Modeling the Skip-and-resurgence of Japanese Encephalitis Epidemics in Hong Kong

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Contents

Supplementary Information

S1 More Fitting Results Under Different Scenarios

S1.1 Baseline fitting results

In this case, the force of infection from mosquitoes to pigs is set as

$$\lambda_{vp} = k \cdot \omega(t) + b,$$

where ω is the time series of ovitrap index in Hong Kong, k and b are model parameters under estimation. The baseline fitting results of the model are shown in Fig S1. Estimated results of model parameters are in Table S1.

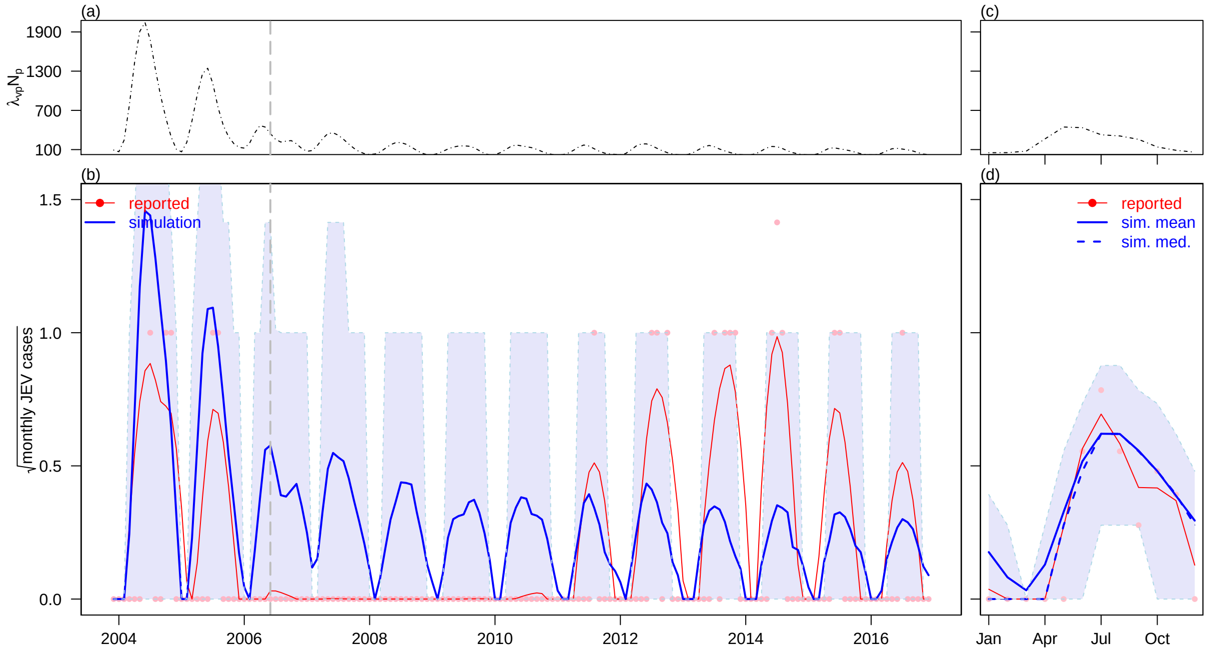

Figure S1: Fitting results of JEV local cases in Hong Kong from 2004 to 2016 under baseline (i.e., no invasion) scenario. Panel (a) and (b) are the scaled force of infection (from vectors to pigs, scaled by the population size of pigs) and simulation results from 2004 to 2016 respectively. Panel (c) and (d) are the one-year-average scaled force of infection and simulation results from 2004 to 2016 respectively. In panel (a) and (b), black dashed lines are the scaled force of infection. In panel (b) and (d), blue lines are the simulation results, shaded regions are 95% quantile interval from simulation, pink dots are the reported (i.e., observed) JEV local cases and red lines are the smoothed (by *loess* function) reported JEV cases. The vertical grey dashed line marks the time point when Hong Kong government triggered the pig rearing licences surrender policy.

Table S1: Summary table of model parameters' estimates under baseline (i.e., no invasion) scenario. X_{p0} denotes the initial proportion of class X_p.

