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A missing layer in COVID-19 studies: Transmission of enveloped viruses in mucus-rich droplets

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Abstract

Here we evaluate the influence of mucus layers on the evaporation time and transport of enveloped viruses, including SARS-CoV-2. Enveloped viruses must remain moist to be fully infective. Yet, the Wells model based on water droplets divides respiratory droplets into either quickly evaporated aerosolized particles termed droplet nuclei (<10 μm) or liquid droplets that fall to the nearest surface, leaving no physical mechanism for airborne transmission of fully infective enveloped viruses over large distances (greater than a few meters). Yet, the role of mucus layers on evaporation times has not been considered even though the formation of mucus shells around liquid cores of respiratory droplets has been shown experimentally. Here we show that mucus shells increase the drying time by orders of magnitude so that enveloped virions may remain well hydrated and, thus, fully infective at substantial distances. This provides a mechanism by which infective enveloped virus particles can transmit as aerosols within buildings and between buildings over extended distances. This analysis is important because public health agencies typically follow the Wells model to establish health policies including social/physical distancing guidelines.

1. Introduction

The long-lasting global COVID-19 pandemic has raised interest in the spread of infectious respiratory disease in the built environment [1–3]. While global and local health organizations acknowledge that SARS-CoV-2 can be transmitted through airborne routes, how much this contributes to the epidemiology of the disease remains incompletely quantified. Some of this lack of clarity arises in part because of reliance on the widely adopted Wells model that divides respiratory droplets into either evaporated aerosolized particles termed droplet nuclei (<10 μm) or liquid droplets that fall to the nearest surface, leaving no pathway for airborne or aerosolized transmission of fully infective enveloped viruses at substantial distances. In 1934, Wells [4] showed that water droplets (perhaps with nonvolatile salts) less than ~120 μm in diameter evaporate in dry air before falling two meters (the approximate height of an adult mouth to a floor below), while droplets larger in diameter fall to the floor or on similar surfaces to enable fomite transmission (i.e., leaving small liquid pools on surfaces that may pass viruses to the mouth, nose or eyes via touch) (see Fig. 1a). Under these conditions, evaporation of a single phase water droplet typically takes a fraction of a second (certainly <10 s when relative humidity is <80%), leaving little time for an enveloped virus to spread out spatially, leaving only droplets that only spread a couple of meters from their source as the primary mode of infection. This dichotomy between liquid droplets and dried aerosol particles proposed by Wells [4] remains the mainstay of public health policy and is a key source of mandates to maintain physical or social distancing and to wear masks that are distinctively effective in stopping transmission of the larger droplets.

Abbreviations: COVID-19, coronavirus disease 2019; SARS, Severe acute respiratory syndrome; SARS-CoV-1, Severe acute respiratory syndrome coronavirus 1; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2.

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2 "It appears, therefore, that transmission of infection through air may take one of two forms depending upon the size of the infected droplet. The form first recognized and most obvious is droplet infection proper. It applies to droplets larger than a tenth millimeter in diameter, which are rapidly removed from the air by gravity, before they can dry, and within a short distance of the source. The second form may be called air-borne infection, and deals with dried infected droplet nuclei, derived directly from droplets less than a tenth millimeter diameter, depending primarily upon air for the buoyancy which keeps them suspended for long times and carries them long distances." (Wells, 1934)

