Taking advantage of pathogen diversity and plant immunity to minimize disease prevalence

Pauline Clin, Frédéric Grognard, Ludovic Mailleret, Florence Val, Didier Andrivon, Frédéric Hamelin. Submitted to Phytopathology.

ModStatSAP
November 24 2020

French context

- Pesticide use impacts public health and biodiversity
- Target: halve pesticide use by 2025
- Constraints:
  - Plant breeding for new disease resistance genes
  - Breakdown and durability of resistance

French context

- Pesticide use impacts public health and biodiversity
- Target: halve pesticide use by 2025
- Constraints:
  - Plant breeding for new disease resistance genes
  - Breakdown and durability of resistance

Wanted

New agro-ecological methods

GRENELLE ENVIRONNEMENT

ÉCOPHYTO
RÉDUIRE ET AMÉLIORER L'UTILISATION DES PHYTOS

French context

- Pesticide use impacts public health and biodiversity
- Target: halve pesticide use by 2025
- Constraints:
  - Plant breeding for new disease resistance genes
  - Breakdown and durability of resistance

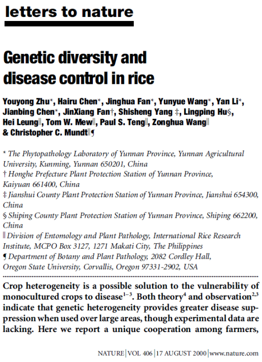
Wanted

New agro-ecological methods

- Host mixtures remain to be optimized
- Plant immunity is key but absent from mathematical models so far

The Yunnan province experimentation (2000)

In mixtures, the prevalence of Rice blast was reduced from 20% to 1% on susceptible varieties compared to susceptible monocultures (dilution effect)


letters to nature

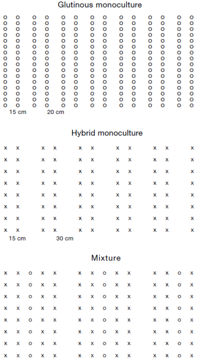
Genetic diversity and disease control in rice

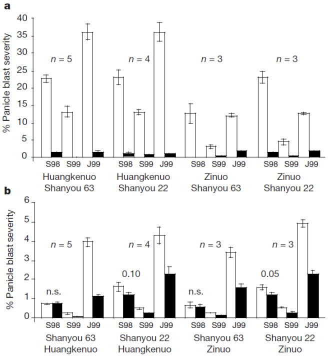
Youyong Zhu*, Hairu Chen*, Jinghua Fan*, Yunyue Wang*, Yan Li*, Jianbing Chen*, JinXiang Fan†, Shisheng Yang ‡, Lingping Hu§, Hei Leung‖, Tom W. Mew‖, Paul S. Teng‖, Zonghua Wang‖ & Christopher C. Mundt‖¶

* The Phytopathology Laboratory of Yunnan Province, Yunnan Agricultural University, Kunming, Yunnan 650201, China
† Honghe Prefecture Plant Protection Station of Yunnan Province, Kaiyuan 661400, China
‡ Jianshui County Plant Protection Station of Yunnan Province, Jianshui 654300, China
§ Shiping County Plant Protection Station of Yunnan Province, Shiping 662200, China
‖ Division of Entomology and Plant Pathology, International Rice Research Institute, MCPO Box 3127, 1271 Makati City, The Philippines
¶ Department of Botany and Plant Pathology, 2082 Cordley Hall, Oregon State University, Corvallis, Oregon 97331-2902, USA

Crop heterogeneity is a possible solution to the vulnerability of monocultured crops to disease[1–3]. Both theory[4] and observation[2,3] indicate that genetic heterogeneity provides greater disease suppression when used over large areas, though experimental data are lacking. Here we report a unique cooperation among farmers,

NATURE | VOL 406 | 17 AUGUST 2000 | www.nature.com

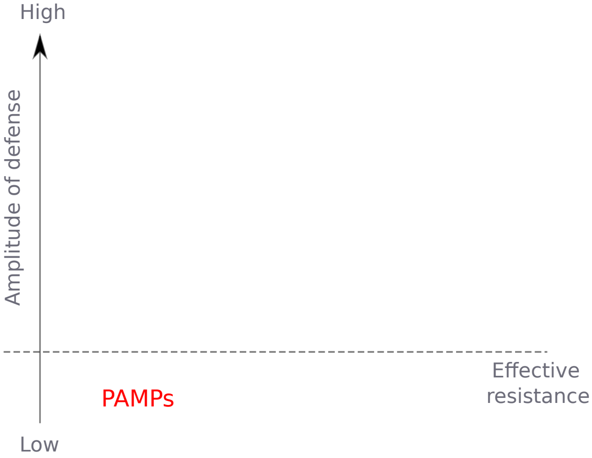




On resistant varieties compared to resistant monocultures, the prevalence decreased from 2% to 1%. Why is that?

