predicts viability during the first 60 min when the biggest loss of infectivity occurs, while Ijaz's model is a long term curve fit (up to 25 h) and neglects the initial loss occurred during the first 15 min.

According to Köhler's theory (Pruppacher and Klett, 1978), the relationship between relative humidity and the size and composition of a spherical aqueous solution droplet suspended in a gas under equilibrium conditions can be described by:

$$\varphi = a_w \, \mathrm{Ke} \tag{3}$$

where φ is the relative humidity and Ke is defined by:

$$\mathrm{Ke} = \exp\left(\frac{4\sigma M_w}{\rho R T d_m}\right) \tag{4}$$

The term Ke is the Kelvin or curvature term and describes the increase of water vapour pressure over a spherical droplet with the surface tension σ and the inverse of the droplet diameter d_m. Here, M_w is the molar mass of water, R is the ideal gas constant, and T is the absolute temperature; σ and ρ are the surface tension and density of the aqueous solution, respectively. The Kelvin effect is negligible when the droplets are bigger than 1 μm in diameter (Martin, 2000). The current model takes into account all of these physical parameters in cases where there are significant differences among carrier droplets.

4. Results

The model developed in this study was tested using the experimental data published by Schaffer et al. (1976) for influenza virus propagated in primary chick embryo cells and aerosolized from culture fluids (Fig. 3). The Kelvin term can be approximated with $\rho = \rho_{medium} = 1012\ \mathrm{kg\,m^{-3}}$ and $\sigma = {}_{medium} = 0.0459\ \mathrm{N\,m^{-1}}$ (Palasz et al., 2000) under the experimental conditions of $T = 298\ \mathrm{K}$ and $d_m = 2.5 \times 10^{-6}\ \mathrm{m}$ (Benbough and Bennett, 1990). Under these conditions the Kelvin value is equal to one. The other parameters used for the model predictions plotted in Fig. 3 were found by fine tuning the model parameters using the data from Schaffer et al. (1976). The recommended values were: $\alpha = 0.13$, $c_1 = 0.6$, $c_2 = 20$, $c_3 = 0.1$, $q = 2$ and $n = 0.5$. Fig. 3b shows the decay of viability as a function of time for influenza virus. The model effectively predicts the variations in viability with relative humidity and time.

With the same parameters used for the influenza virus, but changing α (initial viability rate) to 1.0, the proposed model was applied to the case studied by Benbough (1971) for Langat virus (Fig. 4). The predictions compared well with the experimental data measured at 5 min and 60 min, however, the predictions did not agree so closely with the measurements taken at 1 s.

Benbough (1971) also performed experiments with poliovirus to determine the viability when aerosolized from clarified culture fluids. A comparison between the experimental results obtained by Benbough and the proposed model is shown in Fig. 5. The proposed model predicts the viability of poliovirus at low, mid and high relative humidity in close agreement with the experimental data. Again, the model does not reliably predict the viability for measurements taken at 1 s. The parameters used for poliovirus are the same as those used for the influenza virus, except for $\alpha = 1.0$, $c_1 = 2$ and $a_{cr} = 0.3$. Poliovirus exhibits low viability at low relative humidity which may be due to the lack of a lipid membrane (De Jong and Winkler, 1968; Schaffer et al., 1976). This is the reason for the reduction of the critical water activity parameter, a_{cr}, from 0.5