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However, Wells’ simple but enduring dichotomy may not fully describe the transmission modes of enveloped viruses including SARS-CoV-2. Enveloped viruses must remain in a fluid environment (i.e., more than simply attached waters of hydration) to preserve their infectivity. Enveloped viruses have a lipid coating in addition to a protein shell surrounding a nucleic acid core (see Fig. 1b). Such a lipid layer is absent in nonenveloped viruses. This lipid layer is important because it provides some protection for enveloped viruses from immune system recognition but at the cost of losing infectivity when the virus dries (and permits susceptibility to soaps when washing). Examples of enveloped viruses include the influenza viruses, measles [5], and all corona viruses including SARS-CoV-1 and SARS-CoV-2. Nonenveloped viruses in contrast remain infective when they dry, provided that their protein coats remain intact. Examples of nonenveloped viruses include rhinovirus and polio, which may be highly infective because their dry form may transmit as an aerosol similar to the droplet nuclei proposed by Wells [4]. To preserve infectivity, enveloped viruses often transport in mucus rich droplets. Mucus is a long-chain polymeric protein common in saliva and respiratory fluids that forms an interconnected network that may encapsulate enveloped viruses [6].

However, one key conundrum associated with enveloped viruses is their apparent infectivity at significant distances from their sources. Field studies in the built environment suggest that enveloped viruses spread much farther than social distancing guidelines, challenging the dichotomy of fomite transmission via hydrated droplet on surfaces or dry virus containing particles suggested by Wells [4,7]. Yu, et al., [8] tracked the spread of SARS in the tall Amoy Gardens apartment complex to show that spread seemed to follow wind patterns (e.g., wind at 2 m/s between buildings ~60 m apart), which would not be the case if all droplets that did not hit the floor had completely dried out (whether by coughing or by sewer-formed droplets the same inadequacy exists).

![Diagram](image)

Fig. 1. (a) When a person emits respiratory droplets (e.g., from coughs, sneezes, singing, breathing, talking, laughing), they evaporate and gravitationally settle. The Wells model presents a dichotomy where wet droplets fall to surfaces to enable fomite transmission or remain suspended as dry particles called droplet nuclei. Mucus shells enable a third option that transiently sustains a liquid core to permit enveloped viruses to remain infective for longer times and distances, presenting an alternative to Well’s dichotomy. Blue arrows represent bulk air flow; droplets (microns to millimeters) not to scale. (b) Enveloped viruses have one or more lipid layers surrounding their protein capsid shell in contrast to non-enveloped viruses that do not have lipid layers. Lipid layers protect the virus from the immune systems but leave the virus susceptible to soaps and drying out. (c) Comparison of mucus rich droplets that form mucus shells around liquid cores and mucus poor droplets that do not. Dimensions of droplets include the initial droplet diameter, \(d_{ic}\), shell diameter, \(d_{sc}\), and core diameter, \(d_{cc}\), leaving a shell thickness of \(h = d_{sc} - d_{cc}\). (*Non-infective except in the less likely scenario where infectivity can be restored following rehydration.) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Similarly, Lu, et al., [2] suggest that infectivity of SARS-CoV-2 in an air-conditioned restaurant followed air currents, which would not be feasible if all of the droplets containing enveloped viruses dried within a fraction of a second. Also, Hamner, et al., [9] report 52 choir members became ill from one index patient, suggesting aerosol spread substantially beyond the nominal 6 ft of social distancing in the U.S. Therefore, recent research has begun to focus on mechanisms that would extend the hydrated status of droplets. For example, Xie, et al., [10] revisited the work of Wells to include the influence of droplet evaporation and humidity on viral spread. Increasing humidity decreases the minimum size of liquid droplets that land on surfaces to enable fomite transmission and extends the time to evaporation into 10’s of seconds. Bourouiba, et al., [11] suggest that some small droplets circulate within a cloud that may decrease their evaporation rate. Liu, et al., [12] include the influence of turbulence on spread to show some marginal increase in the droplet distribution pattern due to decaying turbulent eddies. While each of these observations extends the range of infectivity relative to that proposed by Wells, none of these fully explain the apparent infectivity of SARS-CoV-1 between buildings.

