Sciences Economiques et Sociales de la Santé
& Traitement de l'Information Médicale

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Vector-borne transmission dynamics and environmental change: from data to process.

June 2020

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Vector-borne transmission dynamics and environmental change: from data to process.

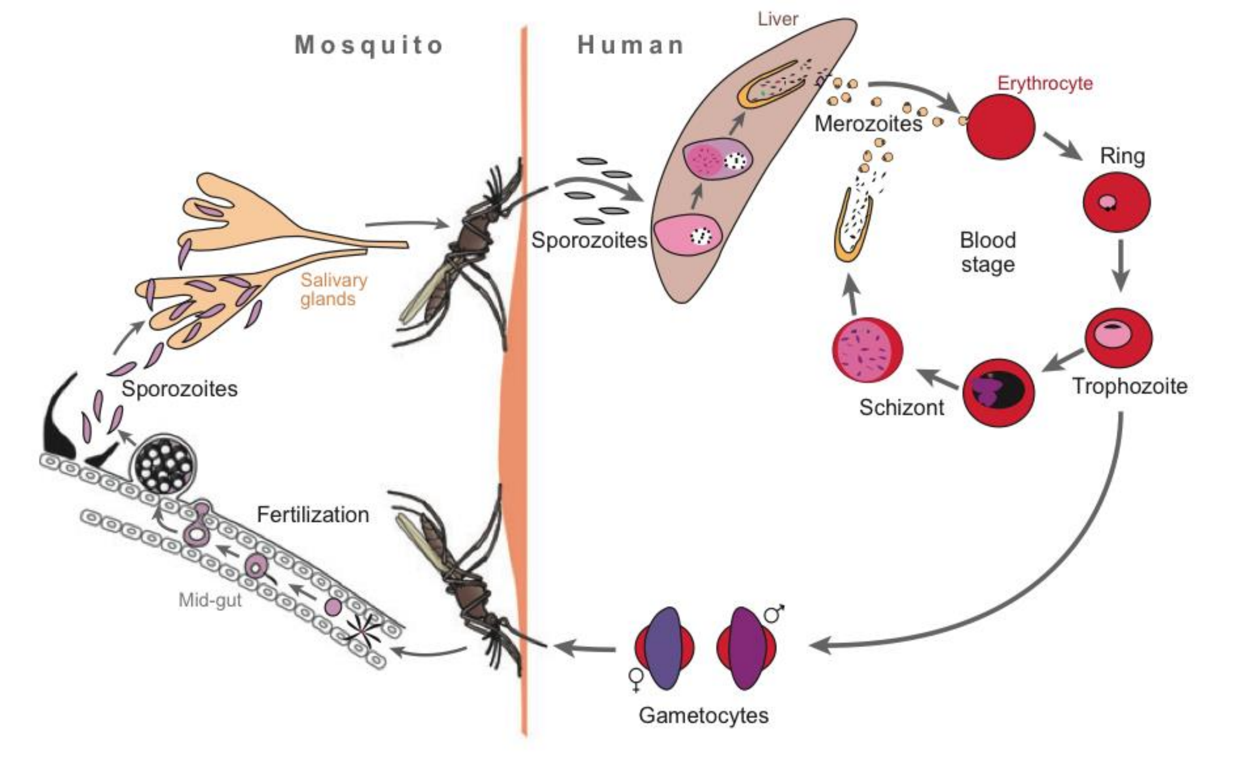
Mercedes Pascual

University of Chicago

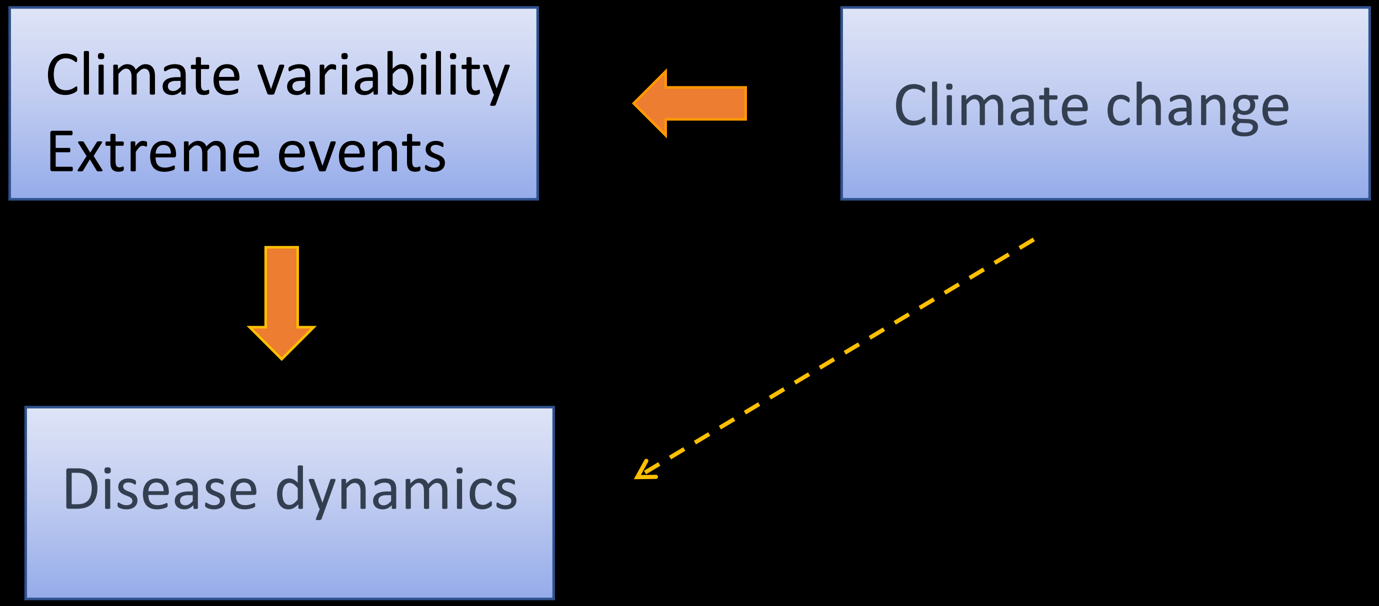
and

The Santa Fe Institute

Plasmodium falciparum malaria

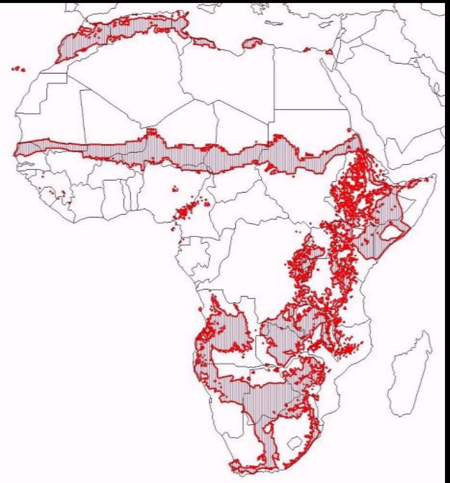


From Scherf 2008
Annual Rev. Microbiology

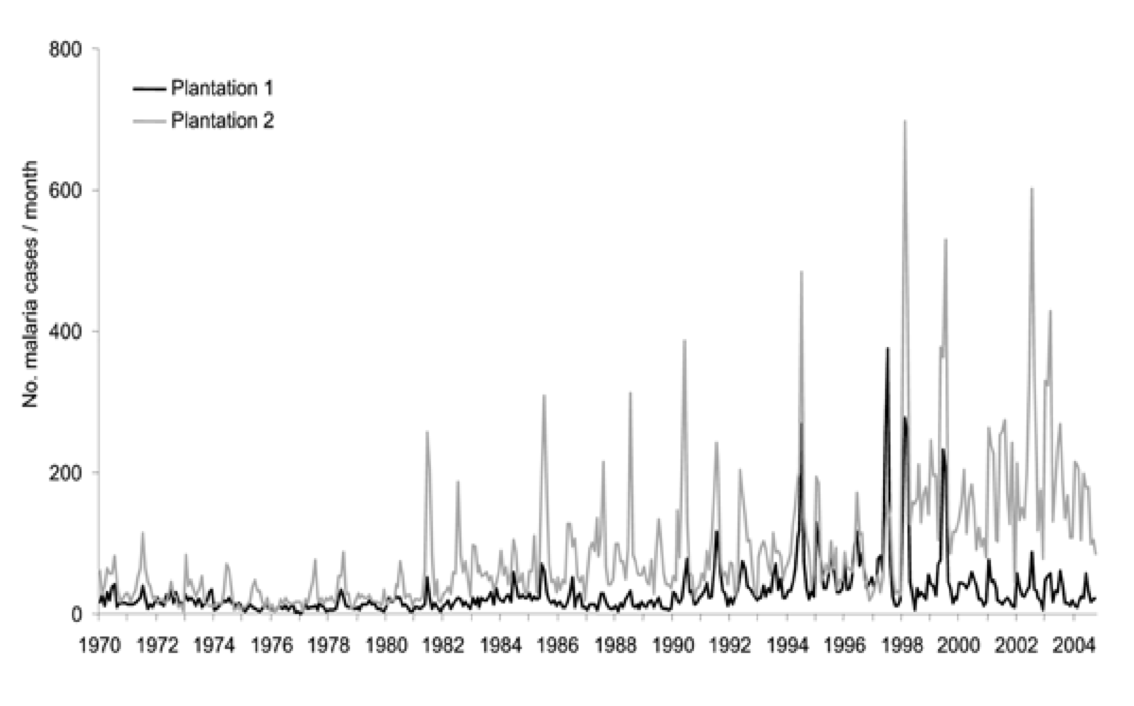


Climate change impacts on infectious diseases occur through seasonal and interannual variability, as well as extreme events

Epidemic or ‘unstable’ malaria exhibits highly dynamic patterns of incidence
Highlands and desert fringes



Areas of Africa
at risk of epidemic malaria
From Grover-Kopec et al, Mal. J. 2005



From Shanks et al. EID 2005

Global warming vs. socio-economic development and intervention

Malaria may not rise as world warms

Studies suggest that strategies to combat the disease are offsetting the impact of climate change.

Of the many climate-change catastrophes facing humankind, the anticipated spread of infectious tropical diseases is one of the most frequently cited — and most alarming. But a paper in this week's *Nature* adds to the growing voice of dissent from epidemiologists who challenge the prediction that global warming will fuel a worldwide increase in malaria.

On the surface, the connection between malaria and climate change is intuitive: higher temperatures are known to boost mosquito populations and the frequency with which they bite. And more mosquito bites mean more malaria.

Yet when epidemiologists Peter Gething and Simon Hay of the Malaria Atlas Project at the University of Oxford, UK, and their colleagues compiled data on the incidence of malaria

Preventative measures such as the widespread use of bed nets have outweighed the effects of climate warming on malaria.

W. DANIELS/PANOS

change per se is not something that should be central to the discussion. The risks have been overstated."

Some earlier analyses painted a dire picture of a malaria-ridden future, but these models often exclusively evaluated the impact of warmer temperatures without taking other factors into consideration, says Paul Reiter, an entomologist at the Pasteur Institute in Paris. The latest assessment of the Intergovernmental Panel on Climate Change noted these concerns: "Despite the known causal links between climate and malaria transmission dynamics, there is still much uncertainty about the potential impact of climate change on malaria at local and global scales."