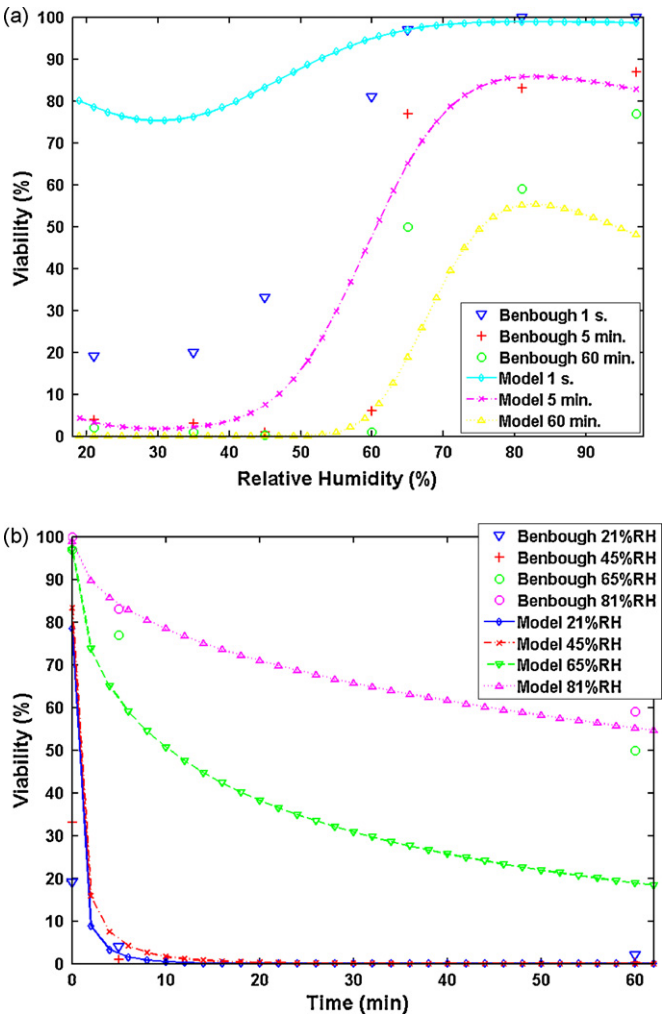

Fig. 5. Comparison between Benbough's (1971) experimental data and the proposed model for viability of poliovirus in aerosols sprayed from culture fluid. (a) Viability versus relative humidity, and (b) viability versus time; RH = relative humidity.

to 0.3. The parameter c_1 was proportional to the minimum viability when $a_w = a_{cr}$. The relatively large change in the value of c_1 from 0.6 for influenza virus to 2 for poliovirus indicated that some experimental information is necessary to predict the minimum viability of a given virus at the critical water activity.

Fig. 6 depicts the model predictions as compared to measurements by Ijaz et al. (1987) for poliovirus. First the same model parameters were used as listed in Table 1 for poliovirus. Then, only one parameter, namely c_3, was varied to assess the sensitivity of the results to such conditions. The predictions improved significantly when c_3 was changed. This change in c_3 could be due to differences in the experimental conditions.

5. Discussion

This paper reports a mathematical model that can be used to predict the viability of aerosolized viruses. As shown in Fig. 2, at high relative humidity, the amount of water in a droplet is high so the percentage weight of solute (NaCl) is low. From Fig. 1, it can be seen that at low percentage weight of solute, the water activity is high (very close to one), which is favourable for virus viability. At mid relative humidity, the water content is low so the solute weight percent will be high, and the water activity will be low. Therefore the virus viability is expected to be minimal in the mid relative