Parameter	Notation	Value	Type	Initial status	Unit
Average force of infection	$\langle\lambda_{vp}\rangle$	0.0019	estimated	time-dependent	per year
Pig latent period	σ_p^{-1}	1.5	fixed	1-2	days
Pig infection period	γ_p^{-1}	3	fixed	2-4	days
Pig convalescent period	δ_p^{-1}	2.5	fixed	1-4	days
Imported infection ratio	η	1.0%	fixed	0.43%-1.45%	Nil
Effective contact rate	β_p	0.0098	estimated	0.0-0.4	per days
Pig living period	ν_p^{-1}	234	fixed	234	days
Pig population	N_p	-	-	time-dependent	pigs
Average spill over ratio	$\langle\rho\rangle$	0.0008	estimated	time-dependent	Nil
Average ovitrap index	$\langle\omega\rangle$	0.0564	given	time-dependent	Nil
Initial susceptible	S_{p0}	0.5847	estimated	45-75%	Nil
Initial exposed	E_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial infectious	I_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial convalescent	C_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial recovered	R_{p0}	0.3123	estimated	25-55%	Nil
BIC	BIC	168.7009	estimated	-	Nil

S1.2 Fitting results of partitioned spill-over rate ρ

This model scenario is associated with explanation **I3**. For partitioned ρ, we assume ρ is increased after new strain invasion as:

$$\rho = \begin{cases} \xi_1 \cdot \omega(t-\tau), & t < T_0 \\ \xi_2 \cdot \omega(t-\tau), & t \geqslant T_0 \end{cases}$$

where τ is the time delay and T_0 is the starting time instant when new JEV strain joined the system.

The fitting results of the new JEV strain invasion scenario with increased λ_{vp} and ρ after invasion are shown in Fig S2. Estimated results of model parameters are in Table S2. The estimate of $\mathcal{R}_{pp}$ is 0.026 (95% C.I.: [0.00,0.30]) under this scenario (see Fig S3).

S1.3 Fitting results of partitioned force of infection

This model scenario is associated with explanation **I2**. In this case, fixing the spill-over ratio, we assume the force of infection under new JEV strain invasion scenario is

$$\lambda_{vp} = \begin{cases} k_1 \cdot \omega(t) + b, & t < T_0 \\ k_2 \cdot \omega(t) + b, & t \geqslant T_0 \end{cases}$$

where T_0 is the starting time instant when new JEV strain joined the system. The situation with no invasion of new strains can be regarded as the special case that $k_1 = k_2$.

The fitting results of the new JEV strain invasion scenario with variable force of infection are shown in Fig S4. Estimated results of model parameters are in Table S3. The estimate