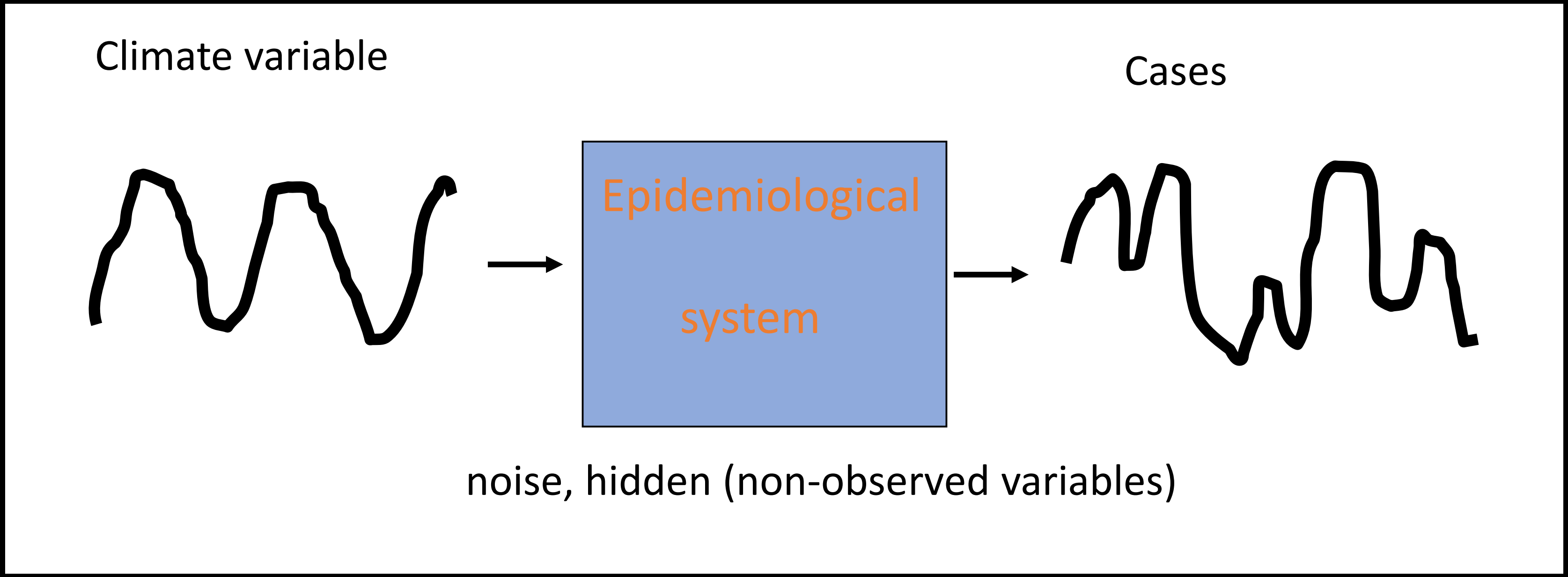
Gething and colleagues' study is the first of its kind to provide a detailed statistical model of global trends over the

Editorial commentary, Nature 2010




Photos: M. Pascual

Climate effects in the context of epidemiology



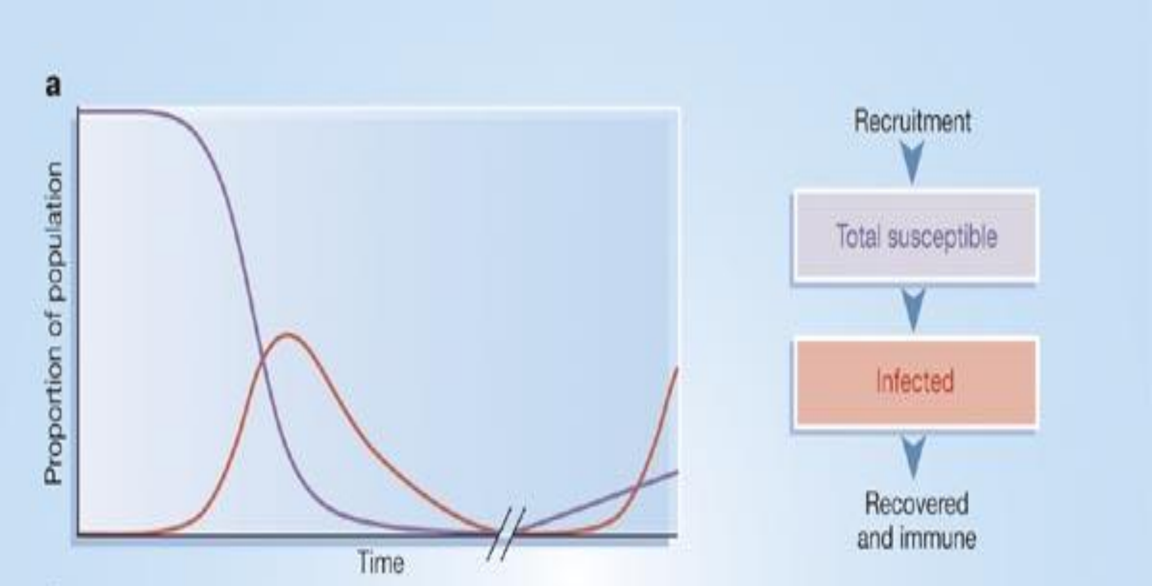
Process-based models + statistical inference methods

Observed cases

Intrinsic dynamics (transmission and immunity)

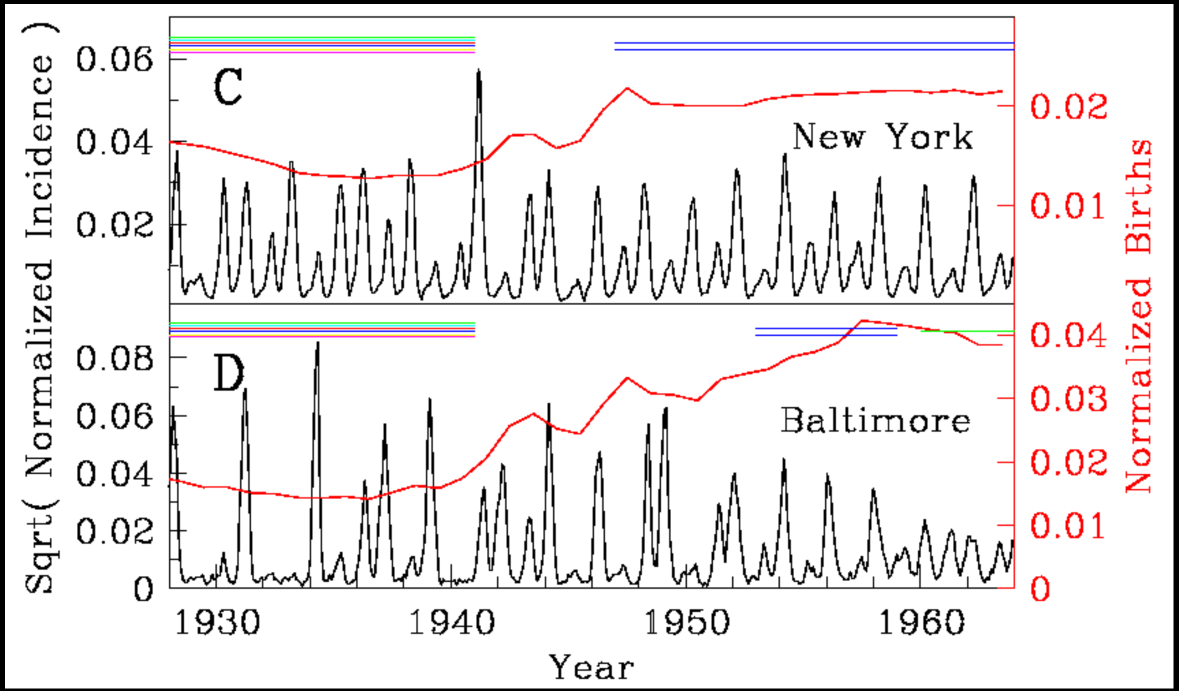
Extrinsic drivers (climate variables)

Infectious Diseases as nonlinear oscillators:



From Bryan Grenfell, Ottar Bjornstad (2004)

add seasonal
transmission



From Earn *et al.*, Science (2000)

$$\beta\left(\frac{I}{N}\right) S$$

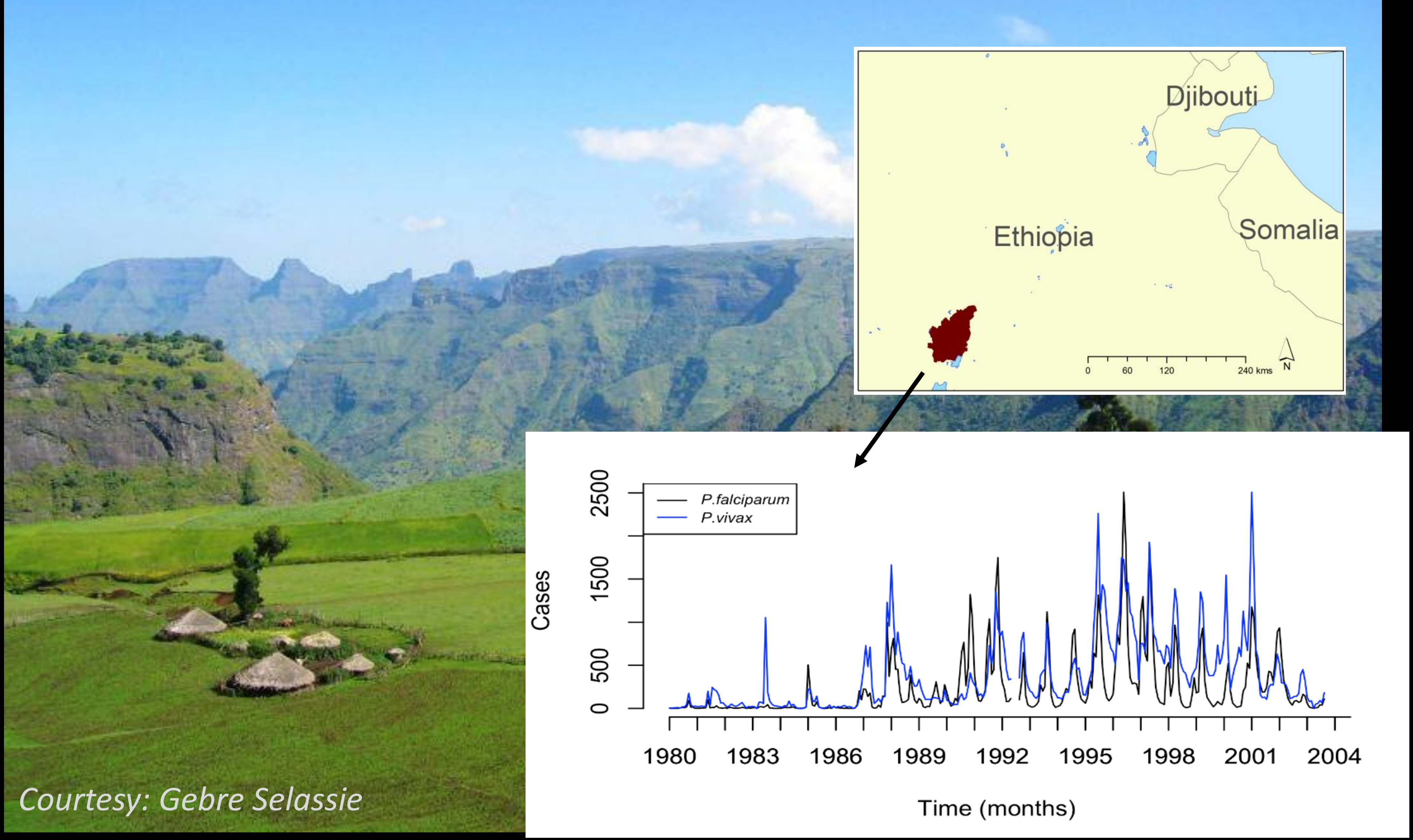
Total transmission rate

Outline

- Highland malaria and climate change (warmer temperatures) in Ethiopia
  Temperature change vs. control?