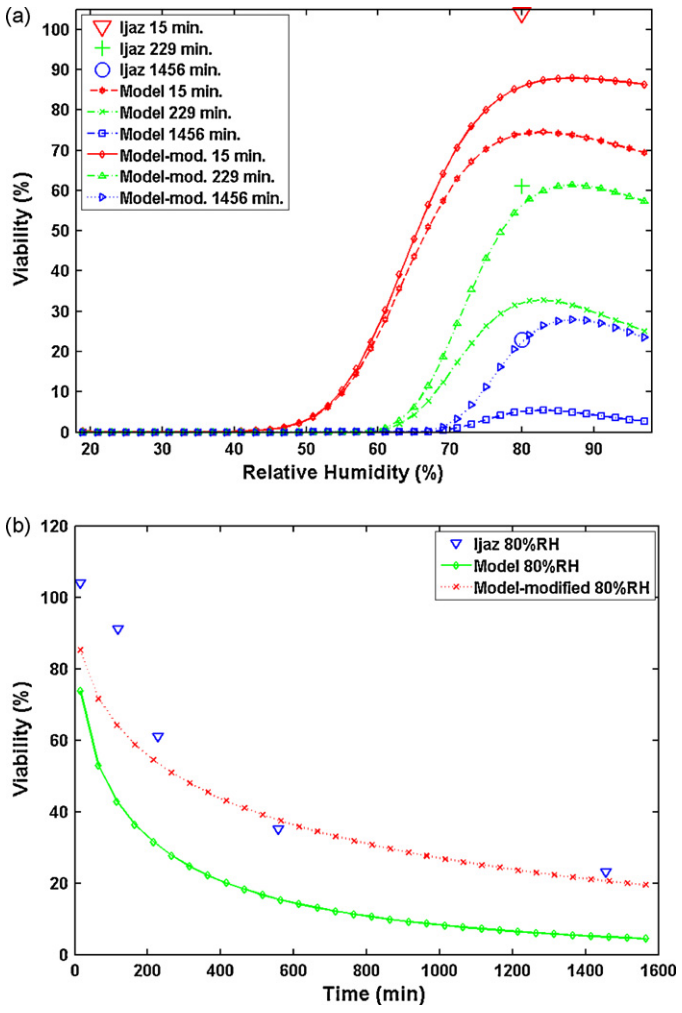

Fig. 6. Comparison between the experimental data from Ijaz et al. (1987) and the proposed model for viability of poliovirus in aerosols sprayed from culture fluid. (a) Viability versus relative humidity, and (b) viability versus time; RH = relative humidity. The parameter c_3 was modified from 0.1 to 0.04.

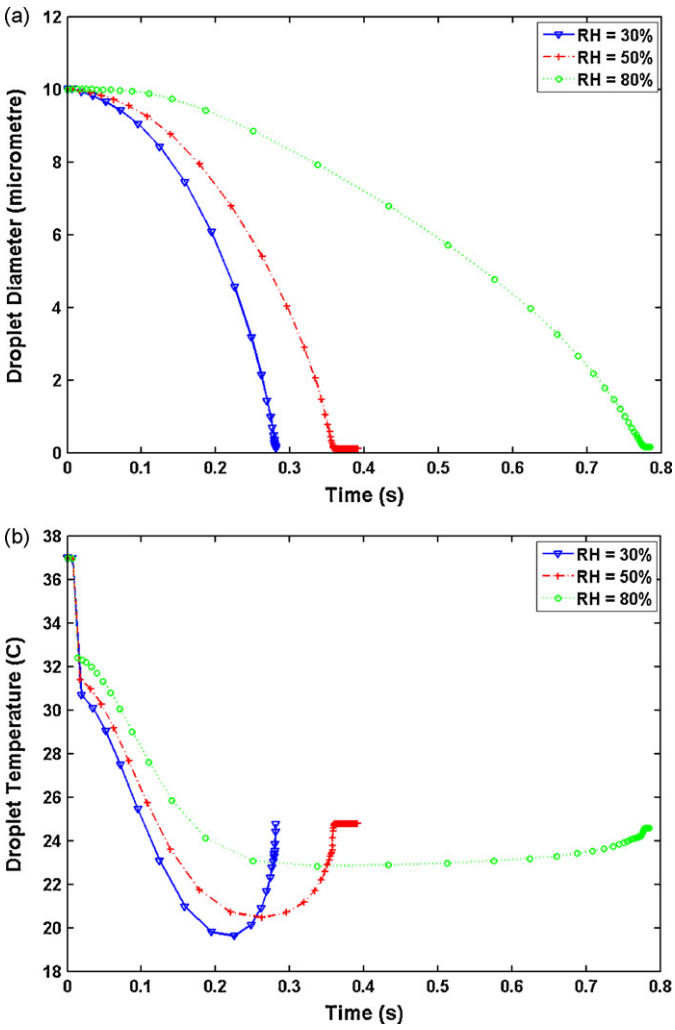

Fig. 7. Time evolution of a water droplet starting with different initial conditions inside a room at constant temperature (T = 25 °C) and constant relative humidity. (a) Diameter, and (b) temperature; RH = relative humidity.

humidity range. The higher viability of some airborne viruses at low relative humidity may be explained by the fact that salts are toxic in solution and non-toxic when in solid form (Benbough, 1971).

The increased viability of enveloped viruses at low relative humidity compared with non-enveloped viruses, like poliovirus, could also be caused by a decrease in the water evaporation rate of the droplet due to the presence of a lipid layer in enveloped viruses. Iwata et al. (1969) measured an approximate four-fold increase in evaporation when the lipid layer was removed from the precorneal tear film of a rabbit. Mathers (2004) also showed that evaporation from the ocular surface is dramatically reduced by the lipid layer which covers it.

