ROLE OF VECTOR PHENOTYPIC PLASTICITY IN DISEASE TRANSMISSION AS ILLUSTRATED BY THE SPREAD OF DENGUE VIRUS BY *AEDES ALBOPICTUS*

Dominic Brass, Christina Cobbold, Bethan Purse, David Ewing, Amanda Callaghan, Steven White

UK Centre for Ecology & Hydrology

MODEL AIMS

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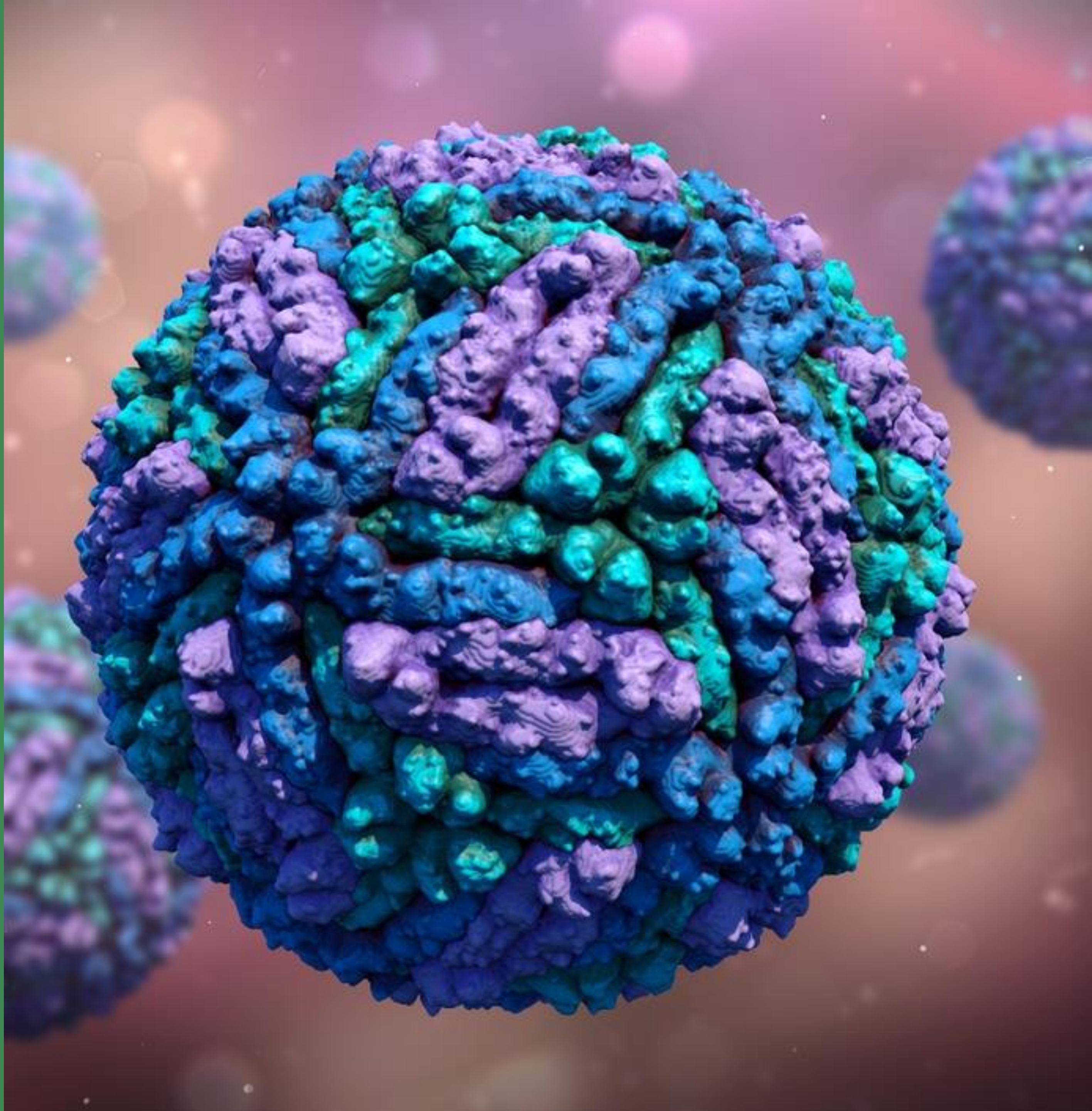
Understand patterns in *Aedes albopictus* driven dengue risk



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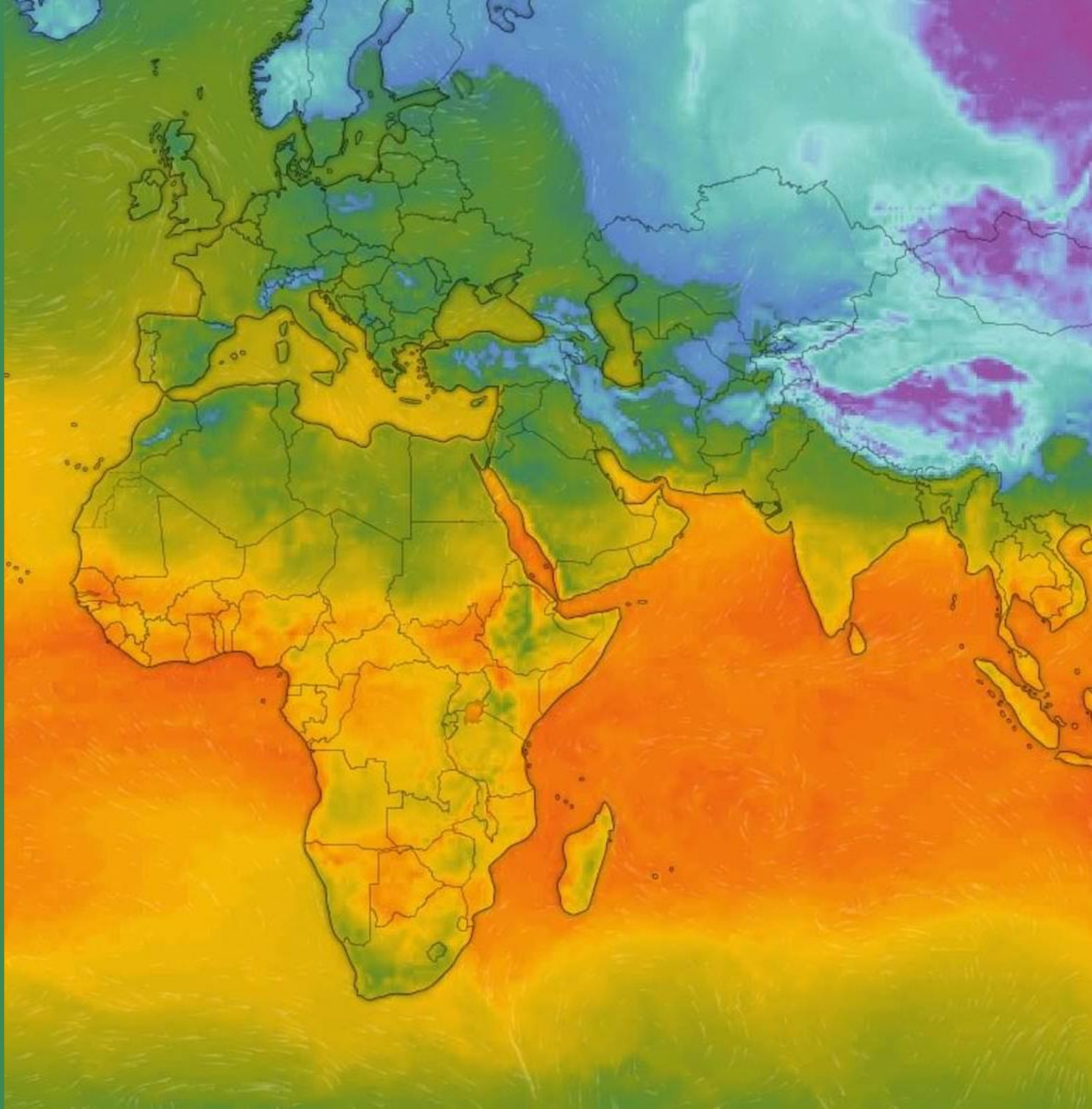
Understand patterns in *Aedes albopictus* driven dengue risk

This requires understanding differences in global vector dynamics

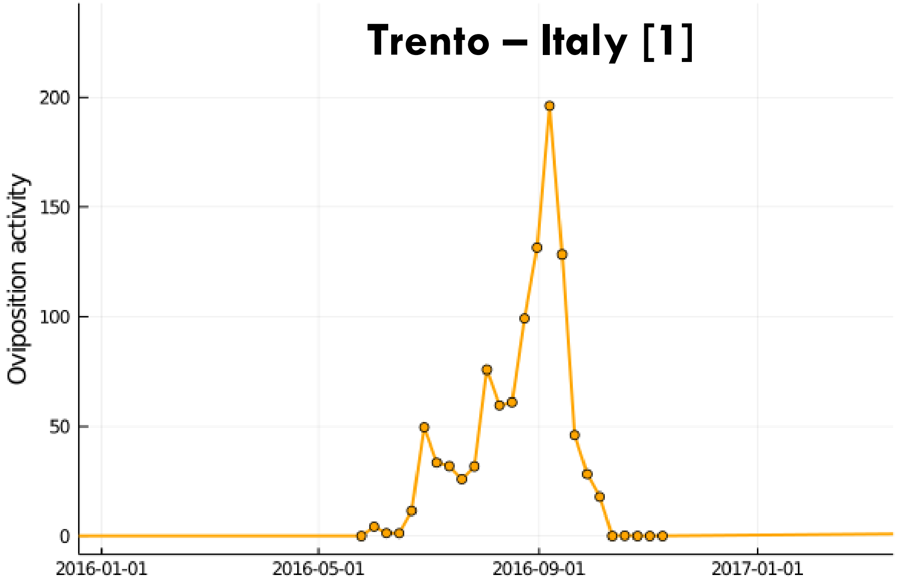


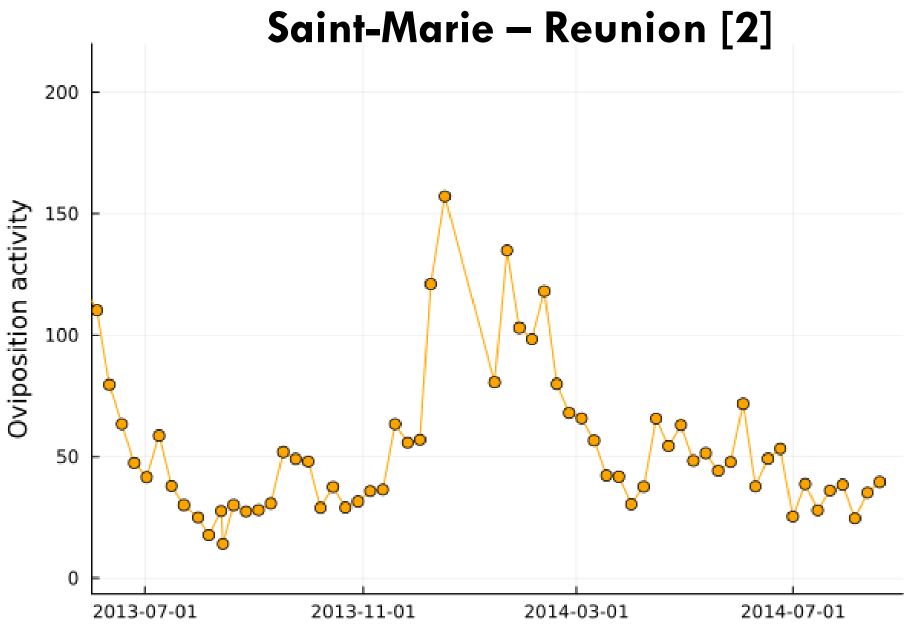
MODEL AIMS

Understand patterns in *Aedes albopictus* driven dengue risk

This requires understanding differences in global vector dynamics

We need a model that makes predictions that generalise between environments





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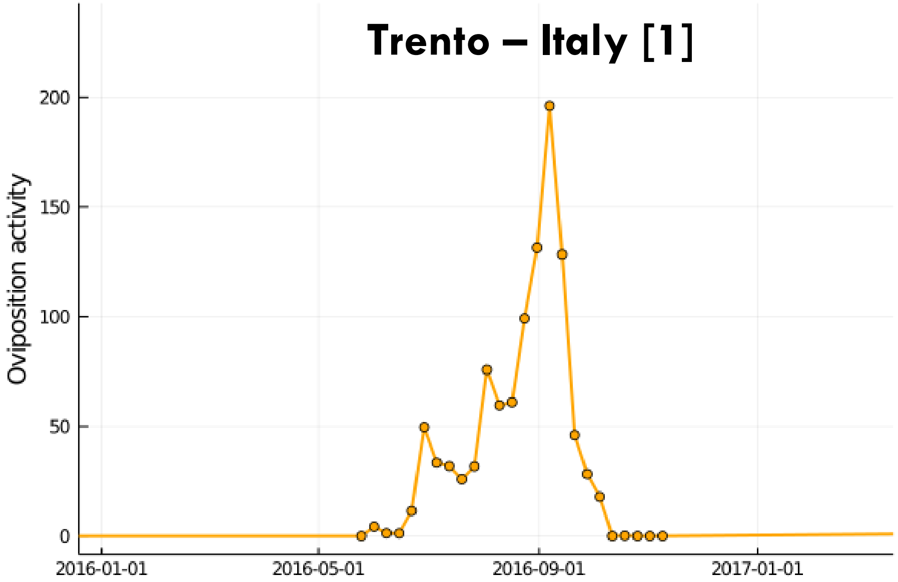
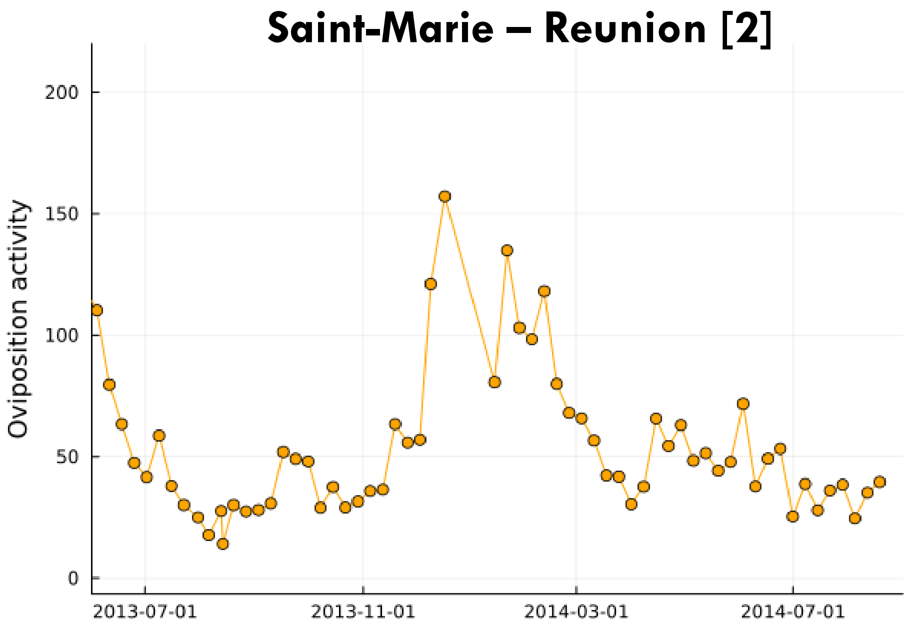
THE IDEA

Accounting for density-dependence





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THE IDEA

Accounting for density-dependence

Traits important for disease transmission exhibit delayed density-dependence

Larval conditions

Temperature Competition

Adult traits

Wing length

Fecundity Survival

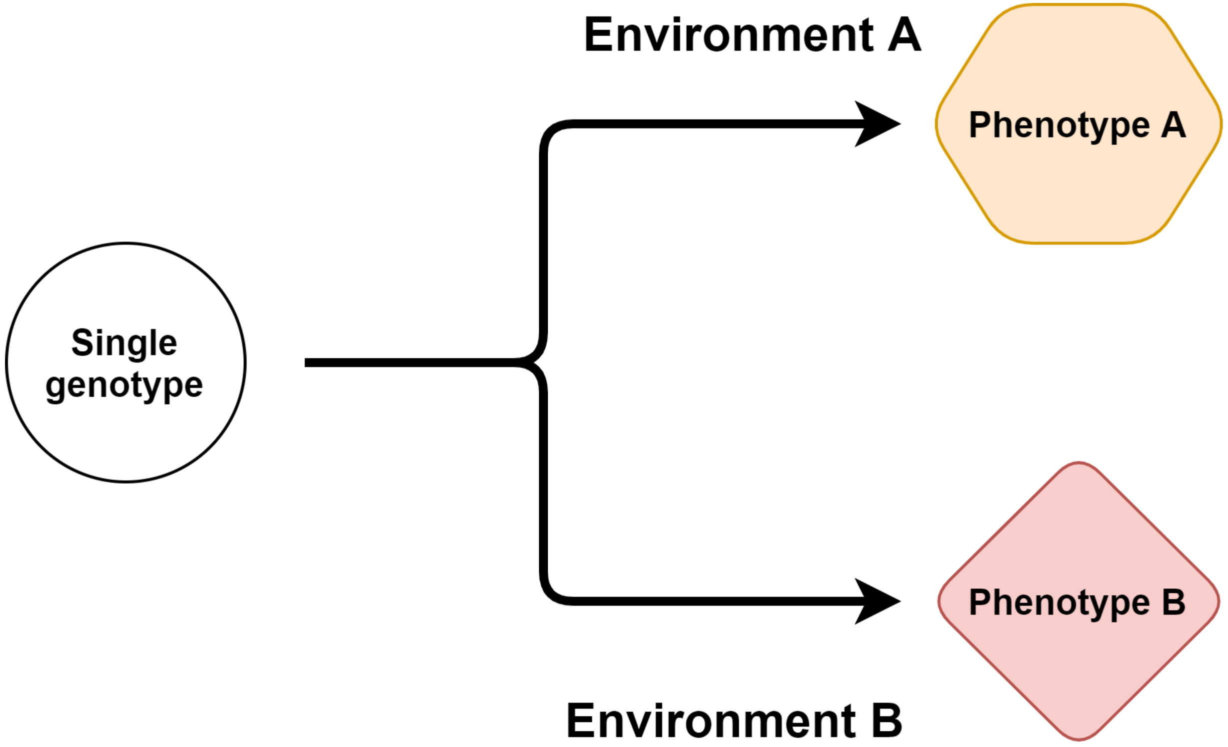
THE IDEA

Accounting for density-dependence

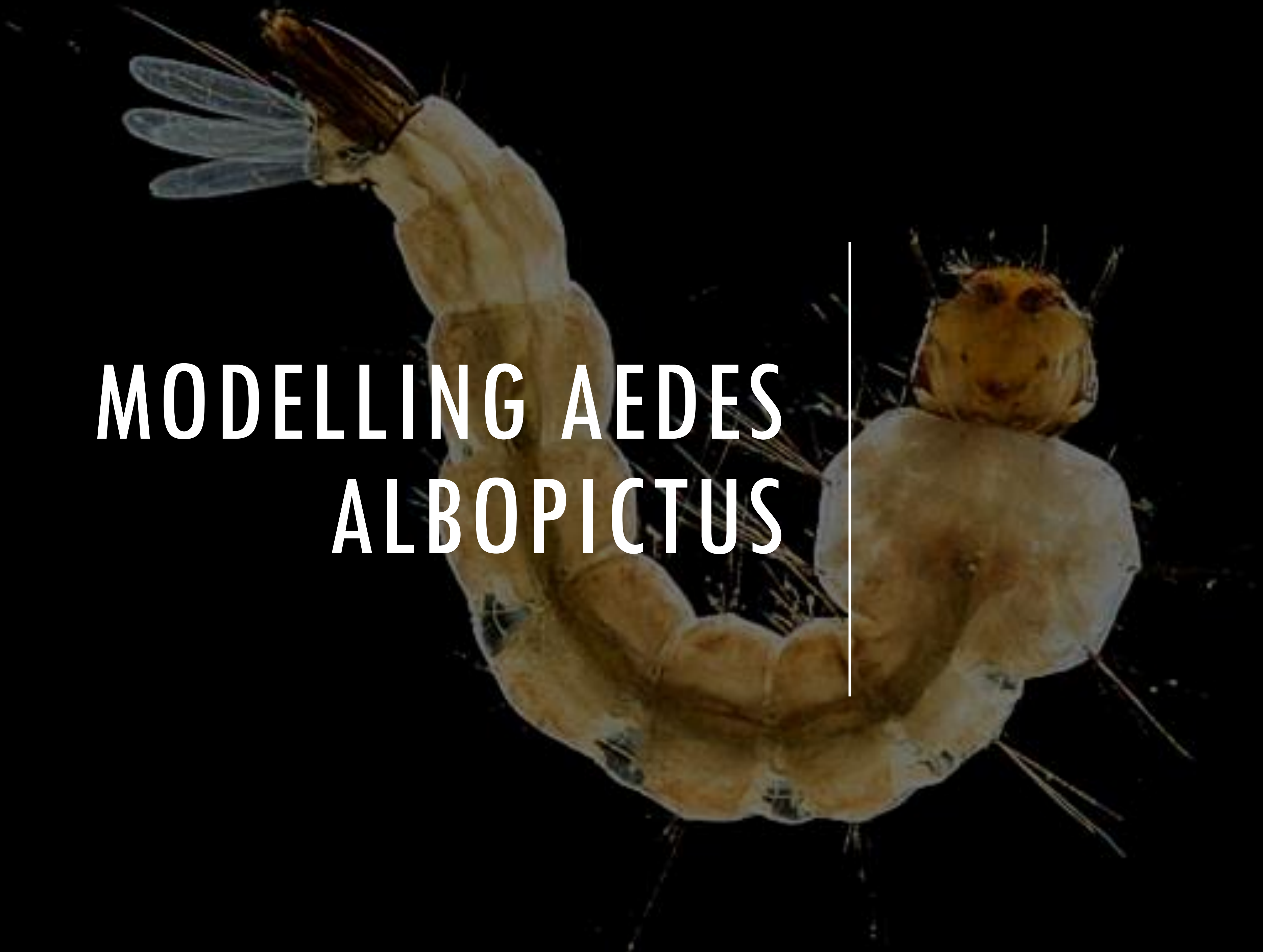
Traits important for disease transmission exhibit delayed density-dependence

