Mini-symposium CANUM 2020 13-17 juin 2022

Hétérogénéités dans les modèles mathématiques d'épidémiologie

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Pauline Clin, Doctorante à l'IGEPP INRAe Rennes, Mélanges d'hôtes pour la lutte contre les maladies des plantes : avantages de la sélection des agents pathogènes et de l'amorçage *immunitaire*.
Youcef Mammeri, MCF HDR au LAMFA, *Modélisation spatio-temporelle de la dyna*mique des lésions entre plantes et pathogènes.

Avec le support du groupe SMAI Mabiome et du GDR Mathématiques, Santé, Sciences de la Vie (MathSAV)
https://mathsav.math.cnrs.fr

Journées Math Bio Santé du GDR MathSAV et du GT Mabiome
3 au 7 octobre à Besançon
https://jmbs2022.sciencesconf.org/

Spatio-temporal modelling of plant-pathogen lesions dynamics

Youcef Mammeri
LAMFA CNRS UMR 7352
Université de Picardie Jules Verne

UMR Institut de Génétique, Environnement et Protection des Plantes

Multidisciplinary joint work with INRAE Bretagne Démécologie Team

Stéphane Jumel, Lydia Bousset (biologist)

Melen Leclerc (stat), Nicolas Parisey (computer)

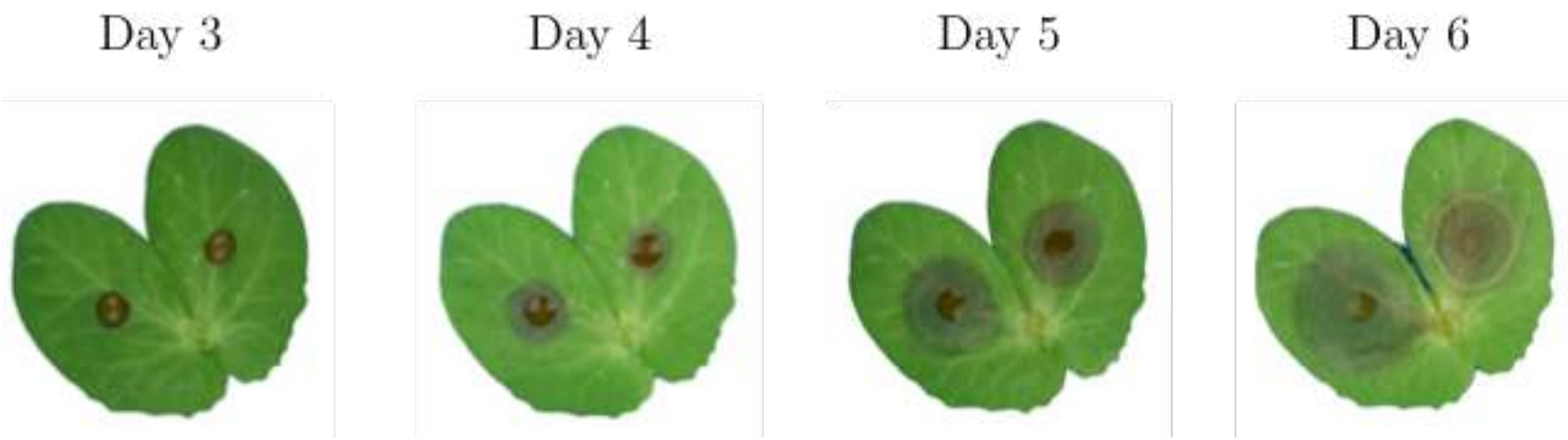
Fréderic Hamelin (modeller)

Biological context

Growing lesions caused by a fungus, e.g. *Peyronellaea pinodes* (blackspot) strongly involved in pea diseases

Growing lesions

Peyronellaea pinodes



Questions

Can we combine imaging with a spatially explicit model that

1. Describe plant-pathogen interactions at lesion scale
2. Compare the aggressiveness and the variability of the infection
3. Predict the adaptation of pathogen populations and optimize the use of different varieties

Combine 2 approaches

Top-down and bottom-up

Combine 2 approaches

Top-down and bottom-up

Image acquisition

Combine 2 approaches

Top-down and bottom-up

Image acquisition

Image processing

Combine 2 approaches

Top-down and bottom-up

Image acquisition

↓

Image processing

↓

Probability map of infection

Combine 2 approaches

Top-down and bottom-up

Image acquisition

↓

Image processing

↓

Probability map of infection

Mechanistic model

Combine 2 approaches

Top-down and bottom-up

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Probability map of infection

Mechanistic model

Calibration

Combine 2 approaches

Top-down and bottom-up

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Probability map of infection

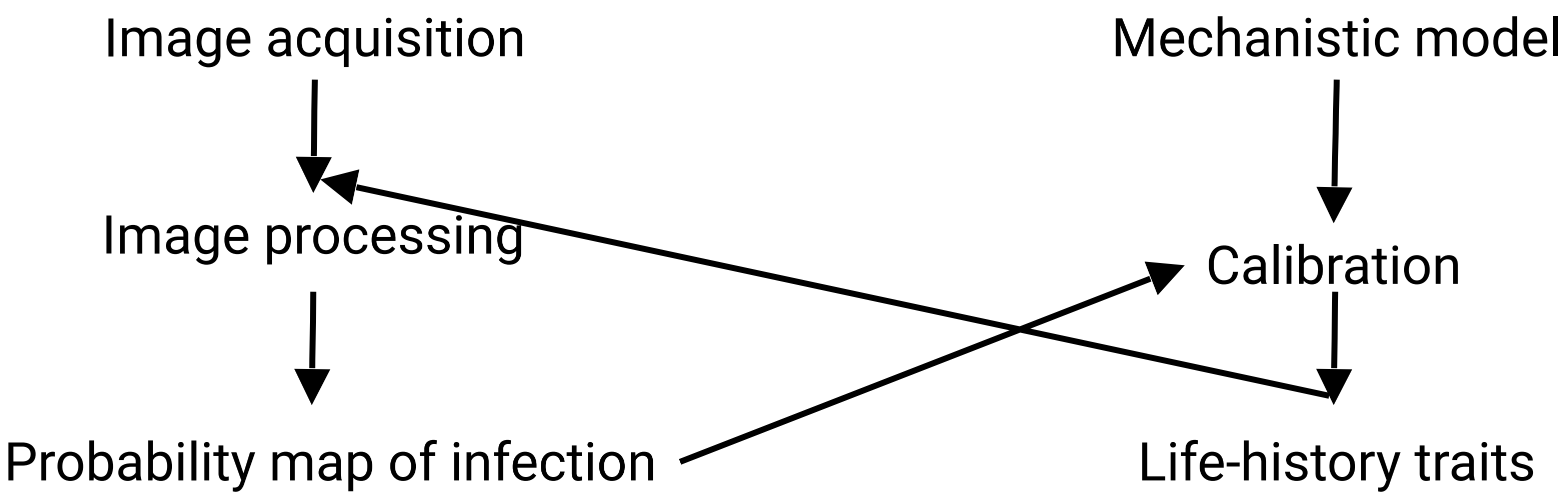
Mechanistic model

Calibration

Life-history traits

Combine 2 approaches

Top-down and bottom-up



Outline

1. Top-down approach: Data generation and classification

2. Bottom-up approach: Diffusion and growth from a spatially explicit model

Short review

Berger-Jones 85: logistic ODE

Individual based model: Calonnec et al 08, Mammeri et al. 10, Calonnec-Mammeri 17

