

Role of environmental persistence in pathogen transmission: a mathematical modeling approach

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Abstract Although diseases such as influenza, tuberculosis and SARS are transmitted through an environmentally mediated mechanism, most modeling work on these topics is based on the concepts of infectious contact and direct transmission. In this paper we use a paradigm model to show that environmental transmission appears like direct transmission in the case where the pathogen persists little time in the environment. Furthermore, we formulate conditions for the validity of this modeling approximation and we illustrate them numerically for the cases of cholera and influenza. According to our results based on recently published parameter estimates, the direct transmission approximation fails for both cholera and influenza. While environmental transmission is typically chosen over direct transmission in modeling cholera, this is not the case for influenza.

Keywords Environmental transmission · Environmental persistence · Direct transmission · Slow–fast dynamics

Mathematics Subject Classification (2000) 92D30 · 92D40 · 93A30

1 Introduction

Modeling infectious diseases that are environmentally transmitted is a field of growing interest. In short, environmental transmission is the process by which a pathogen is passed from an infected to a susceptible individual through the environment. Infected individuals shed pathogen particles in the environment where the pathogen persists

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depending on temperature, humidity, acidity, etc. The pathogen is then *harvested* by susceptible individuals that become infected depending on the ingested dose. This mechanism is in contrast to direct transmission which postulates that the pathogen is acquired through an infectious contact with an infected individual.

Pathogens persist on fomites (Rusin et al. 1998; Reynolds et al. 2005), in water (Pepper et al. 2004) and aerosols (Gralton et al. 2011). Environmental transmission is empirically recognized as an important transmission pathway for human viruses [e.g., gastroenteritis (D'Souza et al. 2006)], animal viruses [e.g., rabbit haemorrhagic disease (Henning et al. 2005)], water-borne pathogens [e.g., cholera (King et al. 2008; Pascual et al. 2002), avian cholera (Blanchong et al. 2006)], bacteria [e.g., tetanus (Roper et al. 2007), salmonella (Xiao et al. 2007), epizootics of plague (Webb et al. 2006)], prions [e.g., chronic wasting disease (Miller et al. 2006)], bovine spongiform encephalopathy (Anderson et al. 1996)] and zoonotic pathogens [e.g., Nipah and Hendra viral diseases (Field et al. 2001)]. Notably, environmental transmission is the preferred mechanism modeled for the transmission of cholera (Codeço 2001; Codeço et al. 2008; Jensen et al. 2006; Pascual et al. 2002; King et al. 2008). It has also been included, together with direct transmission, in modeling transmission of avian influenza in aquatic wild birds (Breban et al. 2009, 2010; Roche et al. 2009; Rohani et al. 2009).

Li et al. (2009) have opened the discussion on the modeling principles of environmental transmission, addressing the topic from a very general perspective. Using a paradigmatic mathematical model, they demonstrated that environmental transmission appears like direct transmission in certain situations where the density of the pathogens in the environment remains approximately constant. Notably, Li et al. (2009) and Spicknall et al. (2010) emphasized that environmental transmission is empirically recognized as mediating the spread of human respiratory diseases such as tuberculosis, SARS and influenza. However, most of the modeling work on these diseases uses a direct transmission mechanism, despite difficulties in defining the notion of infectious contact. The direct transmission incidence term is typically defined based on the principle of proportional mixing between susceptible and infected individuals. Relaxing this principle by using complex contact networks between individuals still relies on the notion of infectious contact. Since direct transmission is widely used in the modeling of environmentally transmitted diseases, it is important to study in what circumstances direct transmission represents a good approximation of environmental transmission.

The purpose of this paper is to show that environmental transmission may be approximated by direct transmission in the case where the pathogen persists little time in the environment. We write the environmental transmission term as an expansion in the persistence time. The first order represents the well-known direct transmission term. Using the second order of the expansion, we formulate conditions for the validity of this modeling approximation and we illustrate them numerically for the cases of cholera and influenza. Using published parameter estimates, we find that the validity conditions do not hold and the approximation is violated in both cases.