We consider the effect of developmental plasticity on disease dynamics

Definition - Phenotypic plasticity
The ability of a single genotype to produce multiple phenotypes when exposed to different environmental conditions



MODELLING AEDES ALBOPICTUS



MODEL FOR AEDES ALBOPICTUS

Developed a stage-phenotypically structured system of delay-differential equations

The Systematic Formulation of Population Models for Insects with Dynamically Varying Instar Duration

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LETTER

ECOLOGY LETTERS WILEY

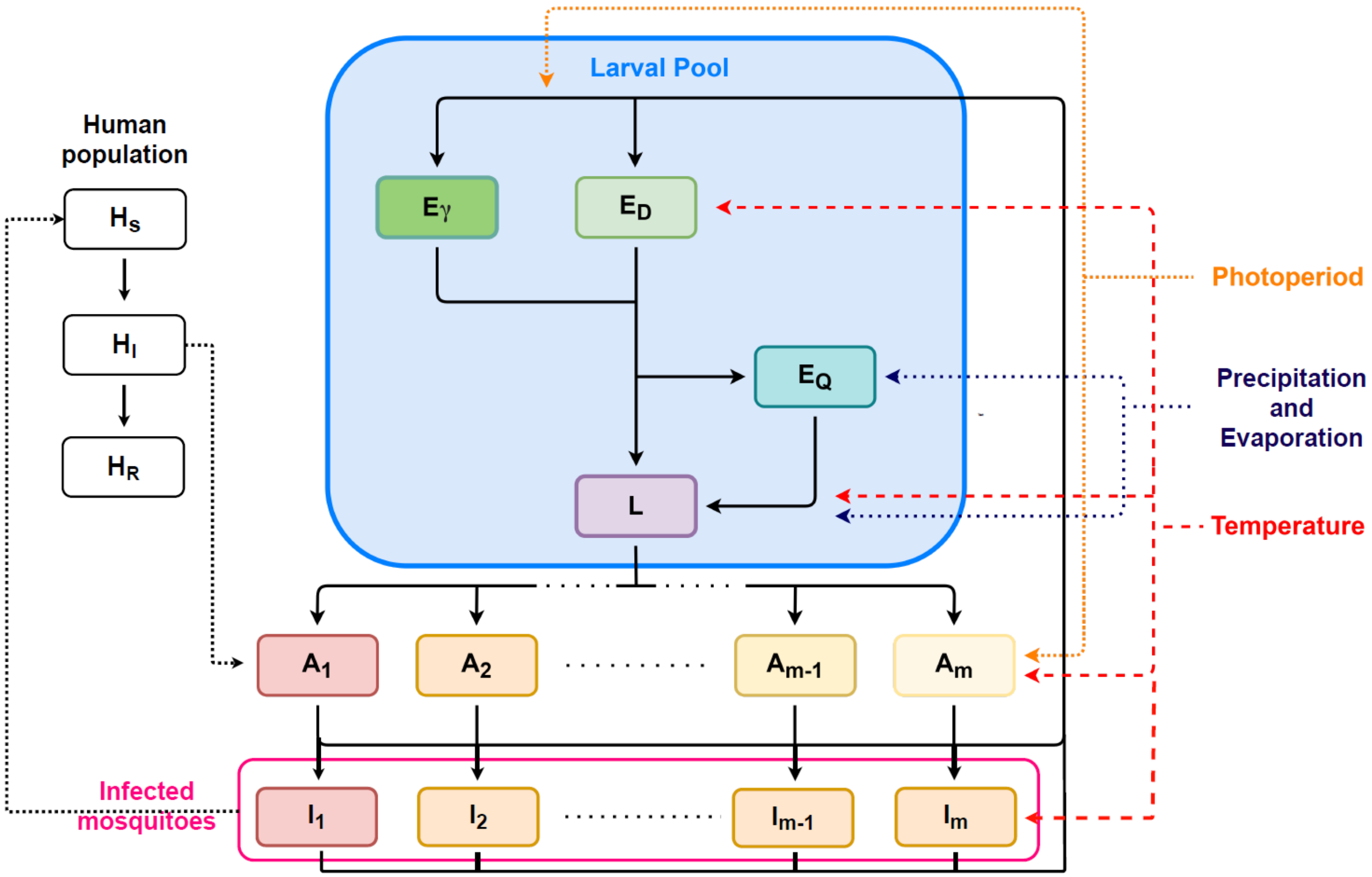
Phenotypic plasticity as a cause and consequence of population dynamics

Dominic P. Brass[1,2] | Christina A. Cobbold[3] | David A. Ewing[4] |
Bethan V. Purse[1] | Amanda Callaghan[2] | Steven M. White[1]

MODEL FOR AEDES ALBOPICTUS

Developed a stage-phenotypically structured system of delay-differential equations

Adult population structured by infection status and wing-length

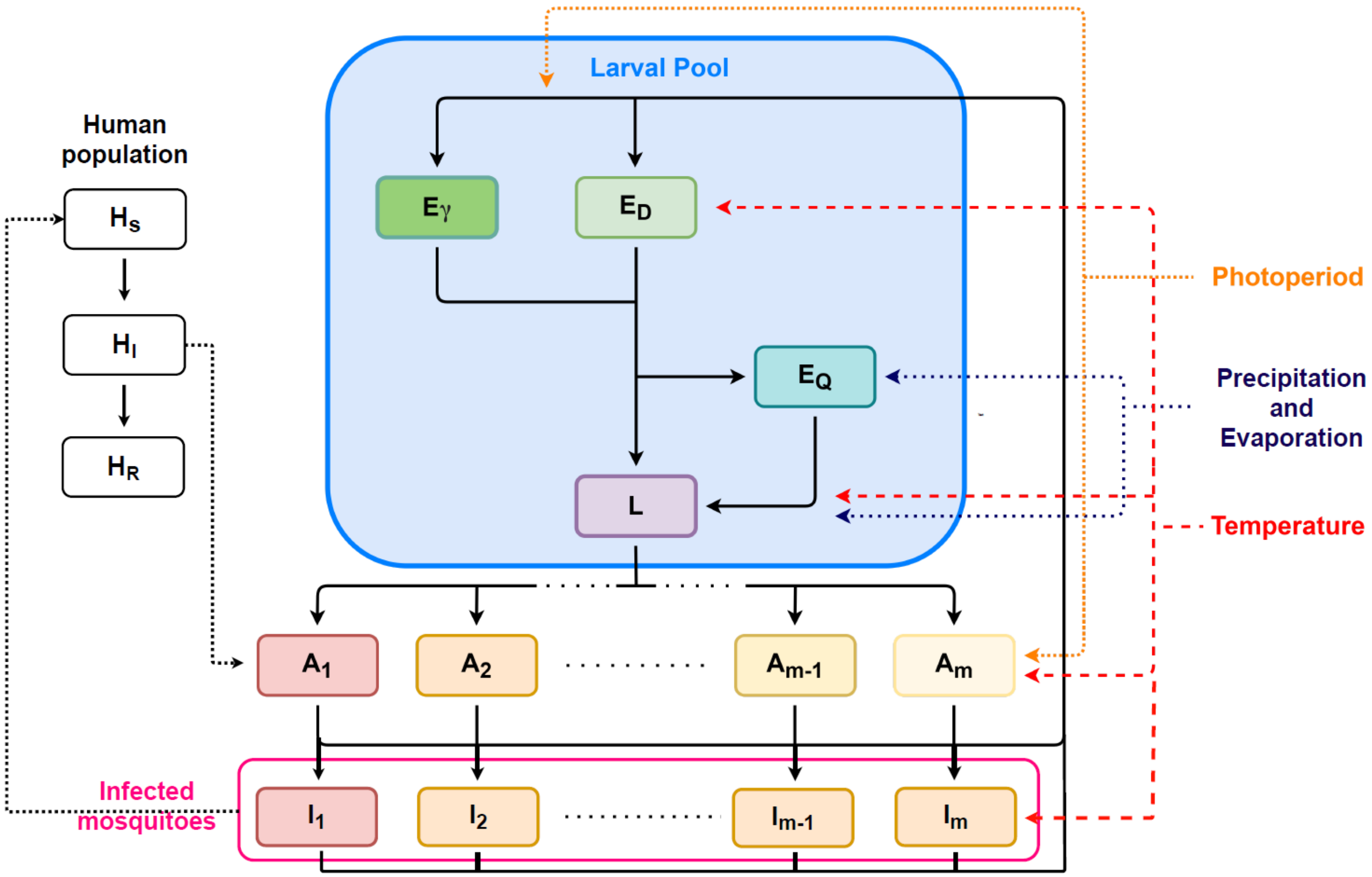


MODEL FOR AEDES ALBOPICTUS

Developed a stage-phenotypically structured system of delay-differential equations

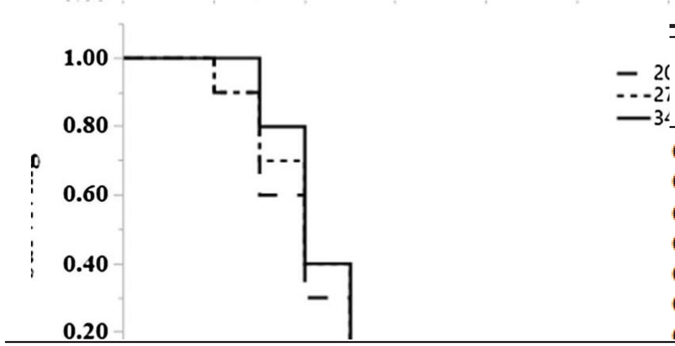
Adult population structured by infection status and wing-length

Use historic experience of larval competition to determine the wing-length of emerging adults



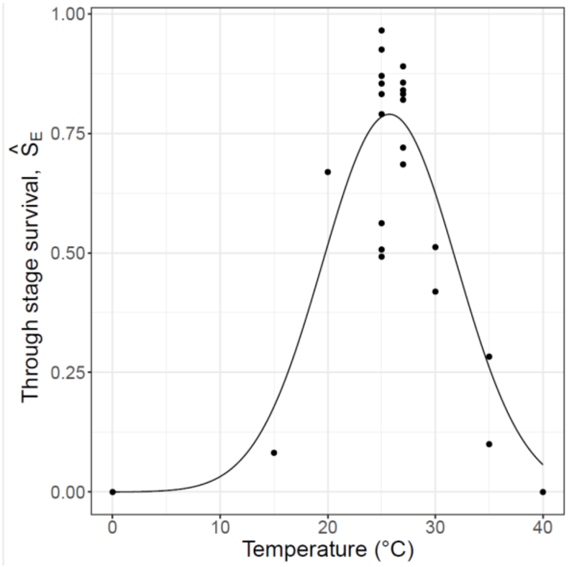
REACTION NORMS

Parametrise reaction norms linking environmental drivers to trait value using laboratory data



	20°C			
	n	Mean	SE	min
Cycle 1	11	6.7	0.8	3 a
Cycle 2	5	8.4	1.6	5 a
Cycle 3	2	13.5	4.5	9 a
Cycle 4	1	10.0		10
Cycle 5				
Cycle 6				
Cycle 7				

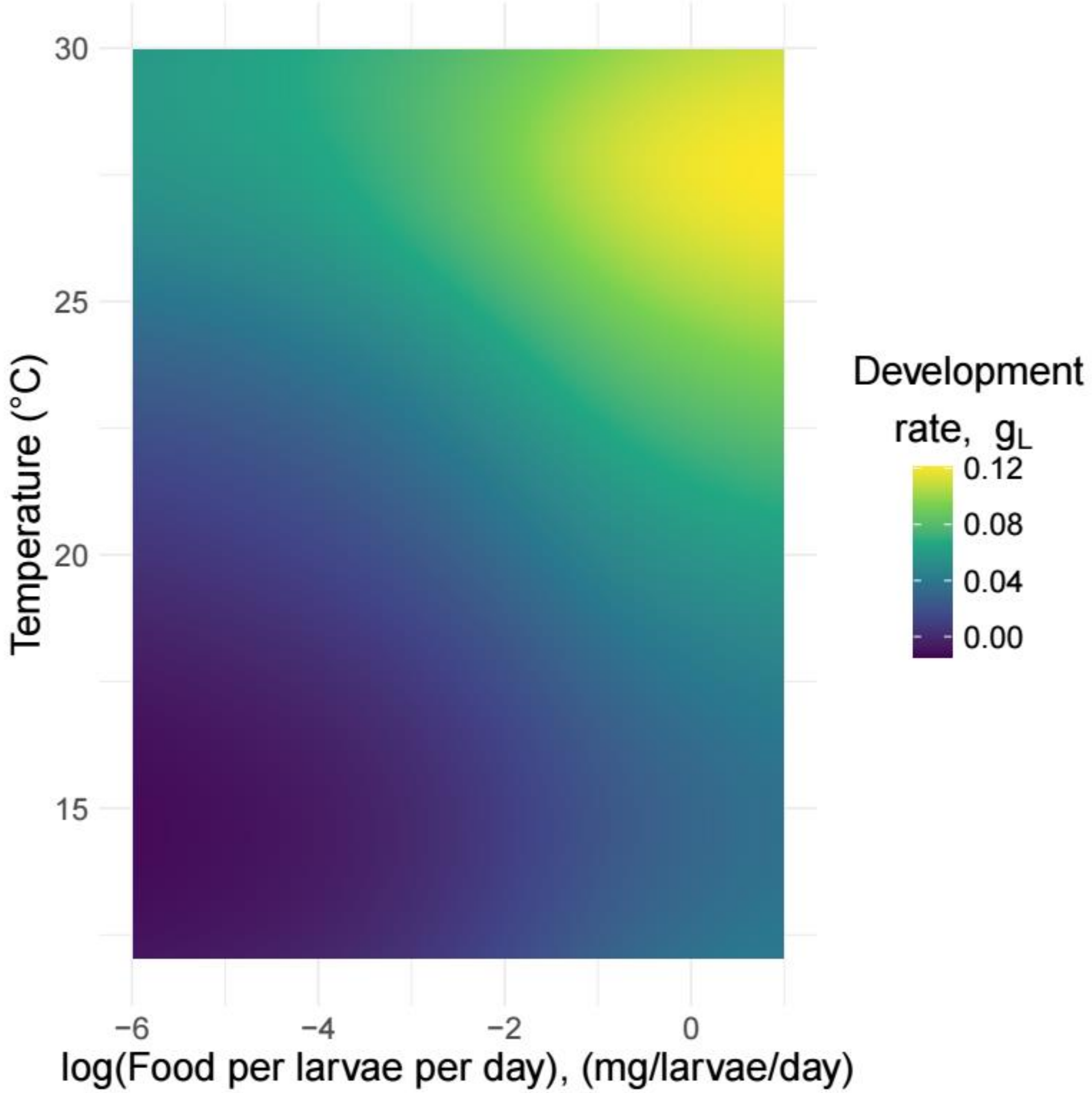
T (°C)	Egg Mean SE	L1 Mean SE	L2 Mean SE	L3 Mean SE	L4 Mean SE	Pupae Mean SE	L1-adult Mean SE	Sex ratio
5	11 ± 1.3							
10	2 ± 0							
15	7.4 ± 1.8 a	5.6 ± 0.3 a	3.3 ± 0.2 a	4.6 ± 0.2 a	13.4 ± 0.8 a	8.7 ± 0.6 a	35.0 ± 0.9 a	47.5%
20	2.9 ± 0.4 b	3.0 ± 0.2 b	1.4 ± 0.2 b	2.1 ± 0.3 b	4.1 ± 0.3 b	4.1 ± 0.2 b	14.4 ± 0.4 b	43.5%
25	4.5 ± 0.7 c	2.1 ± 0.2 c	1.2 ± 0.2 b	1.2 ± 0.1 c	3.3 ± 0.2 c	2.7 ± 0.1 c	10.4 ± 0.7 c	41.0%
30	6.7 ± 0.7 a	1.4 ± 0.1 d	1.3 ± 0.1 b	1.4 ± 0.2 c	3.0 ± 0.3 c	1.9 ± 0.1 d	8.8 ± 0.6 d	46.3%
35	7.1 ± 0.8 a	1.7 ± 0.1 c	1.2 ± 0.1 b	2.4 ± 0.4 b	6.8 ± 1.1 d	1.7 ± 0.7	12.3 ± 0.7	66.6%



REACTION NORMS

Parametrise reaction norms linking environmental drivers to trait value using laboratory data