Plant immune system

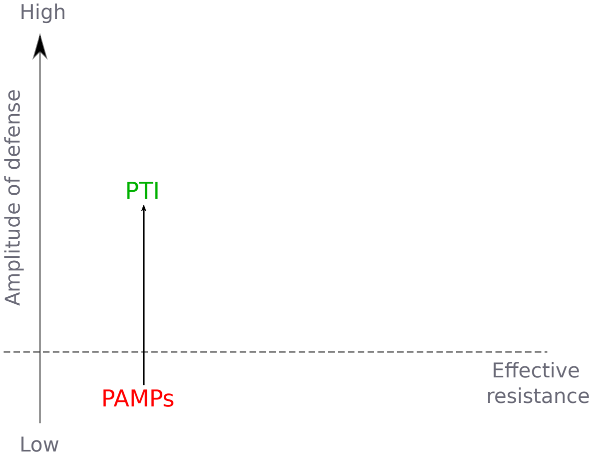
2 levels of immunity (Jones and Dangl, 2006; Milgroom, 2015)



PAMPs = Pathogen molecules, **PTI** = PAMP triggered immunity,
ETI = Effector triggered immunity

Plant immune system

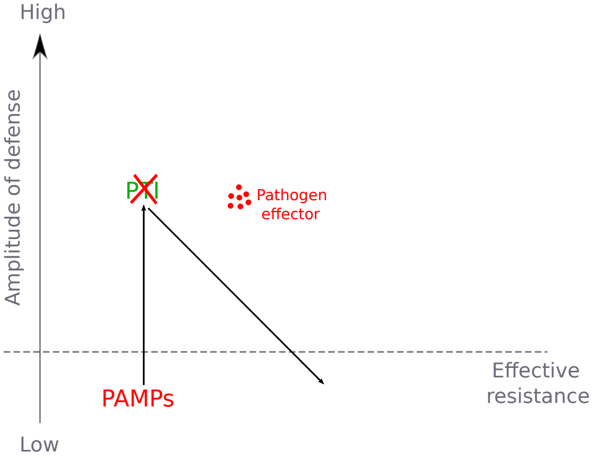
2 levels of immunity (Jones and Dangl, 2006; Milgroom, 2015)



PAMPs = Pathogen molecules, **PTI** = PAMP triggered immunity,
ETI = Effector triggered immunity

Plant immune system

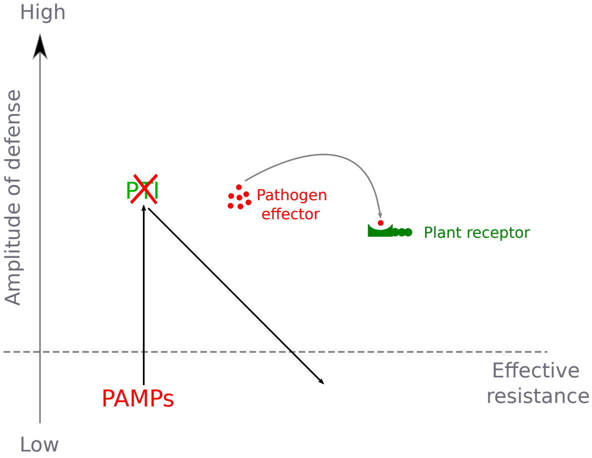
2 levels of immunity (Jones and Dangl, 2006; Milgroom, 2015)



PAMPs = Pathogen molecules, **PTI** = PAMP triggered immunity,
ETI = Effector triggered immunity

Plant immune system

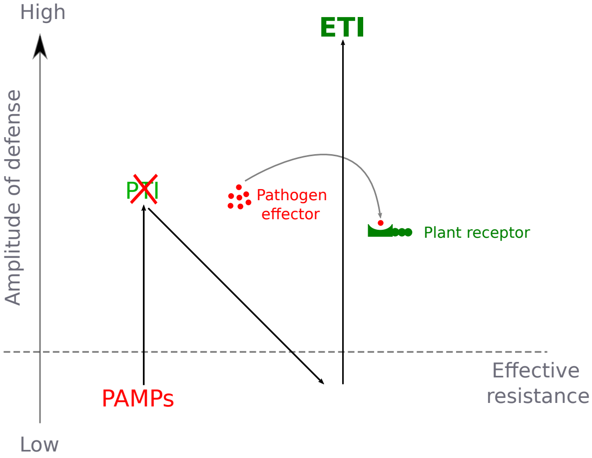
2 levels of immunity (Jones and Dangl, 2006; Milgroom, 2015)



