Modeling the invasion wave of *Wolbachia* for controlling mosquito-borne diseases

Zhuolin Qu

Department of Mathematics
University of Texas at San Antonio

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Outlines

"Mosquitoes cause more human suffering than any other organism."

- dengue fever, chikungunya, Zika (2016 epidemic)

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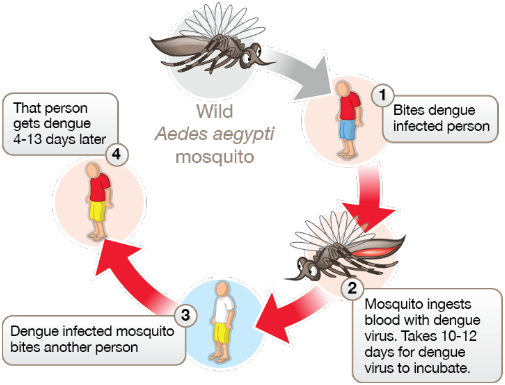
- *Wolbachia*
  - a natural bacteria in 60% insect species
  - blocks the disease transmission

Wolbachia – fight an epidemic with an epidemic



Source: Australias Department of Foreign Affairs and Trade (DFAT) & Eliminate Dengue Program

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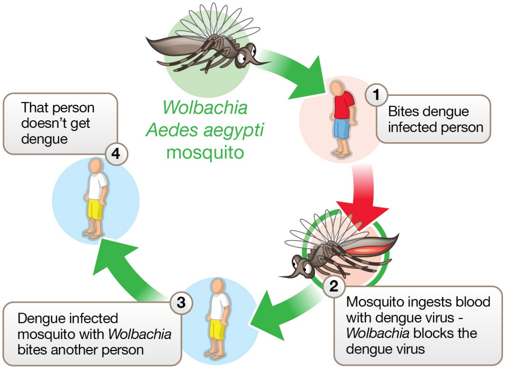

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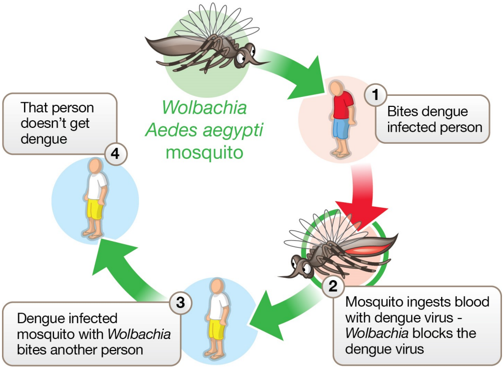

- Releasing *Wolbachia*-infected mosquitoes to create infection

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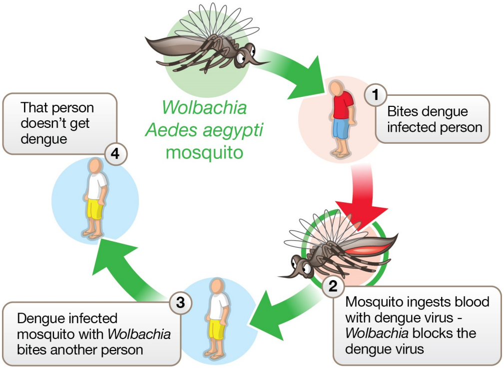

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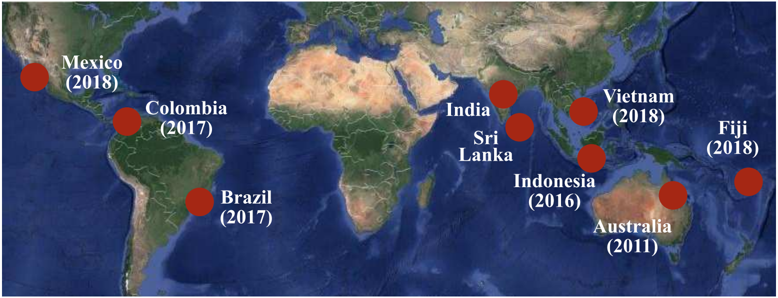

- Releasing *Wolbachia*-infected mosquitoes to create infection
- *Wolbachia* is maternally transmitted among mosquitoes – cost-effective
- Field trials to suppress dengue/Zika

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Q: How many *Wolbachia*-infected mosquitoes need to be released?