A key challenge with prior work is that it has largely been based on the aerosolization of single-phase droplets. In contrast cough, sneeze, and respiratory droplets are decidedly multi-constituent including virus particles, mucus (mucus proteins mucin-2, mucin-5 ac, mucin-5b, and mucin-19 are both secretory and crosslinking), lung surfactant, and a milieu of other constituents that may form multiple phases [13]. Groundbreaking work by Vejerano and Marr [14] shows that mucus may form a shell around a drying droplet collected on a surface potentially preserving its liquid core. This mucus shell may substantially reduce the evaporation rate. These core-shell droplets in turn persist longer and may not rehydrate when surfactants are present in the dried droplets [14]. However, the role of mucus in aerosolized droplet evaporation has
not been explored quantitatively. Therefore, this article explores the influence of mucus shells on drying droplets (Table 1). Furthermore, because aerosolized particles are often driven by surrounding air flow in addition to flow from the jets or puffs associated with the cough or sneeze itself, this article also considers the influence of bulk flow on the transport and fate of respiratory droplets containing infectious species.

2. Materials, methods and models

Consider an aqueous spherical respiratory droplet containing virions and mucus shed or released from a person, child or adult, up to 2 m tall. This analysis starts once the droplet is distinctive and outside the body (i.e., droplets produced by bronchial and larynx mechanisms have been released through nose and mouth and droplets produced by the oral mechanism including coughs and sneezes have completed the fluid break up process and escaped any barriers present). Water in the droplet evaporates as it falls due to gravity with aerodynamic drag reducing its velocity. A key feature of this work is the inclusion of mucus proteins that form a shell on the surface of the droplet as it dries (Fig. 1c) reducing the evaporation rate. The images in Vejerano and Marr [14] confirm mucus shells form and suggest that representative amounts of mucus form a uniform shell that does not buckle, removing buckling and asphericity as a primary component of this analysis. Each of these phenomena are described mathematically in detail below.

The trajectory of a droplet in a bulk velocity field may be described in the absence of hindered settling as

\[
m_d \frac{du_{d}}{dt} = \frac{1}{2} C_d \rho \nu (u_d - u_f) |u_d - u_f| + m_d g \left( 1 - \frac{\rho_d}{\rho_f} \right) \quad (1)
\]

and

\[
\frac{dx_{d}}{dt} = u_d \quad (2)
\]

where \(u_d\) is the drop velocity vector, \(x_d\) is the droplet position vector, \(m_d\) is the mass of the droplet, \(t\) is time, \(\rho_d\) is the surrounding fluid density, \(\rho_f\) is the gas velocity vector, and \(g\) is the gravitational vector. Liu, et al., [12] argues for no virtual mass, Basset history force or Magnus force because the droplet density exceeds the gas density, and particle collisions are neglected in this model due to the moderate density of droplets only a few centimeters from the mouth/nose. The droplet drag coefficient (assuming a spherical droplet) may be expressed as

\[
C_D = \frac{24}{Re_d} \left( 1 + 0.15Re_d^{0.607} \right) \quad (3)
\]

which collapses into the well-known limit of 24/Re \(d\) when \(Re_d\) is small, where \(Re_d = |u_d-u_f|d_d/\nu\), \(d_d\) is the droplet diameter, and \(\nu\) is the kinematic viscosity. This formulation is appropriate because the droplet Reynolds numbers likely remain modest.

The trajectories of the droplets are influenced by the flow field of the surrounding fluid. Liu, et al., [12], Wei, et al., [19] and Xie, et al., [10] argue for representing the respiratory flow field as a circular jet. Dbook and Drikakis [20] argue that coughs should be represented as rectangular jets. Bourouiba, et al., [11] argue that the flow begins as a circular jet and then follows circular puff scaling [21]. For coughs and sneezes, the flow may be approximated as a circular jet with the centerline velocity expressed as

\[
u_t = \frac{h u_o d_o}{z} \quad (4)
\]

in the absence of a significant virtual origin correction, where \(h\) is the velocity decay coefficient, \(u_o\) is the velocity of the cough or sneeze at the mouth or nose, \(d_o\) is the equivalent diameter of the mouth or nose at the start of the jet, and \(z\) is the distance from the mouth or nose along the centerline of the jet [22]. Recognizing \(u_t\) as \(dz/dt\), this expression may be integrated to estimate the distance traveled along the jet centerline at time \(t\) as

\[
z = \sqrt{2hu_o d_o t} \quad (5)
\]

This is the farthest a droplet may transport from the source by coughing, sneezing, or laughing (in the absence of vortex transport). Other respiratory releases (e.g., breathing) that do not form jets do not travel as far. Bulk airflow from room air currents or outside wind may increase this range.