Statistical: Leclerc et al.19

Front propagation: Van den Bosch et al. 88, Powell et al. 05

Reaction-diffusion: Mammeri et al. 14

Outline

1. Top-down approach: Data generation and classification

How we proceed

In the laboratory:

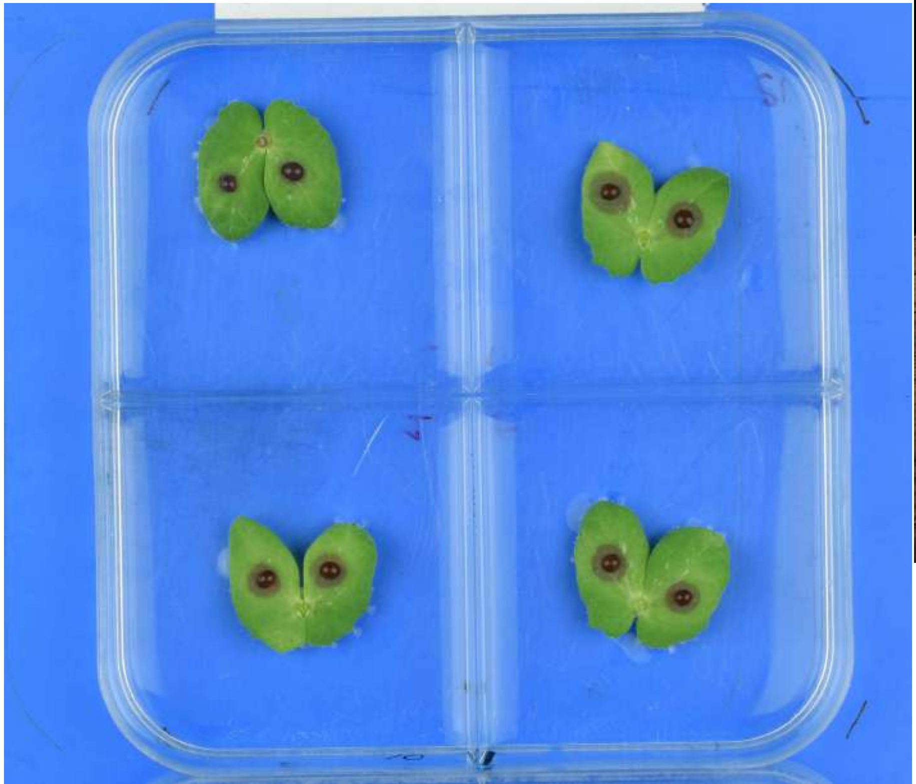
- inoculation of young plants or detached organs (e.g. leaves)
- acquisitions: visible + Chlorophyll Fluorescence x time tracking
- visual scoring or semi-automatic quantification of traits (e.g. disease score or symptom size)

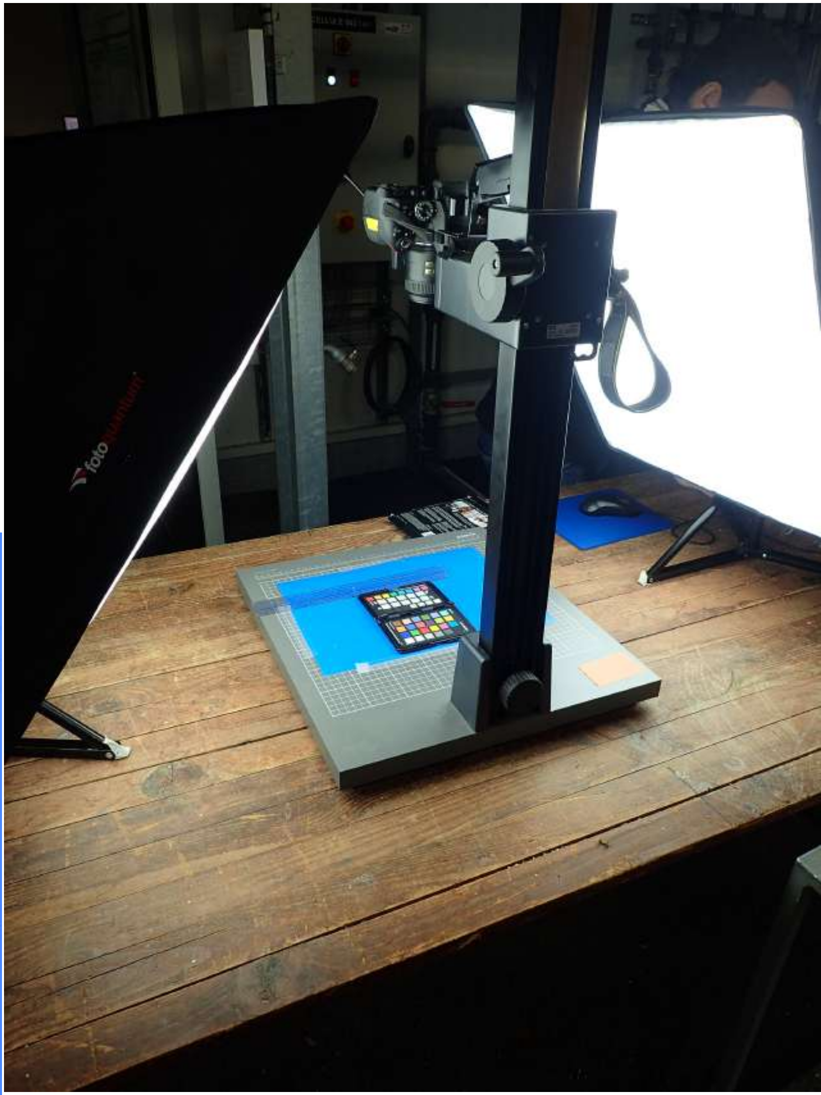
For pea: 500- 1000 spores inoculated, 6 dates measured, 6 seedlings on 60 boxes