- difficult to sustain such infection in a wild mosquito population

- fitness cost due to *Wolbachia* infection
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- small infection will be wiped out by natural mosquitoes
- mathematical model for *Wolbachia* transmission [Qu *et al*, SIAP '18]
  a critical threshold must be exceeded

$$\text{fraction of infection} \begin{cases} < \theta, & \text{infection dies out} \\ > \theta, & \text{stable infection} \end{cases}$$

  - 9-ODE model to capture complex transmission cycle

Qu, Xue, and Hyman, "Modeling the Transmission of *Wolbachia* in Mosquitoes for Controlling Mosquito-Borne Diseases". SIAM Journal on Applied Mathematics, 2018

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- spatial dynamics!
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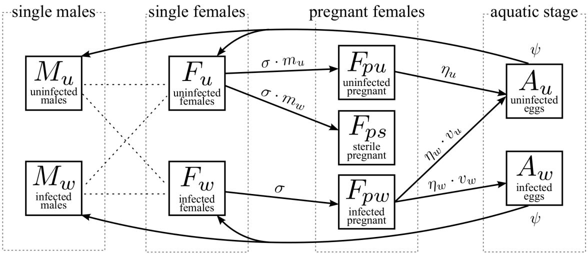
- spatial extension: 2-ODE model $\Rightarrow$ 2-PDE model
  - threshold condition for spatial model?

Qu and Hyman, "Generating a Hierarchy of Reduced Models for a System of Differential Equations Modeling the Spread of *Wolbachia* in Mosquitoes". SIAM Journal on Applied Mathematics, 2019

Outlines

Modeling *Wolbachia* transmission in mosquitoes (2-ODE)



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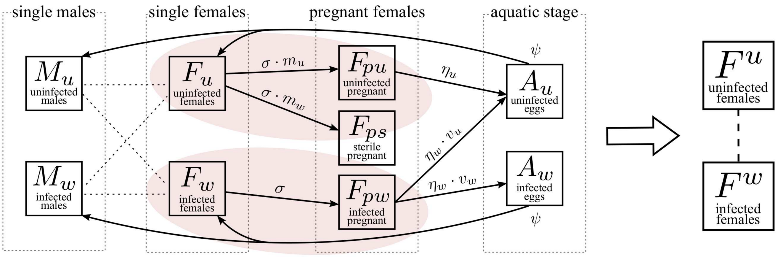

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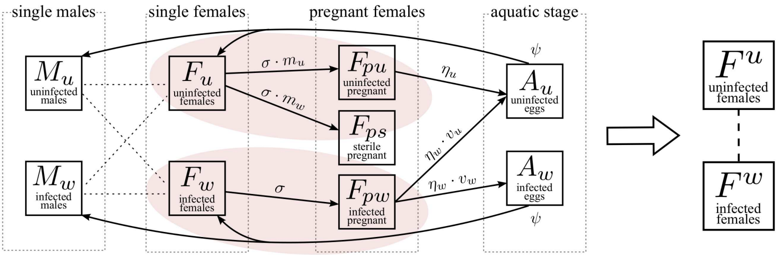

$$\dot{F^u} = b_f \phi''_u \frac{F^u}{F^u + \frac{\mu'_{fw}}{\mu'_{fu}} F^w} \left(1 - \frac{F^u + F^w}{K_f}\right) F^u - \mu'_{fu} F^u$$

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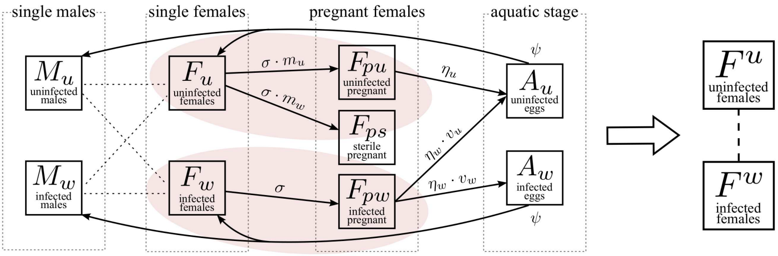

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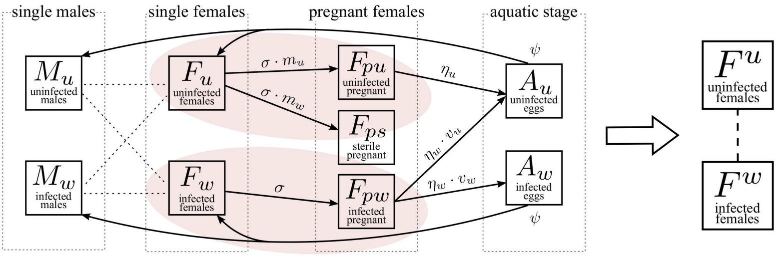