2 Model description

We generalize the SI model with environmental transmission proposed by [Codeço \(2001\)](#), leaving the environmental transmission term broadly specified by several unrestrictive axioms. The equations of our model are

$$dS/dt = \pi - \mu S - \rho S f(V), \quad (1)$$

$$dI/dt = \rho S f(V) - (\mu + \gamma)I, \quad (2)$$

$$dV/dt = \omega I - \eta V, \quad (3)$$

where S , I and V represent the number of susceptible individuals, infected individuals and pathogens in the environment. The parameters $1/\gamma$, $1/\eta$ and ω are the recovery period, the persistence time of the pathogen and the rate at which pathogen is shed by infected individuals; π is the susceptible inflow, μ is the natural death rate of individuals and ρ represents the contact rate with the environment. All variables and parameters are positively defined.

The environmental transmission rate is modeled by the term $\rho S f(V)$. The function $f : [0, \infty) \rightarrow [0, 1]$ represents the probability that an individual is infected when exposed to a population of V pathogens in the environment. It is empirically characterized by ID_{50} , the quantity of pathogen which gives 50% probability of infection. Previous work ([Codeço 2001](#); [Codeço et al. 2008](#); [Jensen et al. 2006](#); [Pascual et al. 2002](#); [King et al. 2008](#); [Breban et al. 2009, 2010](#); [Roche et al. 2009](#); [Rohani et al. 2009](#); [Dennis et al. 1989](#)) has used either a negative exponential

$$f_{NE}(V) = 1 - e^{-\alpha V} \quad (4)$$

or a rectangular hyperbola

$$f_{RH}(V) = \frac{V}{V + \kappa} \quad (5)$$

for the analytic forms of $f(\cdot)$, where α and κ are constants that relate to ID_{50} (i.e., $\alpha = \log_e 2/ID_{50}$ and $\kappa = ID_{50}$). However, currently available data on environmental transmission are too scarce to select an analytical form for $f(\cdot)$ on the basis of empirical evidence. Hence, we leave the function $f(\cdot)$ unspecified and we only make use of properties that derive from its biological meaning. We thus postulate the following ([Breban et al. 2010](#)):

Property 1 *The probability of infection vanishes in absence of pathogen [i.e., $f(0) = 0$] and approaches 1 as the pathogen population becomes large [i.e., $\lim_{V \rightarrow \infty} f(V) = 1$];*

Property 2 *The probability of infection $f(V)$ increases with the pathogen population V ; i.e., $f'(V) > 0$, where prime denotes derivative with respect to the argument.*

Furthermore, for technical reasons, we require

Property 3 $f(V)$ is twice differentiable in the neighborhood of zero and its second derivative is continuous in the neighborhood of zero.

Note that Properties 1 and 3 yield $f(V) = f'(0)V + f''(0)V^2/2! + \mathcal{O}(V^3)$.

3 Model equilibria and epidemic threshold

The model has a unique disease-free state $(S_{\text{DFS}}, I_{\text{DFS}}, V_{\text{DFS}}) = (\pi/\mu, 0, 0)$. All other equilibria have nonzero values for the number of pathogens and infected individuals; they are called endemic states, denoted by (S^*, I^*, V^*) . Their components are as follows. V^* is a positive solution of the equation

$$f(V^*) = (\mu/\rho)V^*/(V_c - V^*) \equiv g(V^*), \quad (6)$$

where $V_c \equiv (\omega/\eta)\pi/(\mu + \gamma)$. Note that V_c represents the amount of the pathogen established in the environmental reservoir in the very extreme case where the inflow of infected individuals equals the inflow of susceptible individuals, π . Hence, V_c is independent of the details of the environmental transmission mechanism and represents the maximum amount of pathogen that could be established in the environmental reservoir.