Density and temperature dependent variable time delays

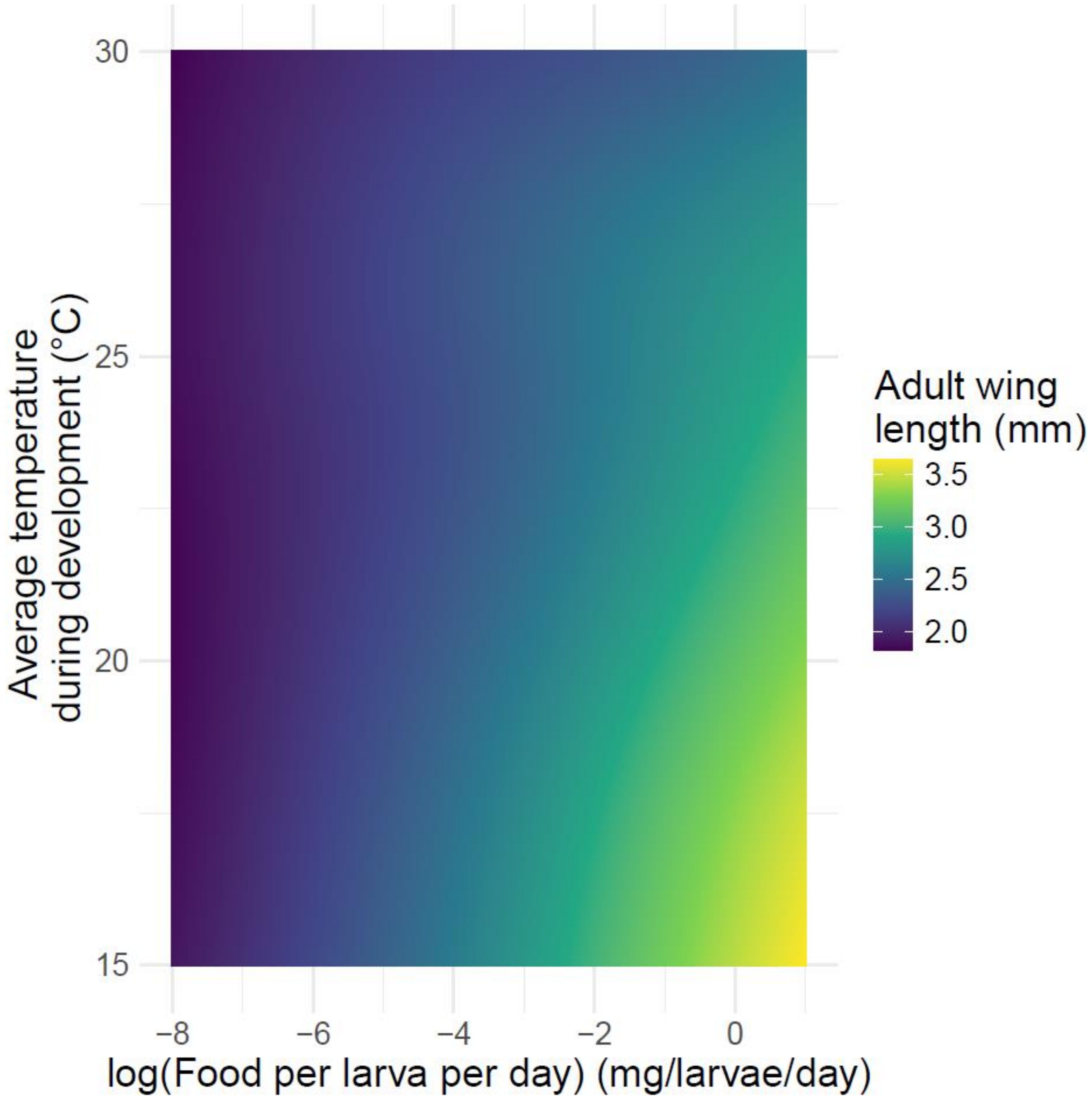


REACTION NORMS

Parametrise reaction norms linking environmental drivers to trait value using laboratory data

Density and temperature dependent variable time delays

Relationship between average larval temperature and average food per larvae per day and adult wing length



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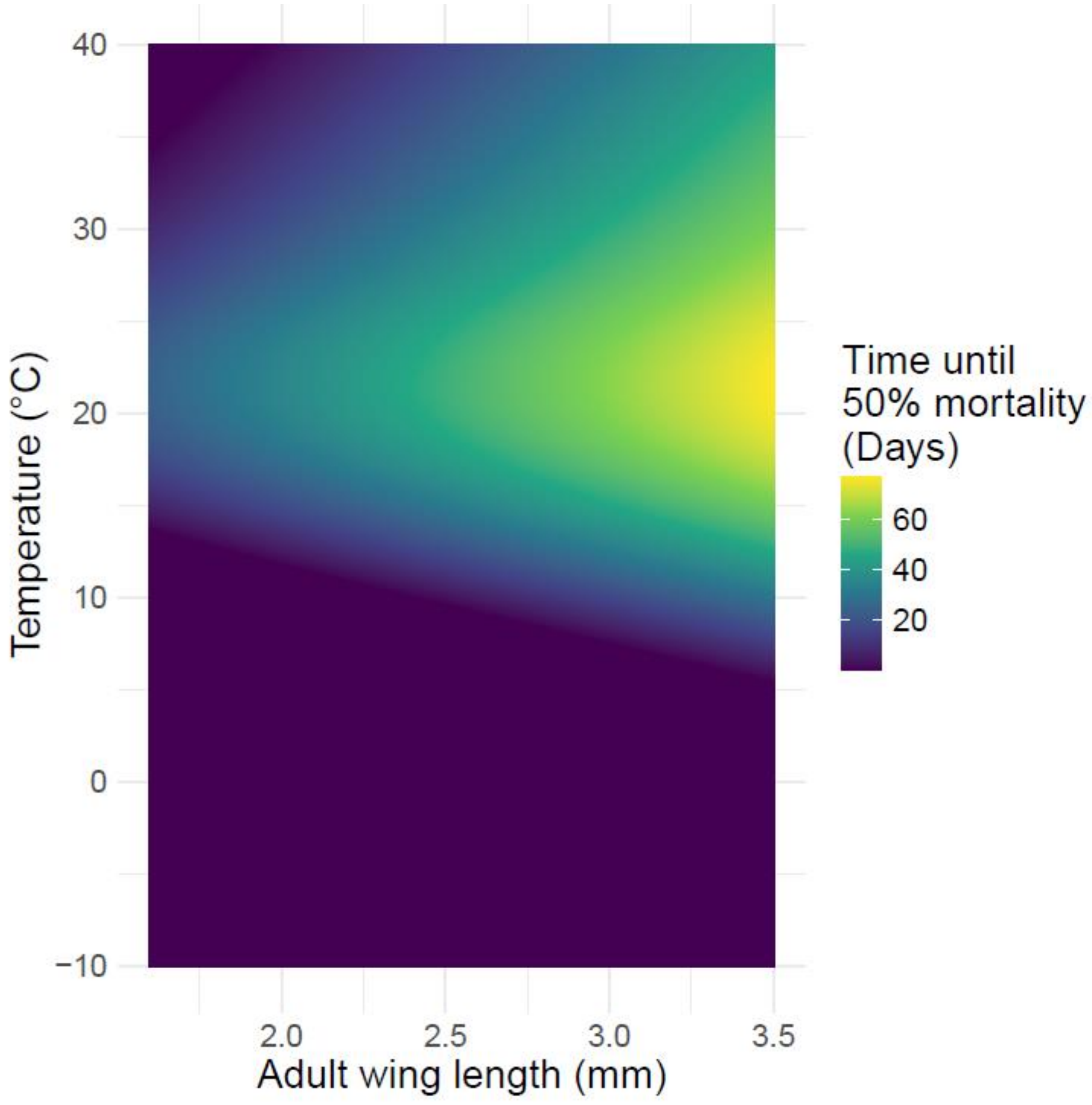


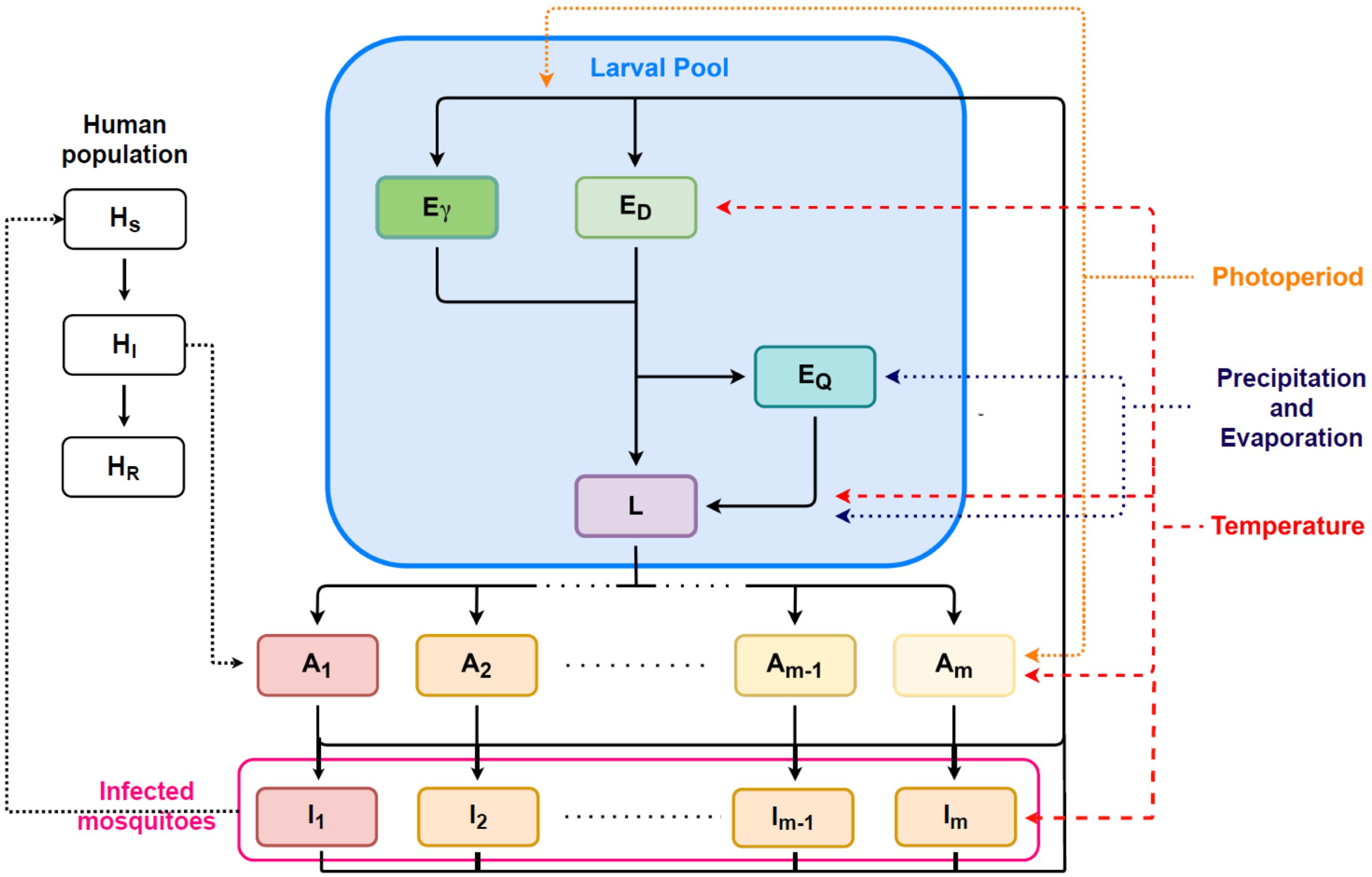
MODEL FOR AEDES ALBOPICTUS

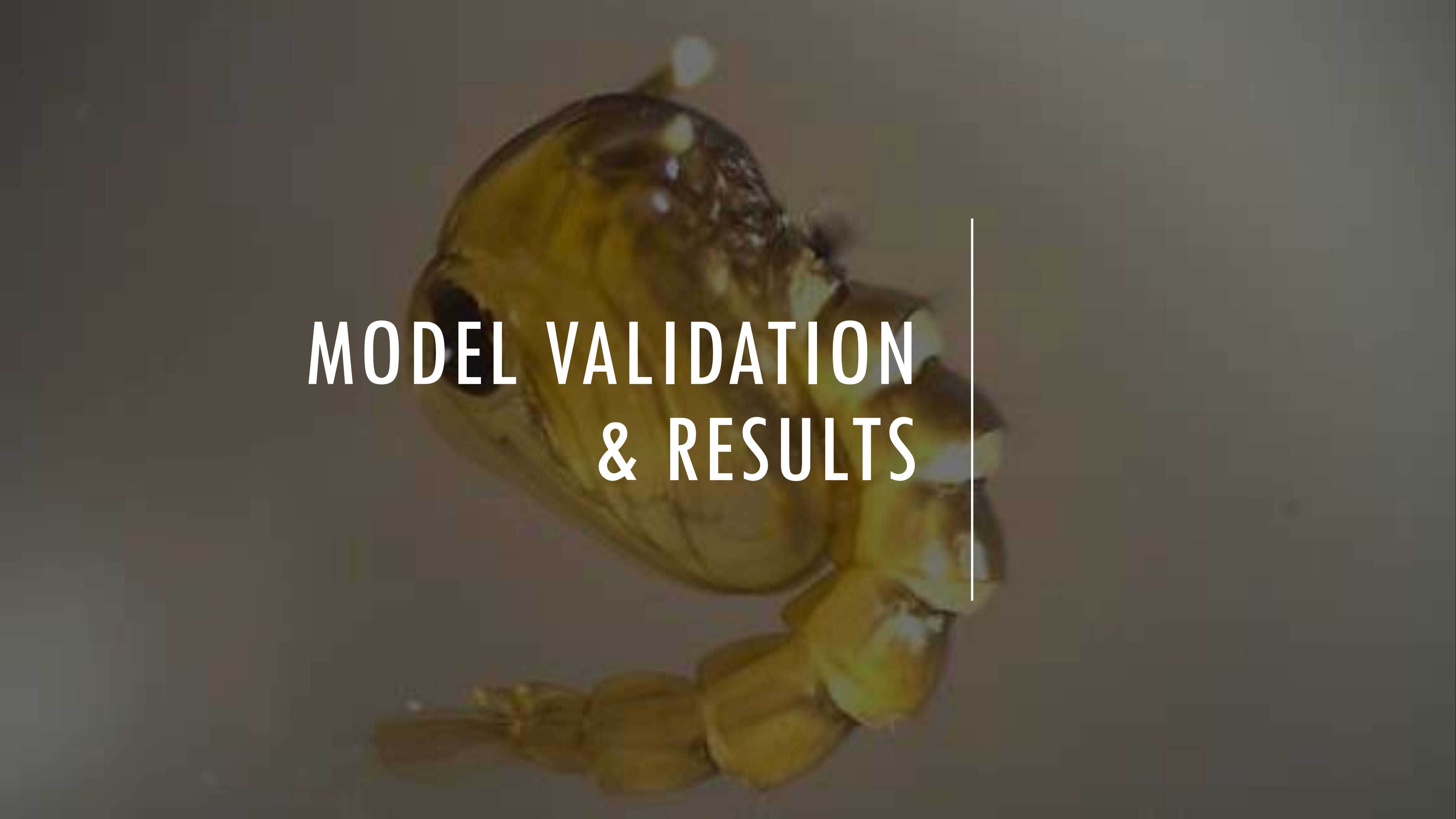
Stage-phenotypically structured delay-differential equations

Input environmental variables

Output population & disease dynamics

No backfitting





MODEL VALIDATION & RESULTS

CARRIERI ET AL. (2011)

Rimini, Italy

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Rimini, Italy

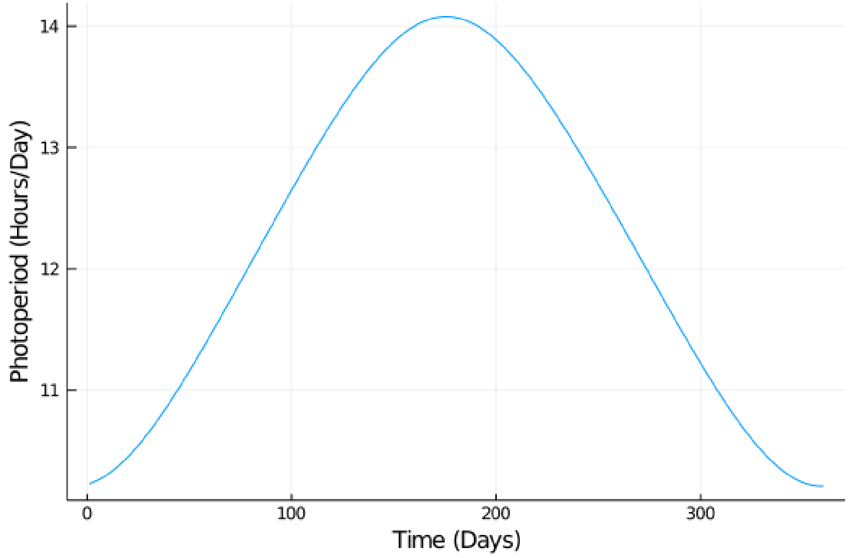
Temperate climate

CARRIERI ET AL. (2011)

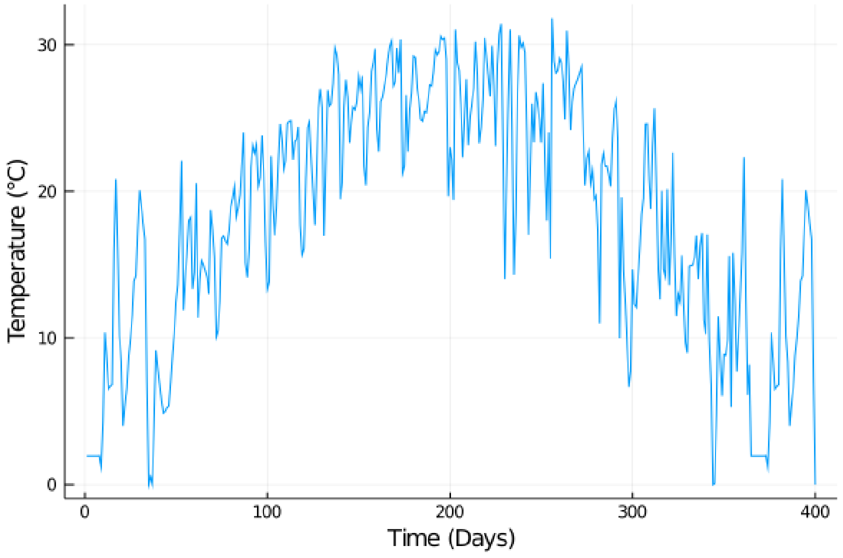
Rimini, Italy

Temperate climate

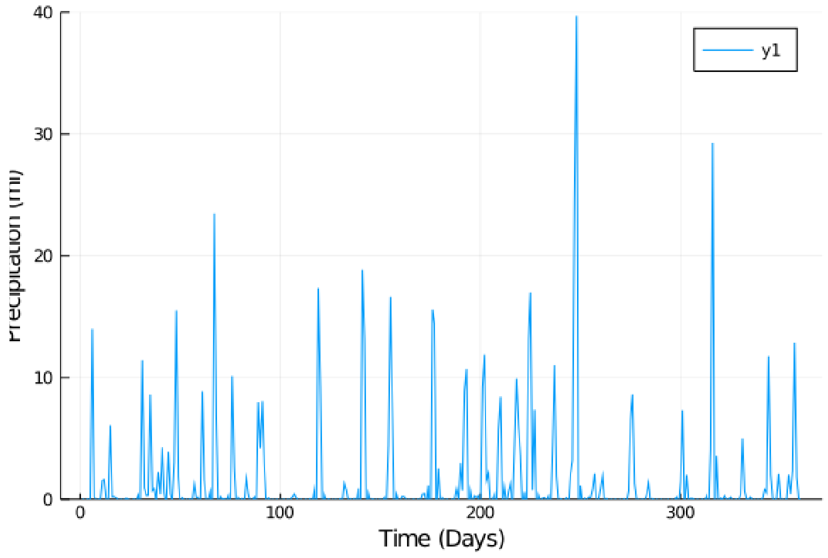
Oviposition activity monitored in 2008



Photoperiod



Temperature



Precipitation

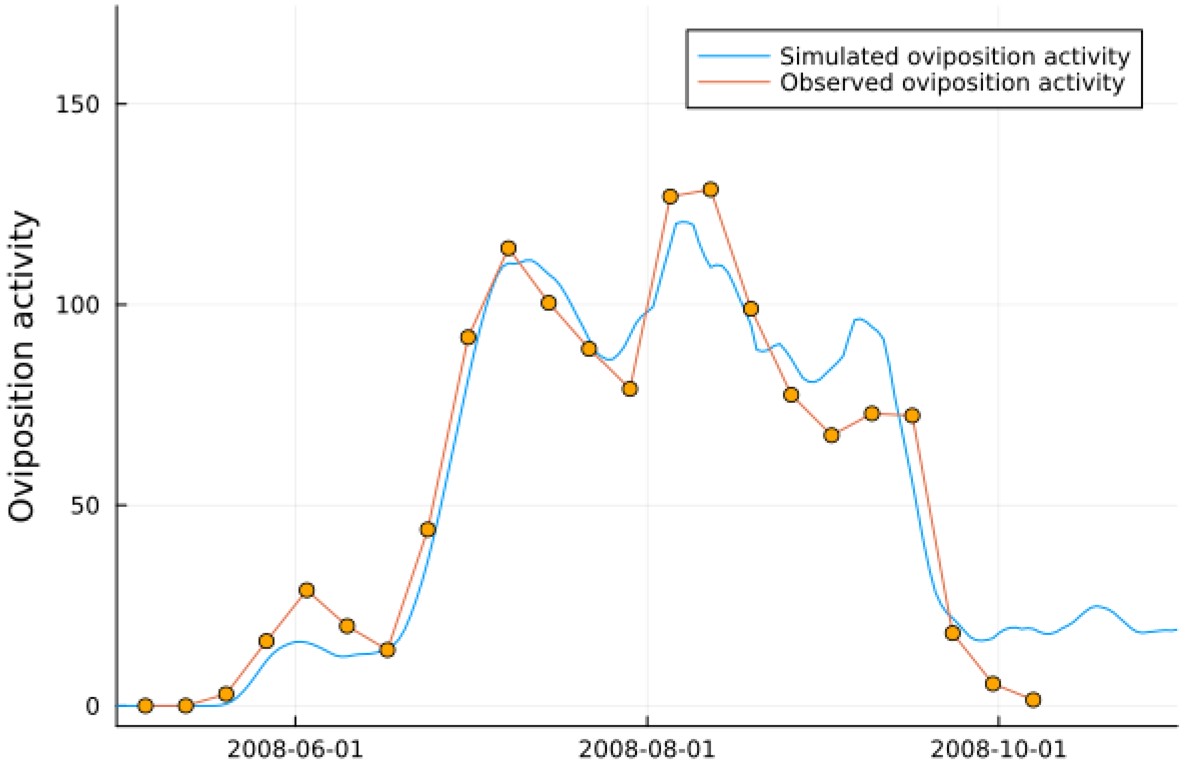
ENVIRONMENTAL CUES

CARRIERI ET AL. (2011)

