# Epidemic malaria and climate variability: a dynamic perspective

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"Water mingles with every kind of natural phenomenon; and more than one might imagine, it has also mingled with the particular destiny of mankind"

--- Fernand Braudel

(from Water, The Epic Struggle for Wealth, Power and Civilization, S. Solomon)

# Etiology of interepidemic periods of mosquito-borne disease

Simon I. Hay*†, Monica F. Myers‡, Donald S. Burke§, David W. Vaughn¶, Timothy Endy‖, Nisalak Ananda‖, G. Dennis Shanks‖**, Robert W. Snow††‡‡, and David J. Rogers*

standing of the factors involved in epidemic genesis. In this report we discuss the potential causes of the interepidemic periods in dengue hemorrhagic fever in Bangkok and of *Plasmodium falciparum* malaria in a highland area of western Kenya. The alternative causes are distinguished by a retrospective analysis of two unique and contemporaneous 33-year time series of epidemiological and associated meteorological data recorded at these two sites. We conclude that intrinsic population dynamics offer the most parsimonious explanation for the observed interepidemic periods of disease in these locations.

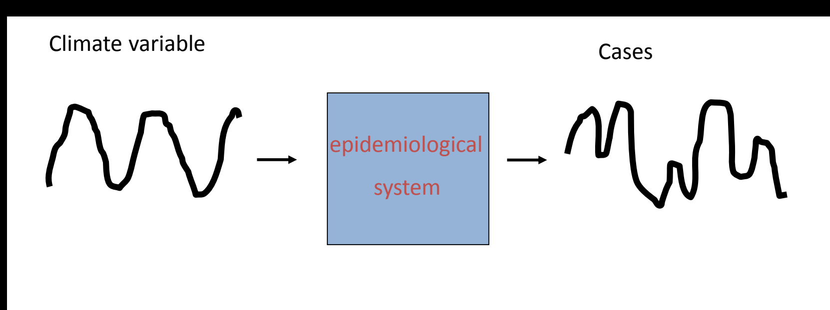
PNAS 2000

JOURNAL OF THE ROYAL SOCIETY Interface

**The interaction of seasonal forcing and immunity and the resonance dynamics of malaria**

Dylan Z. Childs and Michael Boots

*J. R. Soc. Interface* 2010 **7**, doi: 10.1098/rsif.2009.0178 first published online 1 July 2009




Epidemiological model + statistical inference methods


Intrinsic dynamics

Extrinsic drivers

*Koelle and Pascual (Am. Nat. 2004)*
*Koelle, Rodo, Pascual et al. (Nature 2005)*