Given the hyperbolic form of the function $g(\cdot)$ in the right hand side of Eq. (6) and the properties postulated for the function $f(\cdot)$, Eq. (6) has a positive solution (i.e., a solution that can be assigned a biological interpretation) if and only if

$$g'(0) < f'(0) \Leftrightarrow 1 < \frac{\rho\omega f'(0)S_{\text{DFS}}}{\eta(\mu + \gamma)}. \quad (7)$$

Furthermore, if the solution exists, then it is unique and satisfies $0 < V^* < V_c$. The other components of the endemic equilibria are given by

$$I^* = \eta V^*/\omega, \quad (8)$$

$$S^* = S_{\text{DFS}}(1 - V^*/V_c). \quad (9)$$

Hence, the endemic state is unique.

Linear stability analysis shows that the disease-free state and the endemic state switch stability through a transcritical bifurcation when

$$R_0^{\text{env}} \equiv \frac{\rho\omega f'(0)S_{\text{DFS}}}{\eta(\mu + \gamma)} = 1. \quad (10)$$

If $R_0^{\text{env}} > 1$ then the endemic state is stable and the disease-free state is unstable while if $R_0^{\text{env}} < 1$ then the endemic state is unstable [and has non-biological values according to Eq. (6)] and the disease-free state is stable [see Li et al. (2009), Rohani et al. (2009) and Breban et al. (2010) for similar results]. Note that we may have values of R_0^{env} around 1 even though η is large because the shedding rate ω or the number of susceptible individuals at the disease-free state S_{DFS} could be large, as well.

4 The limit of low persistence times

We are interested in the case where the persistence time of the pathogen in the environment is small. That is, pathogen decay is much faster than all the other processes or time scales of the system. We show that, under these conditions, the environmental transmission mechanism appears like a direct transmission mechanism. We start with formally solving Eq. (3) as

$$V(t) = V(0)e^{-\eta t} + e^{-\eta t} \int_0^t ds \omega I(s)e^{\eta s}, \tag{11}$$

which, for $t \gg 1/\eta$, becomes

$$V(t) \approx \int_0^t ds e^{-\eta s} \omega I(t - s). \tag{12}$$

Since η is large, the exponential $e^{-\eta s}$ defines just a narrow time window in the variable s , $[0, 1/\eta]$, where the integrand is significantly different from zero. In this narrow time window, $I(t - s)$ does not change much and can be approximated by its Taylor series expansion around $I(t)$ truncated at the first two terms

$$I(t - s) \approx I(t) - s dI(t)/dt. \tag{13}$$

For moments of time much larger than the persistence time of the virus (i.e., $t \gg 1/\eta$), Eqs. (12) and (13) yield the following expansion up to second order in $1/\eta$

$$V(t) \approx \frac{\omega}{\eta} I(t) - \frac{\omega}{\eta^2} \frac{dI(t)}{dt}, \tag{14}$$

demonstrating that $V(t)$ is small when the persistence time of the virus in the environment is small. Using Eq. (2) to replace the derivative $dI(t)/dt$ in Eq. (14), we obtain

$$V(t) \approx \frac{\omega}{\eta} \left(1 + \frac{\mu + \gamma}{\eta} \right) I(t), \tag{15}$$

since, due to Properties 1 and 3, the term

$$\rho S(t) f(V) \approx \rho S(t) f'(0) V(t) \approx \rho S(t) f'(0) I(t) \omega / \eta, \tag{16}$$

is proportional with $1/\eta$ and does not contribute to the second order in the expansion in $1/\eta$. Substituting $V(t)$ as given by Eq. (15) in Eqs. (1) and (2) and using the expansion of $f(V)$ in the neighborhood of zero, we arrive at the following approximation of our model

$$\frac{dS}{dt} \approx \pi - \mu S - \beta SI \left[1 + \frac{\mu + \gamma}{\eta} + \frac{\omega f''(0)}{2\eta f'(0)} I \right], \tag{17}$$