Rimini, Italy

Temperate climate

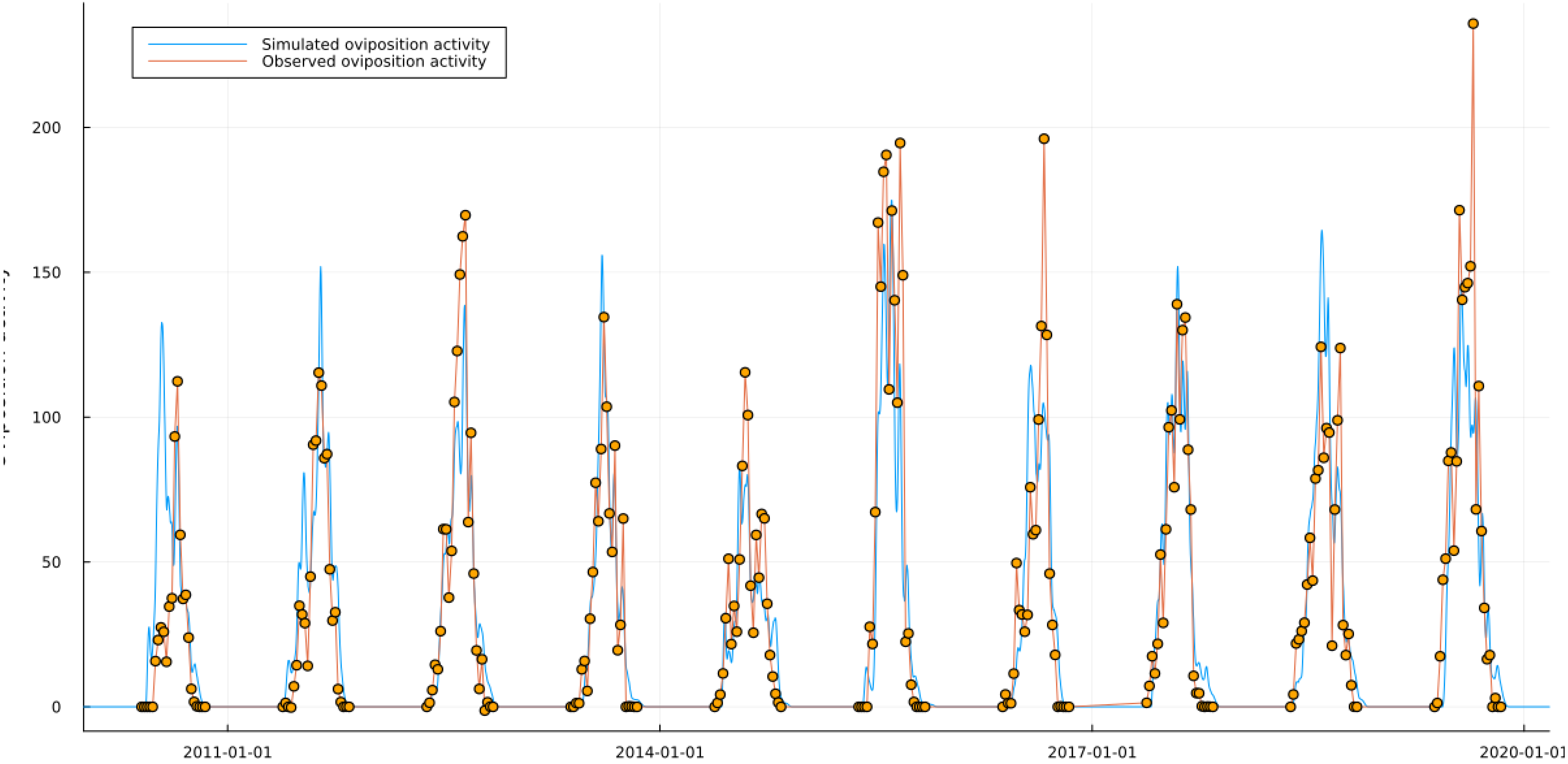
Oviposition activity monitored in 2008



Carrieri, M., Angelini, P., Venturelli, C., Maccagnani, B. & Bellini, R. *Aedes albopictus* (Diptera: Culicidae) Population size survey in the 2007 Chikungunya outbreak area in Italy. II: Estimating epidemic thresholds. *Journal of Medical Entomology* (2012).

TRENTO, ITALY

Oviposition activity monitored over 10 years



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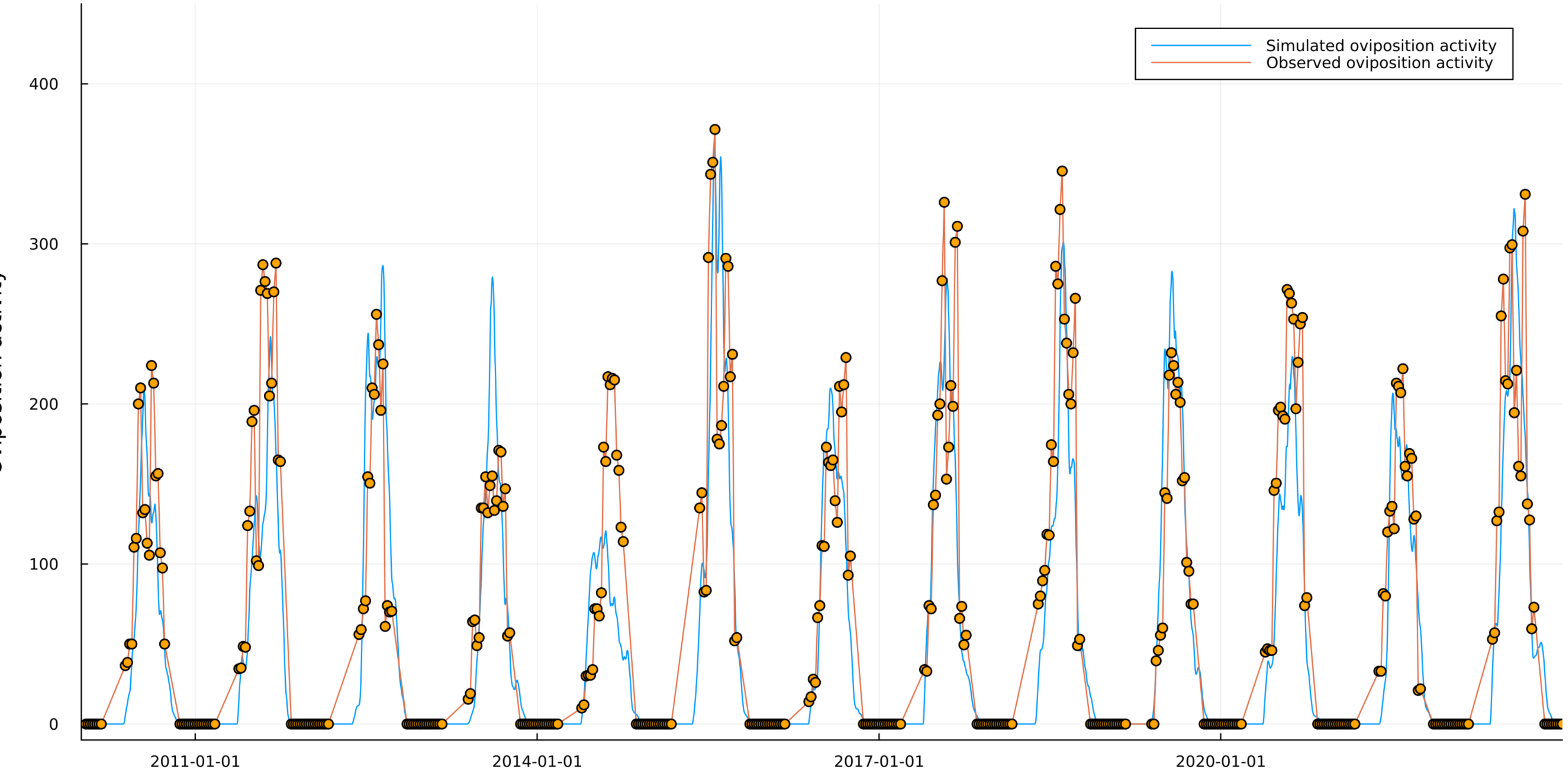
BOLOGNA, ITALY

Oviposition activity monitored over 10 years (taken from VectAbundance)



Simulated oviposition activity
Observed oviposition activity
400
300
200
100
0
2011-01-01
2014-01-01
2017-01-01
2020-01-01
Oviposition activity

WILLIS AND NASCI (1994)

Lake Charles, Louisiana

WILLIS AND NASCI (1994)

Lake Charles, Louisiana

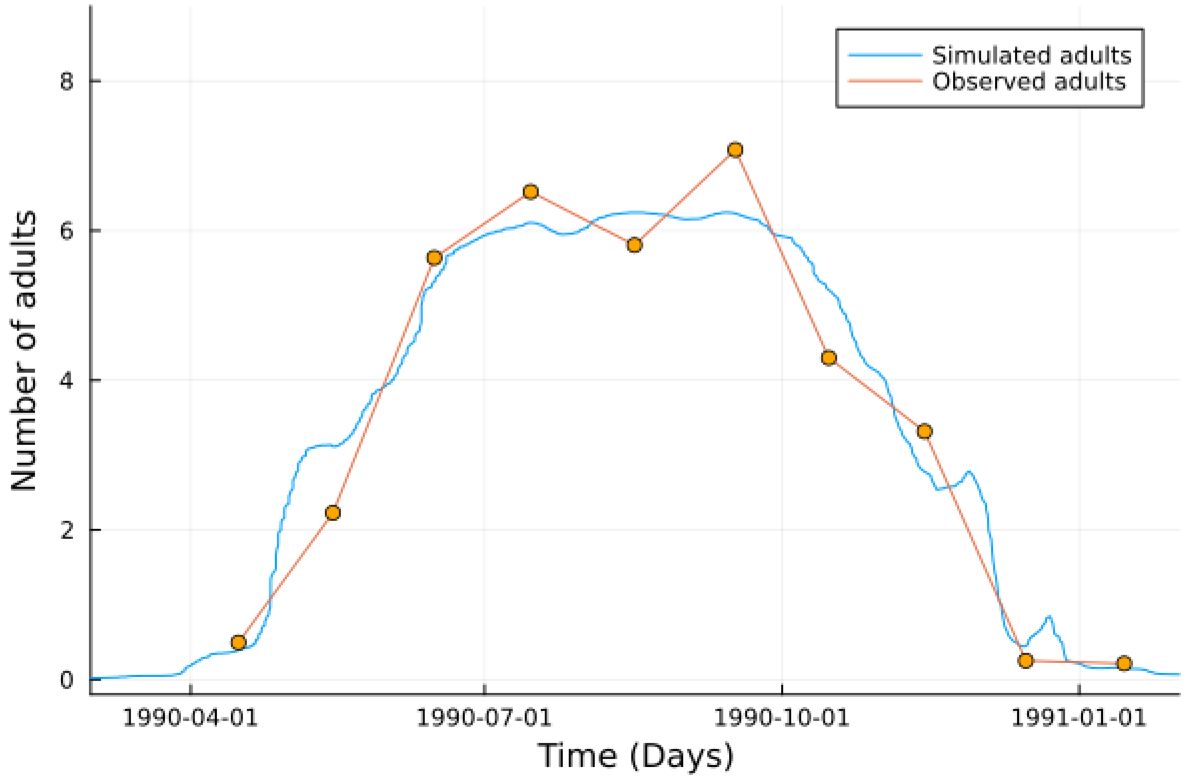
Subtropical climate

WILLIS AND NASCI (1994)

Lake Charles, Louisiana

Subtropical climate

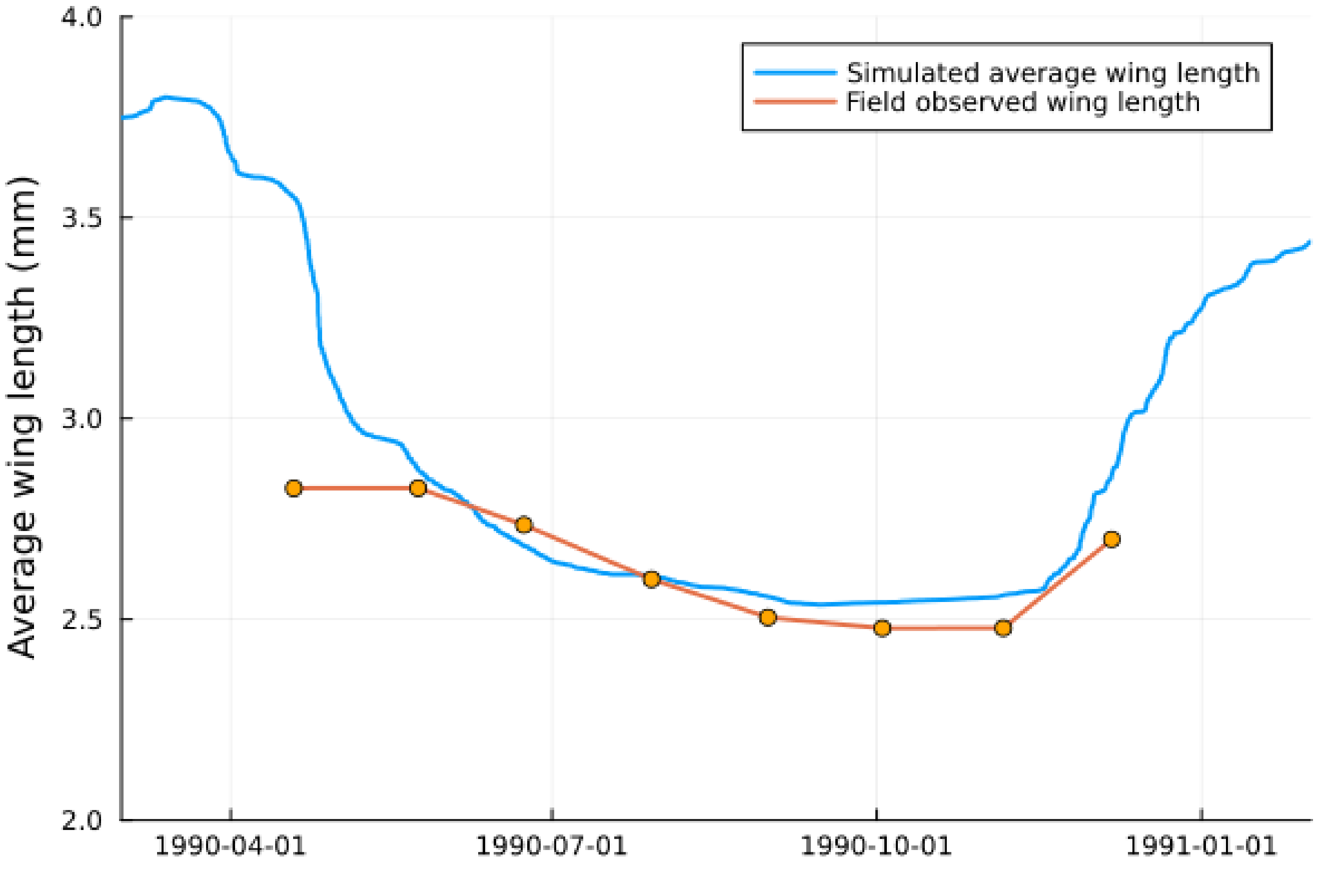
Adults trapped



Willis, F. S. & Nasci, R. S. *Aedes albopictus* (Diptera: Culicidae) population density and structure in southwest Louisiana. *Journal of Medical Entomology* **31**, 594–599 (1994).