The lack of agreement between the model predictions and the experimental results of Benbough (1971) at 1 s for the Langat (Fig. 4) and polio viruses (Fig. 5), may be due to the fast initial decay of viability in the first few seconds following aerosolization. Also, other experimental factors may have a greater impact on viability at such short times. A possible explanation for the need to change the α value between Schaffer's experiments and Benbough's experiments could be that Schaffer did not take into account the viruses inactivated by the shearing forces during injection of the spray.

The least well defined parameter in the present model is c_1 which is related to the minimum value of viability at critical water activity and is associated with the rate at which viability decays with time. It is postulated that c_1 is related to the rate at which water evaporates from, or condenses onto, the surface of the droplet. In other words, it is implicitly related to the change in diameter of the droplet over time, which is not reported in the experiments found in the literature. Such information can be calculated using mathematical models for tracking the droplet evaporation or condensation processes as a function of time. The authors are currently working on a model to predict the dynamic process of droplet evolution in a given environment characterized by a given temperature and relative humidity (Celik et al., 2007), as shown in Fig. 7. This model should predict not only the values of water activity, a_w, but also the diameter and water evaporation rate as a function of time. The rapid changes occurring in the first few seconds after aerosolization may explain why the current model is not very successful at predicting viability at such short times, it is likely that many droplets have not reached an equilibrium state by this time in the experiments considered.

The change in surface tension due to changes in the solution is given by equation 5.19 and Fig. 5.2 in Pruppacher and Klett (1978). Assuming the addition of 10% calf serum to the medium, there will be 0.1 kg of calf serum in 1 L of culture fluid. However, Benbough (1971) aerosolized 10 mL, so 0.001 kg of calf serum would be present in this case. The molecular weight of the major protein component of calf serum (BSA) is 66,432 g/mol, so the num-

ber of moles is 1.505×10^{-5}. Assuming 0.55 mol of the solution and a molecular weight of the solution equal to that of the water (18 g/mol), the molarity will be equal to 1.52×10^{-3} mol/kg. Using equation 5.19 in Pruppacher and Klett (1978) and assuming the slope B is equal to that of NaCl (1.62×10^{-3} N kg/m^{-1} mol^{-1}), the change in surface tension will be 2.46×10^{-6} N/m. This variation in surface tension is very small and can be neglected. The value of the surface tension for medium 199 is 0.0456 N/m. Therefore, the change in the Kelvin term can also be neglected. On the other hand, the Kelvin term is highly affected by the droplet diameter (see Fig. 6.1 of Pruppacher and Klett, 1978). Usually, the precise drop sizes are not provided in the published literature.

6. Conclusions

An empirical model is proposed for predicting the viability of different airborne viruses as a function of relative humidity. In the proposed model, water activity is presumed to be the main variable affecting the viability of the virus when airborne, directly or indirectly. The water activity is a function of the relative humidity and the Kelvin term, and it changes with the type of solute(s) within the droplet, depending on the solute concentration at equilibrium with its surroundings at a prescribed temperature and humidity. The results obtained from the proposed model compared well with the experimental results published by Benbough (1971) and Schaffer et al. (1976) using the influenza, Langat and polio viruses. One of the parameters needed to be adjusted to obtain good agreement with the experimental data for Ijaz et al. (1987). The predictability of the model was found to be improved at exposure times longer than 1 min.

The idea of modelling the culture medium as a solution of water and sodium chloride was a good approximation and provided results very similar to the experimental data. Efflorescence seemed to be the factor responsible for the low viability of enveloped viruses when airborne at mid relative humidity range. The surface tension and the density of the droplet remained largely unchanged with concentration for the cases considered, so the Kelvin term was only significantly affected by the droplet diameter when it was less than approximately 1 μm. Information on droplet sizes was lacking in the previously published experiments. The lipid membrane of the enveloped viruses (influenza and Langat virus) may help explain the longer viability of these viruses compared to the non-enveloped viruses (poliovirus) at low relative humidity.