Neglecting a very rapid initial equilibration of the droplet surface, there are two stages of drying: an early stage when the mucus is dispersed within the liquid droplet and a later stage when the mucus forms a shell around a liquid core [23,24]. The first stage is rapid, while the second stage is longer. Drying and dry refer to sufficient water loss to adversely affect the lipid membrane of the virus but do not require complete removal of free water or waters of hydration. Precipitation of salts and other components is not considered in this first-order analysis. Otherwise, evaporation driving forces are the same between the two stages only the resistance to evaporation changes with the addition of a mucus layer. In the first stage,

\[
\frac{dm_d}{dt} = -2\pi x_d \rho_p M_p D_w Sh_h \ln \left( \frac{1 - R_h x_h}{1 - x_h} \right) \quad (6)
\]

where \(d_d\) is the droplet diameter, \(R\) is the ideal gas constant, \(T_w\) is the temperature far from the surface of the droplet, \(p\) is the pressure, \(M_p\) is the molecular weight of the droplet, \(R_h\) is the relative humidity as a fraction not a percent, \(x_h\) is the mole fraction of water at the droplet surface (which for an ideal gas is the ratio of the saturation pressure divided by atmospheric pressure), \(D_w\) is the diffusion coefficient of air in water vapor or water vapor in air (equal in the pseudo-binary approximation), and \(Sh_h\) is a form of the Sherwood number. This Sherwood number may be estimated by

\[
Sh_h = 1 + 0.38 Re_d^{1/2} Sc^{1/3} \quad (7)
\]

Table 1

| Fate of Respiratory Droplets and Enveloped Viruses. | Droplet Final State | On Surface | Airborne |
|---------------------------------------------------|--------------------|------------|----------|
| **Dry**                                           | Settled Dry Nuclei |            | Dry Nuclei |
|                                                   | Not Infective<sup>a</sup> |            | Not Infective<sup>a</sup> |
| **Wet**                                           | Enables Fomite Transmission | Infective via Contact<sup>b</sup> | Mucus Core-shell Droplets |

<sup>a</sup> Would require effective rehydration and reactivation in the atmosphere or in vivo; Vejerano and Marr [14] show dry particles with mucus and a lung surfactant do not rehydrate. Dry here refers to sufficient evaporation to disturb the lipid envelope, which may or may not necessitate removal of all water molecules.

<sup>b</sup> Trajectory drives social distancing guidance.
where $Sc$ is the Schmidt number \cite{10,12}, Deen \cite{16} indicates that so long as appropriate temperature dependent properties are selected, this equation may be solved independently from the energy balance as

$$d_s = d_o \left[ 1 - \frac{8M_s D_m S_h \ln \left( \frac{1 - R_{pH}}{1 - x_s} \right)}{d_o \rho_s \ln \left( \frac{1 - x_s}{1 - x_c} \right)} \right]$$  \hspace{1cm} (8)

for spherical droplets of density $\rho_d$ here corresponding to the density of liquid waters, where $d_o$ is the initial droplet diameter, when we recognize that droplet mass is the sum of the masses of water and other constituents and only the former change. In this form, the time scale for drying becomes

$$t_1 = \frac{(d_o^2 - d_s^2) \rho_s \ln \left( \frac{1 - x_s}{1 - x_c} \right)}{8 pD_s S_h ln \left( \frac{1 - x_s}{1 - x_c} \right)}$$  \hspace{1cm} (9)

which follows the well-known increase with the square of the diameter as asserted by Wells and subsequent researchers. Complete drying corresponds to $d_s \sim 0$ for pure water droplets or something equivalently small when non-aqueous components are present in the droplet. For typical conditions associated with small (~20 μm) respiratory droplets, this time scale is often less than one second (Fig. 2a). Evaluating the pure water case places an upper limit on the drying time of the first stage, which may be compared to the drying time of the second stage.