- Urban malaria and climate variability (relative humidity) in cities of arid Northwest India
  What determines seasonal epidemic size?

Epidemic malaria in E. African highlands

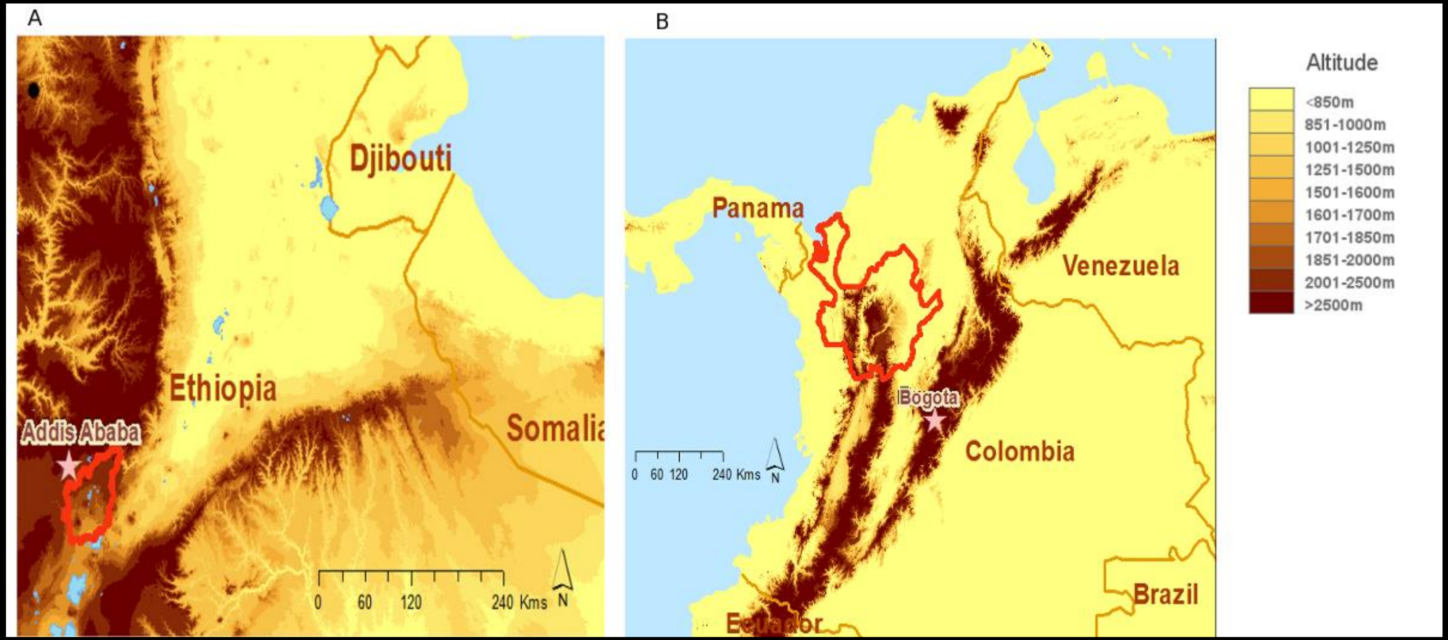


Climate change vs.

- Evolution of drug resistance
- Land-use change
- Increased human movement from lowlands
- Breakdown of public health systems …

Taking advantage of high-resolution spatio-temporal data to address climate change