Most of the experiments on viral viability were performed in small drums at constant temperature and relative humidity. However in reality, environmental factors may lead to significant changes in space and time. When combined with a program to track the movement of the droplets, the proposed model can be used to predict the viable concentration of viruses in a practical working room with spatial variations in temperature and relative humidity across the room.

Future work should focus on modelling the critical water activity for multi-component aerosols. The crystallization water activity for some binary solutions can be found in Tang and Munkelwitz (1994), Chan et al. (2000) and Tang et al. (1997). However, there are not many references reporting the crystallization water activity of multi-component solutions. More experimental work is necessary in order to fill this gap in understanding and enable prediction of the evolution of virus laden droplets in more complex environments.

Collectively, the results indicate that the predictive value of the model can be considered acceptable. However, more research is needed to improve the model further, in particular to account for the variations in the carrier droplet diameter, the constituents of the droplet, as well as the water evaporation rates.

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References

Bateman, J.B., 1968. Long term bacteriological effects of reduced ambient water activity: use of membrane filters support for test organisms. Am. J. Epidemiol. 87, 349.
Benbough, J.E., 1971. Some factors affecting the survival of airborne viruses. J. Gen. Virol. 10, 209–220.
Benbough, J.E., Bennett, A., May 1990. A Test Protocol and Evaluation of Intersurgical's Filta-Therm and Filta-Guard as a Viral Filter. Biosafety Testing Section, Biologics Division, Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire.
Belser, J.A., Blixt, O., Chen, L.M., Pappas, C., Maines, T.R., Hoeven, N.V., Donis, R., Busch, J., McBride, R., Paulson, J.C., Katz, J.M., Tumpey, T.M., 2008. Contemporary North American influenza H7 viruses possess human receptor specificity: implications for virus transmissibility. PNAS 105 (21), 7558–7563.
Blachere, F.M., Lindsley, W.G., Pearce, T.A., Anderson, S.E., Fisher, M., Khakoo, R., Meade, B.J., Lander, O., Davis, S., Thewlis, R.E., Celik, I., Chen, B.T., Beezhold, D.H., 2009. Measurement of airborne influenza virus in a hospital emergency department. Clin. Infect. Dis. 48, 438–440.
Celik, I.B., Redrow, J., Mao, S., 2007. Modelling of bio-aerosol transport and dispersion in a ventilation room. In: Proceedings of the International Conference on Options for the Control of Influenza VI Held in Toronto, Ontario, Canada, pp. 510–512.
Chan, C.K., Ha, Z., Choi, M.Y., 2000. Study of water activities of aerosols of mixtures of sodium and magnesium salts. Atmos. Environ. 34 (28), 4795–4803.
De Jong, J.C., Winkler, K.C., 1968. The inactivation of poliovirus in aerosols. J. Hyg. – Cambridge 66, 557–565.
De Jong, J.C., Trouwborst, T., Winkelr, K.C., 1973. The mechanisms of virus decay in aerosols. In: Hers, J.F.Ph., Winkler, K.C. (Eds.), Airborne Transmission and Airborne Infection. John Wiley & Sons, New York, pp. 124–130.
Hemmes, J.H., Winkler, K.C., Kool, S.M., 1960. Virus survival as a seasonal factor in influenza and poliomyelitis. Nature 188, 430.
Hogan, C.J., Kettleson, E.M., Lee, M.H., Ramaswami, B., Angenent, L.T., Biswas, P., 2005. Sampling methodologies and dosage assessment techniques for submicrometre and ultrafine virus aerosol particles. J. Appl. Microbiol. 99, 1422–1434.
Ijaz, M.K., Karim, Y.G., Sattar, S.A., Johnson-Lussenburg, C.M., 1987. Development of methods to study the survival of airborne viruses. J. Virol. Methods 18, 87–106.
Iwata, S., Lemp, M.A., Holly, F.J., Dohlman, C.H., 1969. Evaporation rate of water from the precorneal film and cornea in the rabbit. Invest. Ophthalmol. Vis. Sci. 8, 613–619.
Lester Jr., W., 1948. The Influence of relative humidity on the infectivity of airborne influenza A virus (PR8 strain). J. Exp. Med. 88, 361–368.
Lowen, A.C., Mubareka, S., Tumpey, T.M., Garcia-Sastre, A., Palese, P., 2006. The guinea pig as a transmission model for human influenza viruses. PNAS 103 (26), 9988–9992.
Lowen, A.C., Mubareka, S., Steel, J., Palese, P., 2007. Influenza virus transmission is dependent on relative humidity and temperature. PLoS Pathog. 3, 1470–1476.
Lowen, A.C., Steel, J., Mubareka, S., Palese, P., 2008. High temperature (30 °C) blocks aerosol but not contact transmission of influenza virus. J. Virol. 82, 5650–5652.
Martin, S.T., 2000. Phase transitions of aqueous atmospheric particles. Chem. Rev. 100, 3403–3453.
Mathers, W., 2004. Evaporation from the ocular surface. Exp. Eye Res. 78, 389–394.
May, K.R., 1973. The collison nebulizer: description, performance and application. J. Aerosol Sci. 4, 235–243.
Morawska, L., 2006. Droplet fate in indoor environments, or can we prevent the spread of infection? Indoor Air 16, 335–347.

