Pathogen Emergence In Seasonal Environments

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Introduction

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$$p_e = 1 - \frac{1}{R_0} = 1 - \frac{\mu}{\lambda}. \tag{1}$$

birth rate λ depends on transmission rate and number of susceptibles

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This is a simple one dimensional model. We shall see more complex model : A ZIKA model in dimension 4.

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For periodic rates (Kendall 1948)

$$\boxed{R_0 = \frac{\bar{\lambda}}{\bar{\mu}}}, \quad \text{with} \quad \bar{\lambda} = \frac{1}{T}\int_0^T \lambda_T(s)\, ds\,, \bar{\mu} = \frac{1}{T}\int_0^T \mu_T(s)\, ds\,.$$

$$p_e(t_0, T) = 1 - \frac{\int_0^T \mu_T(s+t_0) e^{-\varphi_T(s+t_0)}\, ds}{\int_0^T \lambda_T(s+t_0) e^{-\varphi_T(s+t_0)}\, ds}$$

$$\varphi_T(t) = \int_0^t (\lambda_T(s) - \mu_T(s))\, ds\,.$$

Seasonality conclusions

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- If $R_0 < 1$, then $p_e(t_0) = 0$ for all t_0.

Seasonality Conclusions

The formula $p_e(t) \approx \boxed{\text{guess}(t) = 1 - \frac{\mu(t)}{\lambda(t)}}$ is false but sometimes gives a good approximation for large periods, relative to $\frac{1}{\mu}$ = mean infectious period, if

$$\lambda_T(t) = \lambda(t/T)\,, \mu_T(t) = \mu(t/T) \quad (t \in [0,1]).$$

For example

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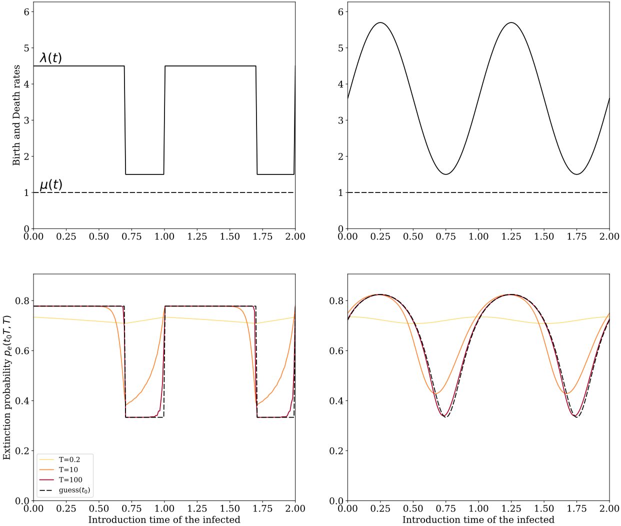
The formula $p_e(t) \approx \boxed{1 - \frac{\bar{\mu}}{\bar{\lambda}}}$ is a good approximation for small periods



$\lambda(t)$
$\mu(t)$
Birth and Death rates
Extinction probability $p_e(t_0 T, T)$
T=0.2
T=10
T=100
guess(t_0)
Introduction time of the infected
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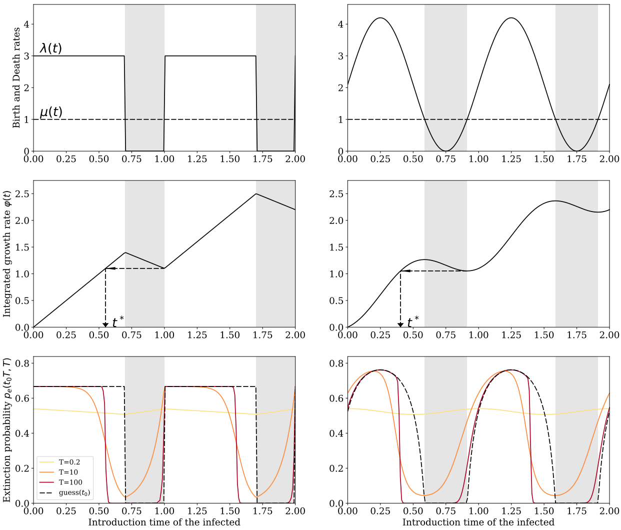
Birth and Death rates
$\lambda(t)$
$\mu(t)$
Integrated growth rate $\varphi(t)$
t^*
t^*
Extinction probability $p_e(t_0T, T)$
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Control Strategies

Replace $\lambda(t)$ by $\lambda_\rho(t) = \lambda(t)(1 - \rho(t))$ with $\rho(t) = \rho_M 1_{(t_1 < t < t_2)}$.