1993-2005

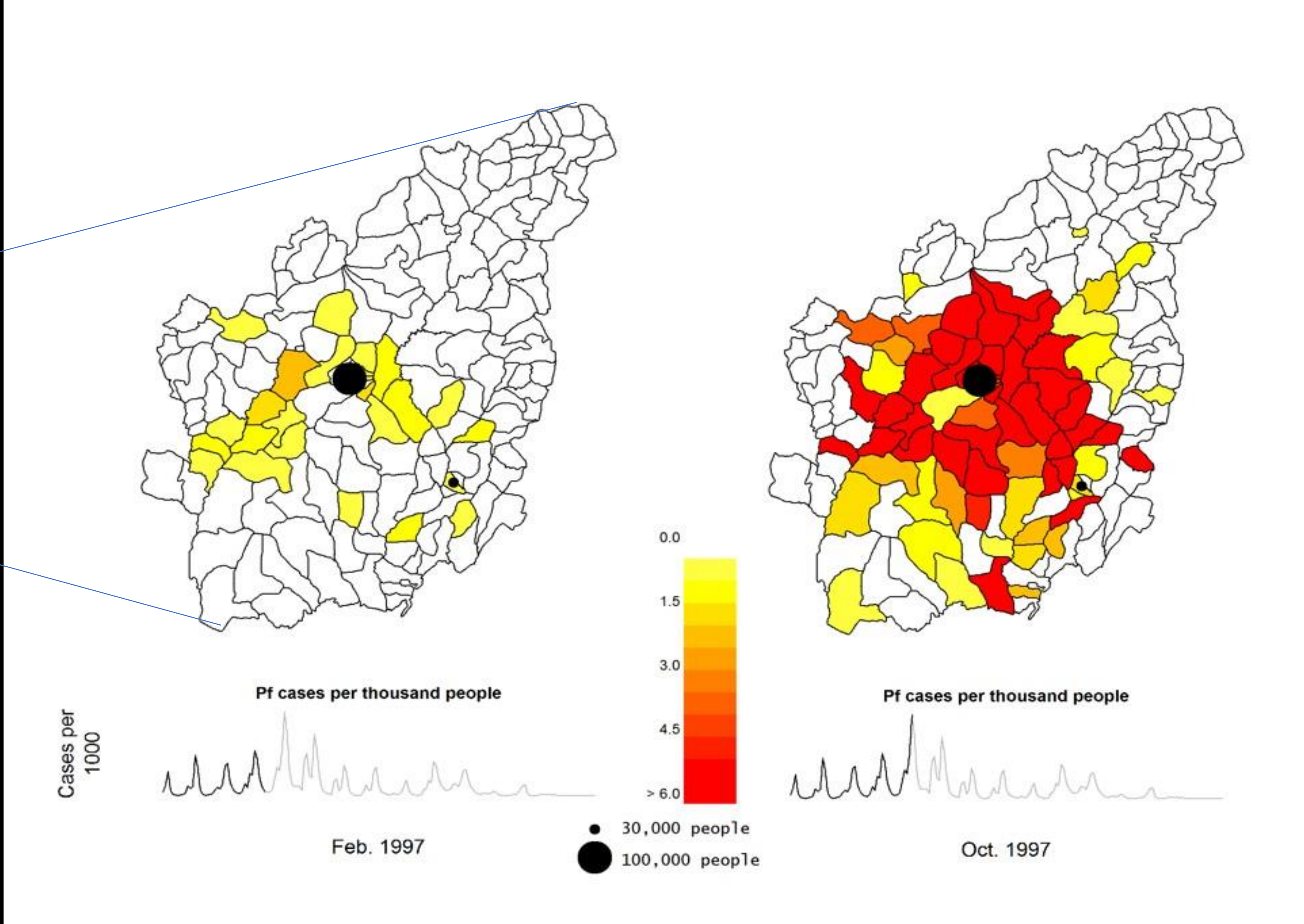


1990-2005

Confirmed monthly cases before major interventions of last decade

Siraj, Santos *et al.*, Science 2014

Expansion of the spatial distribution

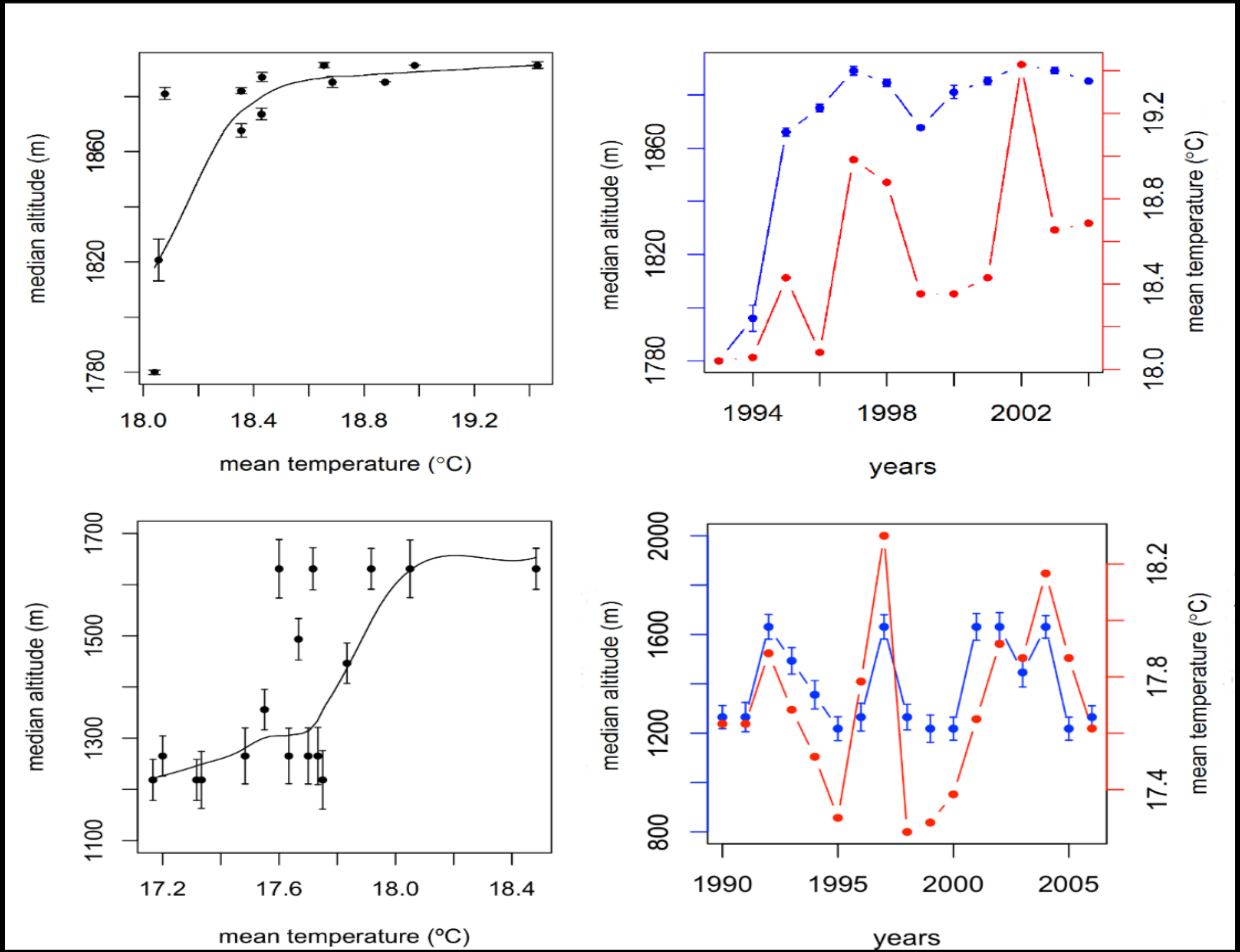


Siraj, Santos-Vega *et al., Science 2014*

The spatial distribution of the disease expands upwards in warmer years

Ethiopia

Colombia



Siraj, Santos-Vega *et al.*, *Science 2014*

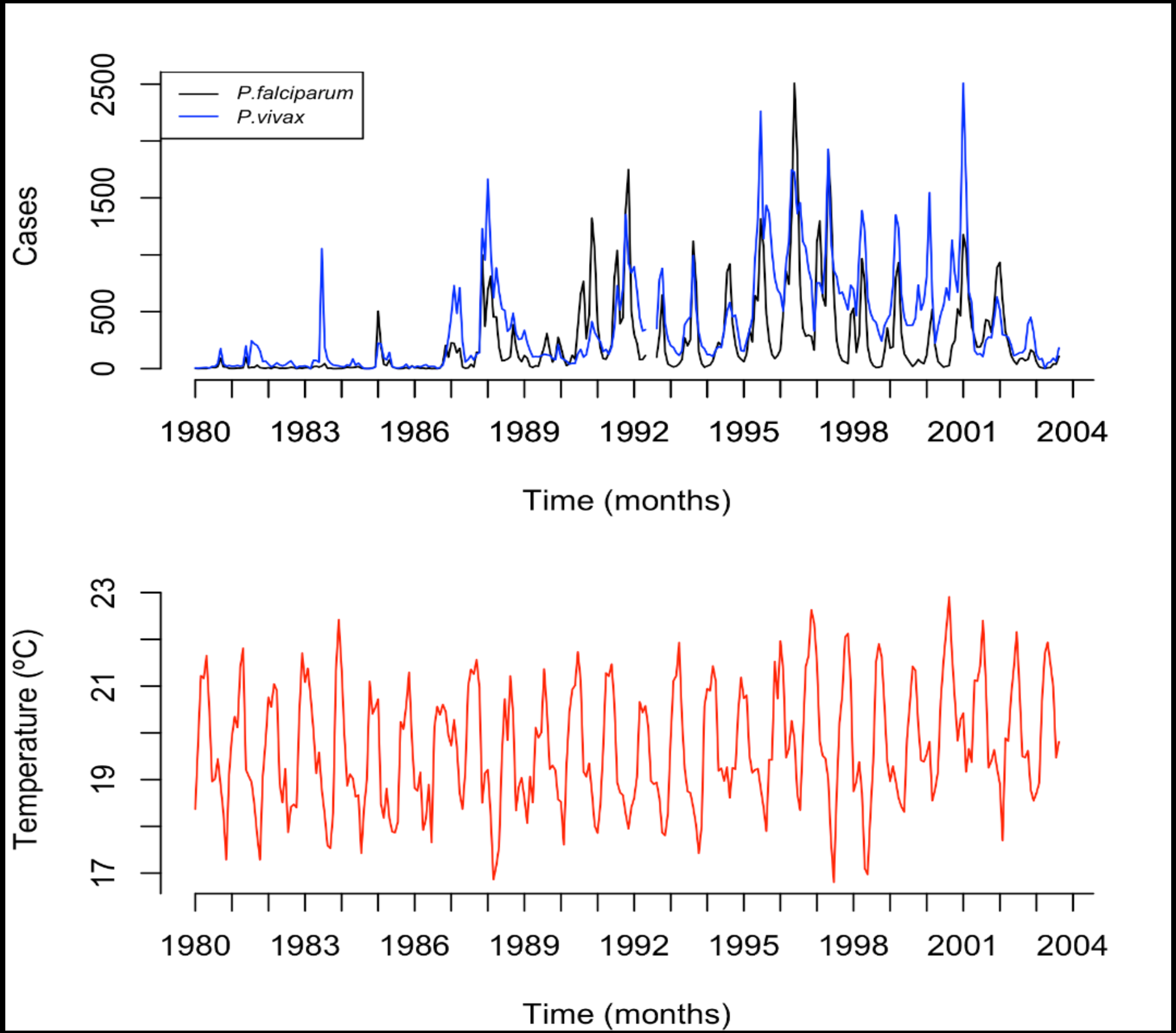
The increase in cases due to altitudinal expansion can explain the long-term trend

From movement in altitudinal distribution

⇨ ~ 1980 cases / degree C

From longer temporal trend

⇨ ~2166 cases / degree C



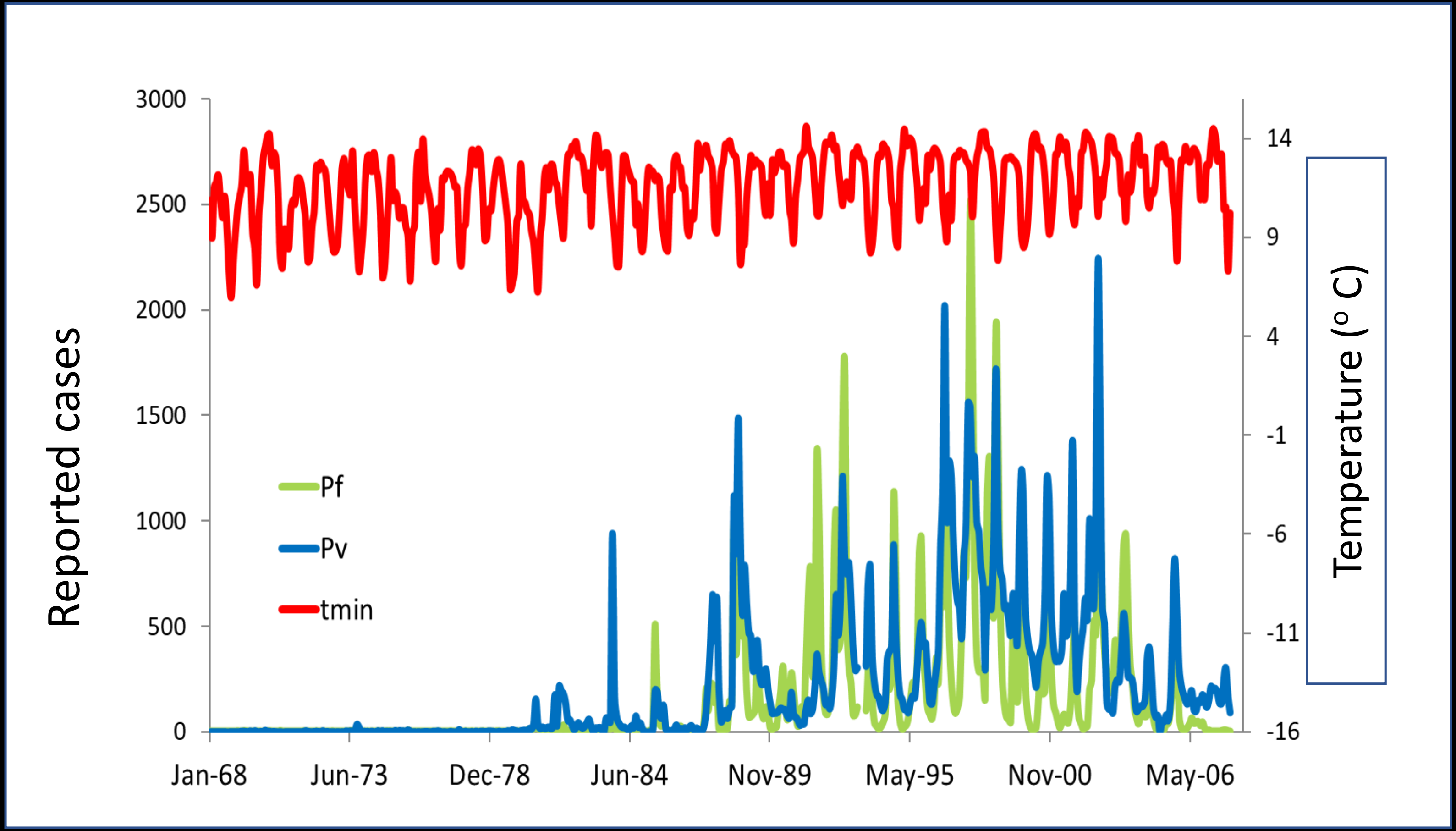
Siraj, Santos *et al.*, Science 2014

For the region as a whole:

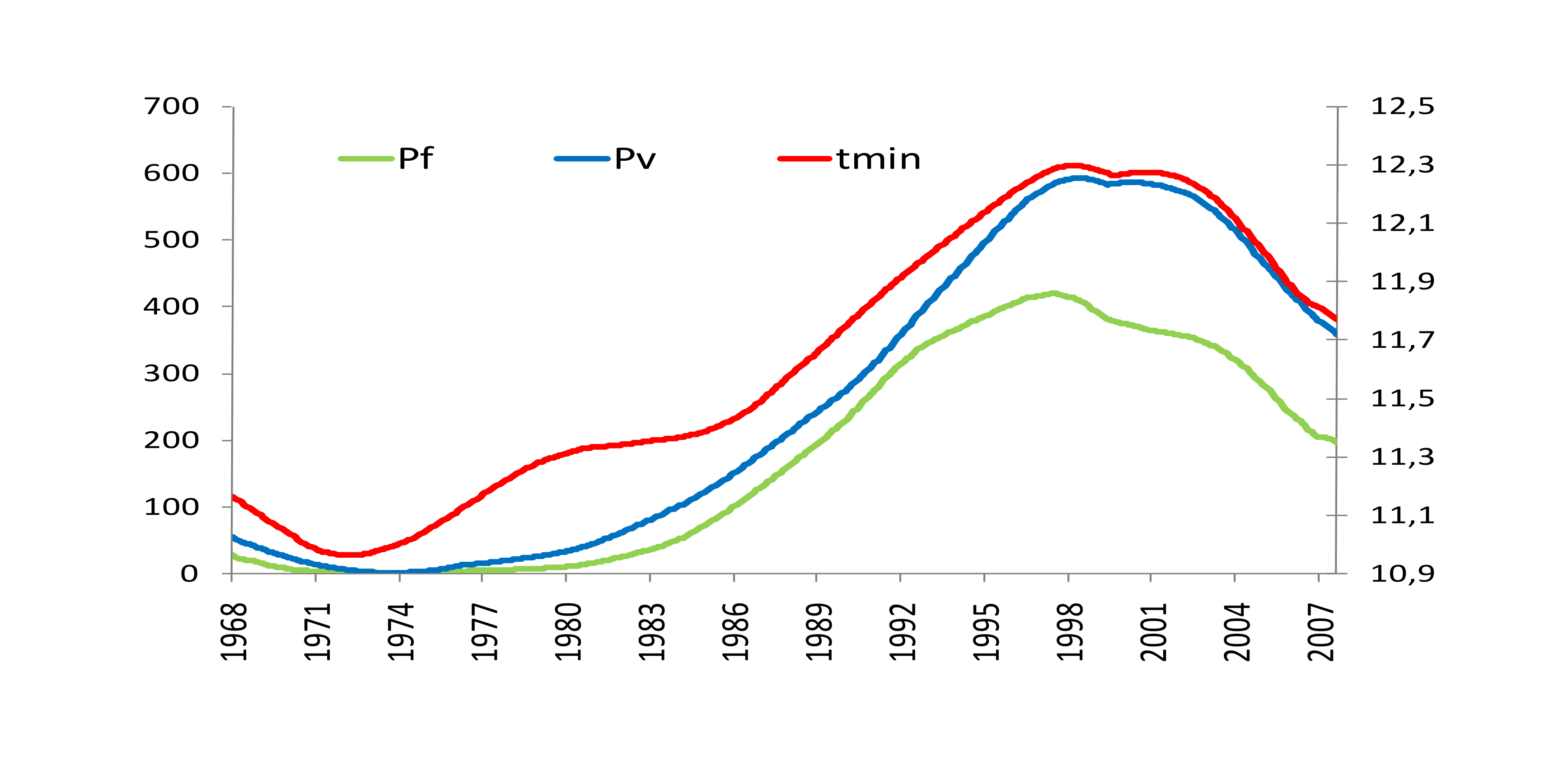
- Climate change will, without mitigation, result in an increase of the malaria burden in the densely populated highlands of Africa.

- For Ethiopia, we estimated a potential addition of 4.9 to 6.1 million cases to the annual national burden from the 1970s to the mid 2000s.
(Bouma and Pascual, 2014, in Butler *et al*. eds. 2015).