WILLIS AND NASCI (1994)

- Lake Charles, Louisiana
- Subtropical climate
- Adults trapped
- Average wing-length of adults measured



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GOUGNA ET AL. (2020)

Saint Paul, Reunion

Tropical climate

Larvae sampled

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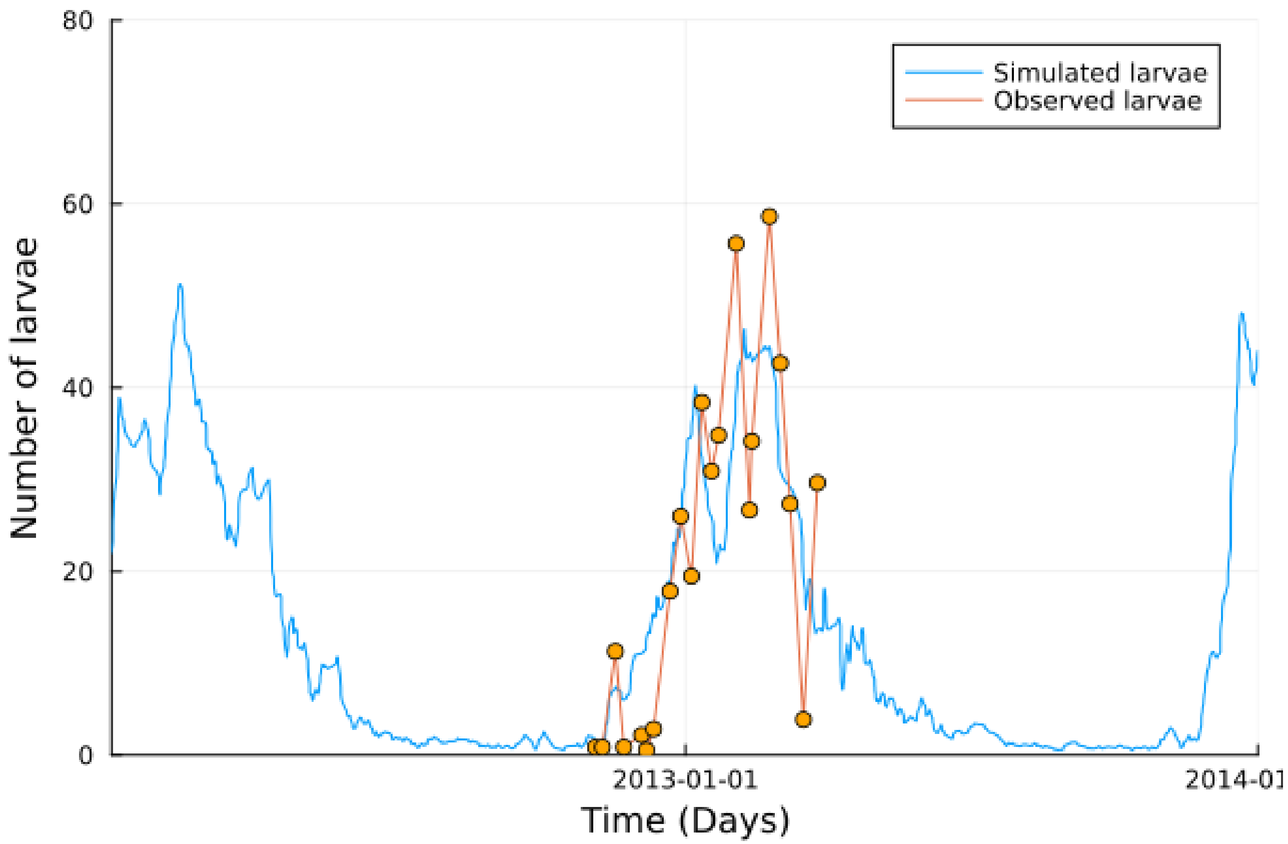

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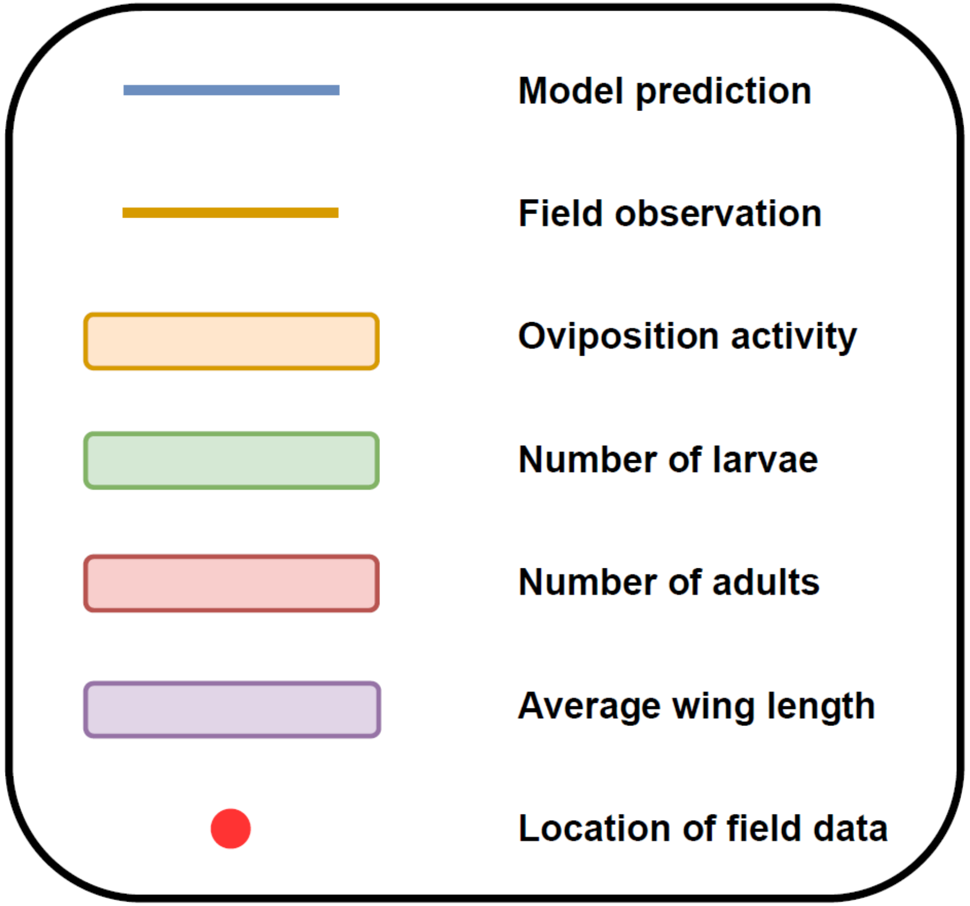

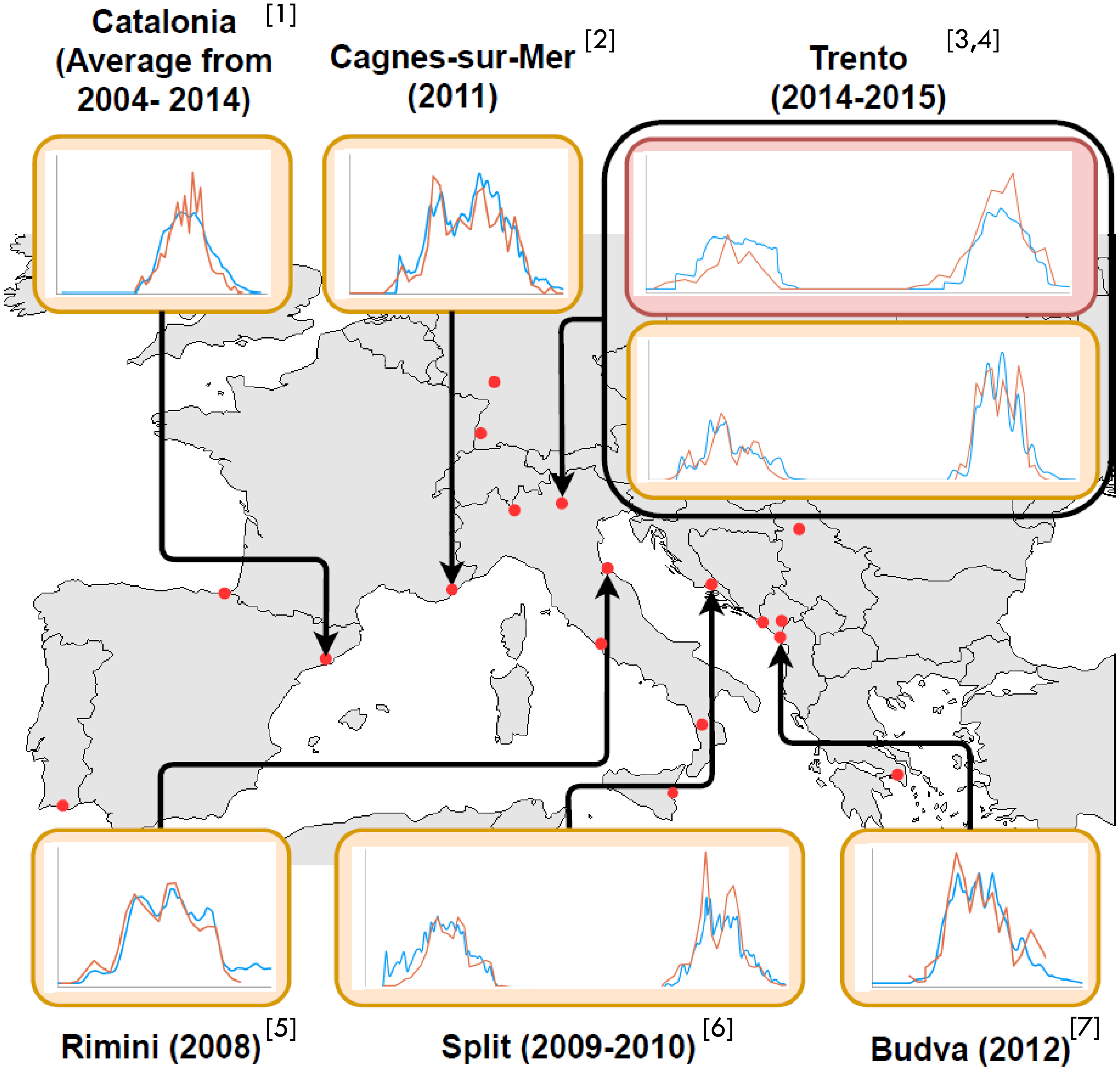

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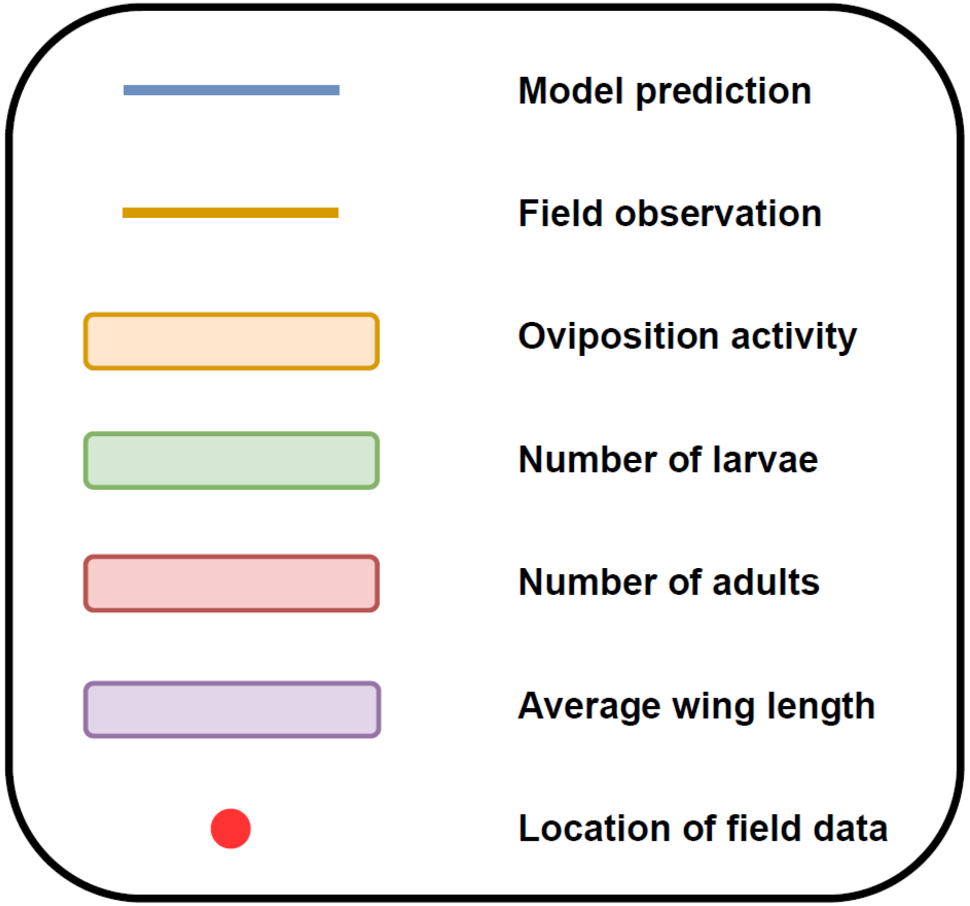

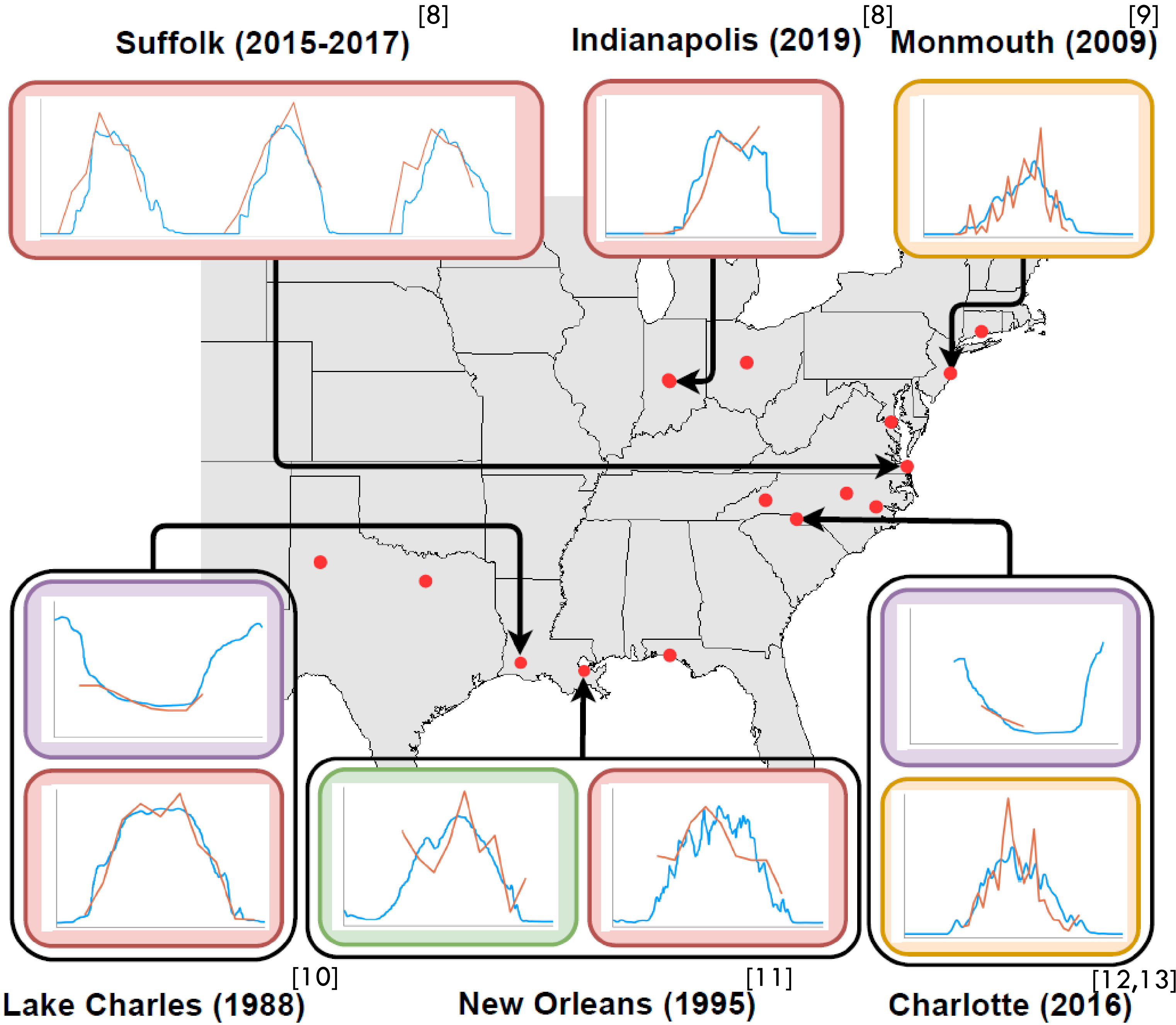

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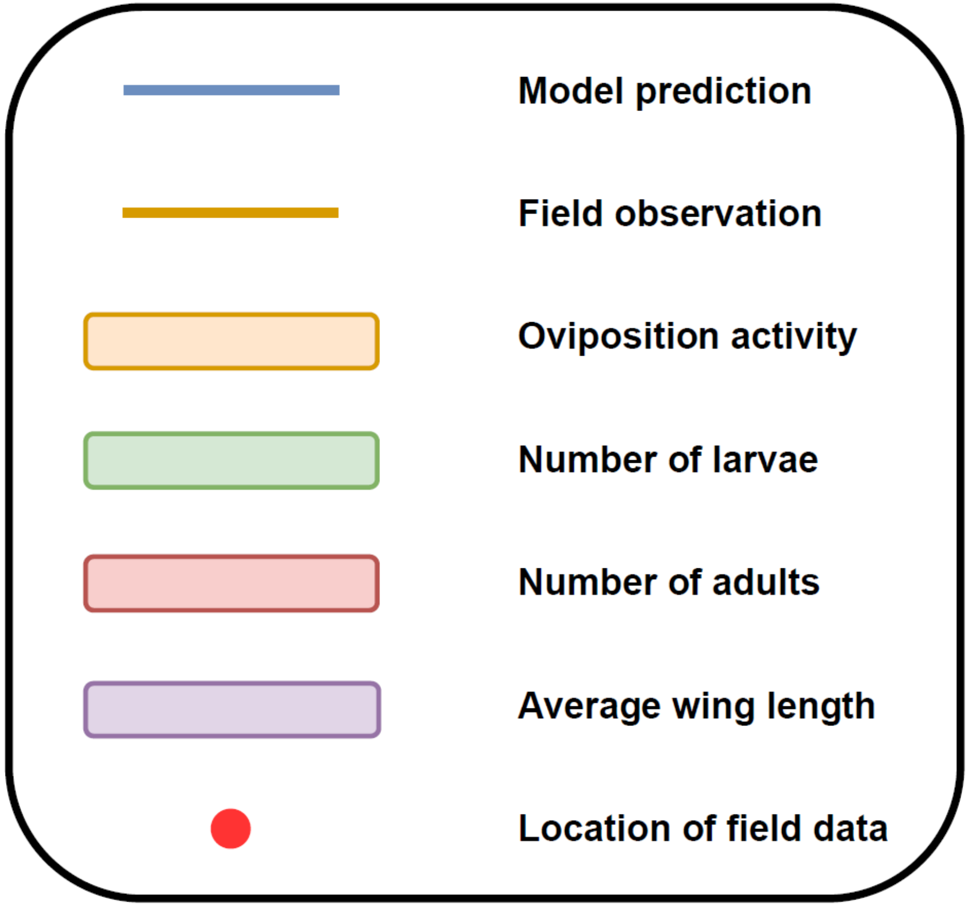