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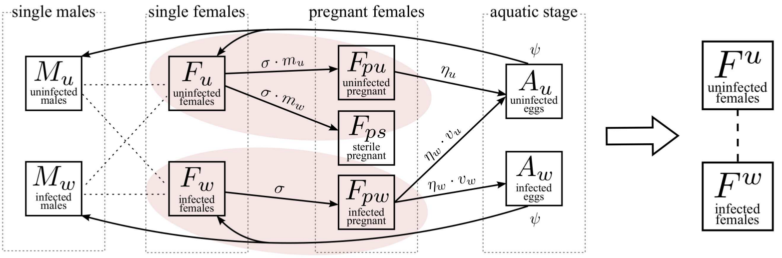

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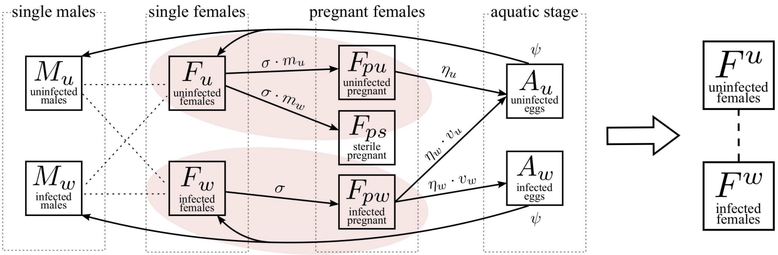

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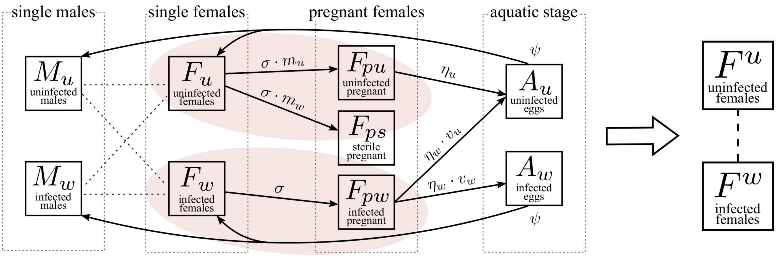

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prob. of mating with uninfected male

death rate

reproduction rate

female birth prob. ~ 1/2

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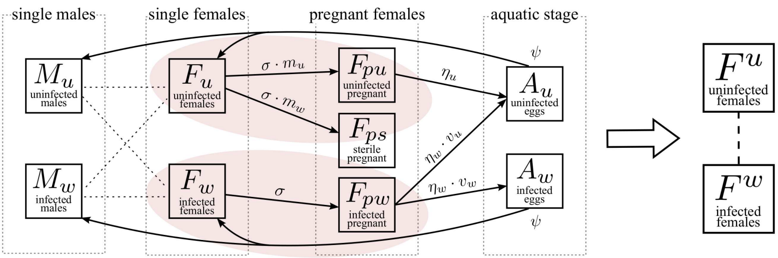

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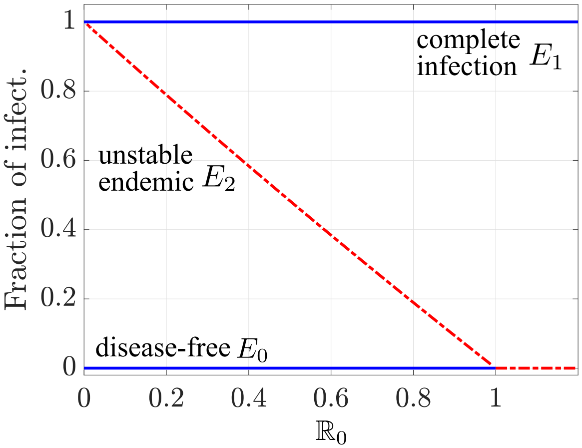
Threshold condition for *Wolbachia* invasion