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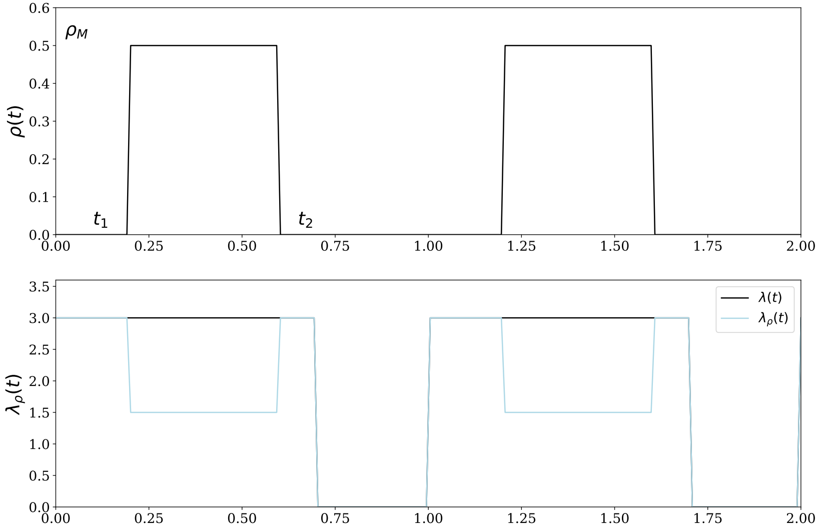
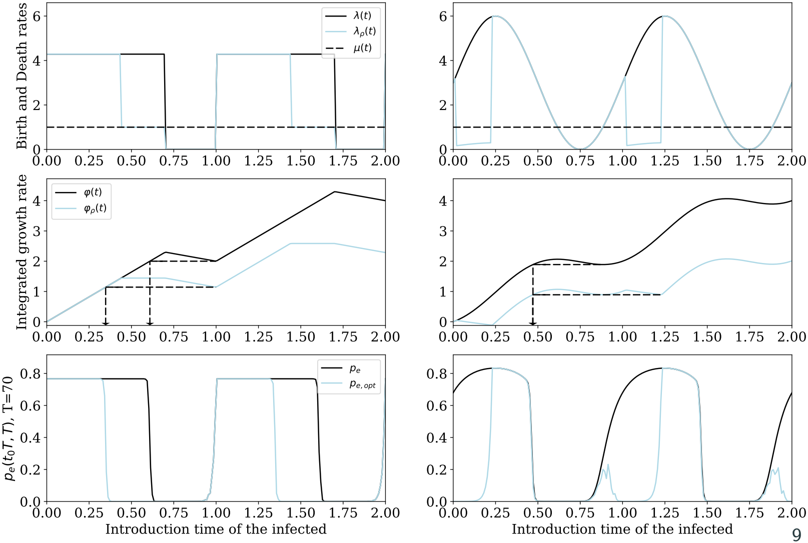
Minimize $< p_{e,\rho} >= \int_0^1 p_{e,\rho}(t_0)\, dt_0$, with fixed cost