Image acquisition

Standardized acquisition (adapted lighting, color test pattern)
→ RGB images

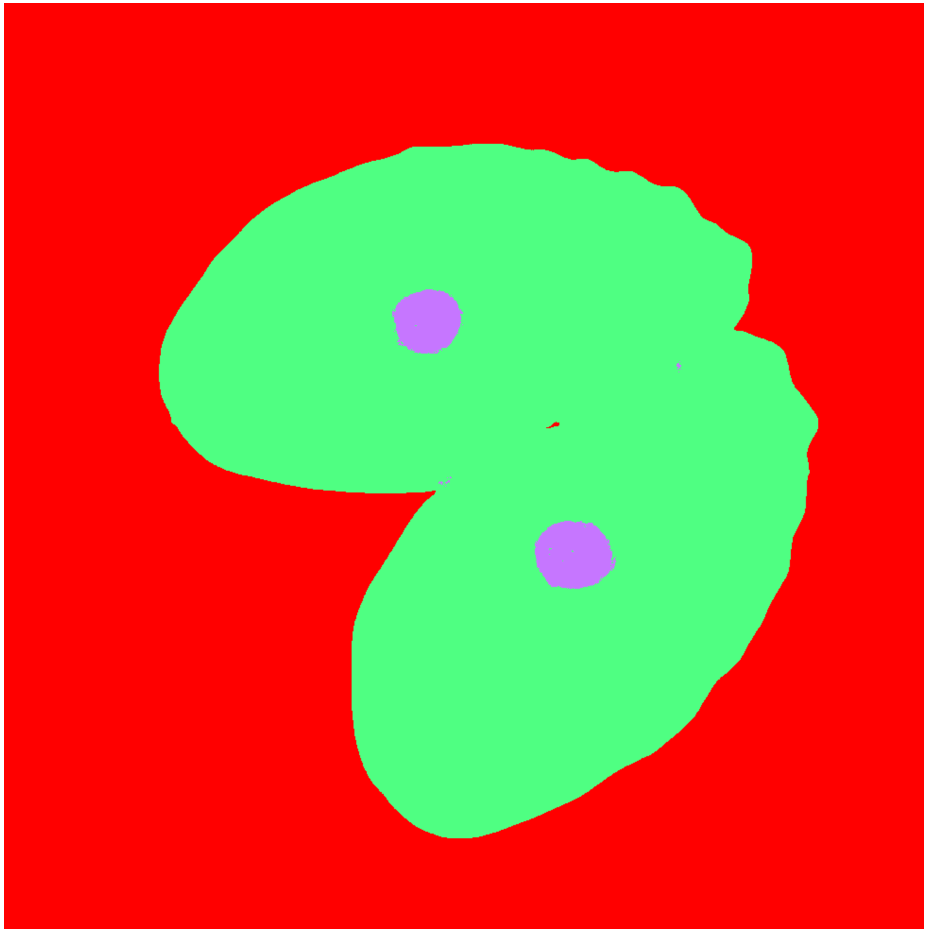
Temporal and multimodal registration for the characterization of plant-pathogen interactions





Images day 3

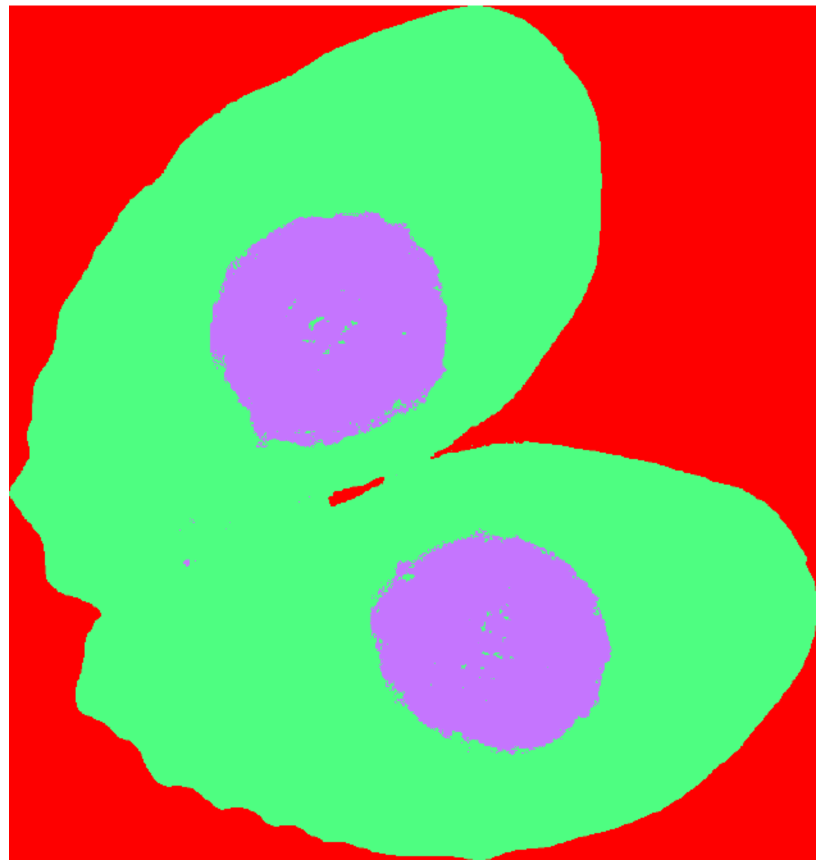
Visible



Fluorescence

Images day 5

Visible



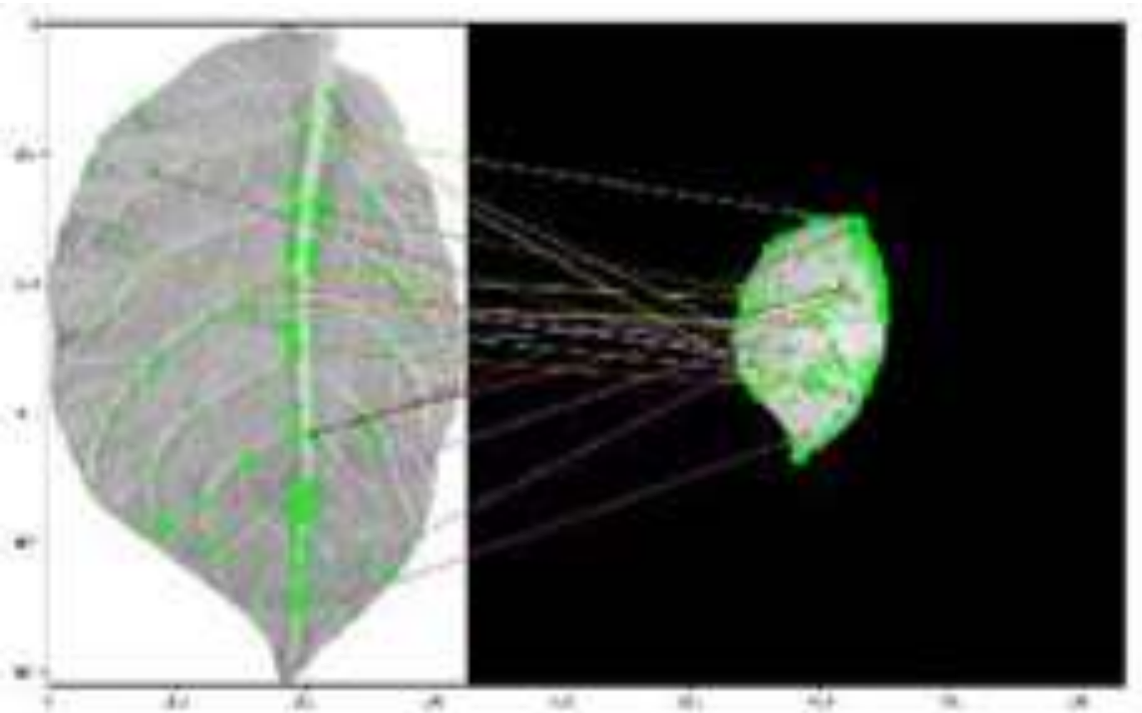
Fluorescence

Image registration

For an inoculated leaf, we have 2 images per day.