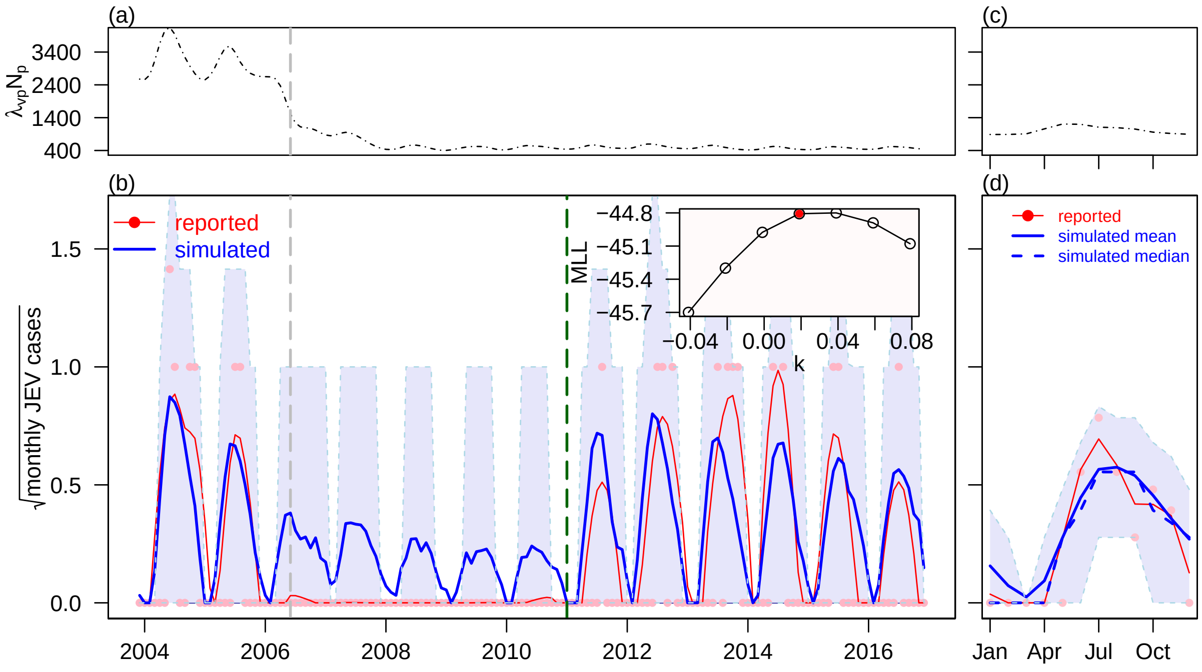

Figure S2: Model fitting results of JEV local cases under the new strain invasion scenario from 2004 to 2016 in Hong Kong. Panels (a) and (b) are the re-scaled force of infection from vectors to pigs, normalized by the pig population sizes and their simulated results, both from 2004 to 2016. Panels (c) and (d) are the one-year average re-scaled force of infection and their simulated results from 2004 to 2016. In panels (a) and (b), black dashed lines are the scaled force of infection. In panels (b) and (d), blue lines are the simulated results, shaded regions are the simulated 95% quantile interval. Pink dots are the observed JEV local cases and red lines are the smoothed observed JEV cases using the *LOESS* function. The vertical grey dashed line is the time where the pig rearing license surrendering policy was implemented. The vertical dark green line is the time when the new strain invasion occurs. The model scenario is associated with explanation **I1**.

of $\mathcal{R}_{pp}$ is 0.0053 (95% C.I.: [0.00,0.31]) under the invasion scenario with partitioned force of infection (see Fig (S5)).

S2 Further Reasoning on Model Parameters and Structure

S2.1 Initial proportions of I_{p0}, E_{p0} and C_{p0}

The proposed modelling framework is relatively novel thus it is difficult to find the exact value of these three values in previous research of pigs. The initial proportions of E_{p0}, I_{p0} and C_{p0} is assumed to be equal for simplicity. Here is the justification. The average period of staying in E_p, I_p or C_p is $(1.5+3.0+2.5)/3 = 7/3$ days (see Table 1 for the parameter values). Then, if a pig is assumed to be infected during its living period and we randomly select one day,

Table S2: Summary table of parameter estimation under new JEV strain invasion scenario with variable ρ. X_{p0} denotes the initial proportion of class X_p.

Parameters	Notations	Values	Types	Initial status	Units/Remarks
Average force of infection	$\langle\lambda_{vp}\rangle$	0.0042	estimated	time-dependent	per year
Latent period of pigs	σ_p^{-1}	1.5	fixed	1-2	days
Infection period of pigs	γ_p^{-1}	3	fixed	2-4	days
Convalescent period of pigs	δ_p^{-1}	2.5	fixed	1-4	days
Infection ratio among imported pigs	η	1.0%	fixed	0.43%-1.45%	Nil
Effective contact rate	β_p	0.0011	estimated	0.0-0.4	per days
Lifespan of pigs	ν_p^{-1}	234	fixed	234	days
Size of pig population	N_p	-	-	time-dependent	pigs
Average spill-over ratio	2004-10:$\langle\rho\rangle$	0.0002	estimated	time-dependent	before invasion
Average spill-over ratio	2011-16:$\langle\rho\rangle$	0.0024	estimated	time-dependent	after invasion
Average ovitrap index	$\langle\omega\rangle$	0.0564	given	time-dependent	Nil
Initial proportion of susceptible	S_{p0}	0.6818	estimated	45-75%	Nil
Initial proportion of exposed	E_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial proportion of infectious	I_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial proportion of convalescent	C_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial proportion of recovered	R_{p0}	0.3152	estimated	25-55%	Nil
BIC	BIC	140.2633	estimated	-	Nil