## Testing hypotheses on disease dynamics and climate forcing by comparing mechanistic models

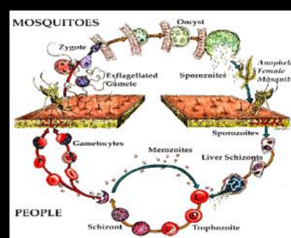
**Best disease models**

**with no climate**

⟺

**Best disease models**

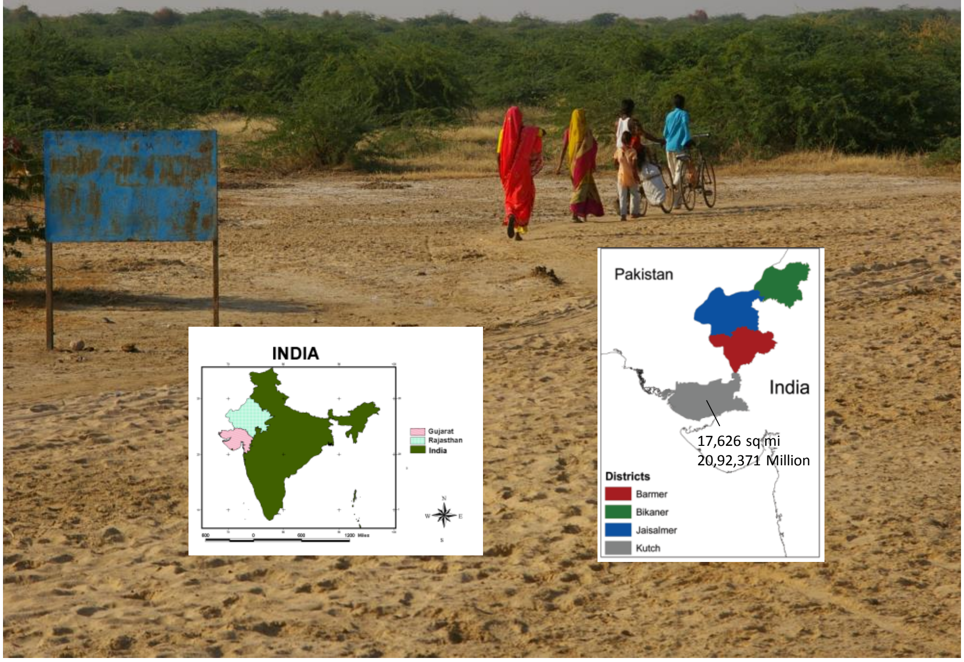
**with climate variability**




# Conceptual outline

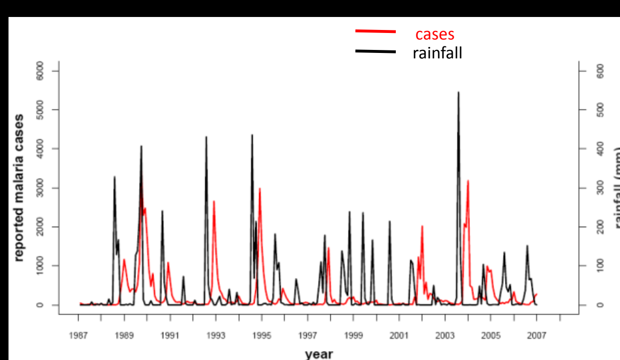
- The effect of climate forcing will be most apparent where climate factors act as strong limiting factors (at the edge of the spatial distribution of the disease, in highland and semi-arid regions). But here, by definition, transmission is low, and therefore, population immunity, is most unlikely to play a strong dynamical role.
- We will see that epidemiological processes matter but primarily at seasonal scales.
- The nonlinear feedbacks that matter most may be primarily the result of 'reactive control'.
- At higher transmission, super-infection/complex processes underlying immunity appear to modify the response to forcing in fundamental ways
- Long-term trends are unavoidable. This does not mean that fitted models are no longer relevant to prediction.

## Epidemic malaria and rainfall variability in semi-arid India

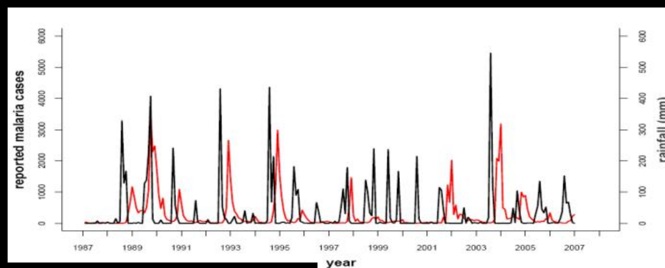



## Typical epidemic behavior of *P. falciparum* cases

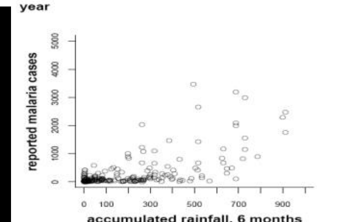
District of Kutch:
30 years
monthly cases




Laneri *et al.* PloS Computational Biology 2010




- does population immunity play a role in the response to climate variability?
- how predictable is the size of outbreaks based on transmission models driven by climate?



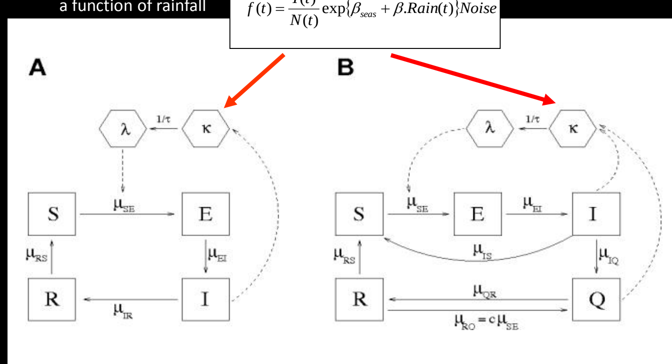

## Transmission models and parameter inference from time series of cases

Force of infection:
a function of rainfall

$$f(t) = \frac{I(t)}{N(t)} \exp\{\beta_{seas} + \beta.Rain(t)\} Noise$$

mosquitoes

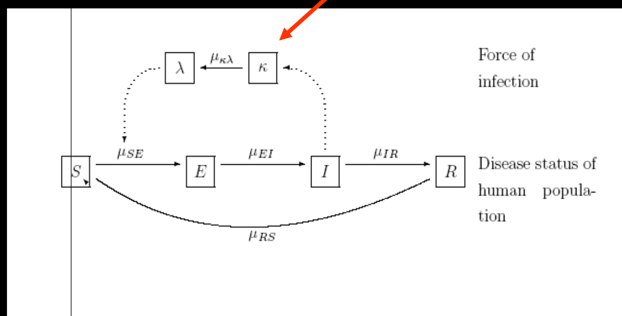
hosts




Novel statistical and computational method to mazimize likelihood (sequential Monte Carlo approach) (Ionides *et al.* PNAS 2006; King *et al.* Nature 2008).