To analyze the spatiotemporal dynamics of the lesion and compare the imaging types we need to: remap (and merge) the images

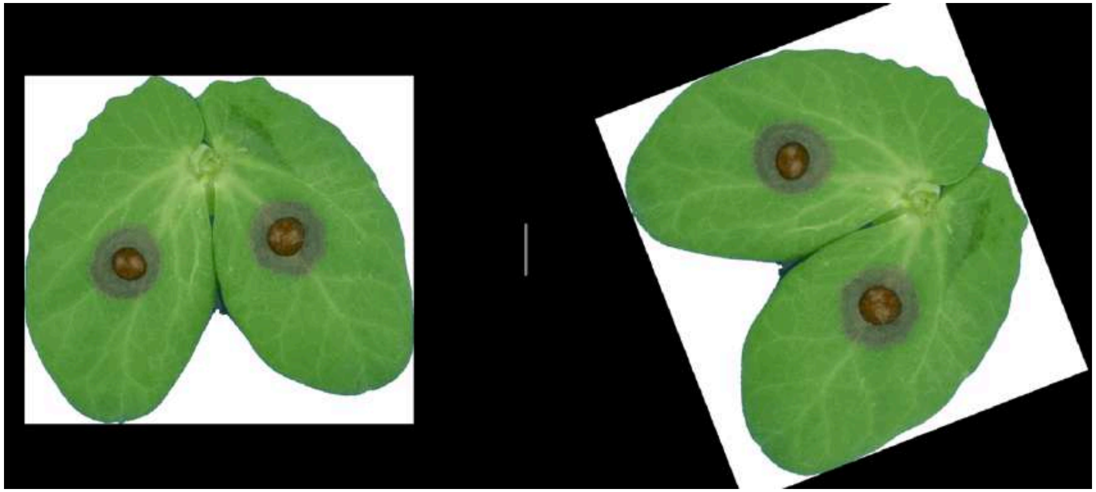
Find the geometrical transformations that allow to go from one image to another



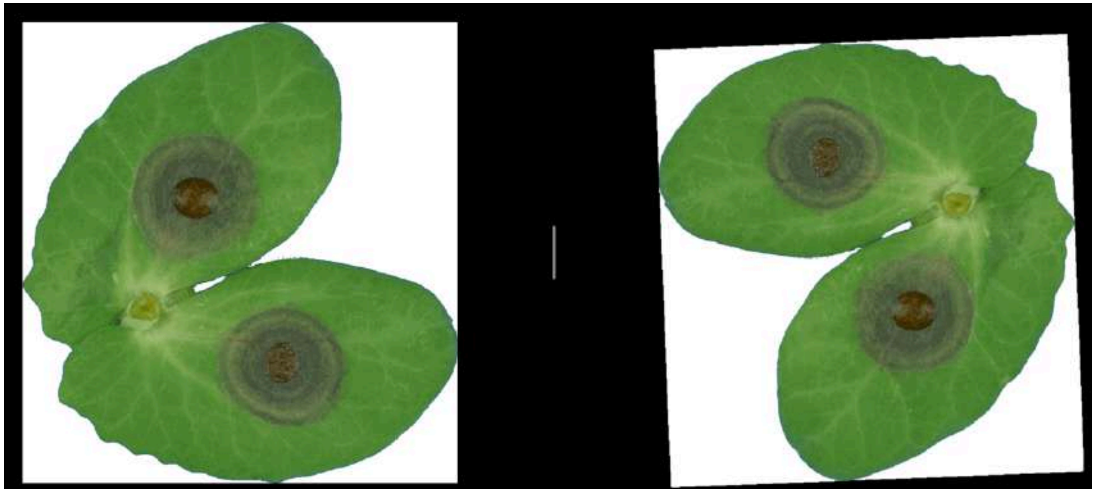
Temporal registration

Coherent Point Drift method (Myronenko-Song 2010): uses the features of the image, e.g. points, contours, regions