What explains the turn-around in the malaria trend at the beginning of new century?



Concordance of trends:



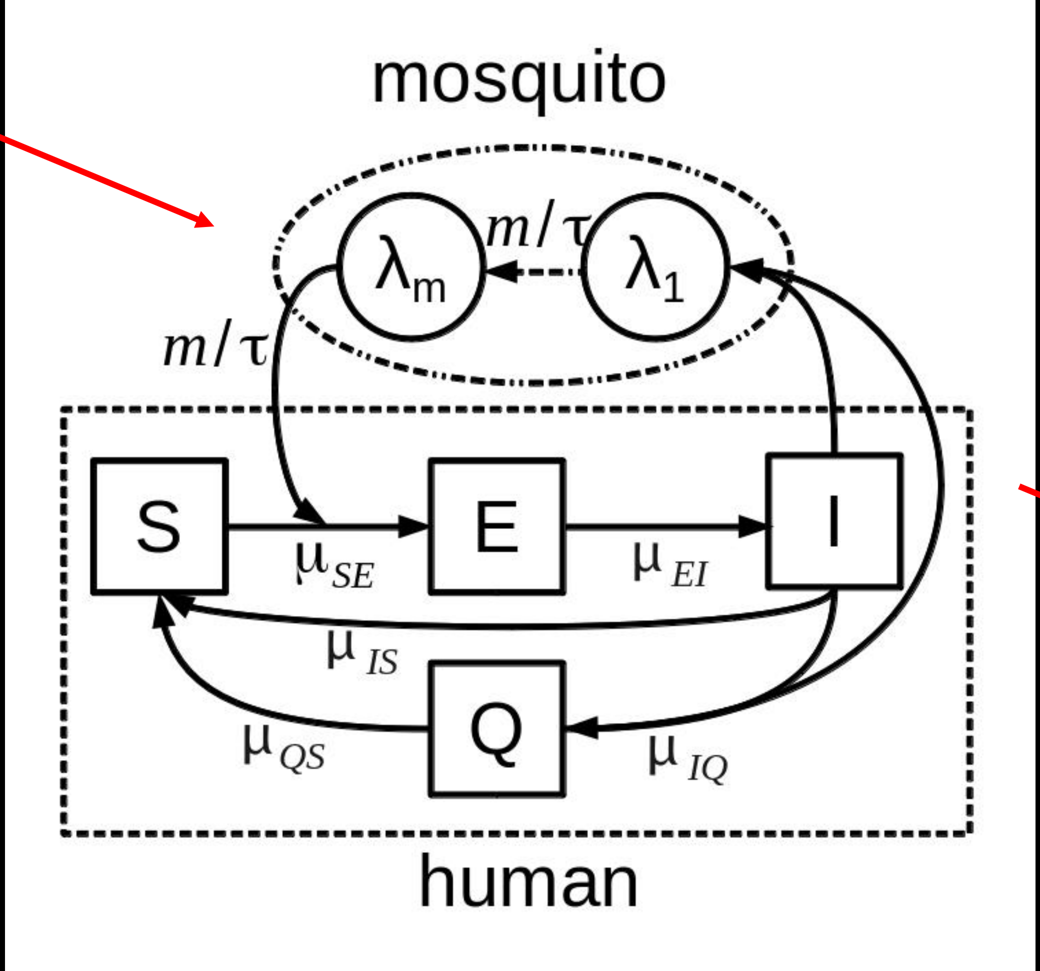
The *Singular Spectrum Analysis - MultiTaper Method* (SSA-MTM) decomposes short, noisy time series into major temporal components

A useful web site: https://dept.atmos.ucla.edu/tcd/singular-spectrum-analysis-ssa

Transmission model to perform a 'counterfactual experiment':

What would have been the temporal pattern of reported cases post 2000, based on transmission dynamics and temperature if everything else had continued as in pre 2000?

Force of Infection
(depends on temperature, season, infection levels and noise)



Reported cases + error
(under-reporting)

Inference method: Likelihood maximization by iterated filtering

(based on sequential Monte Carlo methods --- particle filters)

Major challenges!

- flexible model formulations /structures
- unobserved variables (e.g. susceptible, immune classes)
- stochasticity (environmental and demographic process noise)
- measurement error (under-reporting plus noise in the surveillance)

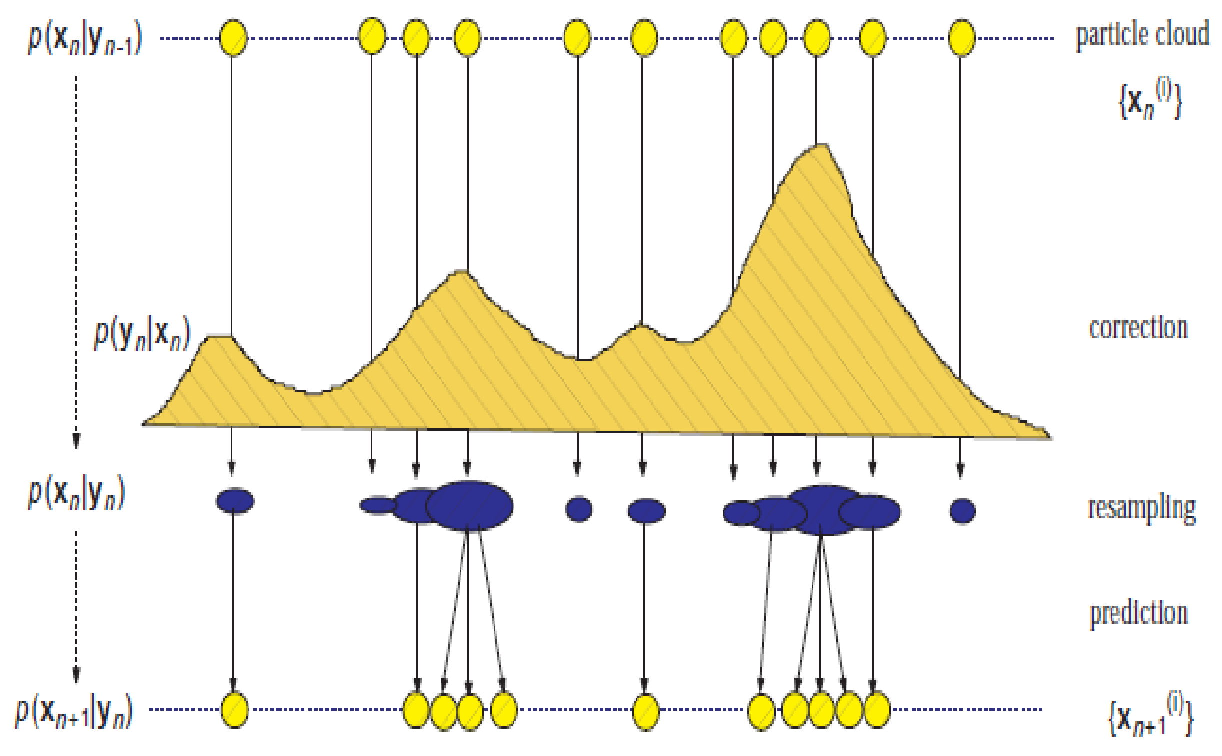
Ionides *et al*. PNAS 2016

King *et al.* Journal of Statistical Software 2016

Statistical Inference for Partially Observed Markov Processes

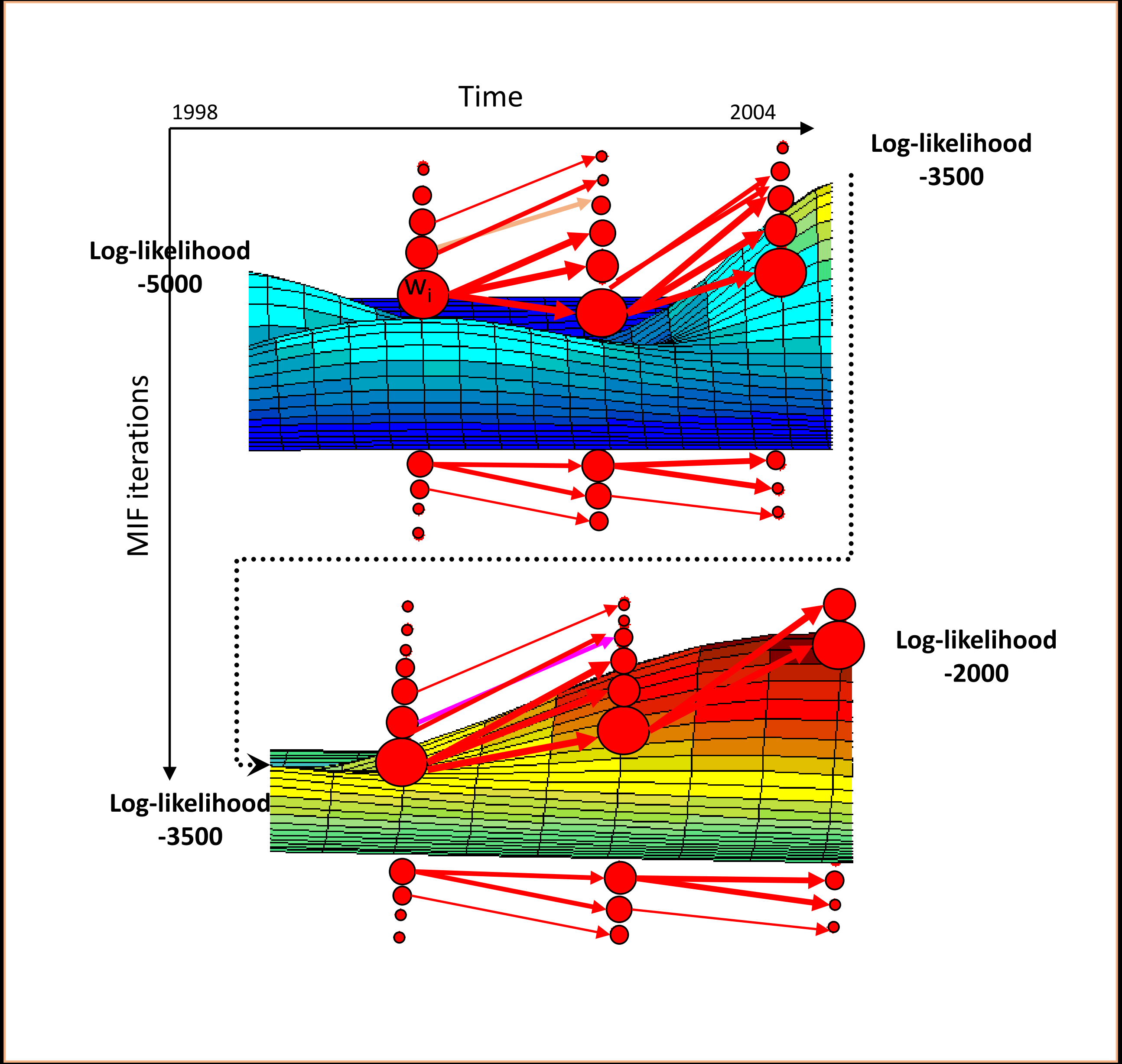
R package **pomp**
at pomp.r-forge.r-project.org