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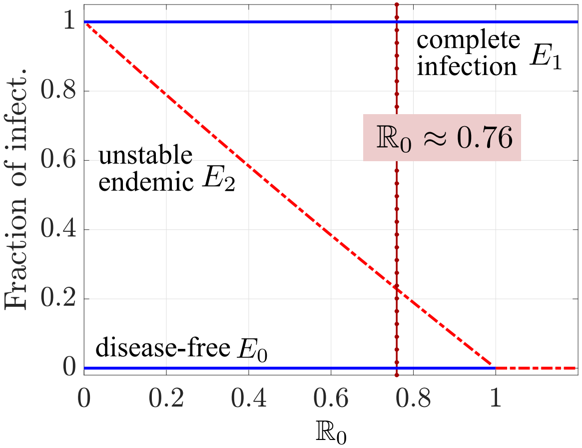

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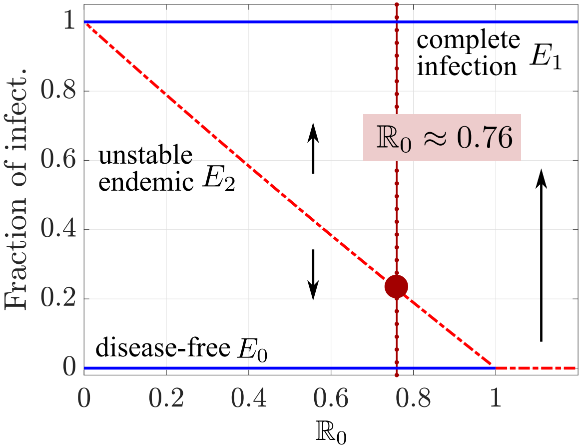

Outlines

Why we need spatial models?

For field releases, we need to consider

- mosquito dispersion and advection

$$\frac{\partial F^u}{\partial t} = ODE\ model + DF^u_{xx}, \quad \frac{\partial F^w}{\partial t} = ODE\ model + DF^w_{xx}$$

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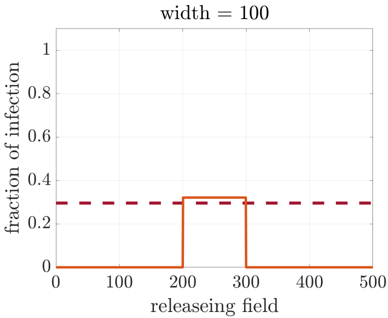

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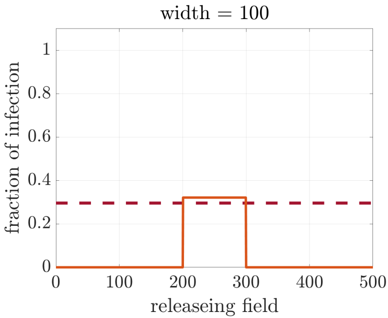

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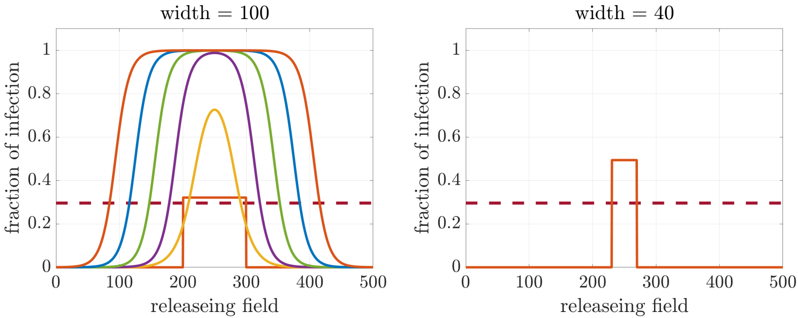

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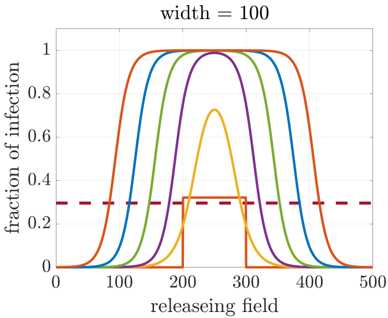