PAMPs = Pathogen molecules, **PTI** = PAMP triggered immunity,
ETI = Effector triggered immunity

Plant immune system

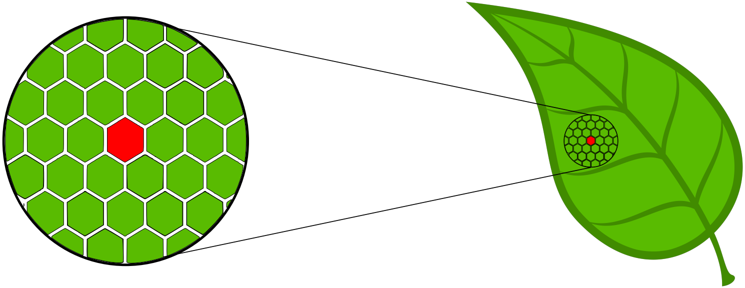
2 levels of immunity (Jones and Dangl, 2006; Milgroom, 2015)



PAMPs = Pathogen molecules, **PTI** = PAMP triggered immunity,
ETI = Effector triggered immunity

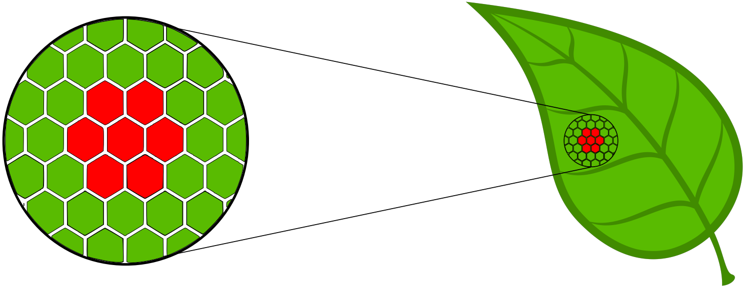
Effector Triggered Immunity (ETI)

Infection by **an avirulent pathogen on a resistant** plant:



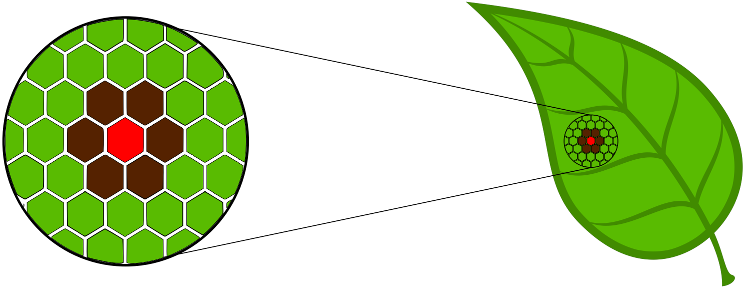
Effector Triggered Immunity (ETI)

Infection by **an avirulent pathogen on a resistant** plant:



Effector Triggered Immunity (ETI)

Infection by **an avirulent pathogen on a resistant** plant:

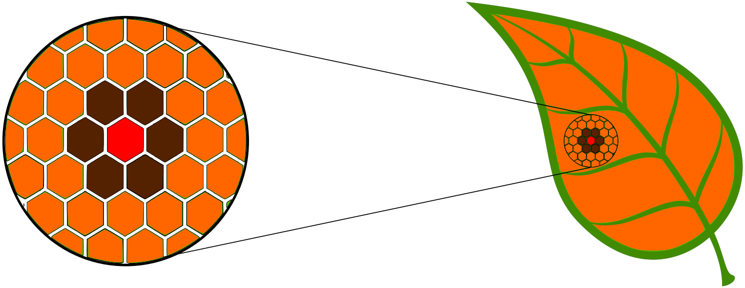


Hypersensitive response

Programmed death of cells located where the infection occurred

HR induces systemic acquired resistance

Infection by **an avirulent pathogen on a resistant** plant:



Systemic acquired resistance SAR
Resistance response that applies to the entire plant
Derives from ETI