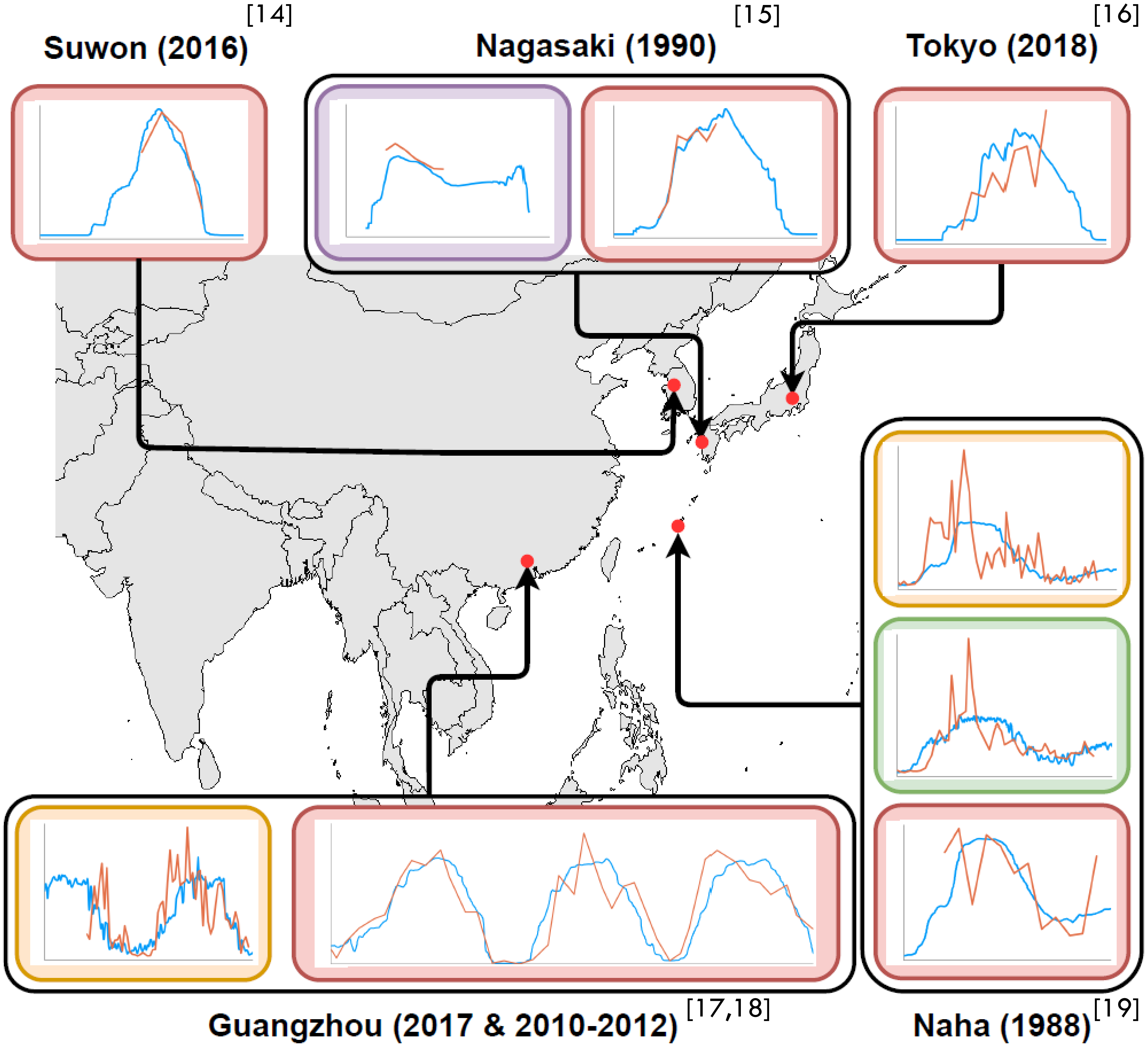

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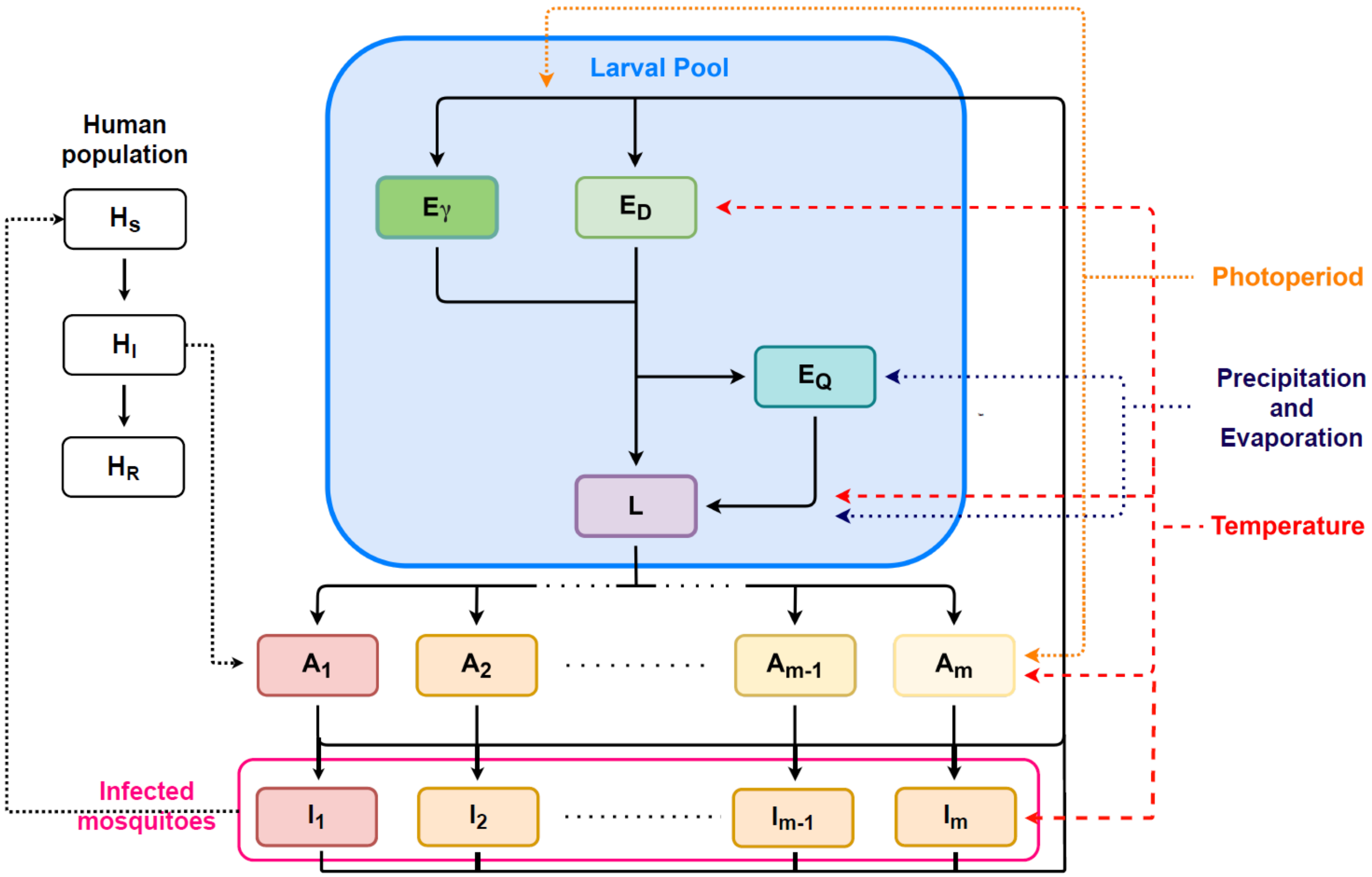
SEIR MODEL

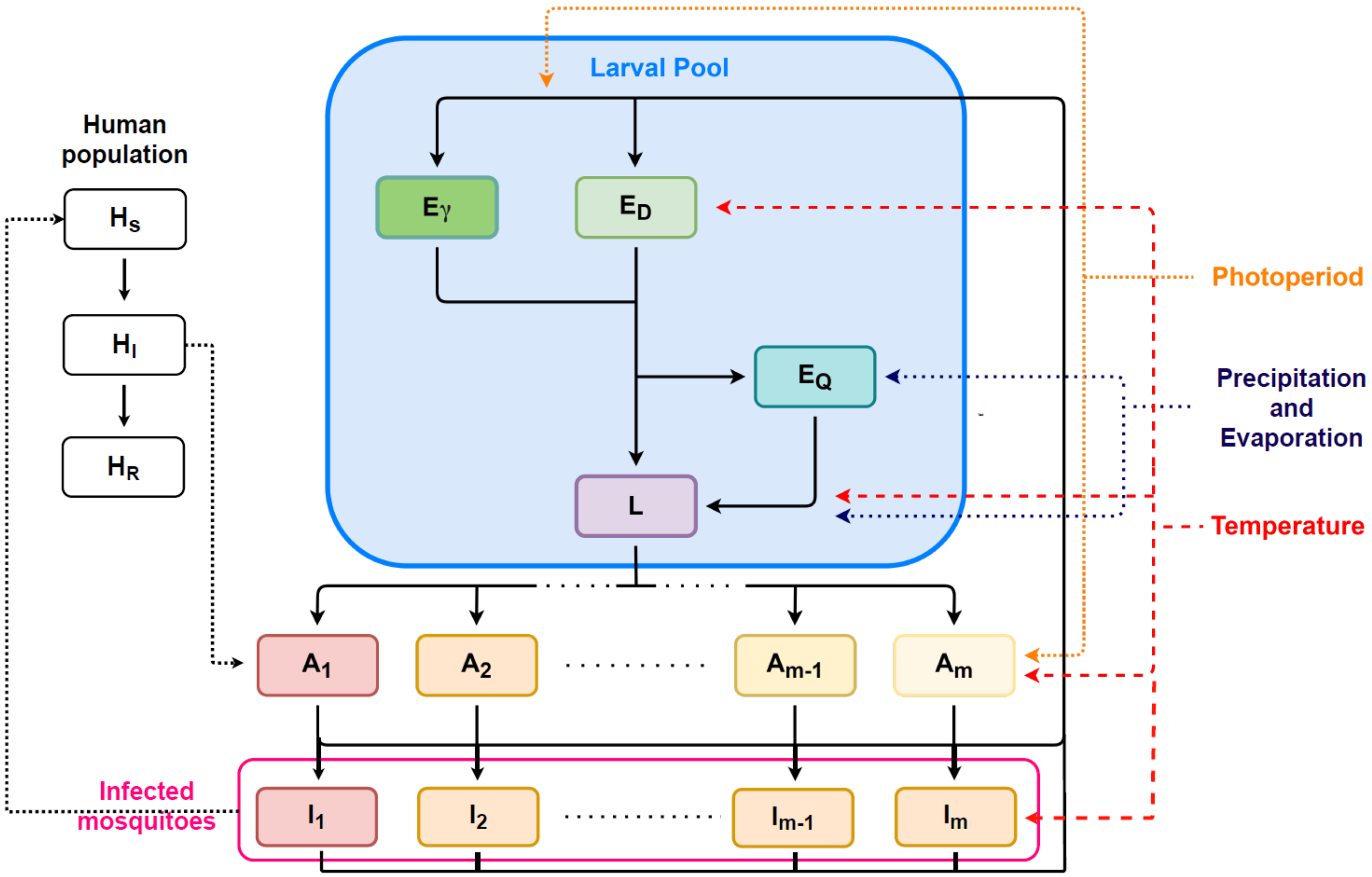
Validate disease dynamics by comparing predictions to historic dengue outbreaks



SEIR MODEL

Validate disease dynamics by comparing predictions to historic dengue outbreaks

We select plausible introduction scenarios for dengue cases based on case reports

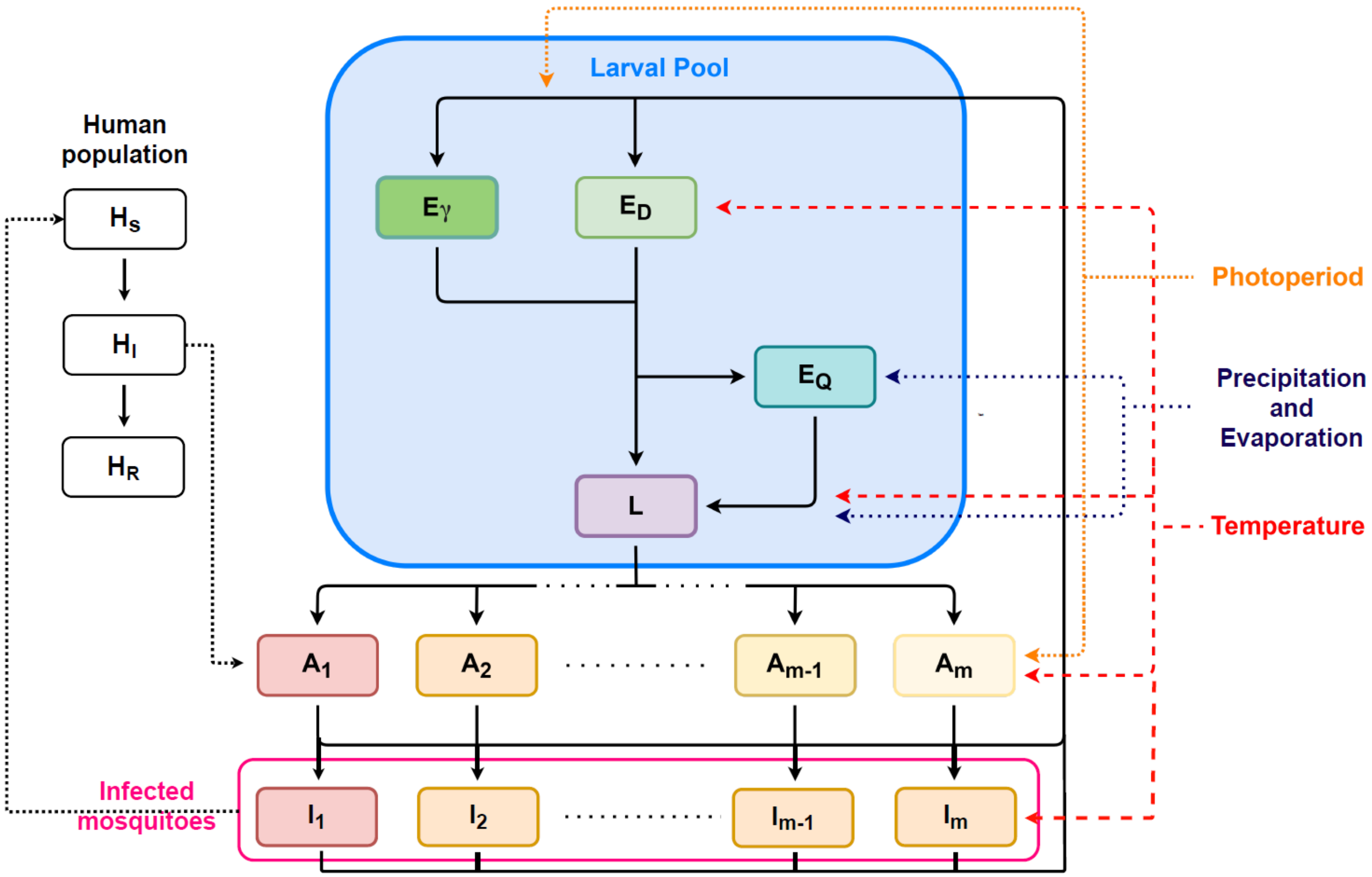


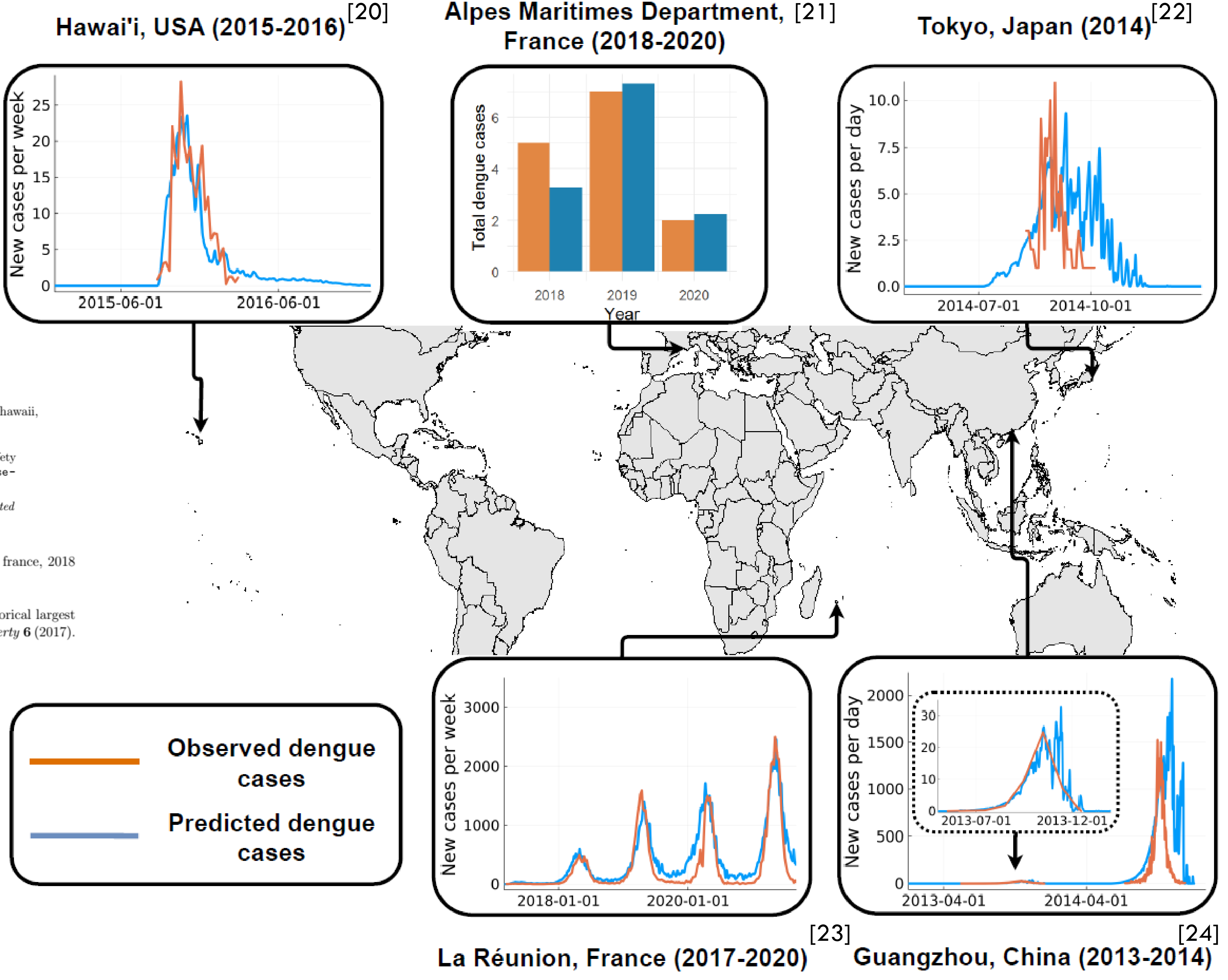
SEIR MODEL

Validate disease dynamics by comparing predictions to historic dengue outbreaks

We select plausible introduction scenarios for dengue cases based on case reports

These are often uncertain





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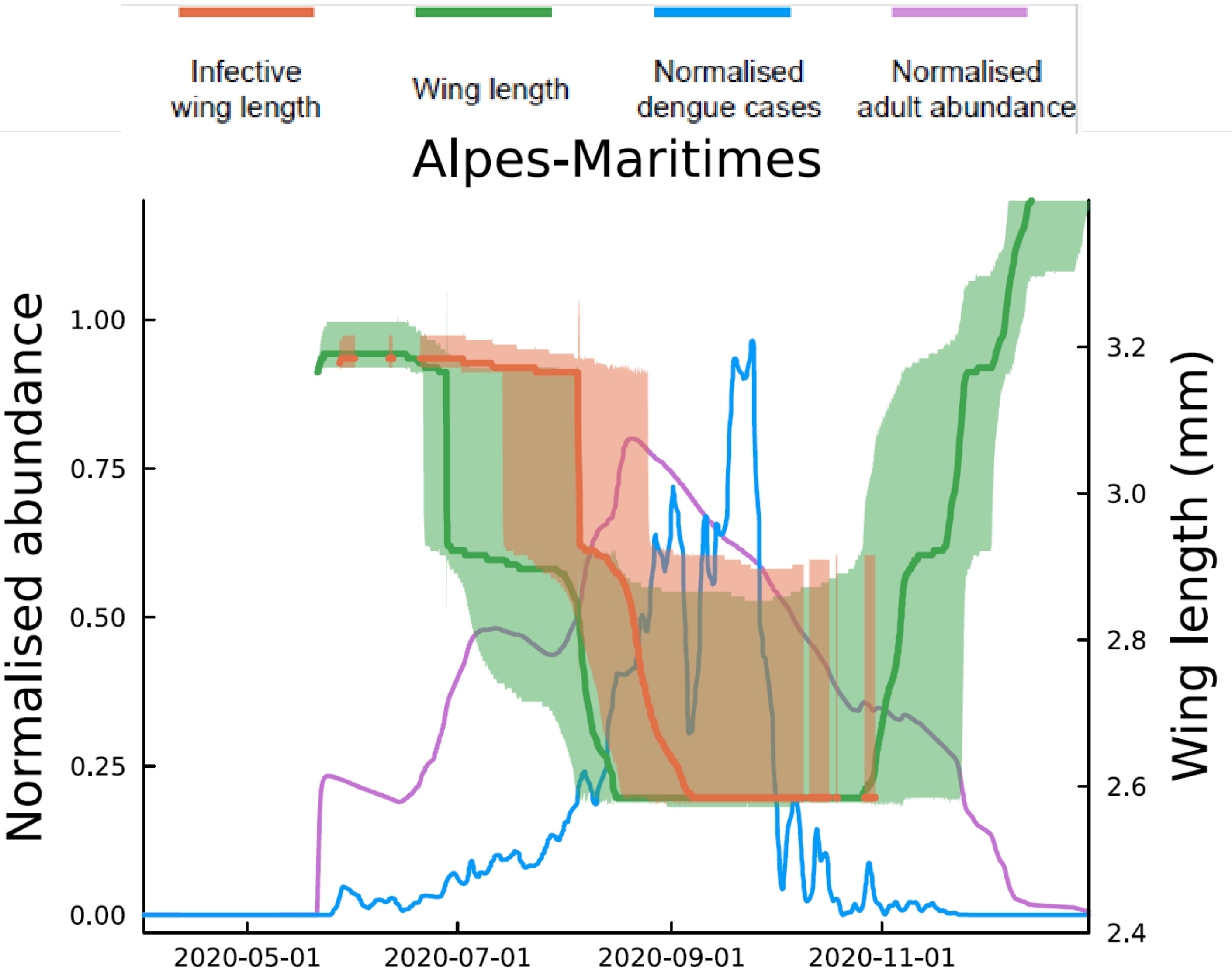
RESULTS