$$\frac{dI}{dt} \approx \beta SI \left[1 + \frac{\mu + \gamma}{\eta} + \frac{\omega f''(0)}{2\eta f'(0)} I \right] - (\mu + \gamma)I, \tag{18}$$

where we introduced the notation $\beta \equiv \rho \omega f'(0)/\eta$. Hence, in the first order in $1/\eta$, Eqs. (17) and (18) represent the expected *SI* model with a direct transmission mechanism of transmissibility β . In addition, we obtained the next order corrections (i.e., second order in $1/\eta$) to the direct transmission term.

We note that our analysis may be difficult to apply to general models with environmental transmission. However, for obtaining results emerging from the first order expansion in the pathogen persistence time (e.g., the direct transmission model and its corresponding transmissibility formula) one may use *the slow-fast dynamics formalism*, a general technique of singular perturbation theory. See the appendix for the application of this technique to our model example.

4.1 Discussion of the correction terms

Both correction terms have transparent biological interpretations. The term $(\mu + \gamma)/\eta$ stands for the fact that a susceptible individual may become infected with pathogen that persisted past the recovery period of the shedder; note that an infectious individual cannot cause infections past their infectious period with a direct transmission mechanism. This term adds transmissibility and becomes important as the persistence time of the pathogen $1/\eta$ becomes larger than the infectious period of the shedder $1/(\mu + \gamma)$.

The second correction term requires a slightly more elaborated discussion. First, we define an infectious dose \widehat{ID} such that, for amounts of pathogen less than \widehat{ID} , the probability of infection is small; hence, $f(\widehat{ID}) \approx 0$. We use the expansion of $f(\widehat{ID})$ in the neighborhood of zero to estimate \widehat{ID}

$$f(\widehat{ID}) \approx f'(0)\widehat{ID} + f''(0)\widehat{ID}^2/2 \approx 0 \Rightarrow \widehat{ID} \approx -2f'(0)/f''(0). \tag{19}$$

We note that, under weak assumptions, the theory of birth processes demonstrates that $f(\cdot)$ is concave [see Breban et al. (2010), Dennis et al. (1989) and references therein]; thus, $f''(0) < 0$. (N.b., both $f_{NE}(\cdot)$ and $f_{RH}(\cdot)$ are concave.) Therefore, Eq. (19) makes biological sense for many reasonable choices of the function $f(\cdot)$. The resulting \widehat{ID} relates to ID_{50} ; e.g., $\widehat{ID} = 2 ID_{50} / \log_e 2$ for $f_{NE}(\cdot)$ and $\widehat{ID} = ID_{50}$ for $f_{RH}(\cdot)$.

Second, we consider the amount of virus shed by I infectious individuals during the persistence time of the pathogen, $\omega I/\eta$. If $\omega I/\eta < \widehat{ID}$, then susceptible individuals are *protected* from infection (as compared to direct transmission) since the pathogen always passes through the environment where it does not accumulate in sufficient amounts to create new infections because it undergoes fast decay. Hence, a term like

$$\frac{\omega I}{\eta \widehat{ID}} = -\frac{\omega f''(0)}{2\eta f'(0)} I \tag{20}$$

would appear as a negative correction to transmissibility.

Table 1 Parameter values for the simulations in Fig. 1

Case	ξ	\hat{I}
A	0.001	100,000
B	0.5	100,000
C	0.001	1,000
D	0.5	1,000

We have chosen $R_0^{env} = 1.5$ and $\gamma = 50 \text{ years}^{-1}$. The vital dynamics parameters are $\pi = 1,000 \text{ years}^{-1}$ and $\mu = 0.01 \text{ years}^{-1}$; i.e., $S_{DFS} = 100,000$. The rest of the parameters are calculated such that ξ and \hat{I} take the values listed below. (N.b., The amount of pathogen is measured in infectious doses; hence $\kappa = 1$.)