However, mucin and other proteins may accumulate near the evaporating surface. When the concentration of these constituents increases to the point that these proteins jam together to achieve gelation (meaning mucin proteins link to span the full droplet circumference) at the surface, this layer of proteins becomes a shell that impedes evaporation. In this model, a mass balance on the non-aqueous components gives

$$\frac{C_s - C_{mo}}{C_{mo}} = \frac{d_s^3 - (d_o - h_s)^3}{d_o^3 - (d_o - h_s)^3}$$  \hspace{1cm} (10)

where $C_s$ is the concentration corresponding to the onset of gelation or surface crosslinking, $C_{mo}$ is the initial mucin concentration, $d_s$ is the droplet shell diameter, and $h_s$ is the initial shell thickness before the core dries. This is used to solve for $d_{do}$. When drying is complete, a hollow vapor core is surrounded by the shell. The hollow core diameter may be estimated by

$$\frac{C_s}{C_{mo}} = \frac{d_{do}^3}{d_o^3 - d_s^3}$$  \hspace{1cm} (11)

where $d_s$ is the core diameter after the core dries. This formulation places limits on the extent of particle shrinkage that bounds settling time variations relative to those based on the initial droplet diameter alone. Fig. 3 presents the core and shell diameters that result from a droplet variations relative to those based on the initial droplet diameter alone.

This mucin protein shell acts like a polymer membrane that slows liquid flow from the core to the outer surface of the shell. Because flow through the increasingly thick shell becomes rate limited, diffusion is assumed to have sufficient time to uniformly mix the solute composition within the core. The flux of water through the shell, $N_{shell}$ as determined at the shell may be derived as

$$N_{shell} = \frac{2pD_{sw}}{d_s^2} \ln \left( \frac{1 - p_{sw}/p}{1 - p_{s}/p} \right)$$  \hspace{1cm} (12)

where $d_s$ is the outer diameter of the shell, $d_o$ is the outer diameter of the core, $D_s$ is the constant diffusion coefficient through the shell, and $C_s$ and $C_{sw}$ are the concentrations at the outer diameters of shell and core, respectively \cite{25,26}. These concentrations may be liquid concentrations of water if the shell is hydrated or be converted into partial pressures of water via the ideal gas law (for example) if the shell is dry. The flux at the outside of the shell is given as

$$N_{shell} = \frac{2pD_{sw}}{d_o^2} \ln \left( \frac{1 - p_{sw}/p}{1 - p_{s}/p} \right)$$  \hspace{1cm} (13)

(similar to Eq. 6), where $p_{sw}$ is the partial pressure of water far from the droplet surface and $p_s$ is the saturation pressure at the surface. At the liquid solid interface, the liquid phase concentration and gas phase concentrations may be related by a partition coefficient or its equivalent (e.g., a Henry’s law constant).