Day 4

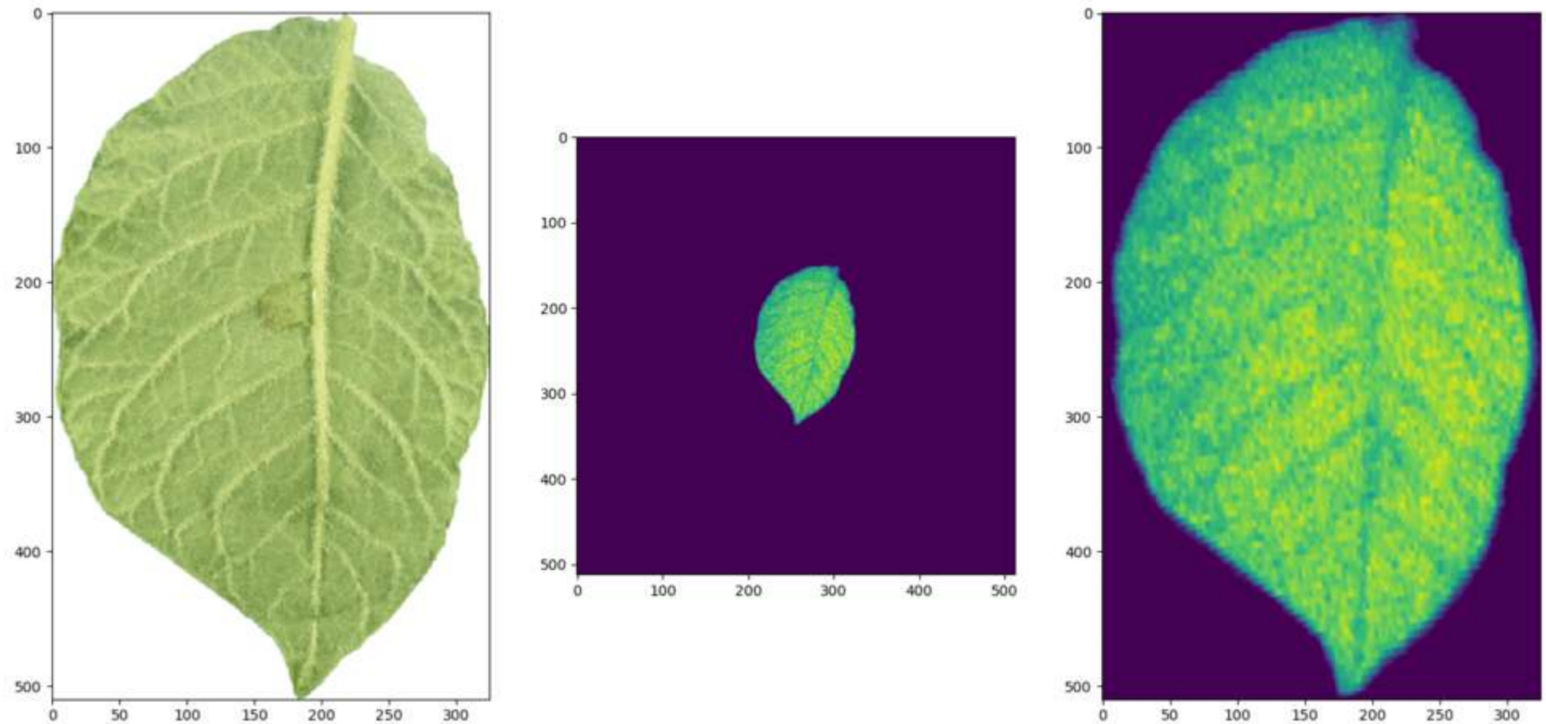


Day 5

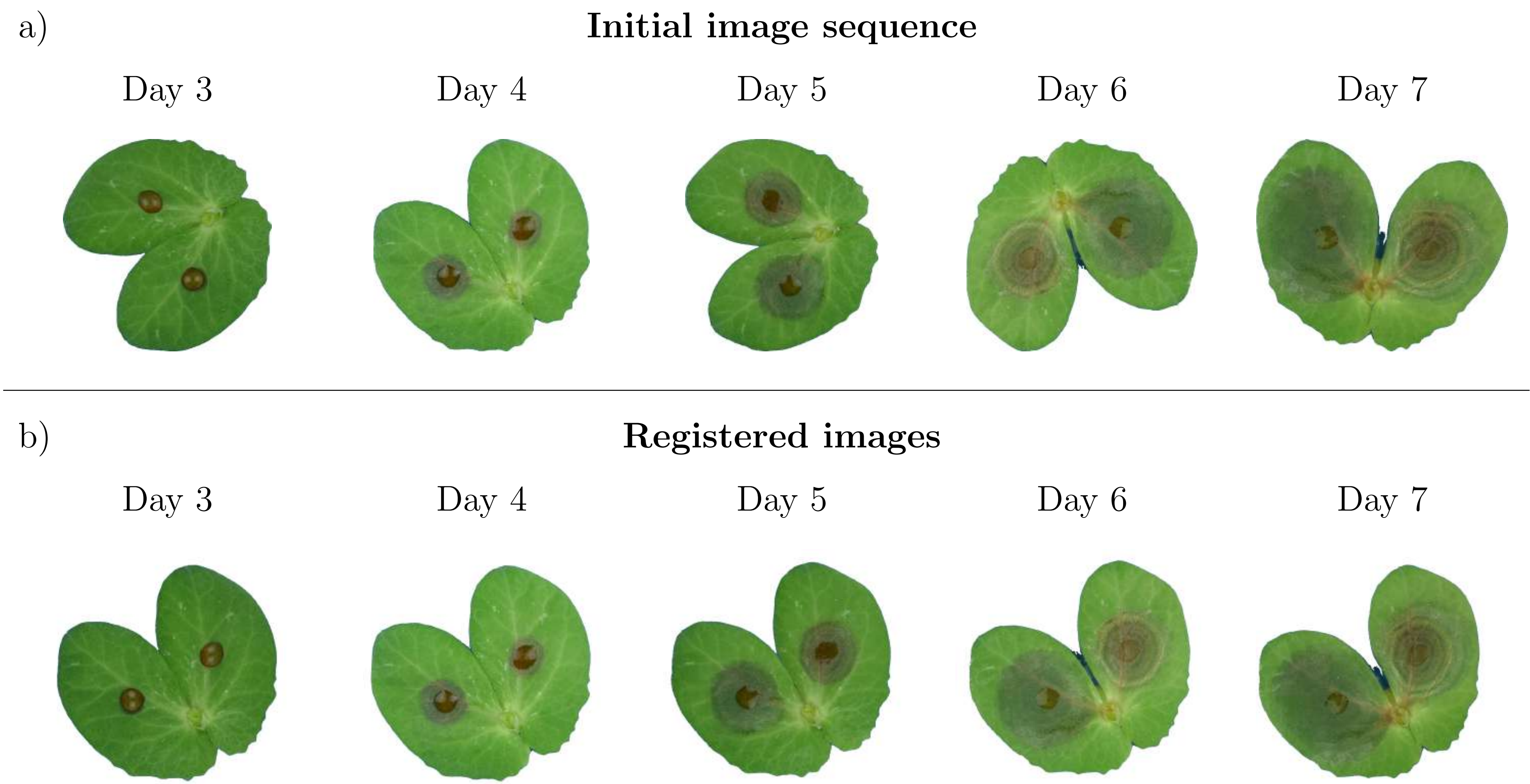


Registration between imaging modes

RGB + Fluo



Raw images to Registered images



Pixel classification

Healthy (H) or Symptomatic (S) (or Background)
in 32x16x(648×756) = 250 822 656 px described by colors, edges, textures

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Random Forest classifiers using the Trainable Waikato Environment for Knowledge Analysis (Weka) (Arganda-Carreras et al., 2017)

Pixel classification

Healthy (H) or Symptomatic (S) (or Background)
in 32x16x(648 × 756) = 250 822 656 px described by colors, edges, textures

Random Forest classifiers using the Trainable Waikato Environment for Knowledge Analysis (Weka) (Arganda-Carreras et al., 2017)