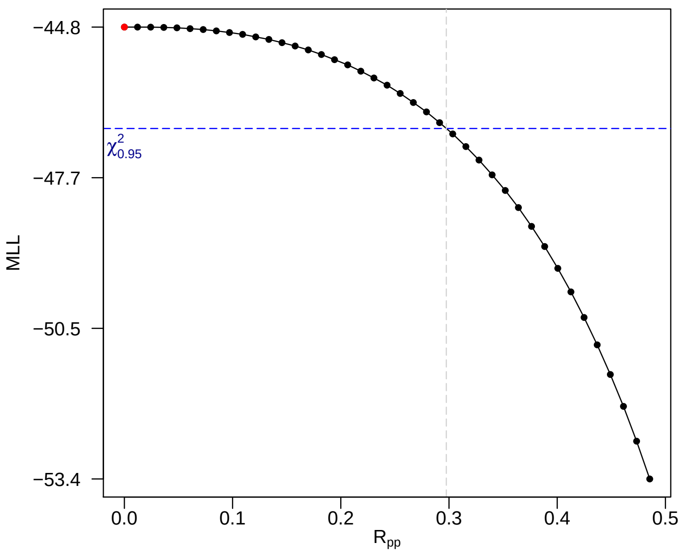

Figure S3: The estimation result of the basic reproduction number of pig-to-pig transmission ($\mathcal{R}_{pp}$) under new JEV strain invasion scenario with both variable λ_{vp} and ρ. The horizontal blue dashed line is the 95% confidence threshold. The model scenario is associated with explanation **I1**.

the probability of "the pig is in E_p, I_p or C_p on the selected day" is $p_1 = (7/3)/234 = 0.01$ (where 234 days are the average pigs' lifespan). According to References, we have $R_{p0} =$ 25% 55% (see Table 1), this implies there is 55%-25%=30%, as a maximum, of locally-reared