ROLE OF TRAIT VARIATION

The wing-length distribution of infected and uninfected mosquitoes are different



ROLE OF TRAIT VARIATION

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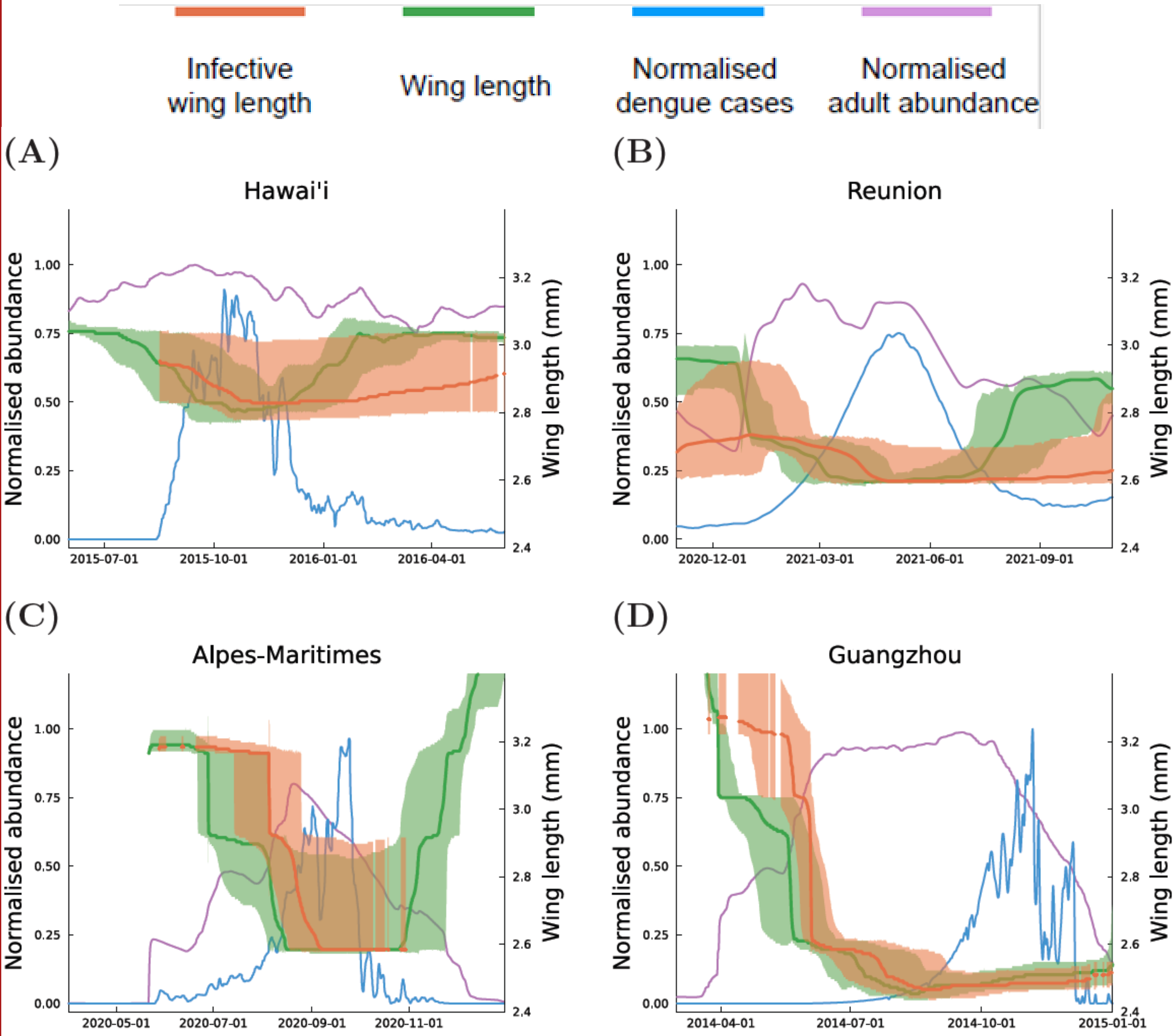
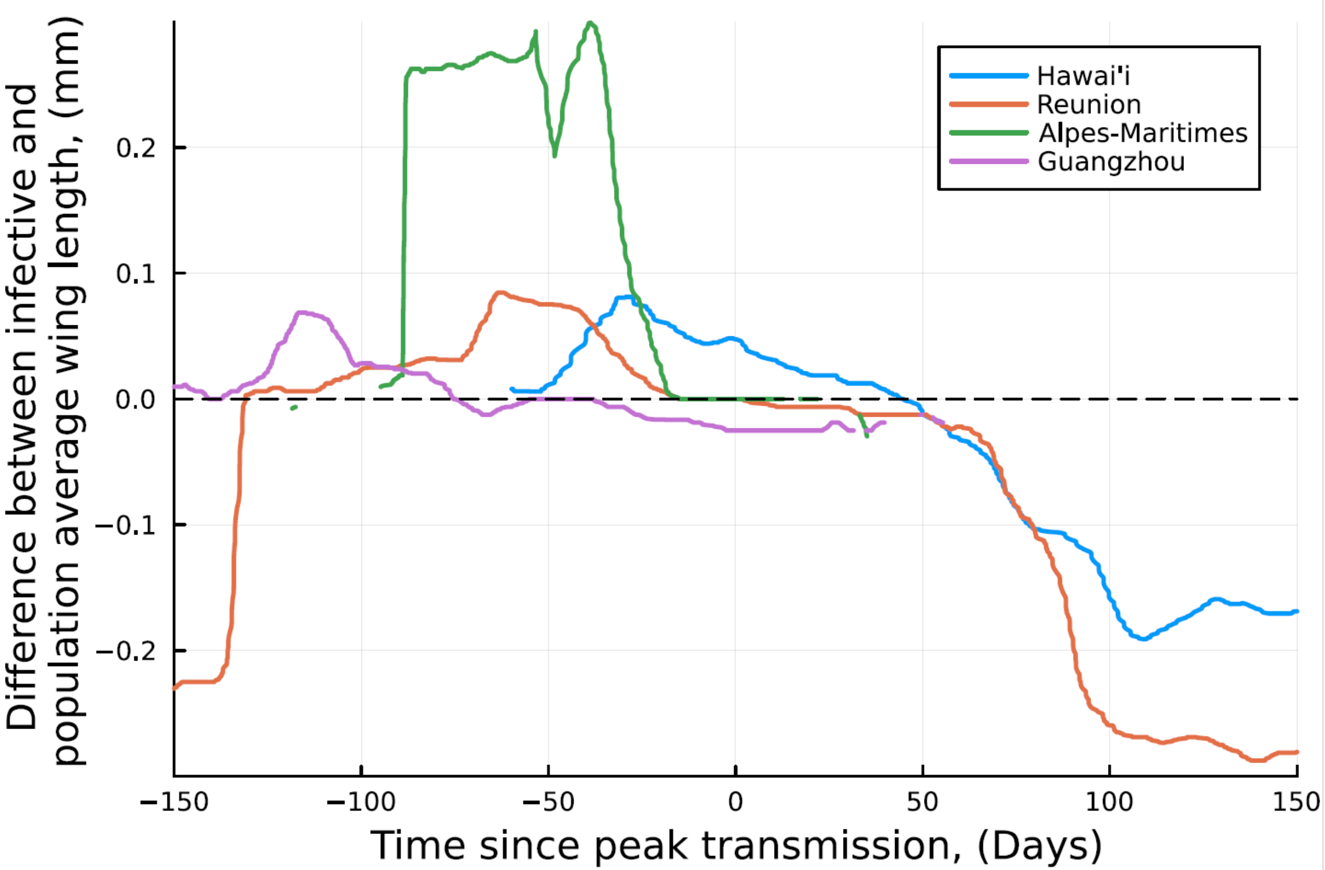


ROLE OF TRAIT VARIATION

The wing-length distribution of infected and uninfected mosquitoes are different

Large mosquitoes drive increase in dengue case numbers before peak infection

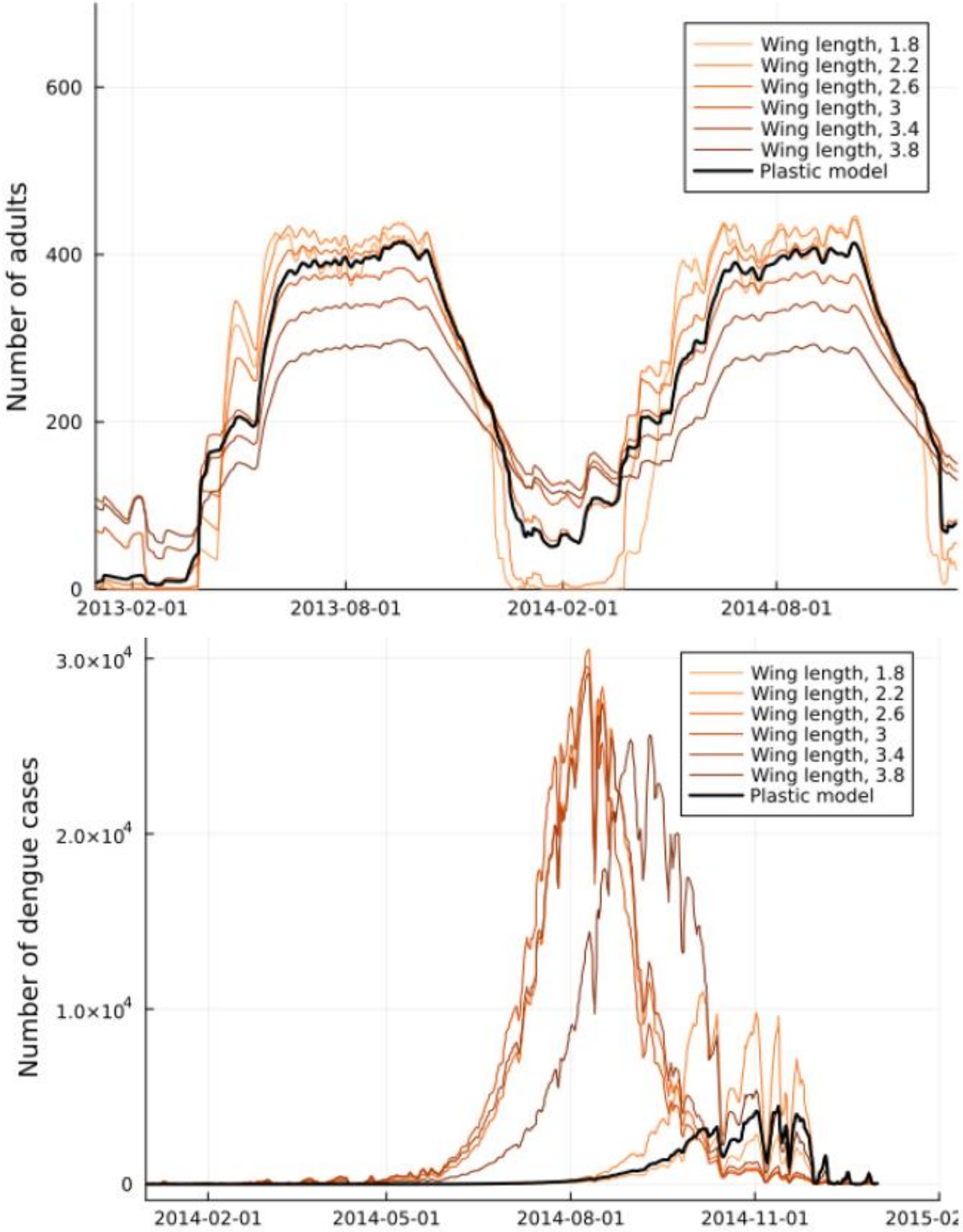


ROLE OF TRAIT VARIATION

The wing-length distribution of infected and uninfected mosquitoes are different

Large mosquitoes drive increase in dengue case numbers before peak infection

Phenotypic plasticity alters disease dynamics



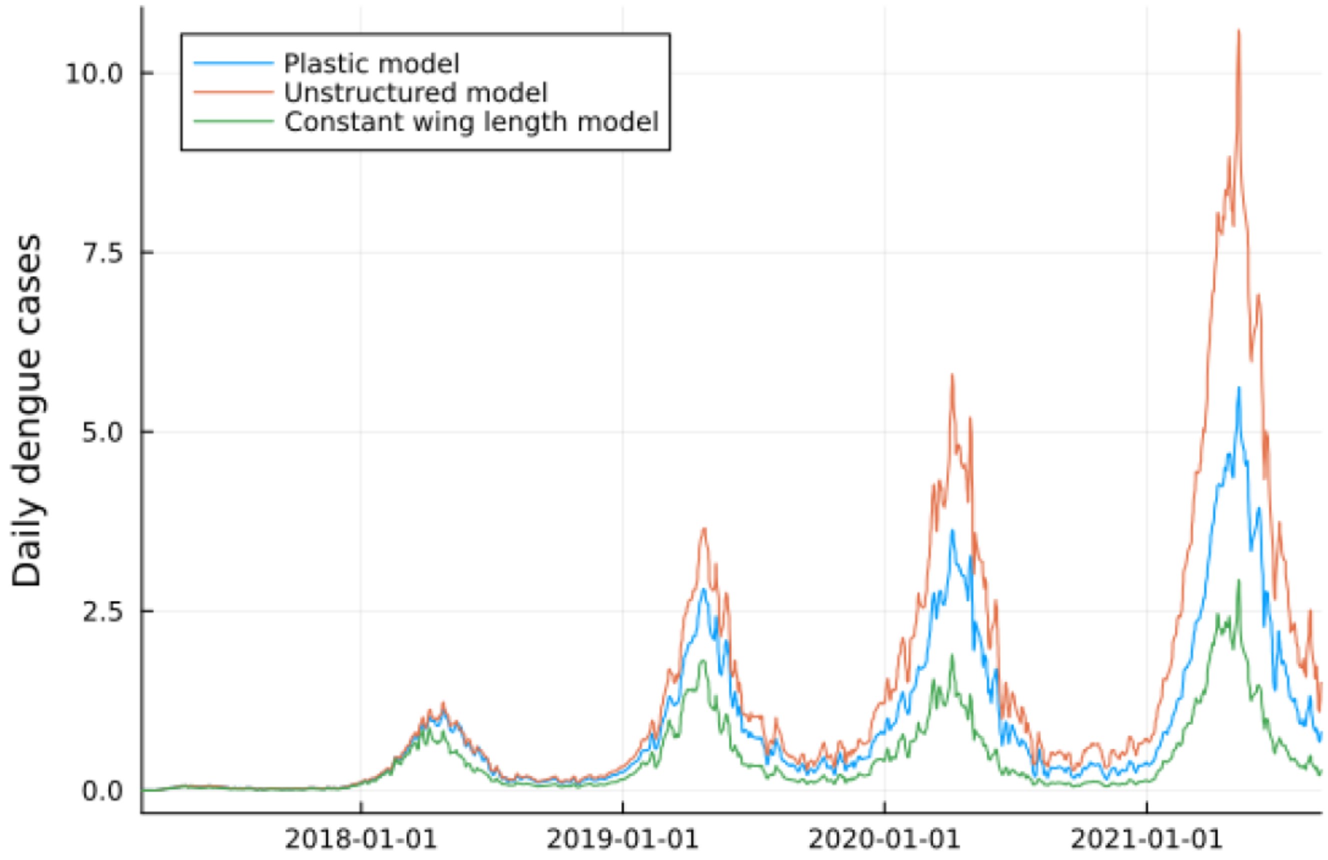
ROLE OF TRAIT VARIATION

The wing-length distribution of infected and uninfected mosquitoes are different

Large mosquitoes drive increase in dengue case numbers before peak infection

Phenotypic plasticity alters disease dynamics

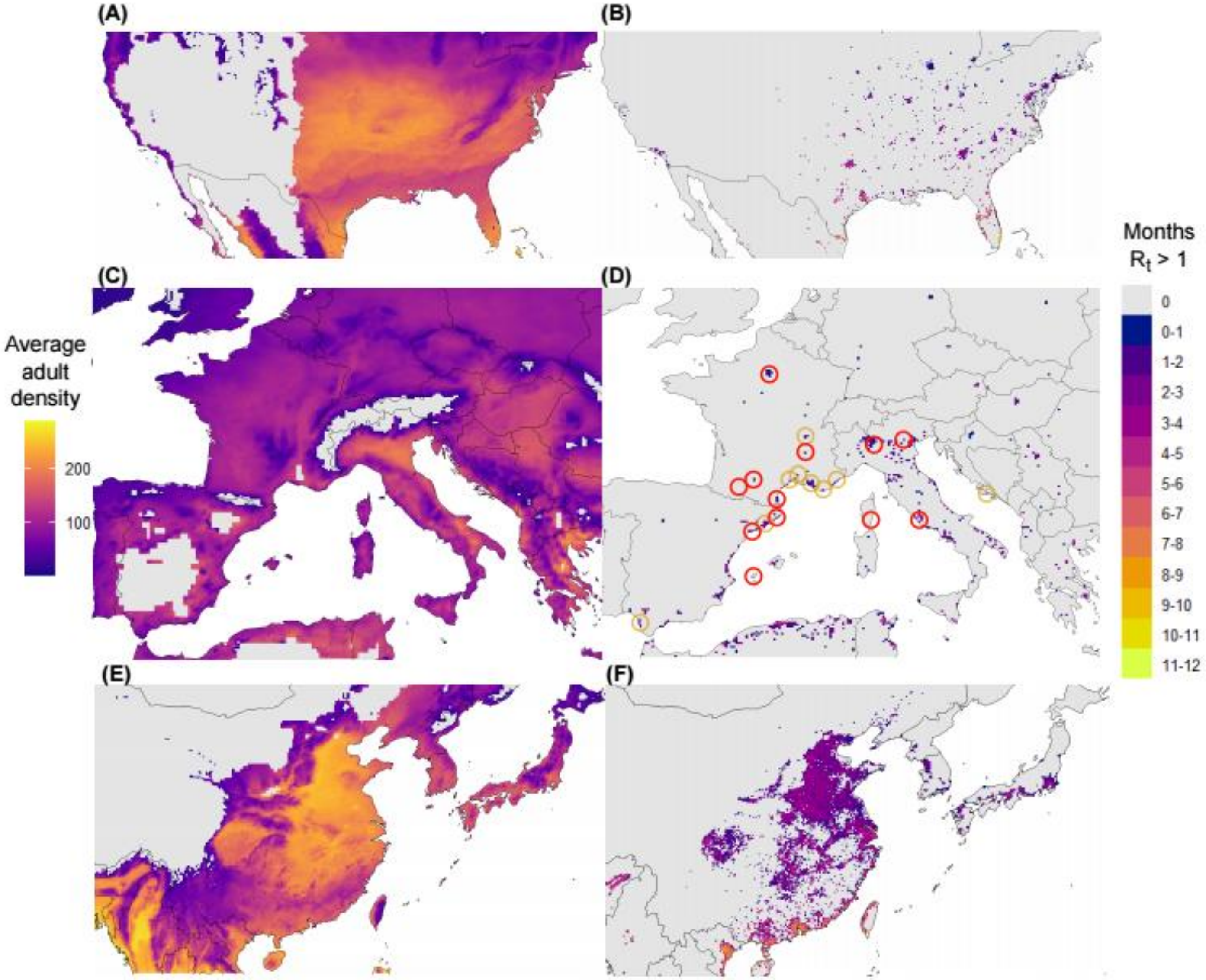
Trait structure alters disease dynamics



GLOBAL RISK

We simulate the model from 2015-2019 and output average months Rt > 1

$$R_{t-\tau_{\mathrm{EIP}}(t)} = \left[\sum_{j=1}^{m}\left(\int_{t}^{t+\tau_{\mathrm{REC}}} \frac{\frac{g_{\mathrm{EIP}}(s)}{g_{\mathrm{EIP}}(s-\tau_{\mathrm{EIP}}(s))} b(s-\tau_{\mathrm{EIP}}(s))h_v(s-\tau_{\mathrm{EIP}}(s))2\kappa A_j(s-\tau_{\mathrm{EIP}}(s))S_{\mathrm{EIP}_j}(s)}{H_T} \times \left(\int_{s}^{s+1/\delta_{A_j}(s)} \frac{b(u)v_h(u)H_s(u)}{H_T} du\right) ds\right)\right]^{\frac{1}{2}}.$$