4.2 Validity conditions for the direct transmission approximation

We use the conditions that the magnitude of each correction term is much smaller than 1 to establish when environmental transmission may be approximated with a direct transmission term. Thus, we obtain

$$\frac{\mu + \gamma}{\eta} \equiv \xi \ll 1, \tag{21}$$

and

$$I \ll \hat{I} \equiv \frac{\eta \hat{ID}}{\omega}. \tag{22}$$

Hence, in the paradigm model that we study here, the direct transmission approximation holds if two conditions are satisfied. First, the persistence time of the pathogen is much less than the recovery period of the shedder. Second, the number of infected individuals is much less than \hat{I} . In practical terms, for the second condition to hold for all time, \hat{I} should be of the order of S_{DFS} .

4.3 Numerical illustration of analytic results

We illustrate numerical simulations of the paradigm model given by Eqs. (1)–(3) for various cases of validity of the conditions (21) and (22). We choose $f(\cdot) \equiv f_{RH}(\cdot)$, where we measure the amount of pathogen in infectious doses ID_{50} ; hence, $\kappa = 1$. We analyze four cases: case A, both approximation conditions hold; case B, the first condition holds but the second fails; case C, the second condition holds and the first fails; and case D, where neither condition holds. The parameter choices are presented in Table 1 and computations of prevalence versus time are illustrated in the corresponding panels of Fig. 1. To maintain some means of comparison between the panels, we fixed $R_0^{env} = 1.5$ in each case.

In case A, the first order expansion in $1/\eta$ (i.e., the direct transmission model illustrated by a thin line) is close to the exact model (thick line) and the second order approximation (dashed line) is even closer. In cases B and D, where $\xi \sim 1$ (i.e., $\eta \sim (\mu + \gamma)$), the direct transmission approximation fails since the pathogen

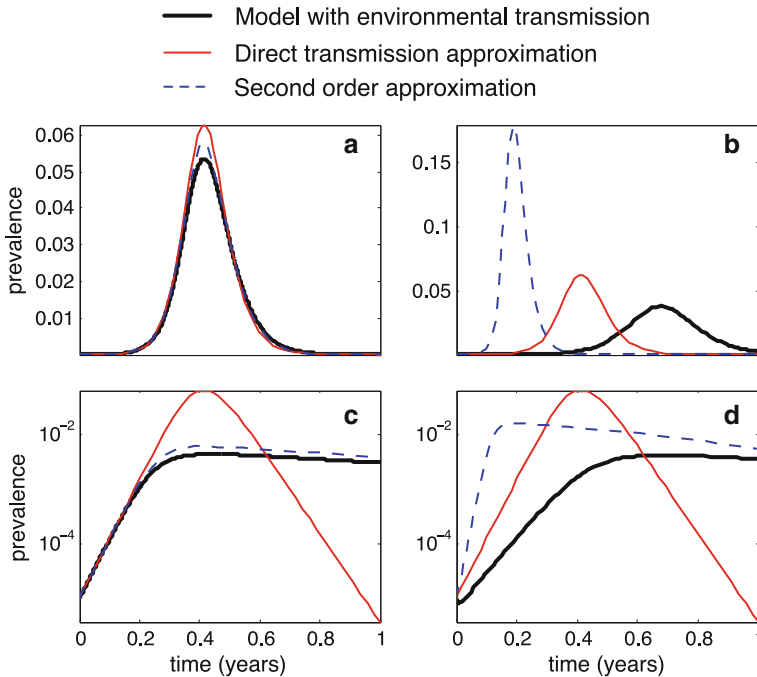


Fig. 1 Successive orders of approximation for a model with environmental transmission (i.e., $f(\cdot) = f_{RH}(\cdot)$). **a** The case where both conditions of the direct transmission approximation hold; $\xi \ll 1$ and $\hat{I} \sim S_{DFS}$. **b** The case where the first approximation condition fails but the second holds; $\xi \sim 1$, but $\hat{I} \sim S_{DFS}$. **c** The case where the first approximation condition holds but the second fails; $\xi \ll 1$, but $\hat{I} \ll S_{DFS}$. **d** The case where both approximation conditions fail; $\xi \sim 1$ and $\hat{I} \ll S_{DFS}$