PRIMING

SAR and priming in host mixtures

Infection probability

Pathogen \ Host	Susceptible	Resistant
Wild-type	1	0
Resistance-breaking	1	1

→ **What is the impact of the priming on epidemiological dynamics?**

SAR and priming in host mixtures

Infection probability

Pathogen \ Host	Susceptible	Resistant
Wild-type	1	**Priming**
Resistance-breaking	1	1

→ **What is the impact of the priming on epidemiological dynamics?**

SAR and priming in host mixtures

Infection probability

Pathogen \ Host	Susceptible	Resistant	Primed resistant
Wild-type	1	**Priming**	0
Resistance-breaking	1	1	1-ρ

→ **What is the impact of the priming on epidemiological dynamics?**

Epidemic model: 3 important parameters

Proportion of resistant hosts p

Resistance-breaking cost c

Decreases the fitness of the resistance-breaking variant on both susceptible and resistant plants

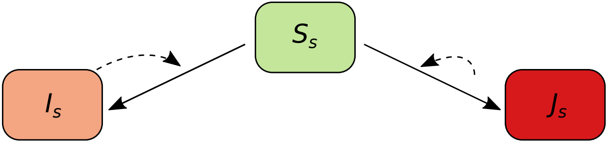
Xanthamonas axonopodis, bacteria (Wichmann and Bergelson, 2004 - Genetics)
Meloidogyne incognita, nematode (Castagnone-Serenoet al, 2007 - Evo. Eco.)
Potato virus Y (Janzac et al, 2010 - MPMI)
Phytophtora infestans, oomycete (Montarry et al, 2010 - Evolutionary Biology)
Soybean mosaic virus (Khatabi et al, 2013 - MPP)
Leptosphaeria maculans, fungi (Bousset et al, 2018 - Evolutionnary applications)

Priming efficiency ρ

Reduces the infection success of the resistance-breaking variant on resistant plants

Tobacco mosaic virus (Ross, 1961 - Virology)
Full priming efficiency (Kuc, 1982 - BioSciences)
A. thaliana (Maleck et al., 2000 - Nature genetics)

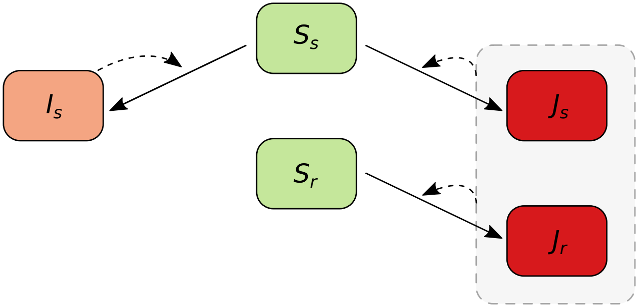
Epidemic model with wild and resistance-breaking variants



$S_s = N_s - I_s - J_s$ and $S_r = N_r - S_r^* - J_r$, where $N = constant$
$\beta =$ pathogen transmission rate and $\alpha =$harvest and replanting rate

$$\begin{cases} \dot{I}_s &= \beta I_s S_s - \alpha I_s \\ \\ \dot{J}_s &= (1-c)\beta(J_s \quad)S_s - \alpha J_s \end{cases}$$

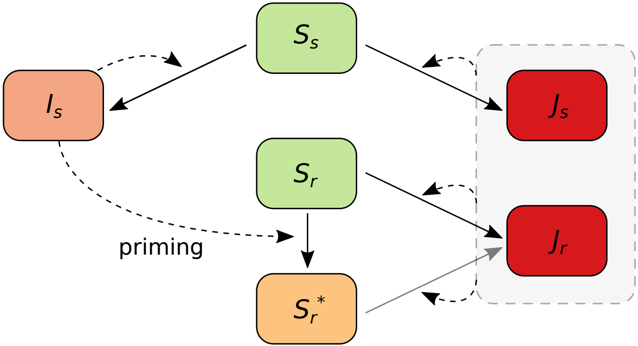
Epidemic model with wild and resistance-breaking variants



$S_s = N_s - I_s - J_s$ and $S_r = N_r - S_r^* - J_r$, where $N = constant$
$\beta =$ pathogen transmission rate and $\alpha =$harvest and replanting rate

$$\begin{cases} \dot{I}_s = \beta I_s S_s - \alpha I_s \\ \\ \dot{J}_s = (1-c)\beta(J_s + J_r) S_s - \alpha J_s \\ \dot{J}_r = (1-c)\beta(J_s + J_r) S_r - \alpha J_r\,. \end{cases}$$