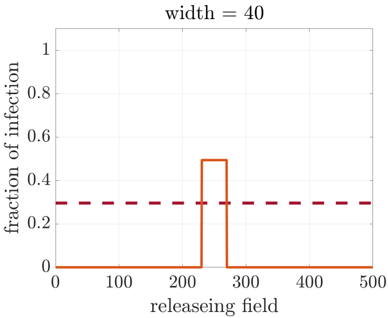

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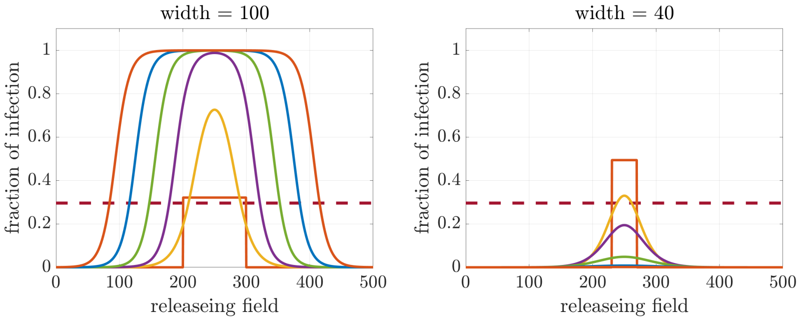

ODE threshold is no longer valid.

Threshold condition for spatial model

$$(F^u)_t = b_f \phi''_u \frac{F^u}{F^u + \frac{\mu'_{fw}}{\mu'_{fu}} F^w} \left(1 - \frac{F^u + F^w}{K_f}\right) F^u - \mu'_{fu} F^u + D_1 (F^u)_{xx}$$

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Threshold condition for spatial model

$$u_t = \frac{u}{u + d\,v}(1 - u - v)u - b\,u + u_{xx} \quad \text{(wild)}$$

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Wolbachia invasion into natural population

- local release, compact support

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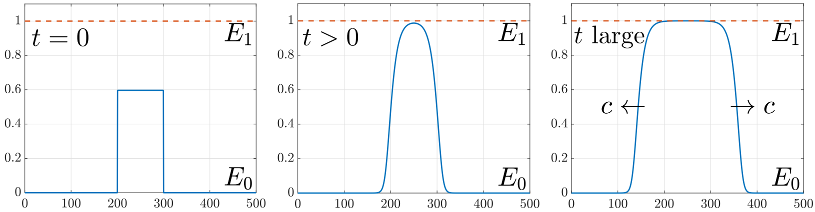

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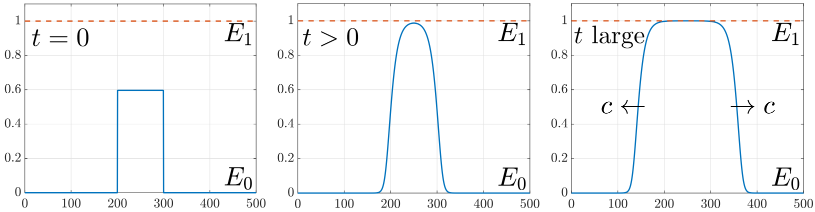

- stage 1: wave initiation to steady-states $\leftarrow$ threshold condition?
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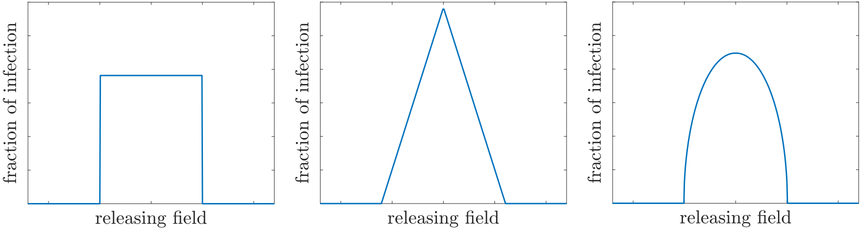
Threshold condition for spatial model

- Different spatial profiles for field releases



Threshold condition for spatial model

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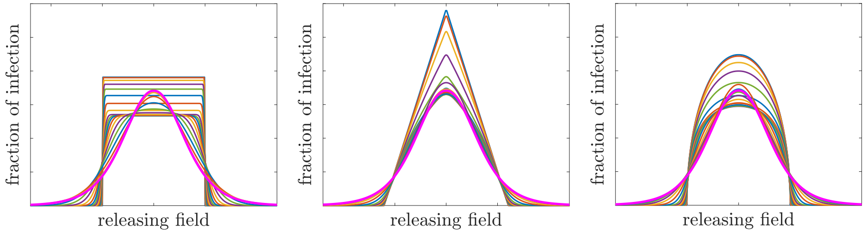