Moser, M.R, Bender, T.R., Margolis, H.S., Noble, G.R., Kendal, A.P., Ritter, D., 1979. An outbreak of influenza aboard a commercial airliner. Am. J. Epidemiol. 110, 1–6.
Mubareka, S., Lowen, A.C., Steel, J., Coates, A.L., Garcia-Sastre, A., Palese, P., 2009. Transmission of influenza virus via aerosols and fomites in the guinea pig model. J. Infect. Dis. 199, 858–865.
Palasz, A.T., Thundathil, J., Verrall, R.E., Mappletoft, R.J., 2000. The effect of macromolecular supplementation on the surface tension of TCM-199 and the utilization of growth factors by bovine ocytes and embryos in culture. Anim. Reprod. Sci. 58, 229–240.
Pruppacher, H.R., Klett, J.D., 1978. Microphysics of Clouds and Precipitation. D. Reidel, Dordrecht.
Schaffer, F.L., Soergel, M.E., Straube, D.C., 1976. Survival of airborne influenza virus: effects of propagating host, relative humidity, and composition of spray fluids. Arch. Virol. 51, 263–273.
Shinya, K., Ebina, M., Shinya, Y., Ono, M., Kasai, N., Kawaoka, Y., 2006. Avian flu: influenza virus receptors in the human airway. Nature 440, 435–436.
Sobsey, M.D., Meschke, J.S., 2003. Virus survival in the environment with special attention to survival in sewage droplets and other environmental media of fecal or respiratory origin. In: World Health Organization Meeting, Rome, Italy 23–25 September.
Stallknecht, D.E., Kearney, M.T., Shane, S.M., Zwank, P.J., 1990. Effects of pH, temperature, and salinity on persistence of avian influenza viruses in water. Avian Dis. 34, 412–418.
Tang, I.N., Munkelwitz, H.R., 1994. Water activities, densities, and refractive indices of aqueous sulfates and sodium nitrate droplets of atmospheric importance. J. Geophys. Res. 99, 18801–18808.
Tang, I.N., Tridico, A.C., Fung, K.H., 1997. Thermodynamic and optical properties of sea salt aerosols. J. Geophys. Res. 102, 23269–23275.
Tang, J.W., Li, Y., Eames, I., Chan, P.K.S., Ridgway, G.L., 2006. Factors involved in the aerosol transmission of infection and control of ventilation in healthcare premises. J. Hosp. Infect. 64, 100–114.
Tellier, R., 2006. Review of aerosol transmission of influenza a virus. Emerg. Infect. Dis. 12, 1657–1662.
Tellier, R., 2009. Aerosol transmission of influenza A virus: a review of new studies. J. R. Soc. Interf., doi:10.1098/rsif.2009.0302.focus.
van Riel, D., Munster, V.J., de Wit, E., Rimmelzwaan, G.F., Fouchier, R.A.M., Osterhaus, A.D.M.E., Kuiken, T., 2006. H5N1 Virus attachment to lower respiratory tract. Science 312, 5772, 399.
WHO (World Health Organization) 2009. Pandemic (H1N1) 2009 – Update 75, November 20, 2009.