Epidemic model with wild and resistance-breaking variants



$$\begin{cases} \dot{I}_s &= \beta I_s S_s - \alpha I_s \\ \dot{S}_r^* &= \beta I_s S_r - (1-\rho)(1-c)\beta(J_s + J_r)S_r^* - (\gamma+\alpha)S_r^* \\ \dot{J}_s &= (1-c)\beta(J_s+J_r)S_s - \alpha J_s \\ \dot{J}_r &= (1-c)\beta(J_s+J_r)S_r + (1-\rho)(1-c)\beta(J_s+J_r)S_r^* - \alpha J_r\,. \end{cases}$$

Model

Let be $x = \dfrac{I_s}{N}$, $m = \dfrac{S_r^*}{N}$, $y = \dfrac{J_s}{N}$, $z = \dfrac{J_r}{N}$, and $t^* = \alpha t$ with

N the number of plants

After nondimensionalization :

Model

Let be $x = \dfrac{I_s}{N}$, $m = \dfrac{S_r^*}{N}$, $y = \dfrac{J_s}{N}$, $z = \dfrac{J_r}{N}$, and $t^* = \alpha t$ with

N the number of plants

After nondimensionalization :

$$\begin{cases} \dot{x} & = & Rx[(1-p) - x - y] - x\,, \\ \dot{m} & = & Rx(p - m - z) - (1-\rho)(1-c)R(y+z)m - \nu m \\ \dot{y} & = & (1-c)R(y+z)[(1-p) - x - y] - y\,, \\ \dot{z} & = & (1-c)R(y+z)(p - m - z) + (1-\rho)(1-c)R(y+z)m - z\,. \end{cases}$$

Model

Let be $x = \dfrac{I_s}{N}$, $m = \dfrac{S_r^*}{N}$, $y = \dfrac{J_s}{N}$, $z = \dfrac{J_r}{N}$, and $t^* = \alpha t$ with

N the number of plants

After nondimensionalization :

$$\begin{cases} \dot{x} &= Rx[(1-p) - x - y] - x\,, \\ \dot{m} &= Rx(p - m - z) - (1-\rho)(1-c)R(y+z)m - \nu m \\ \dot{y} &= (1-c)R(y+z)[(1-p) - x - y] - y\,, \\ \dot{z} &= (1-c)R(y+z)(p - m - z) + (1-\rho)(1-c)R(y+z)m - z\,. \end{cases}$$

where

$R = \dfrac{\beta N}{\alpha}$ the basic reproduction rate and

Model

Let be $x = \dfrac{I_s}{N}$, $m = \dfrac{S_r^*}{N}$, $y = \dfrac{J_s}{N}$, $z = \dfrac{J_r}{N}$, and $t^* = \alpha t$ with

N the number of plants

After nondimensionalization :

$$\begin{cases} \dot{x} &= Rx[(1-p) - x - y] - x\,, \\ \dot{m} &= Rx(p - m - z) - (1-\rho)(1-c)R(y+z)m - \nu m \\ \dot{y} &= (1-c)R(y+z)[(1-p) - x - y] - y\,, \\ \dot{z} &= (1-c)R(y+z)(p - m - z) + (1-\rho)(1-c)R(y+z)m - z\,. \end{cases}$$

where

$R = \dfrac{\beta N}{\alpha}$ the basic reproduction rate and

$\nu = \dfrac{\gamma + \alpha}{\alpha} \geq 1$ where $\gamma \geq 0$ corresponds to the loss of priming,

and $\alpha \geq 0$, the harvest and replanting rate.

Equilibria of the model

- $(0, 0, 0, 0)$: **Disease-free** equilibrium
  Always exists

Equilibria of the model

- $(0, 0, 0, 0)$: **Disease-free** equilibrium
  Always exists

- $(\hat{x}, \hat{m}, 0, 0)$: **Wild-type fixed** equilibrium
  Exists if $R_w = R(1 - p) > 1$

Equilibria of the model

- $(0, 0, 0, 0)$: **Disease-free** equilibrium
  Always exists

- $(\hat{x}, \hat{m}, 0, 0)$: **Wild-type fixed** equilibrium
  Exists if $R_w = R(1 - p) > 1$

- $(0, 0, \hat{y}, \hat{z})$: **Resistance-breaking fixed** equilibrium
  Exists if $R_b = R(1 - c) > 1$