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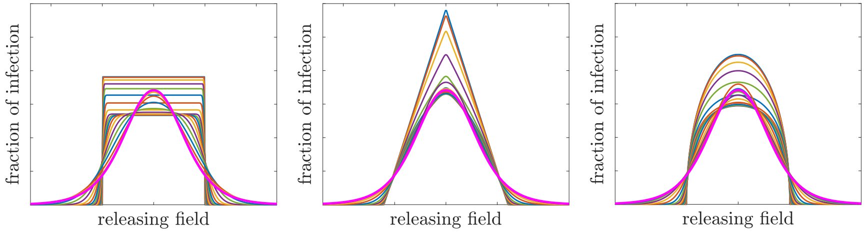

net growth (reaction) diffusion

$$\begin{aligned} u_t &= \frac{u}{u + d\,v}(1-u-v)u - b\,u & \text{vs.} & \quad + u_{xx} \\ v_t &= a(1-u-v)v - b\,d\,v & & \quad + D v_{xx} \end{aligned}$$

"balanced" profile

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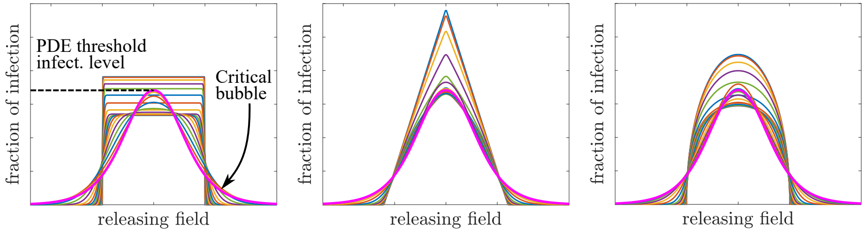

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net growth (reaction)

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Capture the "critical bubble"

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- 1-PDE reduced model: $p = \frac{v}{u+v}$, $u + v = 1 - \frac{b\, d}{a} + \varepsilon$

$$p_t = \frac{b(d - a + ad)}{a + a(d-1)p}\, p\, (p - p_0)(1 - p) + p_{xx}$$

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$$p_t = \frac{b(d-a+ad)}{a+a(d-1)p}\,p\,(p-p_0)(1-p) + p_{xx} = h(p) + p_{xx} = 0$$

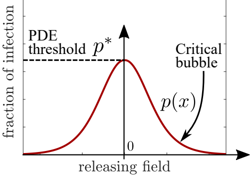
- PDE threshold p^*

$$H(p) = \int_0^p h(y)dy = 0$$

- Critical bubble $p(x)$

$$p'(x) = -\Big(-2H(p)\Big)^{1/2}, \quad p(0) = p^*$$

$$p'(0) = p'(\infty) = 0$$



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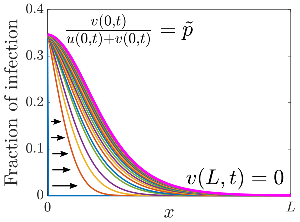
- 2-PDE threshold (numerically)
  - point-release process
  - computationally expensive



Comparison for two approaches

- $D = 1$

$$p^*_{\text{1-PDE}} \approx 0.357, \quad p^*_{\text{2-PDE}} = \frac{v^*}{v^* + u^*} \approx 0.347, \quad \text{discrepancy} \approx 0.01.$$

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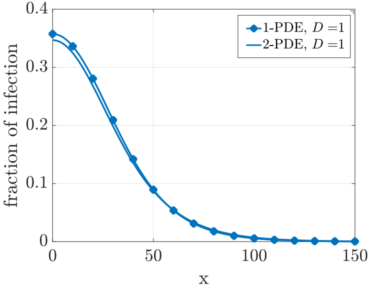

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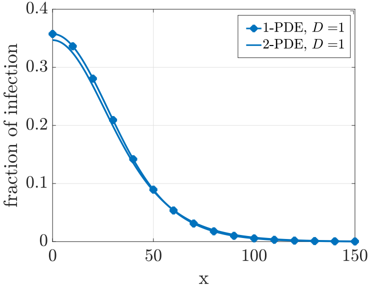
- Varying $D \in [0.5, 1.5]$, $D = D_2/D_1$ (infected/wild)