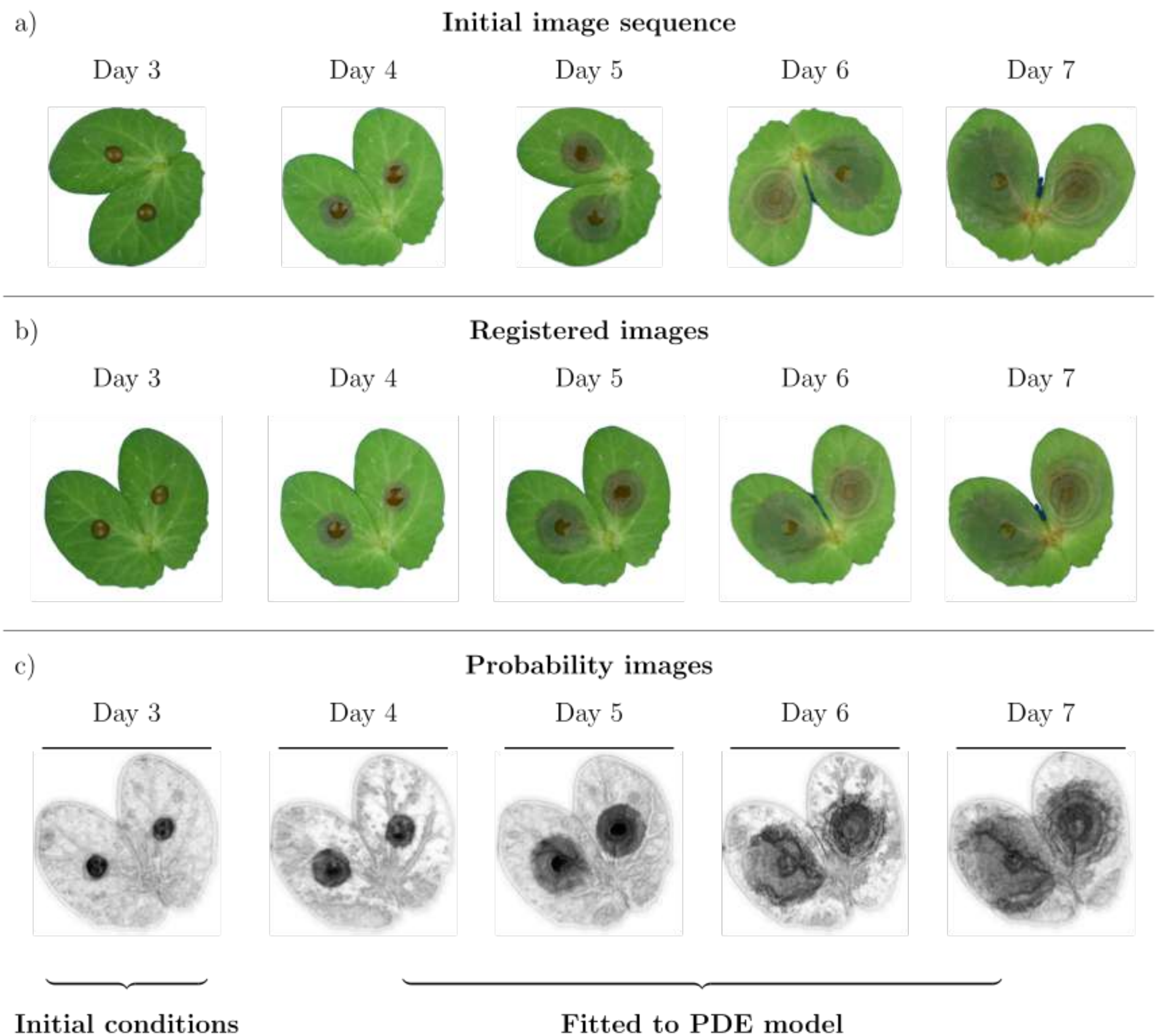
Likelihood function

$$n_{H,i} \sim \mathcal{B}(n_{H,i} + n_{S,i}, 1 - p)$$

$$n_{S,i} \sim \mathcal{B}(n_{H,i} + n_{S,i}, p)$$

Classifiers quality

Classifier	Balanced accuracy	Cohen's κ
Day 3	0.91	0.96
Day 4	0.95	0.95
Day 6	0.85	0.77
Day 7	0.89	0.82


a)
Initial image sequence
Day 3
Day 4
Day 5
Day 6
Day 7
b)
Registered images
Day 3
Day 4
Day 5
Day 6
Day 7
c)
Probability images
Day 3
Day 4
Day 5
Day 6
Day 7
Initial conditions
Fitted to PDE model

Outline

2. Bottom-up approach: Diffusion and growth from a spatially explicit model

Fisher-KPP equation

Ω leaf surface
u local density of pathogen mycelium

$$\frac{\partial u}{\partial t}(\mathbf{x},t) = D\Delta u(\mathbf{x},t) + au(\mathbf{x},t)\left(1 - \frac{u(\mathbf{x},t)}{K}\right).$$

$$\frac{\partial u}{\partial n}(\mathbf{x},t) = 0 \text{ on } \partial\Omega.$$

D diffusion coefficient
a local growth rate of the mycelium
K maximum local biomass
$2\sqrt{aD}$ constant asymptotic speed

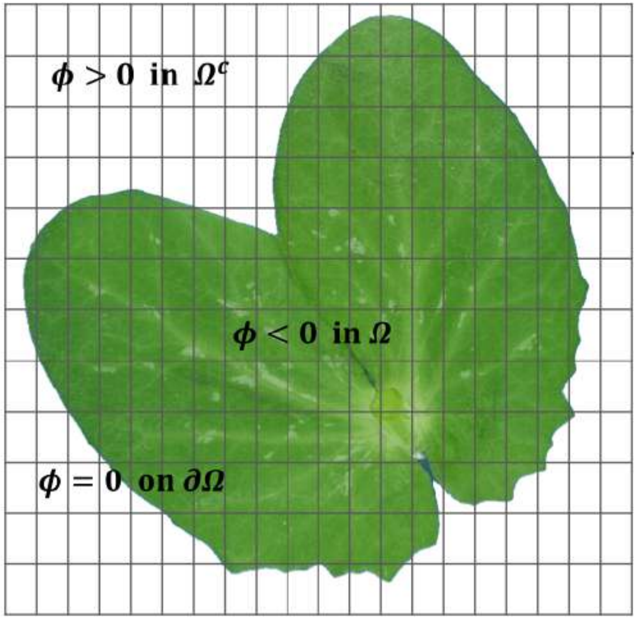
The level-set

Describe Ω leaf surface with a level-set function ϕ

(Osher and Fedkiw 2002; Sethian 1999)

$$\Omega := \{\mathbf{x} \in \mathbb{R}^2;\ \phi(\mathbf{x}) < 0\}$$

$$\vec{n} = \frac{\nabla \phi}{||\nabla \phi||}$$



computational domain

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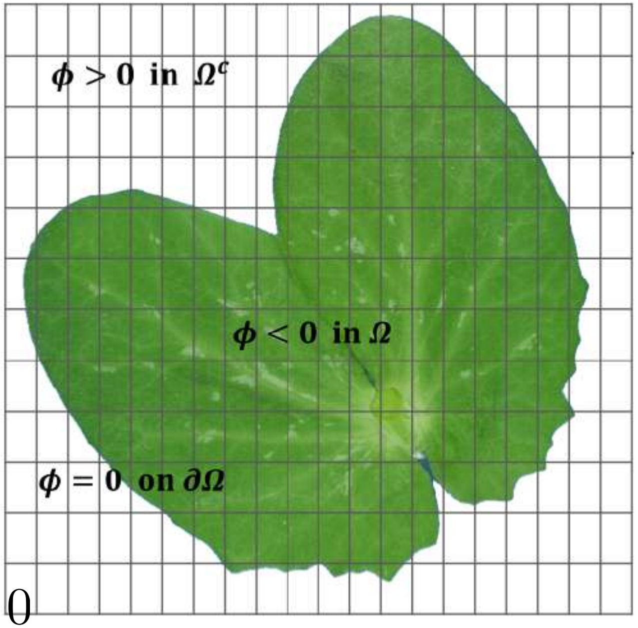
$$\vec{n} = \frac{\nabla\phi}{||\nabla\phi||}$$

$$\frac{\partial\phi}{\partial t} + \vec{v}\cdot\nabla\phi = 0$$

$$\vec{v} = \begin{cases} -\mathrm{sign}(u_{reg}(t_b) - u_{reg}(t_a))\frac{\nabla\phi}{|\nabla\phi|} & \text{if } |\nabla\phi| \neq 0 \\ 0 & \text{if } |\nabla\phi| = 0 \end{cases}$$



computational domain

(Bartalmio et al 2000)