Method: MIF

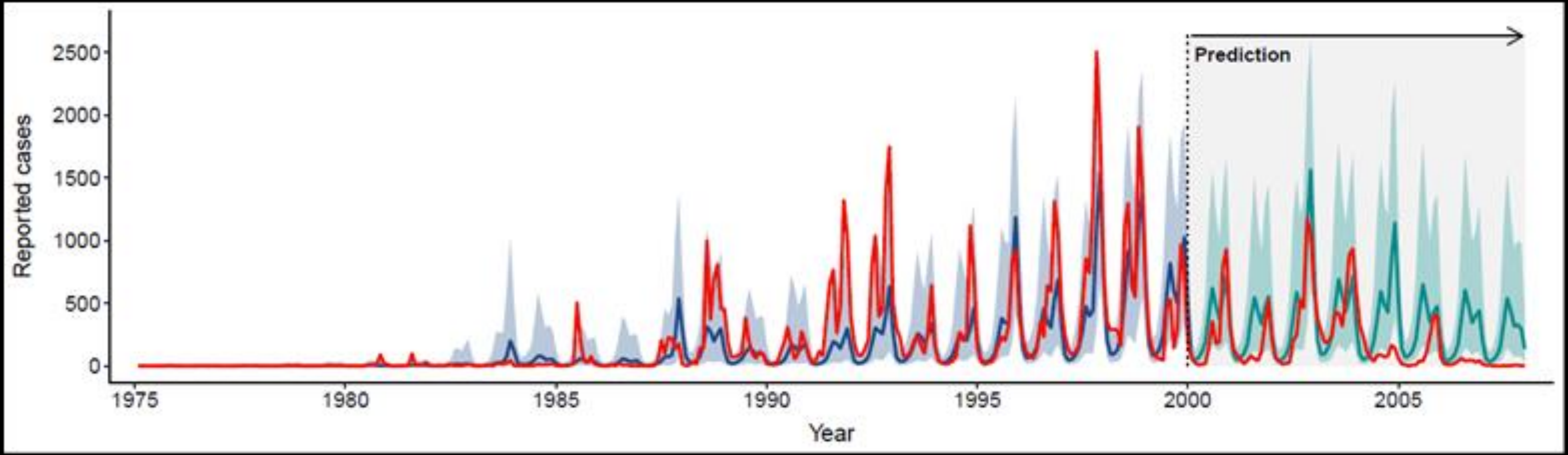


From Z. Chen 2009

The search algorithm iterates the sequential filtering to maximize the likelihood



Model fitted to data up to 2000
"Out-of-fit" predictions post 2000:



Start of strong public health intervention

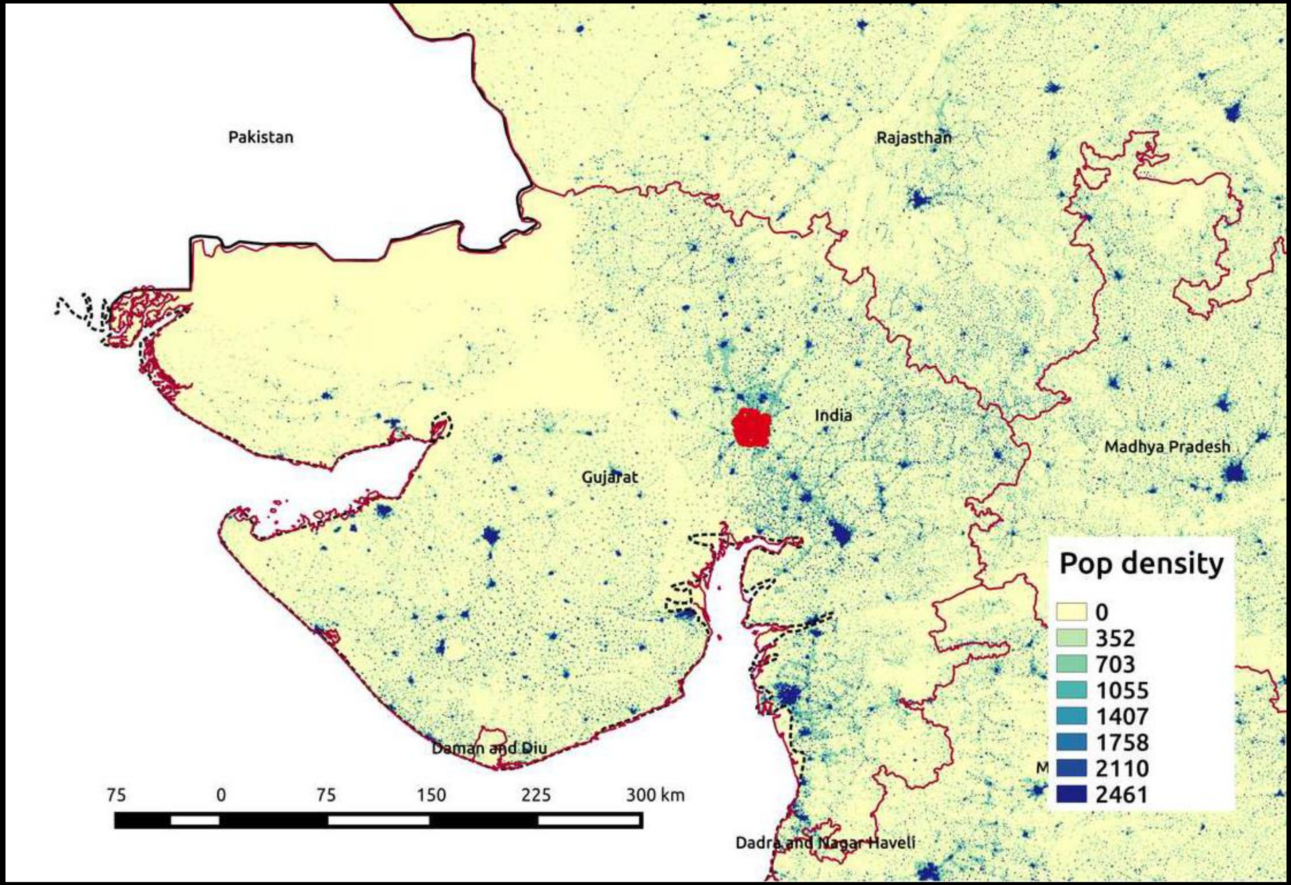
Rodo *et al. in review.*

Some conclusions:

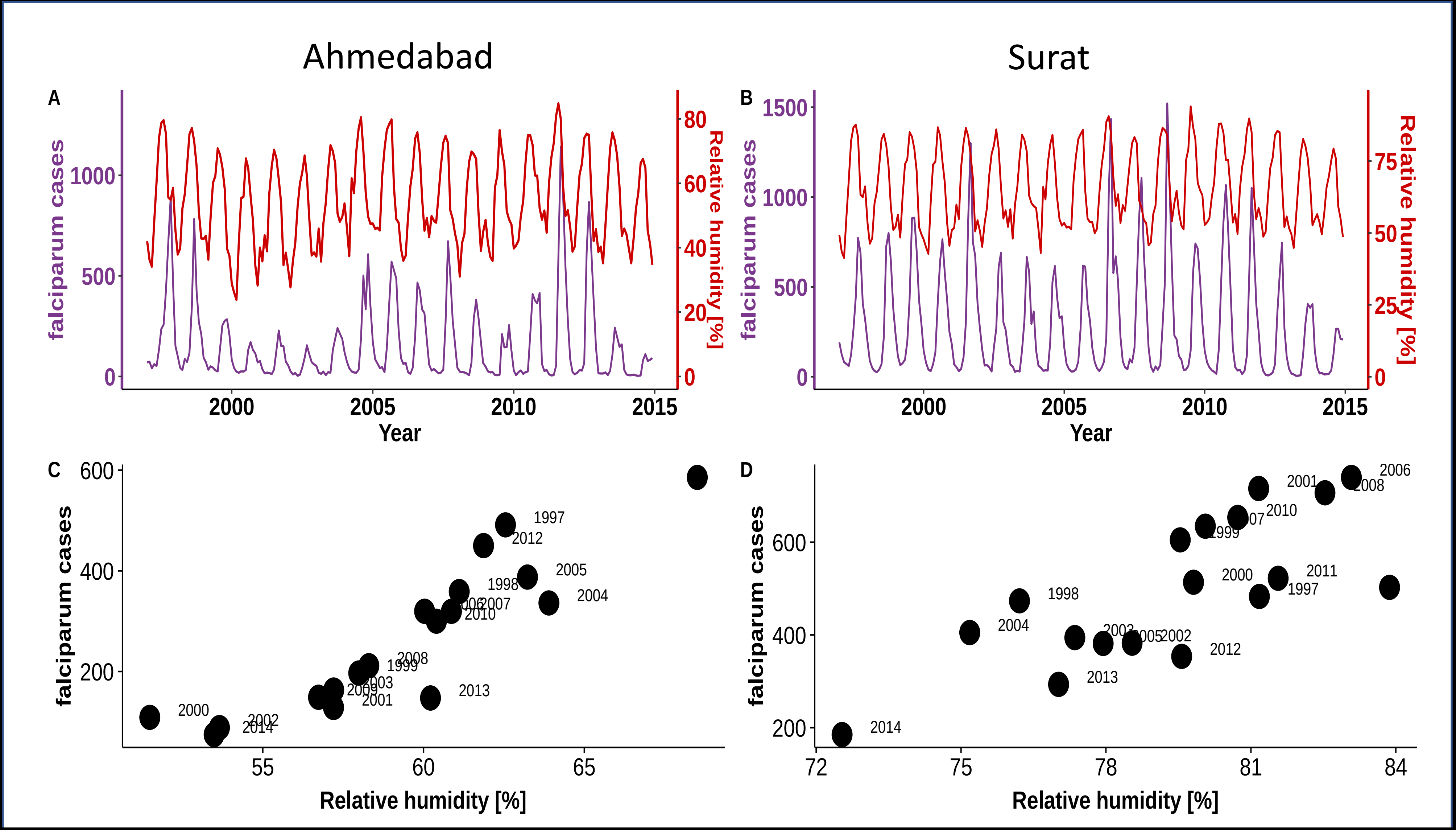
- The slowdown of the malaria trend can be explained by the decadal changes in temperature
- Thus, climate change acted synergistically with control efforts
- Climate conditions should be taken into consideration in other highland regions, and for any relaxation of intervention efforts

Anopheles stephensi:
A truly urban vector in South Asia

Anopheles stephensi
(photo courtesy: Kedar Bhide)



Interannual variability and relative humidity



Mauricio Santos Vega *et al. In review*

Parameter inference and hypothesis testing

www.keywordpictures.com

Climate variability included (Covariate 1)

Climate variability included (Covariate 2)