$$\boxed{C = \int_0^1 \rho(s)\, ds = \rho_M(t_2 - t_1)}.$$

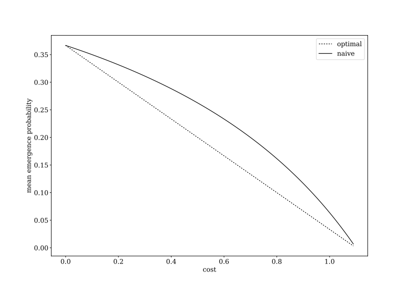
Control Strategy Example

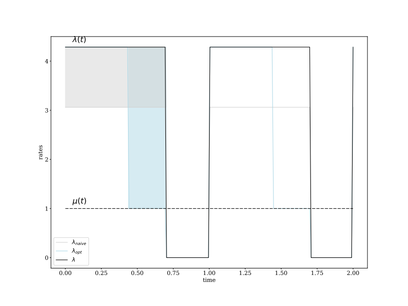


Optimal control strategies

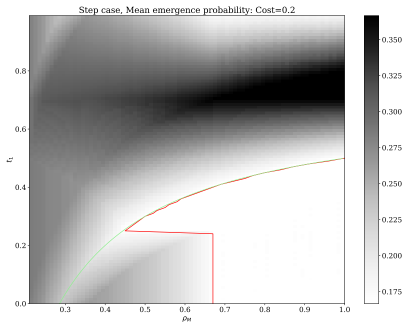


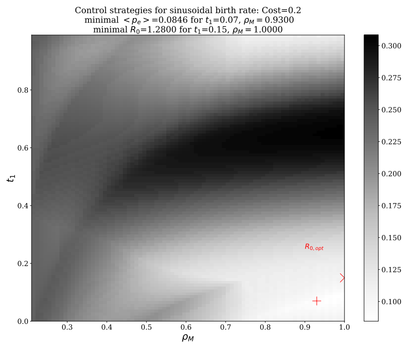
Step Case : naive vs optimal control strategy





Minimizing R_0 vs minimizing $< p_e >$





The ZIKA Virus Example

Common model of (Lourenço & al 2017, Suparit & al 2018, Zhang & al 2017).

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Humans follow stochastic SEIR, Vectors follow stochastic SEI

$$\frac{dS^H}{dt} = \Theta^H - \delta^H S^H - \beta^{VH} I^V S^H \qquad \frac{dS^V}{dt} = \Theta^V - \delta^V S^V - \beta^{HV} I^H S^V$$

$$\frac{dE^H}{dt} = \boxed{\beta^{VH} I^V S^H} - (\gamma^H + \delta^H) E^H \qquad \frac{dE^V}{dt} = \boxed{\beta^{HV} I^H S^V} - (\gamma^V + \delta^V) E^V$$

$$\frac{dI^H}{dt} = \gamma^H E^H - (\kappa^H + \delta^H) I^H \qquad \frac{dI^V}{dt} = \gamma^V E^V - \delta^V I^V$$

$$\frac{dR^H}{dt} = \kappa^H I^H - \delta^H R^H$$

The Associated Branching Process

$$\frac{dE^H}{dt} = \lambda_{I^V,E^H} I^V - \mu_{E^H} E^H , \qquad \frac{dE^V}{dt} = \lambda_{I^H,E^V} I^H - \mu_{E^V} E^V$$

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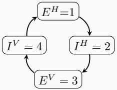
Common parameters : $\frac{1}{\mu^H} = 75$ years, $\mu_{E^H} = \gamma^H + \mu^H$, $\frac{1}{\gamma^H} \approx 7$ days (human mean incubation period), $N^H =$ constant.

The constant rate case (Circular)



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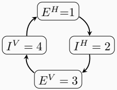

$$R_0^4 = \frac{\prod_i \lambda_{i,i+1}}{\prod_i \mu_i} = \frac{\lambda_{E^H,I^H}\lambda_{I^H,E^V}\lambda_{E^V,I^V}\lambda_{I^V,E^H}}{\mu_{E^H}\mu_{I^H}\mu_{E^V}\mu^{I_V}}$$

$$p_{e,1} = \frac{\prod_{i=1}^{d} \lambda_{i,i+1} - \prod_{i=1}^{d} \mu_i}{\sum_{k=0}^{d-1} \prod_{i=1}^{k} \mu_i \prod_{i=k+1}^{d} \lambda_{i,i+1}}$$

$$guess_1(t_0) = \frac{\prod_{i=1}^{d} \lambda_{i,i+1}(t_0) - \prod_{i=1}^{d} \mu_i(t_0)}{\sum_{k=0}^{d-1} \prod_{i=1}^{k} \mu_i(t_0) \prod_{i=k+1}^{d} \lambda_{i,i+1}(t_0)}$$

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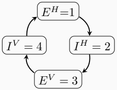

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For $d = 2$, without exposed classes,

$$p_{e,1} = \frac{\lambda_{1,2}\lambda_{2,1} - \mu_1\mu_2}{\lambda_{2,1}(\lambda_{1,2} + \mu_1)}, \qquad p_{e,2} = \frac{\lambda_{1,2}\lambda_{2,1} - \mu_1\mu_2}{\lambda_{1,2}(\lambda_{2,1} + \mu_2)}.$$