If both the core and shell are wet, then a partition coefficient exists at the shell surface to represent the equilibrium between liquid and vapor. (See Appendix A for the case where the shell has dried.) Equating the two fluxes with $K = p_{sw}/C_{mo}$ permits

$$N_{shell} = \frac{2D_s \left( C_s - C_{sw} \right)}{d_s^2 \ln \left( \frac{1 - p_{sw}/p}{1 - p_{s}/p} \right)} = \frac{2pD_{sw}}{d_o^2} \ln \left( \frac{1 - p_{sw}/p}{1 - p_{s}/p} \right)$$  \hspace{1cm} (14)

Fig. 2. (a) Time to complete drying of a pure water droplet as a function of initial droplet diameter at 25°C for relative humidity values of 20% RH (red), 40% RH (orange), 60% RH (light green), and 80% RH (green) along with fall times corresponding to fall distances of 2 m (blue), 1 m (purple), and 0.2 m (black) under quiescent conditions. (b) Time to complete drying of a core-shell mucus particle with a wet shell as a function of initial droplet diameter for gelation to initial concentration ratios of 5 (solid) and 50 (dashed) for relative humidity values of 20% RH (red), 40% RH (orange), 60% RH (light green), and 80% RH (green) along with fall times corresponding to fall distances of 2 m (blue), 1 m (purple), and 0.2 m (black) at 25°C at standard temperature and pressure with a wet shell having a diffusivity of $D_s = 1.0 \times 10^{-7}$ m²/s \cite{16} under quiescent conditions. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
where $K$ is an equilibrium partition coefficient. Solving for $p_{we}$ returns

$$\frac{p_{we}}{p} = C + \frac{a K C_s - p_{we}}{\rho_s D_s} \left( \frac{x}{x - 1} \right) + \frac{\eta_T}{\rho_s D_s}$$

with the use of the first term of a Taylor series expansion ($\ln(1-x) \sim -x - x^2/2 - ...$) when $p_{we}/p < p_{we}/< 1$. The flux then simplifies to

$$N_{net} = \frac{K C_s - p_{we}}{\eta_T} \left( \frac{x}{x - 1} \right) + \frac{\eta_T}{\rho_s D_s}$$

so that

$$\frac{dm}{dt} = -\pi d_s M_s \left( \frac{x}{x - 1} \right) + \frac{\eta_T}{\rho_s D_s}$$

with the same degree of approximation.

Formally the core diameter is time dependent as the shell evaporates. To approximate the time scale, the largest $d_s/d_o$ that occurs when the droplet has completely evaporated was selected. Recognizing that the only mass lost is water, we assert

$$\Delta m_d = -w_o \rho_s h d_i$$

so that

$$t_d = \frac{w_o \rho_s d_o^2}{12 M_s (K C_s - p_{we})} \left[ \frac{K}{D_s} \left( \frac{d_o}{d_i} - 1 \right) + RT \right]$$

where $w_o$ is the weight fraction of water. The total drying time is $t_d + t_o$. However, $t_o >> t_d$ so $t_d$ alone may be considered the drying time.

### 3. Results and discussion

The purpose of this article is to evaluate the implication of mucus shell formation on the drying rates of mucus rich droplets, commonly emitted from the lungs, larynx, and oral cavities [15]. Respiratory droplets are not simply composed of salts and water but contain proteins including the mucins that may cross link together or gel to form a shell as reported by Vejerano and Marr [14]. How this mucus shell affects drying times has not previously been analyzed. This is important because the wet cores within these droplets serve as carriers within which enveloped viruses may remain infective at longer times or longer distances if aerosolized.

Fig. 2a considers the traditional Wells formulation based on single phase droplets (e.g., single phase water and nonvolatile salts) that balances evaporation time with droplet falling rates. Calculated using the equations in the materials, methods, and models section, the figure partitions the time versus the initial droplet diameter space into four regions (see Table 1, Fig. 2, and Fig. S1): a wet aerosol, a dry aerosol, a wet surface droplet, and a dry surface droplet (if nonvolatile are present). Each pairing of intersecting curves provides unique boundaries to these regions. Wells focuses on the dry aerosol and the wet surface droplet regions, with Fig. 2a showing a cutoff between the two regions of ~40–100 μm depending on the vertical fall distance (spanning sitting with mouth 20 cm above a table to standing), the relative humidity (20–80% RH), and local temperature. Droplets falling further away from surfaces transmit further, and droplets falling at shorter vertical distances land on surfaces to enable fomite transmission more quickly. The region of interest to the infectivity of enveloped viruses at distances beyond the social or physical distancing metric of 1–2 m (in a perfectly quiescent environment with no air currents) is the wet aerosol region with the longest lasting water aerosolized droplets drying out in <10 s. Droplets that are larger and wet fall onto the surface to enable fomite transmission via direct contact routes. Droplets that dry out preserve the infectivity of non-enveloped viruses (e.g., polio) but not enveloped viruses (e.g., SARS-CoV-2).