Lagrangian minimization

$$\begin{aligned}
\mathcal{L}(a, D) \quad &= \frac{1}{2}\int_{t_3}^{t_7}\int_{\Omega}(u(\mathbf{x}, t, \theta) - u_{reg}(\mathbf{x}, t))^2 d\mathbf{x}dt \\
+ \quad & \int_{t_3}^{t_7}\int_{\Omega}\left(\frac{\partial u(\mathbf{x}, t, \theta)}{\partial t} - D\Delta u(\mathbf{x}, t, \theta)\right. \\
&\quad \left. - au(\mathbf{x}, t, \theta)\left(1 - \frac{u(\mathbf{x}, t, \theta)}{K}\right)\right)\lambda(\mathbf{x}, t, \theta)d\mathbf{x}dt.
\end{aligned}$$

Lagrangian minimization

$$\begin{aligned}\mathcal{L}(a,D) &= \frac{1}{2}\int_{t_3}^{t_7}\int_{\Omega}(u(\mathbf{x},t,\theta)-u_{reg}(\mathbf{x},t))^2 d\mathbf{x}dt \\ + & \int_{t_3}^{t_7}\int_{\Omega}\Bigg(\frac{\partial u(\mathbf{x},t,\theta)}{\partial t} - D\Delta u(\mathbf{x},t,\theta) \\ & \qquad - au(\mathbf{x},t,\theta)\left(1-\frac{u(\mathbf{x},t,\theta)}{K}\right)\Bigg)\lambda(\mathbf{x},t,\theta)d\mathbf{x}dt.\end{aligned}$$

<u>gradient</u>

$$\begin{cases}\dfrac{\partial \mathcal{L}}{\partial D} = -\displaystyle\int_{t_3}^{t_7}\int_{\Omega}\nabla u(\mathbf{x},t)\nabla\lambda(\mathbf{x},t)d\mathbf{x}dt \\ \dfrac{\partial \mathcal{L}}{\partial a} = \displaystyle\int_{t_3}^{t_7}\int_{\Omega}u(\mathbf{x},t)\left(1-\frac{u(\mathbf{x},t)}{K}\right)\lambda(\mathbf{x},t)d\mathbf{x}dt.\end{cases}$$

Lagrangian minimization

$$
\begin{aligned}
\mathcal{L}(a, D) \quad &= \frac{1}{2}\int_{t_3}^{t_7}\int_{\Omega}(u(\mathbf{x},t,\theta) - u_{reg}(\mathbf{x},t))^2 d\mathbf{x}dt \\
+ \quad & \int_{t_3}^{t_7}\int_{\Omega}\Bigg(\frac{\partial u(\mathbf{x},t,\theta)}{\partial t} - D\Delta u(\mathbf{x},t,\theta) \\
& \qquad - au(\mathbf{x},t,\theta)\left(1 - \frac{u(\mathbf{x},t,\theta)}{K}\right)\Bigg)\lambda(\mathbf{x},t,\theta)d\mathbf{x}dt.
\end{aligned}
$$

<u>gradient</u>

$$
\begin{cases}
\dfrac{\partial \mathcal{L}}{\partial D} = -\displaystyle\int_{t_3}^{t_7}\int_{\Omega}\nabla u(\mathbf{x},t)\nabla\lambda(\mathbf{x},t)d\mathbf{x}dt \\
\dfrac{\partial \mathcal{L}}{\partial a} = \displaystyle\int_{t_3}^{t_7}\int_{\Omega}u(\mathbf{x},t)\left(1 - \frac{u(\mathbf{x},t)}{K}\right)\lambda(\mathbf{x},t)d\mathbf{x}dt.
\end{cases}
$$

<u>λ solution of backward PDE</u>

$$
-\frac{\partial\lambda}{\partial t} = D\Delta\lambda(\mathbf{x},t) + a\left(1 - \frac{2u(\mathbf{x},t)}{K}\right)\lambda(\mathbf{x},t) + (u(\mathbf{x},t) - u_{reg})
$$

Initial guess

By splitting the PDE

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$$D \simeq \frac{\langle r^2 \rangle}{16t}$$ = 98% of population (Shigesada and Kawasaki, 1997)

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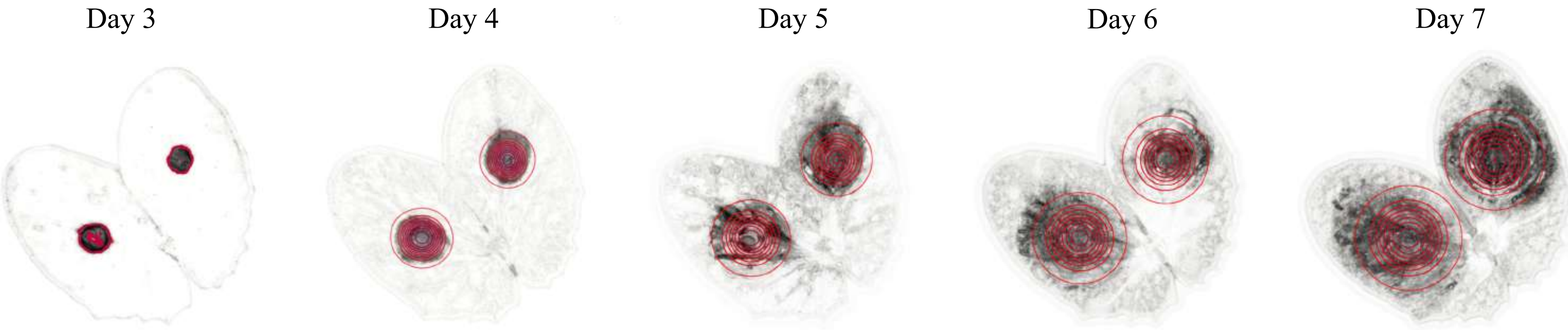
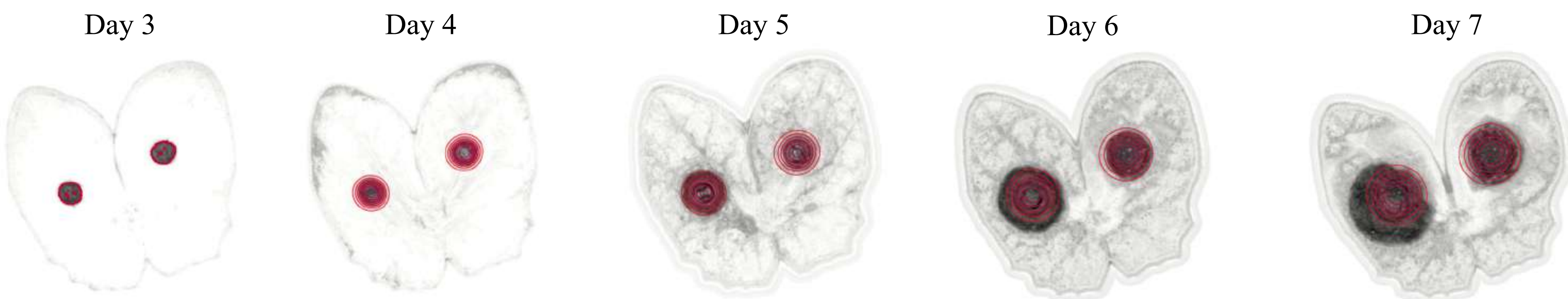
$$a = -\frac{1}{(t_b - t_a)} \ln \left(\frac{\frac{K}{u(t_b)} - 1}{\frac{K}{u(t_a)} - 1} \right)$$