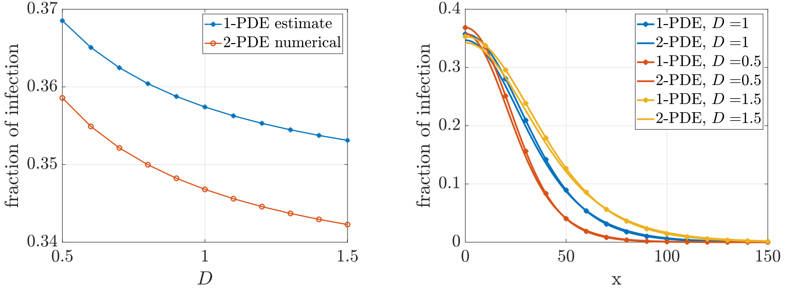


Comparison for two approaches

- $D = 1$

$$p^*_{\text{1-PDE}} \approx 0.357, \quad p^*_{\text{2-PDE}} = \frac{v^*}{v^* + u^*} \approx 0.347, \quad \text{discrepancy} \approx 0.01.$$

- Varying $D \in [0.5, 1.5]$, $D = D_2/D_1$ (infected/wild)



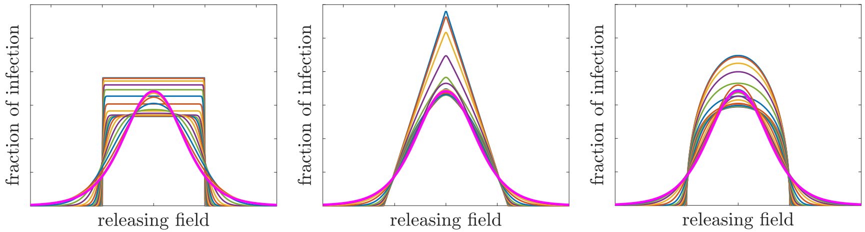
- larger D (diffusion for infected), lower threshold, fatter tail
- $p^*_{\text{ODE}} \approx 0.228 < p^*_{PDE}$

Outlines

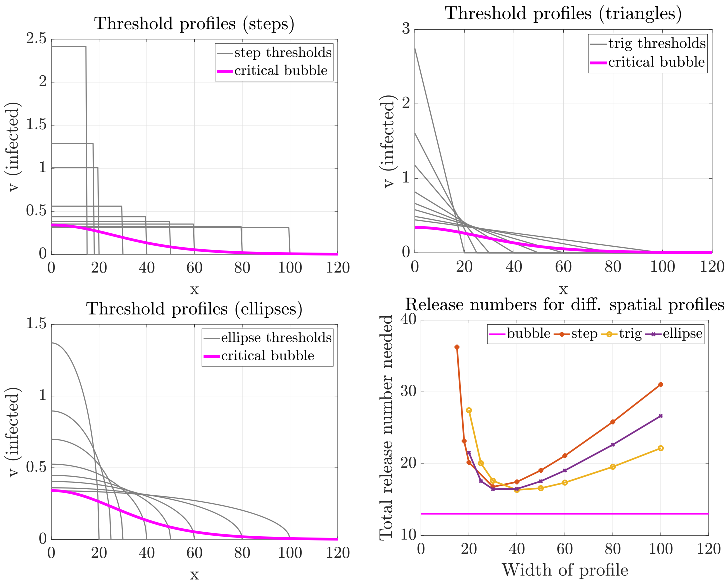
Compare critical bubble with other shapes

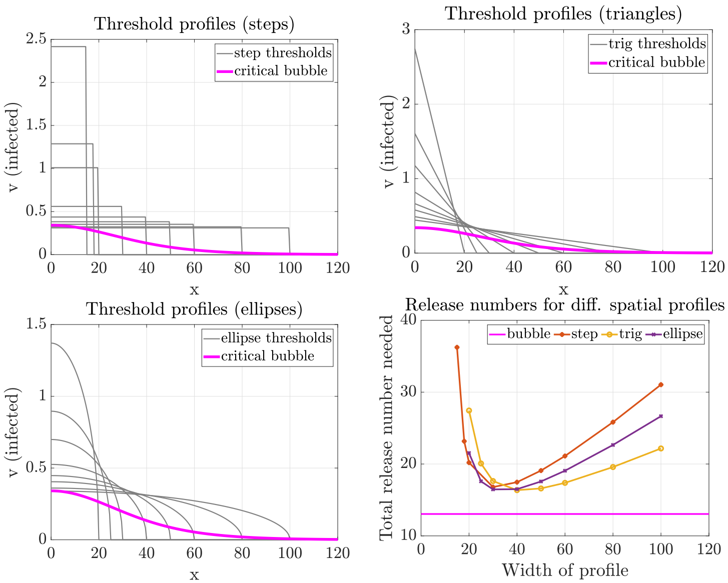
Question

If the critical bubble represents an "optimal" distribution of infection to give rise of the invasion wave?