Quick drying times substantially limit the distance over which these mucus-poor droplets can transmit active virus. For example, if a droplet remains at the centerline of a circular jet, these droplets would travel ($2h$ $w_o d_o d_o)$, where $h$ is the velocity decay coefficient, $w_o$ is the initial velocity of the cough jet, $d_o$ is the opening corresponding to the start of the jet, and $t$ is the time. Using typical parameters ($h = 6, w_o = 10$ m/s in the absence of a mask, $d_o = 20^{-4} m^2$), the droplets would only transfer travel $-3.5$ m in 10 s before drying. (An unimpeaded sneeze with the same parameters but a much higher starting velocity, $w_o < 120$ m/s, would drive droplets <12 m before drying.) These estimates are conservative, because coughs quickly become puffs with less momentum that do not drive droplets as far, all jets become circular jets at some distance from a nozzle (here the mouth or nose), and many droplets fall out of the jet centerline to fall to shorter distances, though substantial air currents (thermal or forced) can meaningfully extend the distance over which droplets Spread. Doubling or quadrupling this distance provides some conservatism to account for statistical variation, high humidity environments (e.g., >80% RH), vortical spread beyond the average, and limited buoyancy as the warm air from the respiratory tract cools to ambient temperatures. This mucus-poor analysis would suggest that most findings of nucleic acids from enveloped viruses further than 3-12
proteins and sugars. While reductionist approaches are often helpful in teasing out the essential physics, they risk oversimplifying the problem. Such is the case with mucus-rich droplets from the respiratory system, where the role of network forming mucus molecules has been neglected as a means of preserving the infectivity of enveloped viruses. Vejerano and Marr [14] have shown that the mucins can form core-shell particles on substrates and this study extends their findings to aerosol droplets.

Fig. 2b shows mucus-rich droplets, which form shells, persist orders of magnitude longer than simple water or saltwater droplets. The figure shows that the mucus-rich droplets that begin in the range of 3–30 μm may persist as wet aerosols for 100 s to 2000 s (~1/2 of an hour). The drying time depends on the ratio of the mucus concentration to the amount of mucin needed to crosslink into a shell. Droplets that gel at lower concentration retain their liquid core longer as shown in the figure. Surprisingly, relative humidity makes but a modest difference (less than a factor of 3), because here it is the shell that governs the drying time, perhaps explaining the frequent anticipation that humidity should strongly influence the spread of respiratory illnesses in contrast to epidemiological data that suggests a modest influence. Using the same approach as above, a droplet that persists for 100–2000 s on the centerline of an unimpeded jet moves away from the emitter ~10–170 m. However, with these very long persistent times, there is significant potential for these droplets to be carried along other air flows (mechanical ventilation, etc.). For example, a light breeze with a velocity of 2.6 m/s (5 knots on Beaufort scale) permits respiratory droplets to transport significant distances between buildings, even between buildings that may not be adjacent. This risk is not negligible given the superspreading event at the Amoy Garden [8]. These results suggest that mucus composition may be a major factor in the transmission of respiratory droplets within and between buildings and should be considered as a possible factor in superspreading phenomena.