No climate variability

↓

PARAMETER ESTIMATION

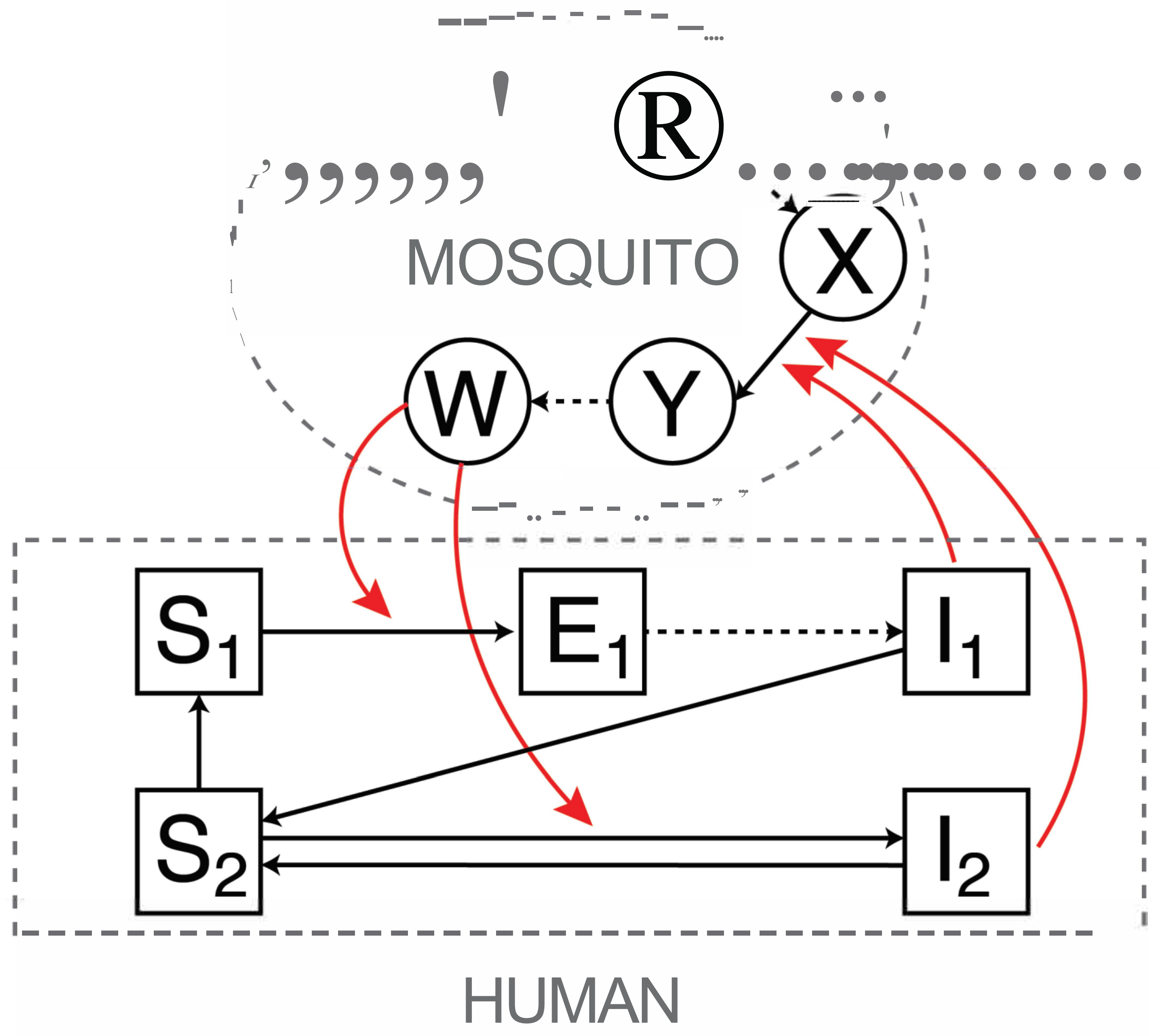
Sequential Monte Carlo method

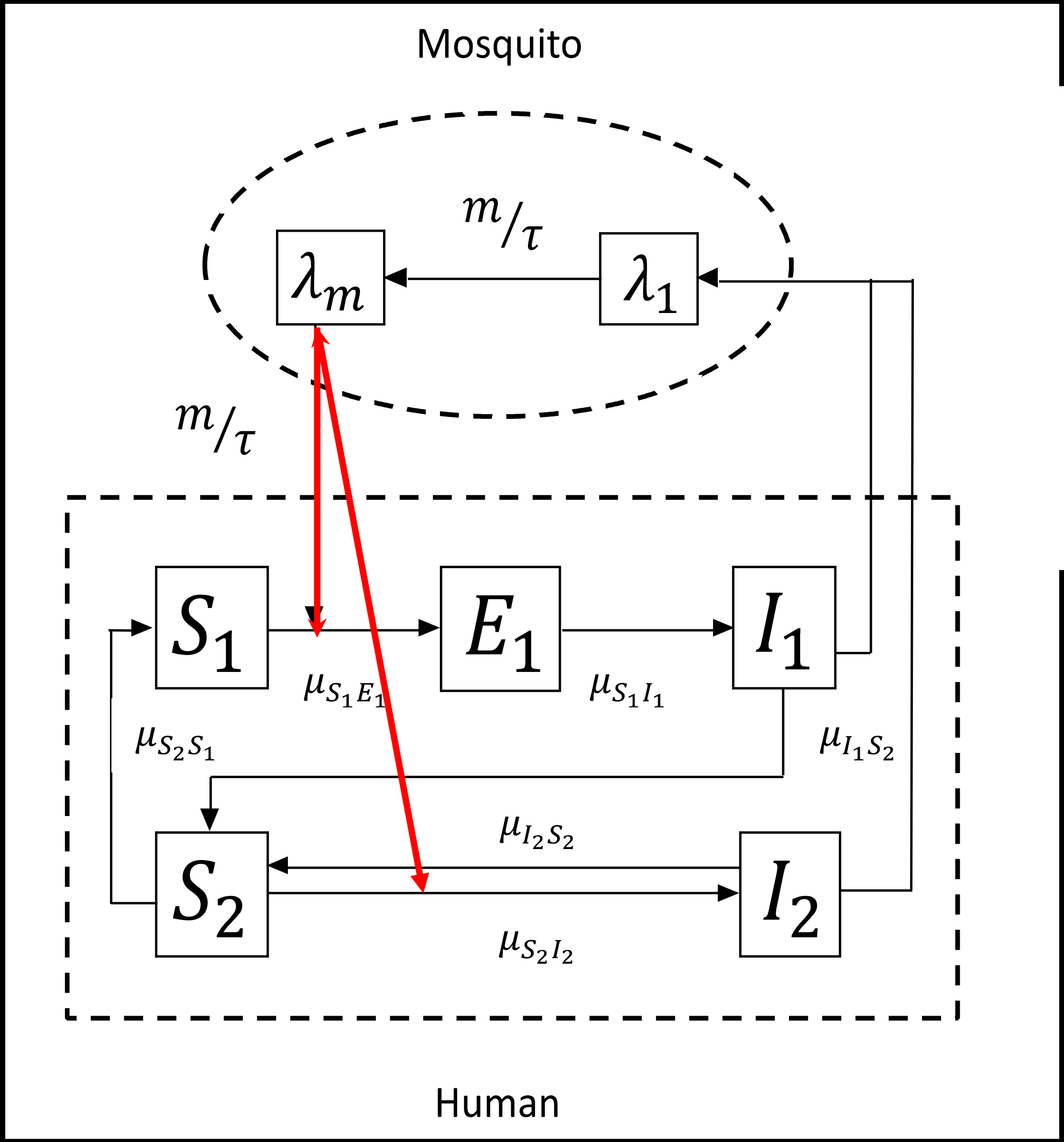
↓

MODEL COMPARISON

Based on log-likelihood/
Model selection criteria (AIC)

Parameters are estimated with a method that ***maximizes the likelihood : MIF in R-package Pomp***


R
MOSQUITO
X
Y
W
S1
E1
I1
S2
I2
HUMAN



$$dS_1/dt = (\delta P + dP/dt) + \mu_{S_2S_1}S_2 - \mu_{SE}(t)S_1 - \delta S_1,$$

$$dE/dt = \mu_{SE}(t)S_1 - \mu_{EI_1}E - \delta E,$$

$$dI_1/dt = \mu_{EI_1}E + \mu_{I_1S_2}I_1 - \delta I_1,$$

$$dS_2/dt = \mu_{I_1S_2}I_1 + \mu_{I_1S_2}I_2 - \mu_{S_2S_1}S_2 - \mu_{SE}(t)S_2 - \delta S_2,$$

$$dI_2/dt = \mu_{SE}(t)S_2 + \mu_{I_2S_2}I_2 - \delta I_2,$$

Seasonality, interannual forcing, environmental noise, measurement noise

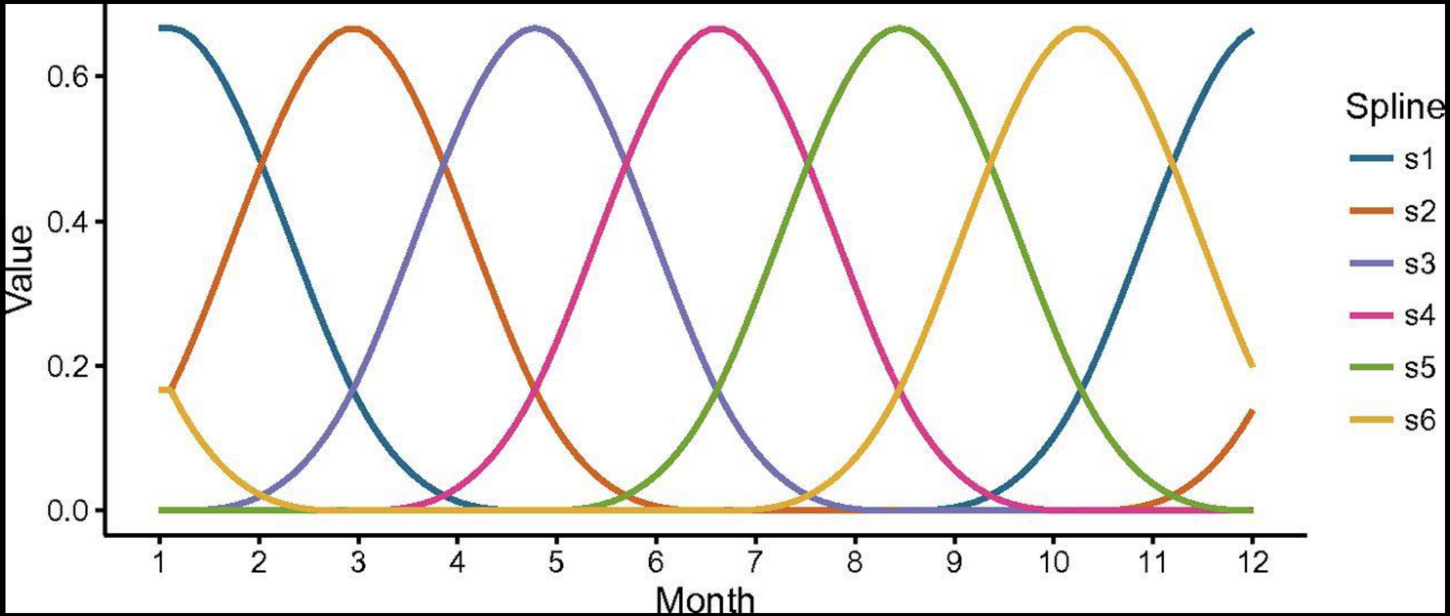
1) Transmission rate

$$\beta(t) = \exp\left[\sum_{k=1}^{6} b_k S_k + b_{RH} S_4 C\right]\left[\frac{d\Gamma}{dt}\right]$$

Noise (Gamma distributed)

Seasonality and interannual forcing

We represent the seasonal variation with 6 B-spline basis functions.