For each configuration, for a given width, identify the threshold height.


Threshold profiles (steps)
step thresholds
critical bubble
v (infected)
x
Threshold profiles (triangles)
trig thresholds
critical bubble
v (infected)
x
Threshold profiles (ellipses)
ellipse thresholds
critical bubble
v (infected)
x
Release numbers for diff. spatial profiles
bubble
step
trig
ellipse
Total release number needed
Width of profile



"Critical bubble" is an optimal spatial distribution of infection.

Invasion success: above threshold

What is the “optimal” target infection level for field release?

- time to establish an invasion
- total amount of release needed

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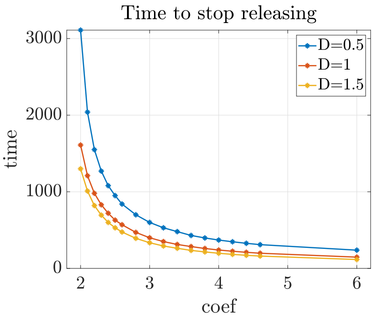

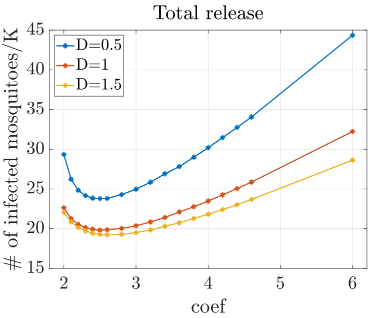

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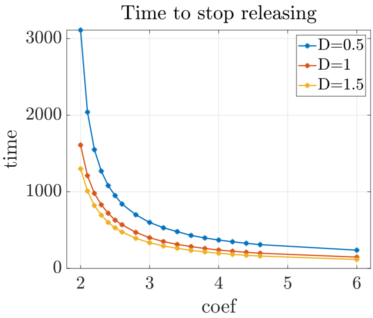
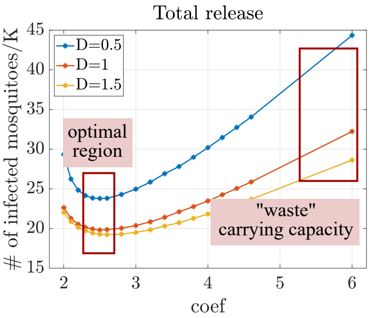
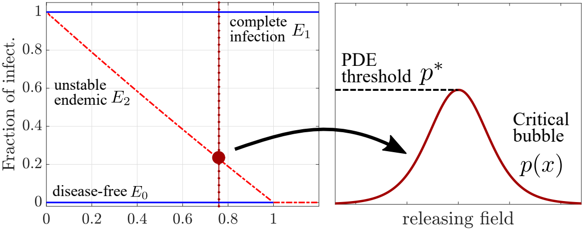


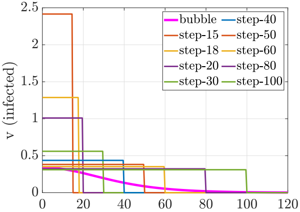


Threshold condition for *Wolbachia* invasion wave

$$u_t = \frac{u}{u + d\,v}(1 - u - v)u - b\,u + u_{xx} \quad \text{(wild)}$$

$$v_t = a(1 - u - v)v - b\,d\,v + D v_{xx} \quad \text{(infected)}$$

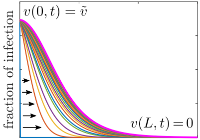




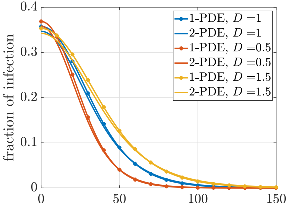
1-PDE (analytically)

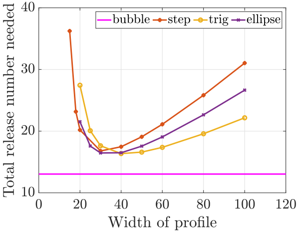
$$p_{xx} + h(p) = 0$$

2-PDE (numerically)



1-PDE vs. 2-PDE





Slides available at
zhuolinqu.github.io