These curves are particularly informative in light of the reported size distributions of respiratory droplets. Johnson, et al., [15] indicate this mode of log normal distributions of bronchial and larynx droplet generation mechanisms in the range of 1–3 μm, while the mode of the oral mechanism centers around 120–150 μm and is quite broad. Even accounting for a factor of two variation in measurement approaches among authors, comparison of these sizes to Fig. 2b suggests that the wet aerosol droplets (~3–20 μm in diameter) that persist the longest (and, thus, spread the farthest) correspond to the lower wing of the oral distribution associated with coughing/sneezing, though a modest contribution from the upper wing of the bronchial and larynx breathing distributions cannot be dismissed. Respiratory droplets with sizes near the center of their distributions dry out or fall to a surface in approximately ~100 s, limiting their spread. This is consistent with the findings of Yang and Marr [17], who show that the larger respiratory droplets are removed from single rooms by gravitational settling leaving smaller droplets consistent with the 3–20 μm peaks in Fig. 2b.

We hasten to emphasize that this is but one mechanism of viral degradation. Viruses may degrade due to biological, photonic, thermal and other degradation mechanisms. Susceptibility may also be humidity dependent for other reasons as well including the extent of hydration of a person’s mucus membranes. However, if the droplet dries out first, other mechanisms do not have a chance to govern the time scale of infectivity retention.

We recognize the possibility that salt crystalized pathogens might remain active and possibly infective, and this study does not finally prove or disprove whether dried out enveloped viruses (perhaps with waters of hydration) can become infective upon rehydration. We recognize that some rehydration of dry nuclei may occur in the atmosphere [27]. However, the experiments of Vejerano and Marr [14] suggest that rehydration may be limited and even then restoration of infectivity may be questionable. Indeed, disruption of the lipid envelope and protein capsid layers of enveloped viruses is known to substantially decrease the amount of infective virus relative to enveloped viruses that remain in free liquids, suggesting that mucus shells may prove to be the dominant mechanism to preserve enveloped viruses in the aerosol form.

In summary, this analysis presents mucus shell structures as a third option to Wells’ dichotomy of dry “nuclei” and liquid droplets that enable fomite transmission. Mucus shells increase the drying time by orders of magnitude so that enveloped virions may remain well hydrated and, thus, fully infective at substantial distances, consistent with real-world observations [2,3,8,18]. Finally, although this analysis says that viruses transmit much further than Wells would have argued, it also provides another mechanism to deactivate enveloped viruses that limits the duration of their infectivity. This is important particularly to those involved in cleaning of HVAC systems or design of mechanical ventilation systems to remove particles from breathing zones.

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None.

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Appendix A

If the shell is dry (and the core is wet with a small air bubble in the core) then

$$N_{\text{droplet}} \approx \frac{2 \rho D_t \left( \frac{1}{\lambda_{\text{vr}}} - \frac{1}{\lambda_{\text{ps}}} \right)}{RT \lambda_{\text{ch}}^2 \left( \frac{1}{\lambda_{\text{vr}}} - \frac{1}{\lambda_{\text{ps}}} \right)}$$

where $p_{\text{rt}}$ and $p_{\text{sr}}$ are the pressures at the core and surface and $T_c$ and $T_s$ are the temperatures at the core and surface. Solving for $p_{\text{rt}}$ returns
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Fig. S1. (a) Time to complete drying of a pure water droplet as a function of initial droplet diameter at 37°C for relative humidity values of 20% RH (red), 40% RH (orange), 60% RH (light green), and 80% RH (green) along with fall times corresponding to fall distances of 2 m (blue), 1 m (purple), and 0.2 m (black) under quiescent conditions. (b) Time to complete drying of a core-shell mucus particle with a wet shell as a function of initial droplet diameter for gelation to initial concentration ratios of 5 (solid) and 50 (dashed) for relative humidity values of 20% RH (red), 40% RH (orange), 60% RH (light green), and 80% RH (green) along with fall times corresponding to fall distances of 2 m (blue), 1 m (purple), and 0.2 m (black) under quiescent conditions. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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