Equilibria of the model

- $(0, 0, 0, 0)$: **Disease-free** equilibrium
  Always exists
- $(\hat{x}, \hat{m}, 0, 0)$: **Wild-type fixed** equilibrium
  Exists if $R_w = R(1-p) > 1$
- $(0, 0, \hat{y}, \hat{z})$: **Resistance-breaking fixed** equilibrium
  Exists if $R_b = R(1-c) > 1$
- $(\bar{x}, \bar{m}, \bar{y}, \bar{z})$: **Coexistence** equilibrium
  Exists if

$$\left\{ c > p\,,\ R_w > 1\,,\ \text{and } \rho < \frac{[pR_v - c][R_w + \nu - 1]}{[R_b - 1]R_v p} \right\} \rightarrow R_v > 1\,.$$

Equilibria of the model

- $(0,0,0,0)$: **Disease-free** equilibrium
  Always exists
- $(\hat{x},\hat{m},0,0)$: **Wild-type fixed** equilibrium
  Exists if $R_w = R(1-p) > 1$
- $(0,0,\hat{y},\hat{z})$: **Resistance-breaking fixed** equilibrium
  Exists if $R_b = R(1-c) > 1$
- $(\bar{x},\bar{m},\bar{y},\bar{z})$: **Coexistence** equilibrium
  Exists if

$$\left\{ c > p\,,\ R_w > 1\,,\ \text{and}\ \rho < \frac{[pR_v - c][R_w + \nu - 1]}{[R_b - 1]R_v p} \right\} \to R_v > 1\,.$$

Equilibria stability ?

Cooperative systems

Hal Smith, 2008 ; Hirsch, 1989

Conditions

- Positive interactions between variables,
- Irreducible jacobian matrix.

Cooperative systems

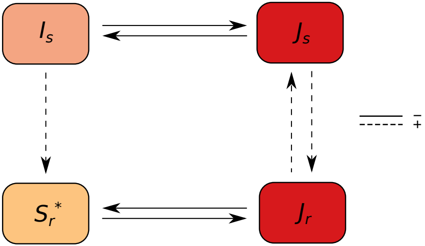
Hal Smith, 2008 ; Hirsch, 1989

Conditions

- Positive interactions between variables,
- Irreducible jacobian matrix.

Jacobian matrix

$$J = \begin{pmatrix} * & 0 & - & 0 \\ + & * & 0 & - \\ - & 0 & * & + \\ 0 & - & + & * \end{pmatrix}$$



Cooperative systems

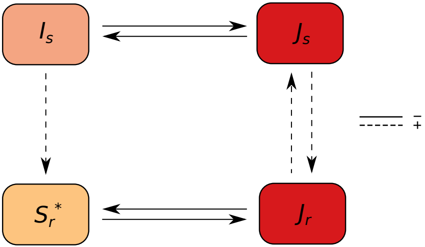
Hal Smith, 2008 ; Hirsch, 1989

Conditions

- Positive interactions between variables,
- Irreducible jacobian matrix.

Jacobian matrix

$$J = \begin{pmatrix} * & 0 & - & 0 \\ + & * & 0 & - \\ - & 0 & * & + \\ 0 & - & + & * \end{pmatrix}$$



Only positive loops

$\Longrightarrow$

The system converges towards an equilibrium

Cooperative systems

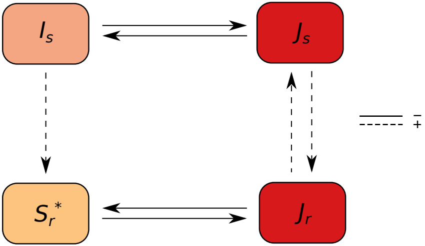
Hal Smith, 2008 ; Hirsch, 1989

Conditions

- Positive interactions between variables,
- Irreducible jacobian matrix.

Jacobian matrix

$$J = \begin{pmatrix} * & 0 & - & 0 \\ + & * & 0 & - \\ - & 0 & * & + \\ 0 & - & + & * \end{pmatrix}$$



Only positive loops

$\Longrightarrow$

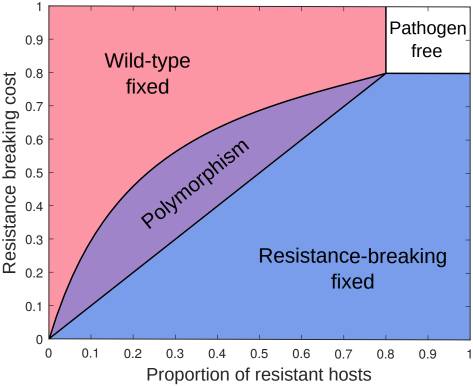
The system converges towards an equilibrium which can only be the coexistence equilibrium!