Seasonality in ZIKA Model

Seasonality comes through temperature

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The transmission rate from infected vectors to humans is proportional to the number of vectors (see Zhang 2017)

$$\lambda_{I^H,E^V} \propto N_H \propto \exp\left\{-(T - T_{opt})^2/\delta_T\right\}$$

Computation of R_0 and $p_{e,i}(t_0)$ in dimension $d \geq 2$

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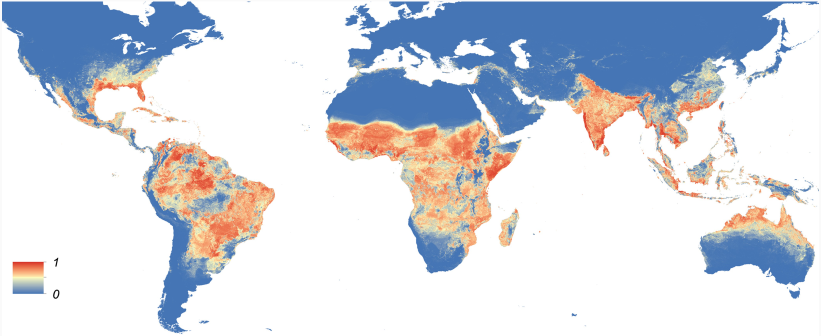
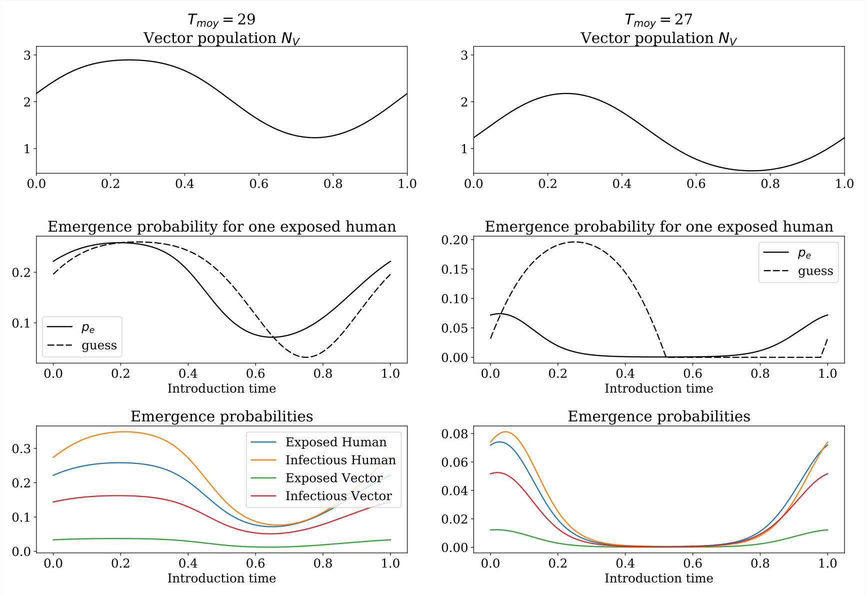
(Bacaer & al 2006) gives a numerical algorithm to compute R_0 that we did not use.

Global map of the predicted distribution of Ae. aegypti. : Kramer & al, eLife 2015;4:e08347



Influence of Geography through mean temperature



Conclusions and Perspectives

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- The formulas for constant rate may give a good guess for $p_{e,i}$, for large periods.
- We can compute optimal control strategies.
- With the right models for seasonal transmission and death rates, we can build risk maps yielding for each fixed month, a map of emergence probabilities, thus replacing the existing prediction maps

Citation from Diekmann, Heesteerbek and Britton

p.429 When there is temporal variation that affects epidemiological ingredients, it will matter for the potential number of secondary cases produced by a given infected individual when exactly that individual became infected. This means that the *epidemiological life* of the individual will depend on the moment of *epidemiological birth*. In other words : individual are not born (epidemiologically speaking) in the same way, and the concept of a generation of infected individuals becomes questionable. Because the definition of R_0 is directly dependent on the generation view, and in particular the biological interpretation is intimately linked to the generation concept, we see that, under temporal variation, a threshold quantity is unlikely to have the same biological meaning as R_0.