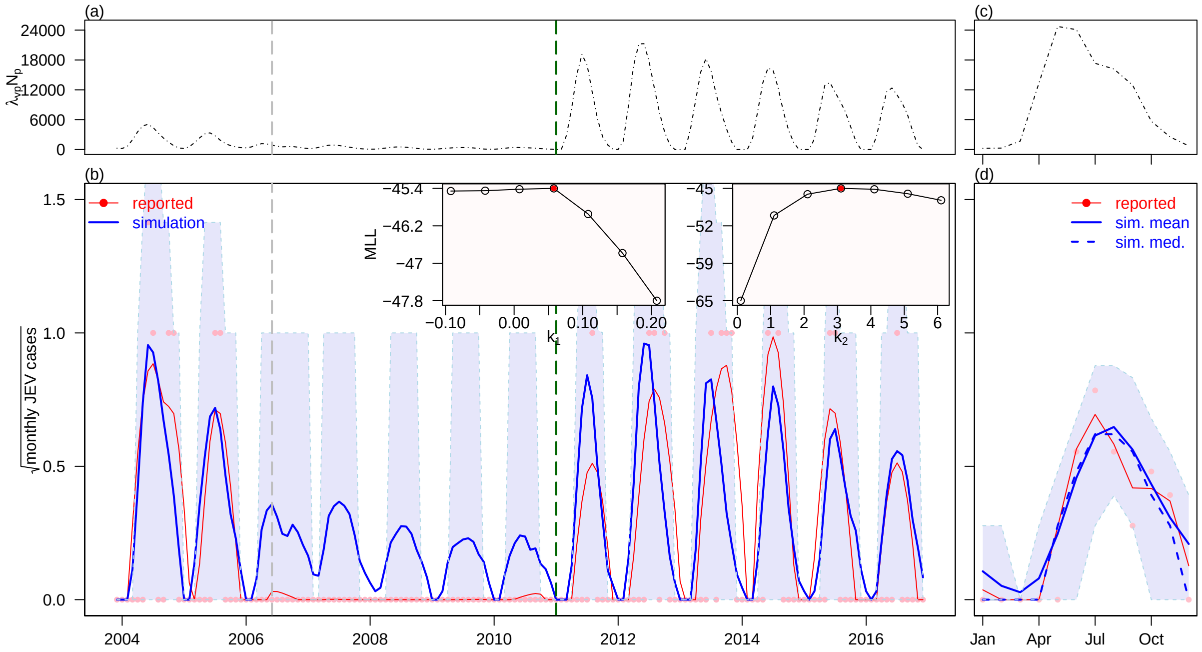

Figure S4: Fitting results of JEV local cases in Hong Kong from 2004 to 2016 under new JEV strain invasion scenario with variable force of infection (λ_{vp}). Panel (a) and (b) are the scaled force of infection (from vectors to pigs, scaled by the population size of pigs) and simulation results from 2004 to 2016 respectively. Panel (c) and (d) are the one-year-average scaled force of infection and simulation results from 2004 to 2016 respectively. In panel (a) and (b), black dashed lines are the scaled force of infection. In panel (b) and (d), blue lines are the simulation results, shaded regions are 95% quantile interval from simulation, pink dots are the reported (i.e., observed) JEV local cases and red lines are the smoothed (by *loess* function) reported JEV cases. The vertical grey dashed line marks the time point when Hong Kong government triggered the pig rearing licences surrender policy. The vertical dark green dashed line marks the time point when the new JEV strain introduced to the pigs' population. The inset panel shows the maximum log-likelihood (MLL) values of different k_1s and k_2s , the red dot with the highest MLL are selected for fitting in main panels. The model scenario is associated with explanation **I2**.

pig would be infected annually. Therefore, we have the probability of "a randomly selected locally-reared pig will be infected during its life time" is $p_2 = 30\% * (234/365.25) = 0.19$ (where 365.25 days are the average time period of a year). By further assuming the events of p1 and p2 are independent, we have the probability of "a randomly selected locally-reared pig is infected (i.e., in E_p, I_p or C_p) on a randomly select day" is $p = p_1 p_2 = 0.0019$ (as upper bound). It is obvious that the lower bounds of E_{p0}, I_{p0} and C_{p0} are all 0. Hence, we have the average of upper and lower bounds: $(0.0019 + 0)/2 = 0.001 = 0.1\%$ as assumed. Furthermore, as the initial proportions of E_{p0}, I_{p0} and C_{p0} are believed to be very small, slightly changes of these three parameters will not affect our main results.

Table S3: Summary table of model parameters' estimates under new JEV strain invasion scenario with variable force of infection (λ_{vp}). X_{p0} denotes the initial proportion of class X_p.

Parameter	Notation	Value	Type	Initial status	Unit/Remarks
Average force of infection	2004-10:$\langle\lambda_{vp}\rangle$	0.0044	estimated	time-dependent	before invasion
Average force of infection	2011-16:$\langle\lambda_{vp}\rangle$	0.1763	estimated	time-dependent	after invasion
Pig latent period	σ_p^{-1}	1.5	fixed	1-2	days
Pig infection period	γ_p^{-1}	3	fixed	2-4	days
Pig convalescent period	δ_p^{-1}	2.5	fixed	1-4	days
Imported infection ratio	η	1.0%	fixed	0.43%-1.45%	Nil
Effective contact rate	β_p	0.0022	estimated	0.0-0.4	per days
Pig living period	ν_p^{-1}	234	fixed	234	days
Pig population	N_p	-	-	time-dependent	pigs
Average spill over ratio	$\langle\rho\rangle$	0.0003	estimated	time-dependent	Nil
Average ovitrap index	$\langle\omega\rangle$	0.0564	given	time-dependent	Nil
Initial susceptible	S_{p0}	0.5767	estimated	45-75%	Nil
Initial exposed	E_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial infectious	I_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial convalescent	C_{p0}	0.001	assumed	0.0-0.25%	Nil
Initial recovered	R_{p0}	0.4203	estimated	25-55%	Nil
BIC	BIC	141.2743	estimated	-	Nil