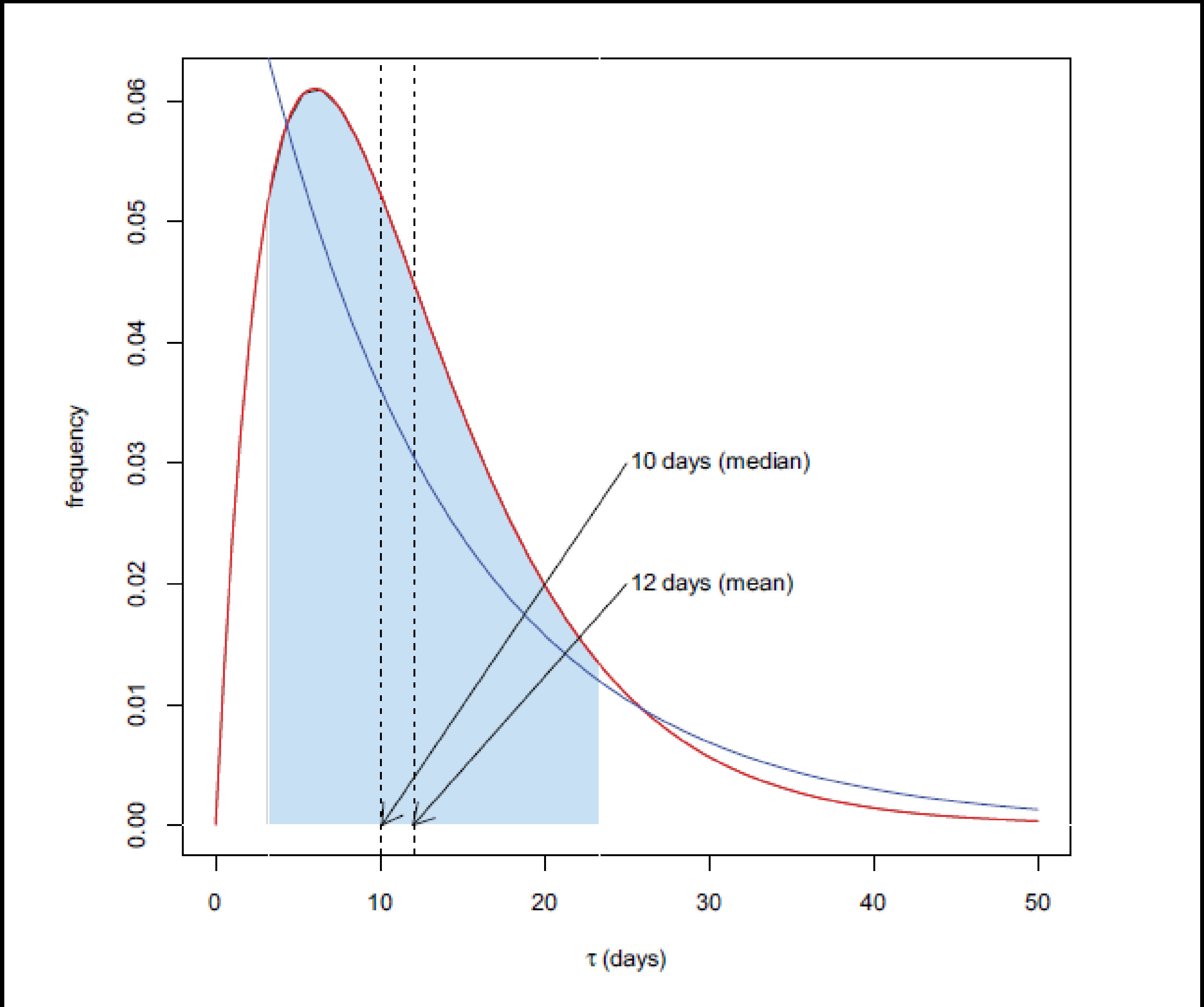


Implicit representation of transmission via mosquitoes:

2) The force of infection per susceptible individual is introduced with a distributed delay:

We feed the following "potential" force of infection through a chain of classes

$$\lambda = \left(\frac{I_1 + I_2}{P(t)}\right)\beta$$



Comparing the best model to the data

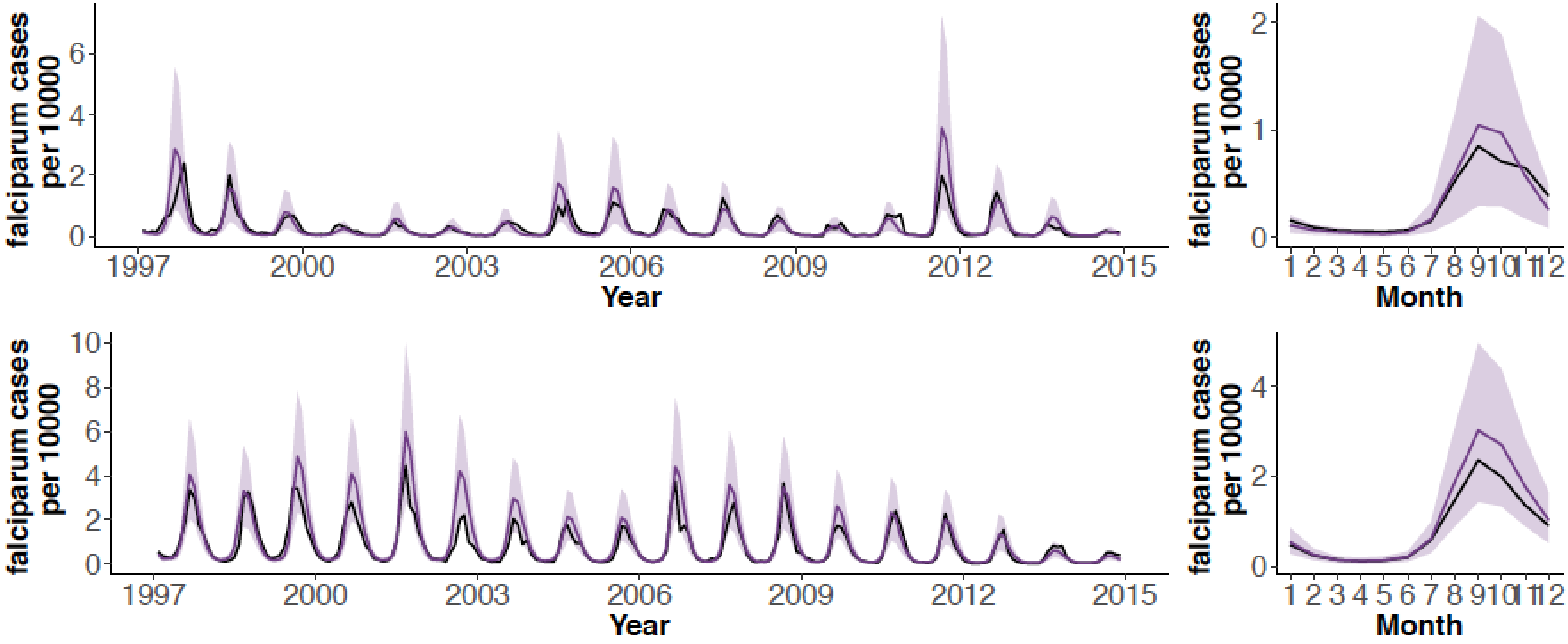
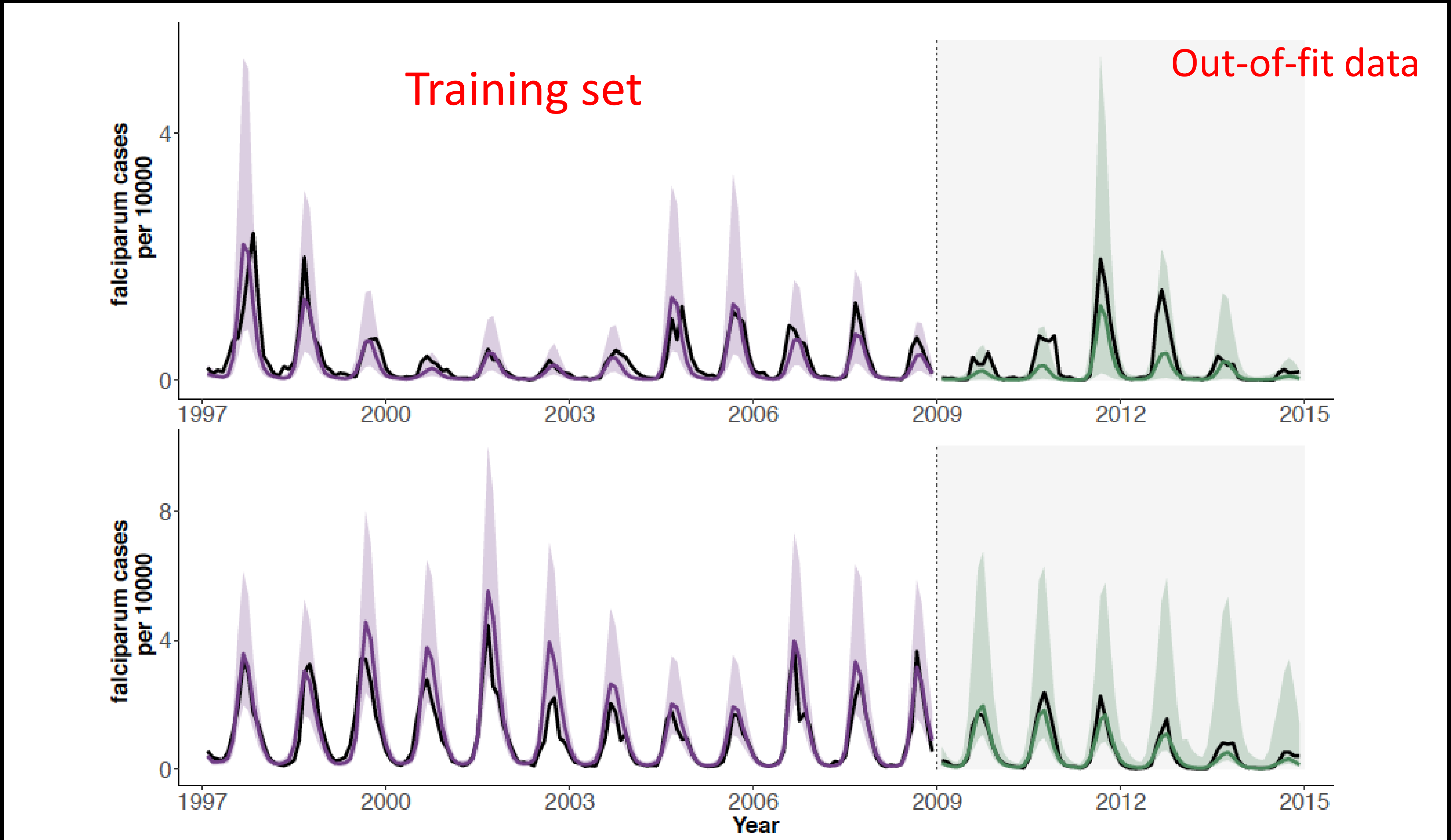


Figure 2. **Comparison of observed and simulated monthly cases with the best model for both cities.**

Santos-Vega *et al. submitted*

Even better: predicting the upcoming season



Santos-Vega *et al. in review*

Comparing models:

Akaike Information Criterion (AIC)

model	log likelihood	SE	# parameters	Delta AIC	LRT
Surat					
RH	-1166.9011	0.1254	25	--	<0.001
Temp	-1176.2280	0.2174	25	-18.6539	
NO RH	-1181.6492	0.1885	24	-27.4962	
Ahmedabad					
RH	-1111.3123	0.3664	25	--	<0.001
Temp	-1120.9340	0.3210	25	-19.2434	
NO RH	-1123.9829	0.2657	24	-23.3411	

Mauricio Santos-Vega *et al. In review*

To close,

- Climate factors should play an important role in the epidemiology of urban vector-borne infections

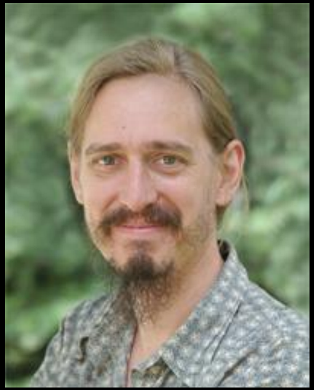
- Beyond temperature, the neglected effects of humidity should be taken into account

- In the heterogeneous landscapes of cities, a much better understanding is needed of fine-scale variation in population density, how it affects transmission dynamics, together with its covariation with temperatures.

(see for dengue, Romeo-Aznar *et al. Proc. Roy. Soc. London B* 2018).

Thank you!

Aaron King, UM



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NSF-NIH, DSM – NIMGS
Uchicago: FACCTS and
Research Computing Center

$$d\lambda_1/_{dt} = (\lambda - k_1)k\tau^{-1}$$

$$d\lambda_j/_{dt} = (k_{j-1} - k_j)k\tau^{-1} \quad for\; j = \; 2$$