Epidemiological dynamics stabilize genetic polymorphism

Two conditions:

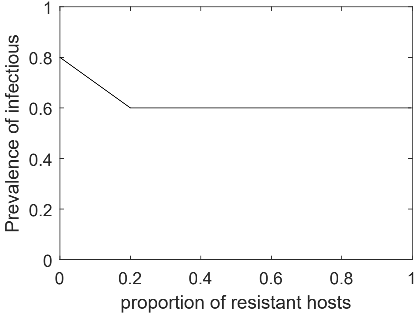
$$c > p \text{ and } \rho < \frac{(R(1-p)+\nu-1)(R(1-c)p-c)}{Rp(1-c)(R(1-p)-1)} = \frac{[pR_v - c][R_a+\nu-1]}{[R_a-1]R_v p}$$

For given $R = 5$, $\nu = 1$, and $\rho = 0.8$:



Priming increases the effectiveness of host mixtures

Prevalence of the disease, $P = I_s + J_s + J_r$, when ρ (Priming effectiveness) increases:



$\rho = 0$ **for black line**

$\rho = 0.2$ *for blue line*

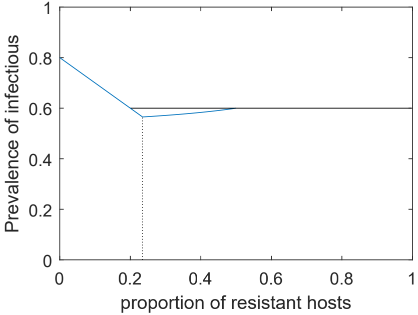
$\rho = 0.5$ *for red line*

$\rho = 0.8$ *for yellow line*

Existence of an **Optimal proportion of resistant hosts** $p^\star$

Priming increases the effectiveness of host mixtures

Prevalence of the disease, $P = I_s + J_s + J_r$, when ρ (Priming effectiveness) increases:



$\rho = 0$ *for black line*

$\rho = 0.2$ **for blue line**

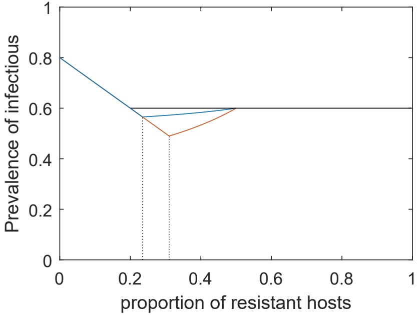
$\rho = 0.5$ *for red line*

$\rho = 0.8$ *for yellow line*

Existence of an **Optimal proportion of resistant hosts** $p^\star$

Priming increases the effectiveness of host mixtures

Prevalence of the disease, $P = I_s + J_s + J_r$, when ρ (Priming effectiveness) increases:



$\rho = 0$ *for black line*

$\rho = 0.2$ *for blue line*

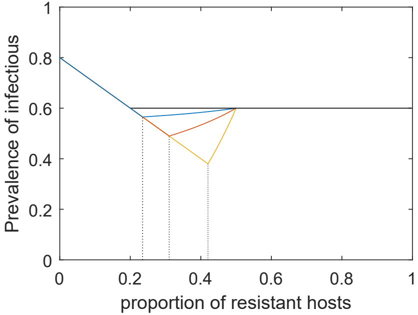
$\rho = 0.5$ **for red line**

$\rho = 0.8$ *for yellow line*

Existence of an **Optimal proportion of resistant hosts** $p^\star$

Priming increases the effectiveness of host mixtures

Prevalence of the disease, $P = I_s + J_s + J_r$, when ρ (Priming effectiveness) increases:



$\rho = 0$ *for black line*

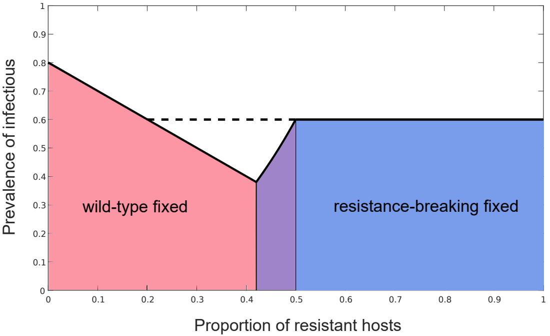
$\rho = 0.2$ *for blue line*

$\rho = 0.5$ *for red line*

$\rho = 0.8$ **for yellow line**

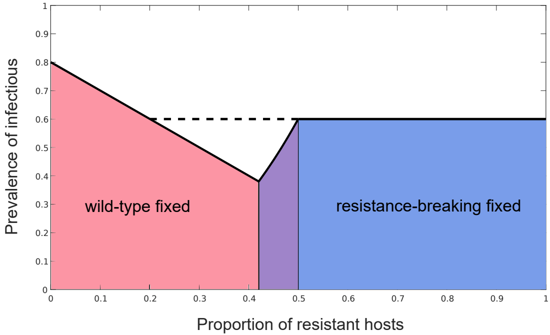
Existence of an **Optimal proportion of resistant hosts** $p^\star$