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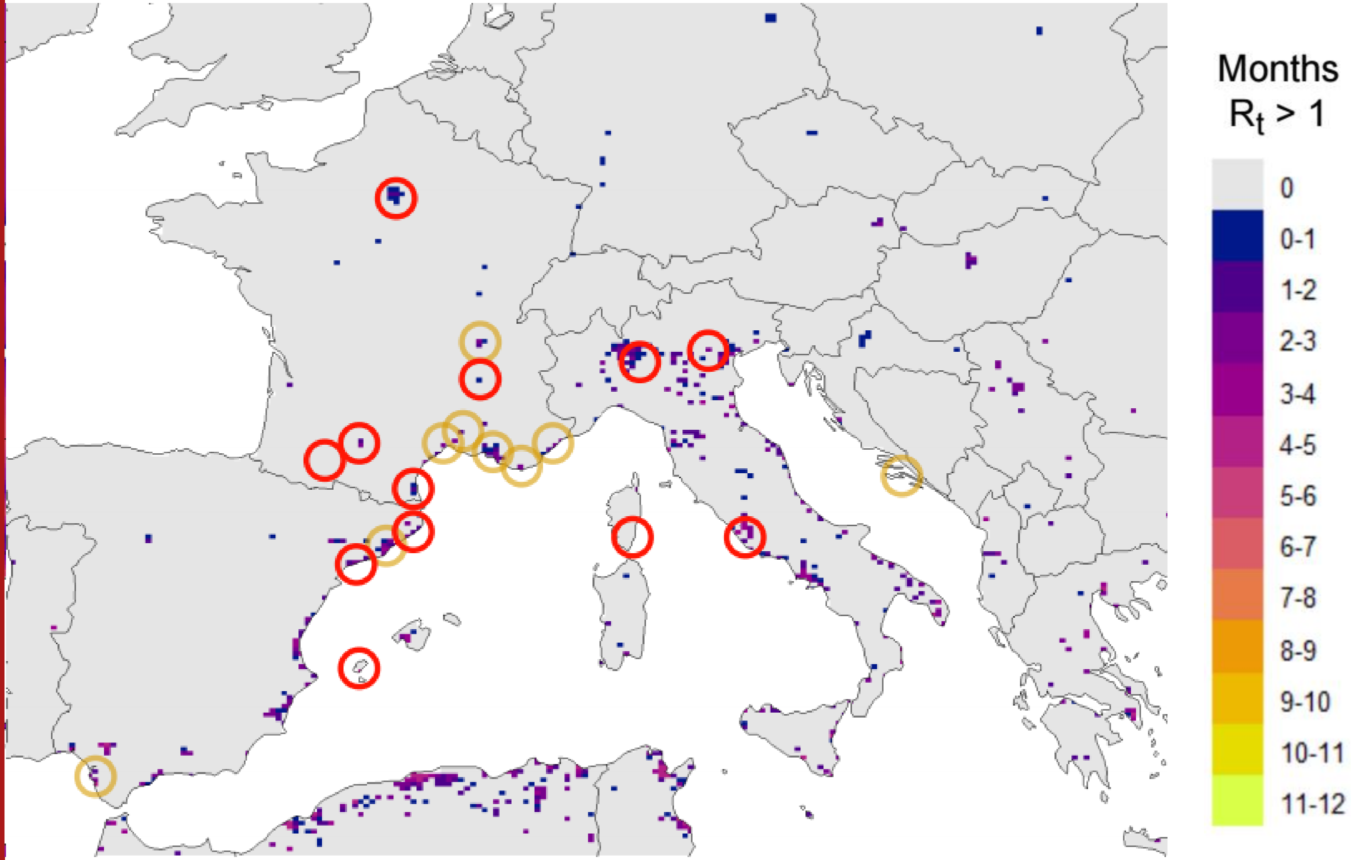

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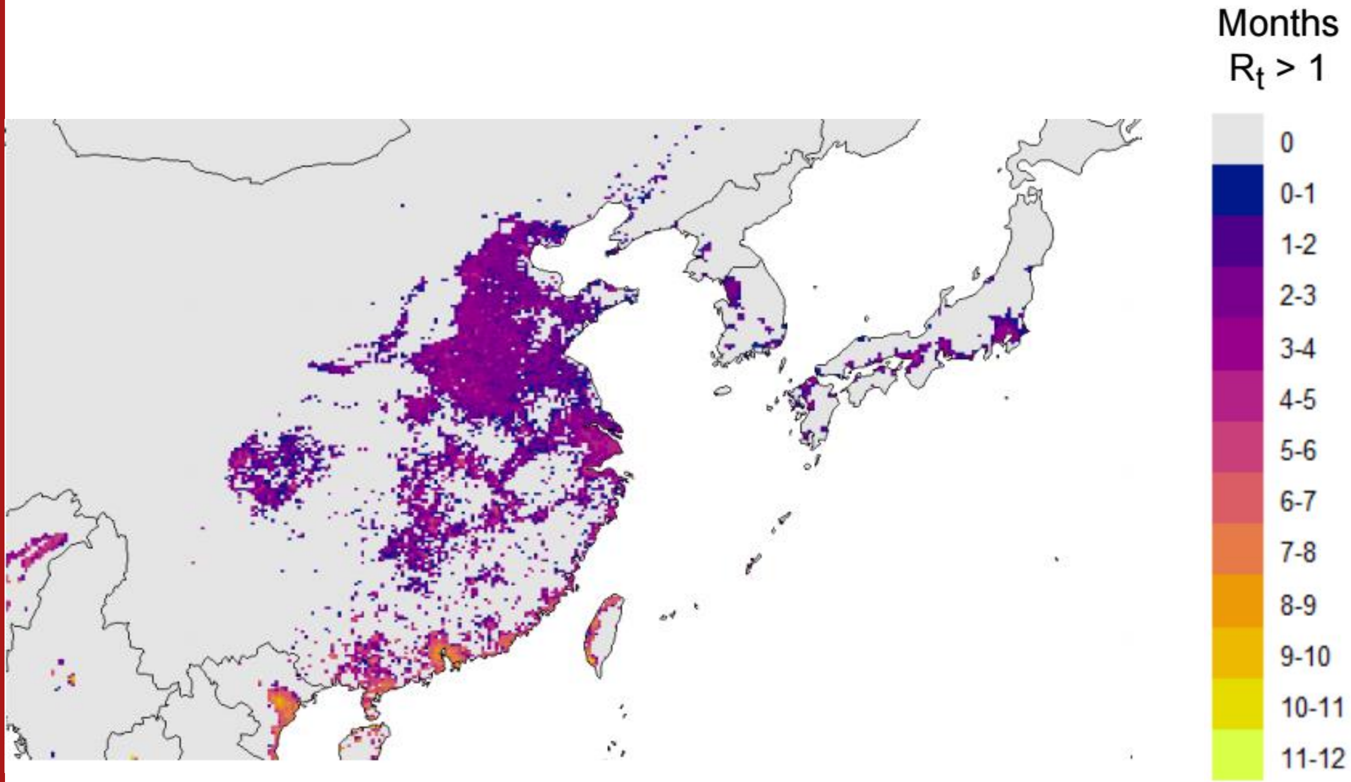

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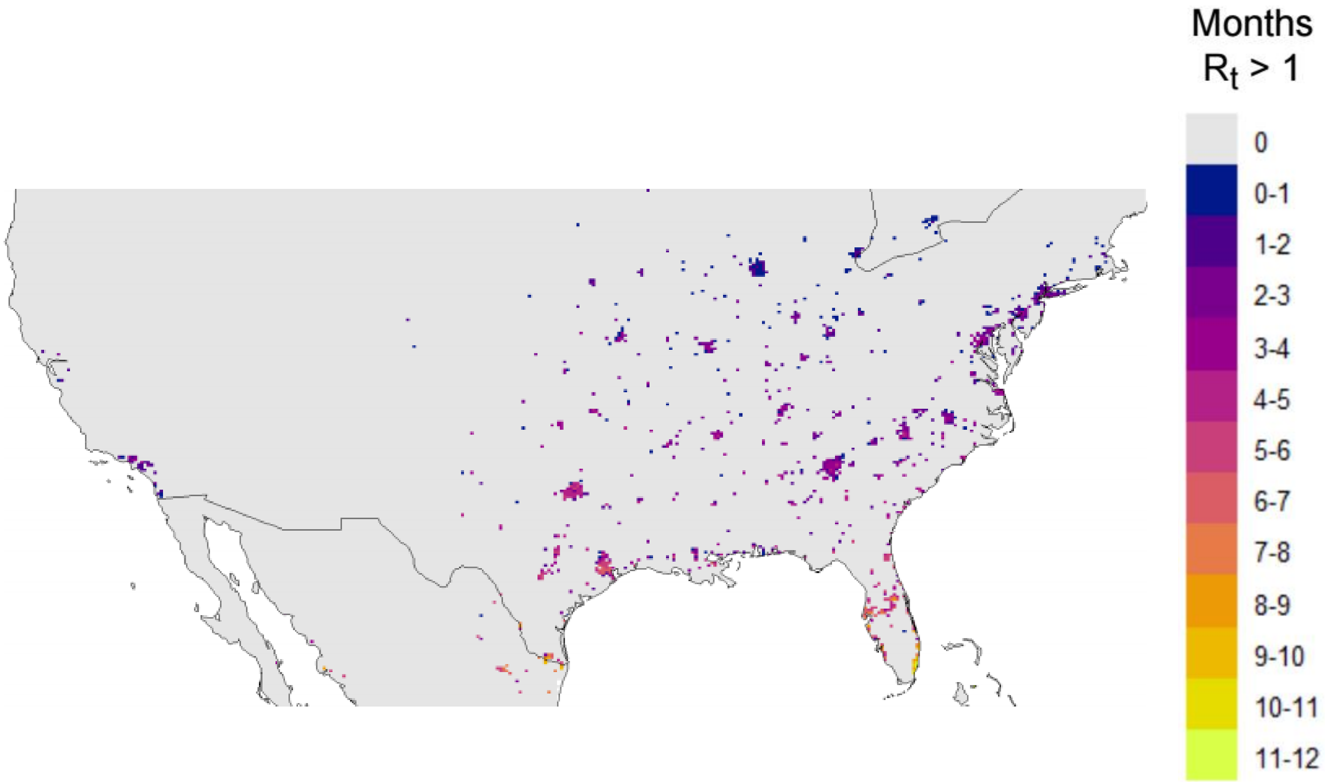

CONCLUSIONS

We have produced a globally validated model of mosquito and disease dynamics

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This can be used to produce accurate predictions of relative disease risk

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Mosquito trait variation in response to developmental environmental experience alters disease dynamics

TICKSOLVE

STAGE-STRUCTURED DELAY-DIFFERENTIAL EQUATIONS FOR *IXODES RICINUS*

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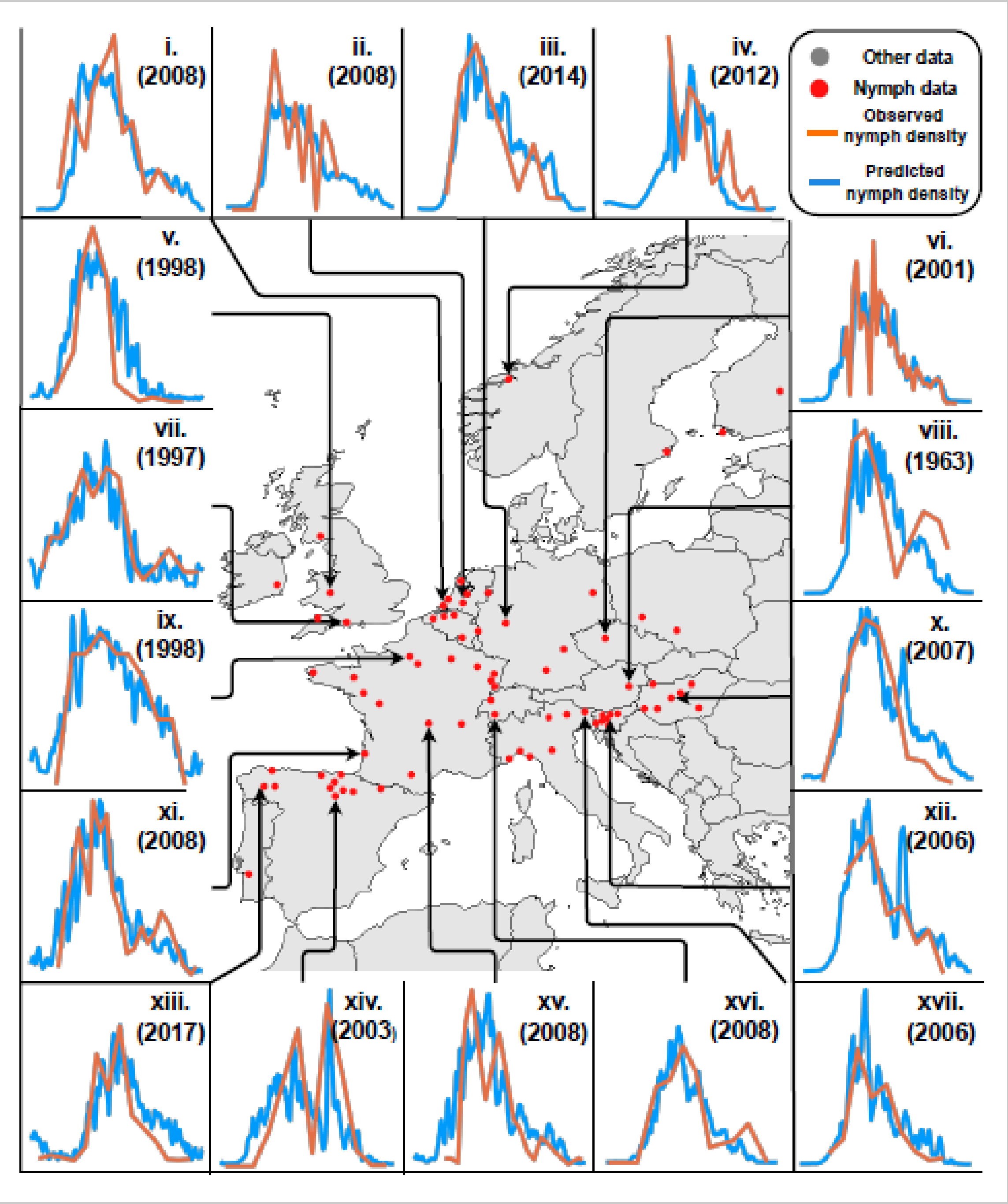

THANKS FOR LISTENING!

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UK Centre for Ecology & Hydrology

THE MODEL

E_γ (t) – Active eggs

E_D (t) – Diapausing eggs

E_Q (t) – Quiescent eggs

L(t) – Larvae

A_j (t) – Adults in environmental class j

R – Recruitment terms

M – Maturation terms

P – Survival

δ – Mortality rate

τ – Stage duration

$$\frac{dE_\gamma(t)}{dt} = R_{E_\gamma}(t) - M_{E_\gamma}(t) - \delta_{E_\gamma}(t)E_\gamma(t),$$

$$\frac{dE_D(t)}{dt} = R_{E_D}(t) - M_{E_D}(t) - \delta_{E_D}(t)E_D(t),$$

$$\frac{dE_Q(t)}{dt} = R_{E_Q}(t) - M_{E_Q}(t) - \delta_{E_Q}(t)E_Q(t),$$

$$\frac{dL(t)}{dt} = R_L(t) - M_L(t) - \delta_L(t)L(t),$$

$$\frac{dA_j(t)}{dt} = R_{A_j}(t) - M_{A_j}(t) - \delta_{A_j}(t)A_j(t), \quad \text{for } \ \mathrm{j} \in 1, \ldots, \mathrm{m}$$

$$\frac{dI_j(t)}{dt} = M_{A_j}(t) - \delta_{I_j}(t)I_j(t), \quad \text{for } \ \mathrm{j} \in 1, \ldots, \mathrm{m}.$$

RATE OF DEVELOPMENT

$$\frac{d\tau_{E_\gamma}(t)}{dt} = 1 - \frac{g_{E_\gamma}(t)}{g_{E_\gamma}(t - \tau_{E_\gamma}(t))},$$

$$\frac{d\tau_L(t)}{dt} = 1 - \frac{g_L(t)}{g_L(t - \tau_L(t))},$$

$$\frac{d\tau_P(t)}{dt} = 1 - \frac{g_P(t)}{g_P(t - \tau_P(t))},$$

$$\frac{d\tau_{\mathrm{EIP}}(t)}{dt} = 1 - \frac{g_{\mathrm{EIP}}(t)}{g_{\mathrm{EIP}}(t - \tau_{\mathrm{EIP}}(t))}.$$

SURVIVAL EQUATIONS

$$\frac{dS_{E_\gamma}(t)}{dt} = S_{E_\gamma}(t)\left(\frac{g_{E_\gamma}(t)\delta_{E_\gamma}(t-\tau_{E_\gamma}(t))}{g_{E_\gamma}(t-\tau_{E_\gamma}(t))} - \delta_{E_\gamma}(t)\right),$$

$$\frac{dS_L(t)}{dt} = S_L(t)\left(\frac{g_L(t)\delta_L(t-\tau_L(t))}{g_L(t-\tau_L(t))} - \delta_L(t)\right),$$

$$\frac{dS_P(t)}{dt} = S_P(t)\left(\frac{g_P(t)\delta_P(t-\tau_P(t))}{g_P(t-\tau_P(t))} - \delta_P(t)\right), \qquad (63)$$

$$\frac{dS_{\mathrm{EIP}_j}(t)}{dt} = S_{\mathrm{EIP}_j}(t)\left(\frac{g_{\mathrm{EIP}}(t)\delta_{A_j}(t-\tau_{\mathrm{EIP}}(t))}{g_{\mathrm{EIP}}(t-\tau_{\mathrm{EIP}}(t))} - \delta_{A_j}(t)\right), \quad \text{for } j \in 1,\dots,m.$$

TRANSITION FUNCTIONS

$$\bar{\alpha}(t) = \frac{\int_{t-\tau_P(t)-\tau_L(t-\tau_P(t))}^{t-\tau_P(t)} \frac{F(s)}{L(s)} ds}{\tau_L(t-\tau_P(t))}.$$

$$w_j(T_{avg}(t), \bar{\alpha}(t)) = \begin{cases} 1, & \text{if } g(w(T_{avg}(t), \bar{\alpha})(t)) = w_j \\ 0, & \text{otherwise} \end{cases}$$

RT

$$
\begin{aligned}
R_{t-\tau_{\mathrm{EIP}}(t)} \quad &= \quad \left[\sum_{j=1}^{m} \left(\int_{t}^{t+\tau_{\mathrm{REC}}} \frac{\frac{g_{\mathrm{EIP}}(s)}{g_{\mathrm{EIP}}(s-\tau_{\mathrm{EIP}}(s))} b(s-\tau_{\mathrm{EIP}}(s)) h_{v}(s-\tau_{\mathrm{EIP}}(s)) 2\kappa A_{j}(s-\tau_{\mathrm{EIP}}(s)) S_{\mathrm{EIP}_j}(s)}{H_T} \right. \right. \\
&\times \quad \left. \left. \left(\int_{s}^{s+1/\delta_{A_j}(s)} \frac{b(u) v_h(u) H_s(u)}{H_T} du \right) ds \right) \right]^{\frac{1}{2}}.
\end{aligned}
$$