Simulation: movie

Solara



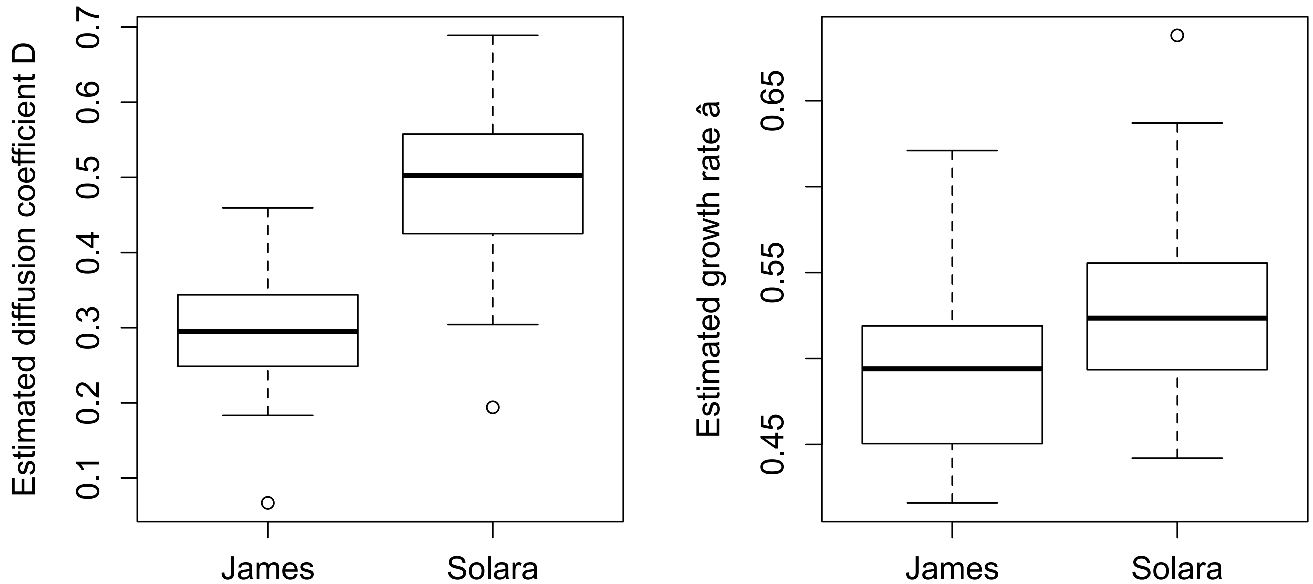
James



Convergence

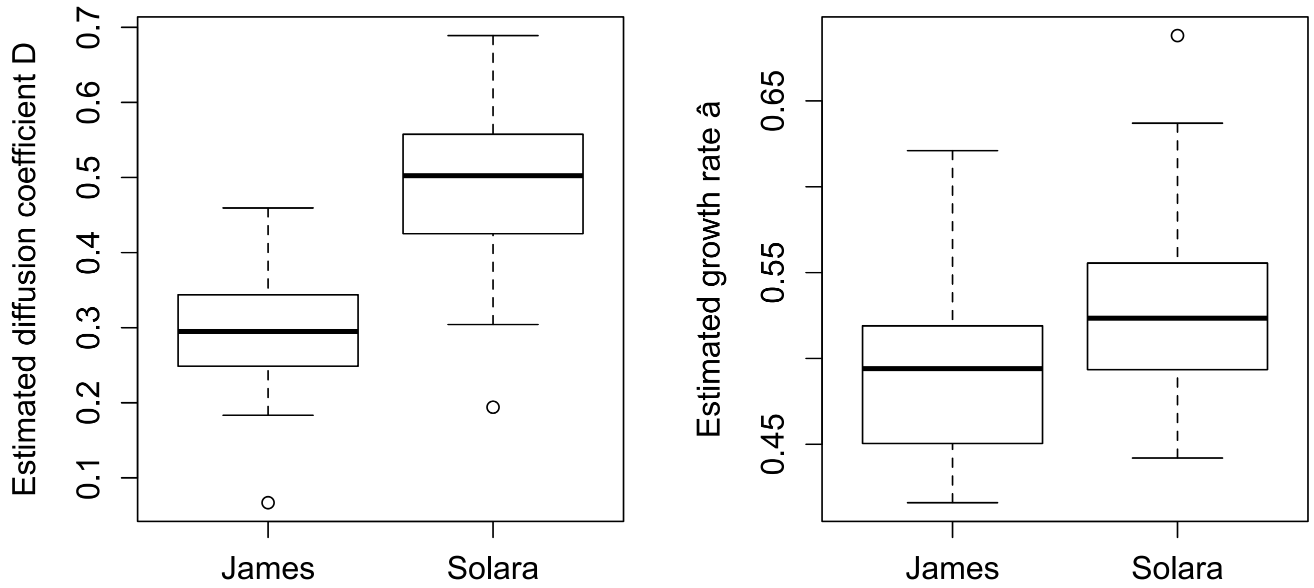
	Cultivar						
1	Solara	size	512×514	614×617	717×720	819×822	922×925
		$\hat{a}$	0.4788	0.4835	0.4845	0.4852	0.4841
		$\hat{D}$	0.4597	0.4511	0.4529	0.4534	0.4584
17	James	size	512×514	614×617	717×720	819×822	922×925
		$\hat{a}$	0.4472	0.4492	0.4530	0.4550	0.4543
		$\hat{D}$	0.2367	0.2367	0.2368	0.2366	0.2368

Results



		Df	Sum Sq	Mean Sq	F value	Pr(>F)
Diffusion $\hat{D}$						
	Cultivar	1	0.31	0.31	24.95	2.36e-05
	Residuals	30	0.37	0.01		
Growth rate $\hat{a}$						
	Cultivar	1	0.01	0.01	3.56	6.90e-02
	Residuals	30	0.11	0.00		

Results



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Growth rate $\hat{a}$						
	Cultivar	1	0.01	0.01	3.56	6.90e-02
	Residuals	30	0.11	0.00		

P. pinodes spread at a higher speed and more virulent
on Solara than on James

Conclusion

We propose a simple PDE able to predict the lesion growth from imaging data

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Other pathosystems: *phytophthora infestans* – potato
phoma medicaginis – pea
powdery mildew - vine

Account for the host physiology (age, senescence, veins…):

MERCI DE VOTRE ATTENTION!

Merci au groupe SMAI Mabiome
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