Take-Home Messages



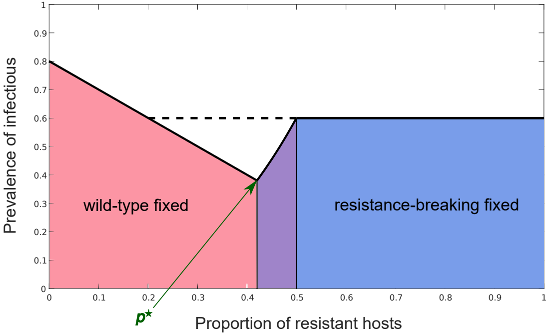
- Host mixtures can be beneficial

Take-Home Messages



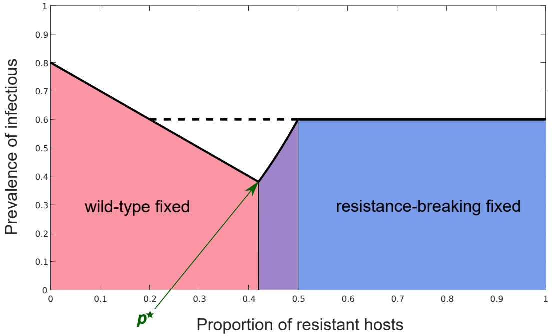
- Host mixtures can be beneficial
- Priming is **key** to host mixtures efficiency

Take-Home Messages



- Host mixtures can be beneficial
- Priming is **key** to host mixtures efficiency
- Optimal proportion $p^\star$ of resistant hosts to minimize virus prevalence

Take-Home Messages



- Host mixtures can be beneficial
- Priming is **key** to host mixtures efficiency
- Optimal proportion $p^\star$ of resistant hosts to minimize virus prevalence
- Priming induced direct **Cross-protection** between hosts

Discussion

- Evidence of the interest of priming in host mixtures shown annalytically for the first time on an epidemiological model.
- Good agreement with experimental studies, which indicate that:

  - Priming may account for 20% to 40% of the disease reduction in mixtures

  (Lannou & Pope 1997, Calonnec et al 1996)
- The use of an optimal proportion of resistants, $p^\star$, prevents the emergence of virulent pathogens.

Discussion

- Evidence of the interest of priming in host mixtures shown annalytically for the first time on an epidemiological model.
- Good agreement with experimental studies, which indicate that:

  - Priming may account for 20% to 40% of the disease reduction in mixtures

  (Lannou & Pope 1997, Calonnec et al 1996)
- The use of an optimal proportion of resistants, $p^{\star}$, prevents the emergence of virulent pathogens.

In addition to reducing the prevalence of the disease :

Host mixtures and priming increase durability of resistances.

Thanks for listening!
Questions ?

Behavioural epidemiology:
Influence of new control method $\rightarrow$ Optimal proportion of resistant in a mixture, $p^{\star}$.

Behavioural epidemiology

Behavioural epidemiology:
Influence of new control method $\rightarrow$ Optimal proportion of resistant in a mixture, $p^\star$.

How do farmers' strategic choices influence disease dynamics?

- p as a dynamic variable.
- Conformism vs Stubbornness vs Responsiveness behavior, Mcquaid et al, 2017.

Behavioural epidemiology

Behavioural epidemiology:
Influence of new control method $\rightarrow$ Optimal proportion of resistant in a mixture, $p^{\star}$.

How do farmers' strategic choices influence disease dynamics?

- p as a dynamic variable.
- Conformism vs Stubbornness vs Responsiveness behavior, Mcquaid et al, 2017.

$$\left.\begin{array}{l}\text{Behavioural model}\\ \text{Epidemiological model}\end{array}\right\}\text{linked by a decision variable, } p\,.$$

Transient phase

Prevalence is minimized at equilibrium, i.e. after a long periode of time.
What happens in the transient phase, before the equilibrium?

Transient phase

Prevalence is minimized at equilibrium, i.e. after a long periode of time.
What happens in the transient phase, before the equilibrium?