persists well in the environment. In case C, where the persistence time of the pathogen is short, the direct transmission approximation works as long as the number of infected individuals does not grow above \hat{I} (i.e., a prevalence of $\sim 10^{-3}$). Once $I > \hat{I}$, the prevalence curves of the exact model and the direct transmission model differ substantially. The curve of the exact model achieves a maximum in the neighborhood of \hat{I} , then declines steadily. In contrast, the prevalence curve of the direct transmission model continues to rise significantly higher than \hat{I} , then declines sharply. The phenomenon of epidemic decline after disease invasion is known as *depletion of susceptibles* and, in this case, appears less significant for the model with environmental transmission than for its corresponding model with direct transmission.

In Table 2, we illustrate the conditions under which the direct transmission approximation holds for cholera (Codeço 2001) and influenza (Li et al. 2009). For each of these diseases, the approximation fails in a different way. For cholera, direct transmission could properly model the infection of tens of thousands of individuals. However, its long persistence time (in aquatic environment) renders ξ comparable to 1; the situation is similar to that presented in panel B of Fig. 1. In contrast, influenza viruses persist much less (in air or on fomites); hence, in this case, ξ is significantly less than 1. However, given that influenza viruses are shed at high rates in the environment, direct

Table 2 Numerical check of the conditions that a direct transmission mechanism could be used to model environmental transmission

Disease	Persistence environment	ξ	\hat{I}	References
Cholera	Water	0.61	33,000	Codeço (2001)
Influenza	Air	0.023	0.17	Li et al. (2009)
Influenza	Frequently touched fomites	0.070	5.5	Li et al. (2009)
Influenza	Infrequently touched fomites	0.070	0.028	Li et al. (2009)

transmission does not accurately model more than several infections. The situation is similar to that presented in panel C of Fig. 1.

5 Discussion and conclusions

Although many pathogens are transmitted from person to person through an intermediary environmental reservoir, most modeling work on their epidemic spread is based on the concepts of infectious contact and direct transmission. Hence, it is important to study the circumstances where direct transmission represents a good approximation of environmental transmission.

In this work, we have shown using a paradigm model that direct transmission holds as an approximation for the environmental transmission mechanism in the case where the persistence time of the pathogen in the environment is short. We derived a second order expansion of the model with environmental transmission in the persistence time of the pathogen. The first order in the expansion is a model possessing the well-known direct transmission mechanism. Using the second order of the expansion, we derived two explicit conditions for when the first order approximation holds: (1) the persistence time of the pathogen is much less than the recovery period of the shedder, and (2) the number of infected individuals is much less than a certain bound given in terms of model parameters.

Whenever applicable, the direct transmission approximation has the advantages that it reduces (i) the dimensionality of the model by excluding the dynamics of the pathogen population in the environment and (ii) the number of parameters by combining some of them into the direct transmissibility β . We note that when the direct transmission approximation fails, adding higher order corrections no longer collapses the parameter space. This is readily obvious in the next order correction that we obtained here. Using the framework of Breban et al. (2010), the results of this paper could be easily generalized for the case of models describing several strains with perfect strain-transcending cross-immunity.

Two human diseases have been modeled so far using environmental transmission terms: cholera and influenza. While it appears that there is consensus in modeling cholera using environmental transmission, this is not the case for influenza where most work uses direct transmission. However, according to our results based on the parameters developed by Li et al. (2009) and Spicknall et al. (2010), the direct transmission approximation fails for influenza. A large shedding rate and a low persistence

time of the virus in the environment causes much virus to decay before reaching susceptible individuals. Consequently, the environmental transmission model reveals less depletion of susceptibles than its counterpart having a direct transmission mechanism.