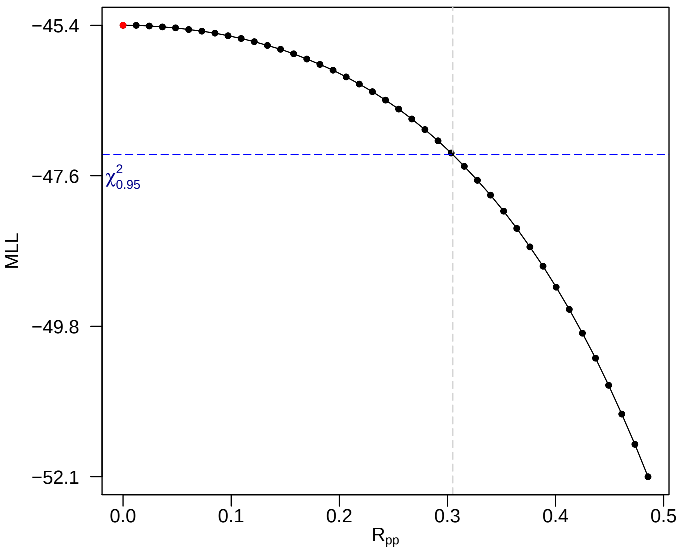

Figure S5: The estimation result of the basic reproduction number of pig-to-pig transmission ($\mathcal{R}_{pp}$) under new JEV strain invasion scenario with variable λ_{vp}. The horizontal blue dashed line is the 95% confidence threshold. The model scenario is associated with explanation **I2**.

S2.2 Further Reasoning on Model Structure

Why to design the model for pig population rather than human? We list the major reasons as follows:

1. For JEV transmission, human hosts are the incidental and dead-end host of the disease

transmission (since humans can not develop sufficient viraemia to infect mosquitoes). However, pigs serve as reservoir for the disease transmission.

2. The human infection risk is proportion to mosquito infections, which is in turn proportion to the infection rate of reservoir, pigs. Thus, by modelling JEV transmission among pigs, human infections can be inferred by using a spill-over rate (ρ).

3. Undoubtedly, one can model all of reservoirs, hosts and vectors population explicitly. However, the model would be very complicated, which may lead to over-fitting issue. As we can see, the current model fits the data well, and also simplified the modelling frameworks.

Why to formulate the vector-free model? The purpose (at least one major purpose) of the vector (mosquito) population is to keep tracking the mosquito density. However, we found a mosquito index (i.e., the ovitrap index) from observation. Thus we directly use this mosquito index as the replacement of the vector (i.e., mosquito in this work) population. This approach saved us from explicitly modeling the mosquito population. Alternatively, we could have formulate a two-host model with both pig and mosquito. Then we aim to fit simultaneously the observed human cases and the observed mosquito index. That will be a challenging future work.

S2.3 $\mathcal{R}_0$ and CCS after New JEV Invasion

New $\mathcal{R}_0$ and CCS before/after the invasion of the new JEV strain It is hard to directly estimate the $\mathcal{R}_0$ with the simplified model (as we avoid model the mosquito and human population explicitly), but we can estimate the percentage change on $\mathcal{R}_0$ before/after new strain invasion. As we wrote in paragraph "Force of Infection from Vectors to Reservoirs" (from mosquito to pig) in "Parameter Estimation" section, λ_{vp} can be further expressed as $\lambda_{vp} = a\theta_{vp}I_v/N_p$. Then, the model is similar to the ODE system proposed in Gao *et al.* [1] by regarding pigs as "host" and mosquito as vector. Biologically, the new (more infective) JEV strain could only increase the transmission probability (i.e., θ_{vp}) via mosquito bites. Then, the effect of term θ_{vp} on $\mathcal{R}_0$ is equivalent to the terms $\sqrt{bc}$ in the $\mathcal{R}_{hv}$ expression at the end of Gao *et al.* [1] (please note that we do not have term λ_{pv} from pig to mosquito in our current model, but as for compensations, our term λ_{vp} covers the effect of the potential term λ_{pv}). Therefore, the percentage change on term θ_{vp} equals to percentage change in λ_{vp}, and the roughly equals to the percentage change in $\mathcal{R}_0$ (by ignore the effect of pig-to-pig transmission, i.e., $\mathcal{R}_{pp}$, because it is estimated to be very small). According to our estimation in scenario **I3**, the changing fold in λ_{vp} is $0.0071/0.0043 = 1.65$. If we presume $\mathcal{R}_0 = 1.15$ (with CCS around $150,000$ in Fig. 8) before invasion, the new $\mathcal{R}_0 = 1.65 \times 1.15 = 1.90$ (which is out of the bound of current Fig. 8) after new JEV invasion, and the new CCS is around $15,000$ (by using Eqn. (10)), which is much less than current local pig population (roughly $60,000$). This is likely to explain the mechanism of JEV resurgence in 2011.

References

[1] Gao D, Lou Y, He D, Porco TC, Kuang Y, Chowell G, et al. Prevention and Control of Zika as a Mosquito-Borne and Sexually Transmitted Disease: A Mathematical Modeling Analysis. Sci Rep. 2016;6:28070.