Our findings may bring insight into recent studies revisiting the role of depletion of susceptibles in influenza epidemiology. Theoretical studies using models with direct transmission advocate for the importance of this phenomenon in curbing down the epidemic and public health applications (Vardavas et al. 2007; Ballesteros et al. 2009; Chowell et al. 2007; Handel et al. 2007). However, analyses of epidemic curves find that depletion of susceptibles does not play the expected role in epidemic decline and stress out the potential impact of behavior change during epidemics (Caley et al. 2008; Goldstein et al. 2009). Our new results suggest that this discrepancy may be resolved by using models with environmental transmission to describe influenza epidemics.

In conclusion, our work discusses environmental transmission in the case where the persistence time of the pathogen in the environment is small. Using a paradigm model, we established the conditions under which environmental transmission can be approximated by direct transmission. We found that these conditions are violated for both cholera and influenza. While the case of cholera is fairly well understood, much remains to be investigated about human influenza viruses, given their strain diversity and multitude of parameters driving their environmental persistence.

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Appendix

A Calculation of the direct transmissibility parameter using the slow–fast dynamics formalism

We approach the problem through the slow–fast dynamics formalism (Fenichel 1979; Sakamoto 1990; Berglund and Gentz 2006), a technique that belongs to the singular perturbation theory. Indeed, in the case where the persistence time of the pathogen is small (i.e., η is large and t is thought as a *slow* time), V is a fast variable (i.e., $|dV/dt| = \mathcal{O}(\eta)$) while S and I are slow variables (i.e., $|dS/dt| = \mathcal{O}(1)$, $|dI/dt| = \mathcal{O}(1)$). However, a direct approach using $1/\eta$ as the only small parameter does not provide the expected outcome: V vanishes in the zeroth order in $1/\eta$ [c.f., Eq. (3)] and the resulting slow system has only a disease free state and no epidemic threshold.

For pathogen to remain present in the environment when its decay rate is large (i.e., $\eta \gg 1$) and the number of shedders is small (i.e., $I = \mathcal{O}(1)$) during disease invasion, we must also have that shedding rates are large; i.e., $\omega/\eta = \mathcal{O}(1)$. Hence, the *slow system* associated to our model is given by

$$dS/dt = \pi - \mu S - \rho S f(\tilde{V}(I)), \quad (23)$$

$$dI/dt = \rho S f(\tilde{V}(I)) - (\mu + \gamma)I, \quad (24)$$

where

$$\tilde{V}(I) \equiv (\omega/\eta)I. \quad (25)$$

defines the plane $(S, I, \tilde{V}(I))$ as a stable *slow manifold*. A well-established theorem ensures that the dynamics of a slow–fast dynamical system having a stable slow manifold converges to the manifold (Fenichel 1979; Sakamoto 1990; Berglund and Gentz 2006). Furthermore, the system is dimensionally reduced (as a first order approximation) to its corresponding slow system evolving within the slow manifold. Applying these results to our model, we have that Eqs. (23), (24) and (25) provide an approximation of our original model given by Eqs. (1)–(3) once $t \gg 1/\eta$.

The incidence term $\rho Sf'(\tilde{V}(I))$ can be further rewritten using the approximation $f'(\tilde{V}(I)) \approx f'(0)\tilde{V}(I)$ (Properties 1 and 3) since η is large and thus $\tilde{V}(I)$ is small. We obtain

$$\rho Sf'(\tilde{V}(I)) \approx [\rho\omega f'(0)/\eta]SI, \quad (26)$$

which represents a direct transmission term with transmissibility $\beta = \rho\omega f'(0)/\eta$. Hence, in the slow system, environmental transmission is approximated by a direct transmission mechanism.

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