# Malaria model

$$f(t)=\frac{I(t)}{N(t)}\exp\{\beta_{seas}+\beta.Rain(t)\}Noise$$




Latent force of infection | Force of infection

$$\kappa=\lambda_0 \Rightarrow \lambda_1 \Rightarrow \lambda_2 \Rightarrow \lambda$$

Parasite's development in surviving mosquitoes

## Inference method:

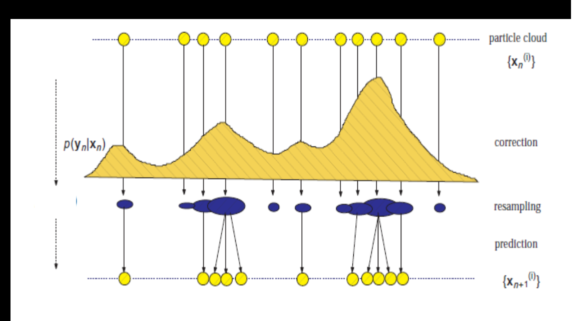
Ionides *et al.* (PNAS 2006); King *et al.* Nature 2008

Likelihood maximization by iterated filtering (based on sequential Monte Carlo methods --- particle filters)

can accommodate:

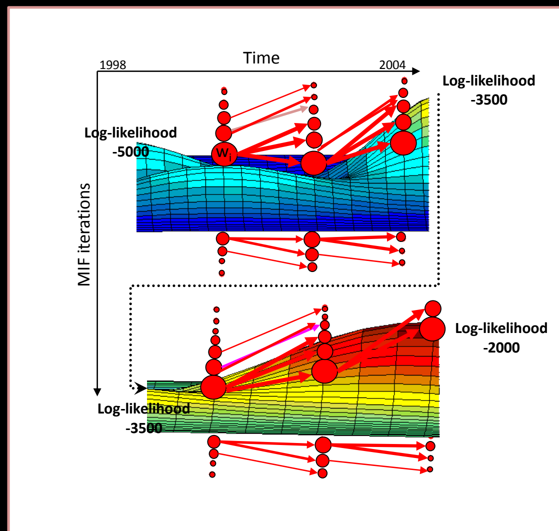
- flexible model formulations ; continuous time
- unobserved variables (e.g. susceptibles)
- stochasticity , trends
- measurement error (under-reporting)

See Laneri et al (PloS Comp. Biol.) for inclusion of covariates and pseudo-code in a malaria example




From Z. Chen 2009

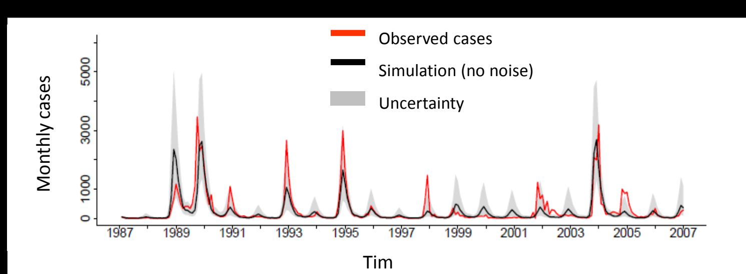
## Inference method:




Likelihood maximization by iterated filtering (based on sequential Monte Carlo methods -- - particle filter ; Ionides and King PNAS 2006)

## Both rainfall and clinical immunity are included in the 'best' model

- Clinical immunity is important at seasonal scales
- This model outperforms a 'standard' non-mechanistic, linear autoregressive, model that includes rainfall




Laneri *et al.* PloS Computational Biology 2010
Bhadra *et al*. J. American Statistical Association 2011

# Model comparison

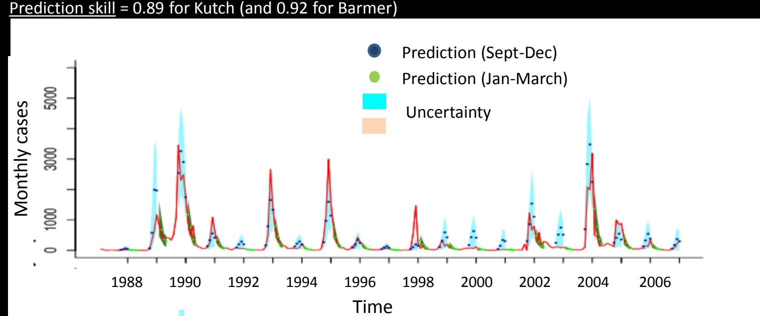
**Table S1. Table of log-likelihood ($\ell$) and AIC of the fitted models for Kutch and Barmer.**

| model | p | log-likelihood ($\ell$) | | AIC | |
|---|---|---|---|---|---|
| | | Kutch | Barmer | Kutch | Barmer |
| VSEIRS model without rainfall | 19 | -1275.0 | -984.1 | 2588.0 | 2006.2 |
| VSEIRS model with rainfall | 20 | -1265.0 | -978.6 | 2570.0 | 1997.2 |
| $VS^2EI^2$ model without rainfall | 24 | -1261.1 | -975.3 | 2570.2 | 1998.6 |
| $VS^2EI^2$ model with rainfall | 25 | -1251.0 | -970.5 | 2552.0 | 1991.0 |
| SARIMA $(1,0,1) \times (1,0,1)_{12}$ without rainfall | 6 | -1329.0 | -983.7 | 2670.0 | 1979.4 |
| SARIMA $(1,0,1) \times (1,0,1)_{12}$ with rainfall | 7 | -1322.6 | -977.0 | 2659.2 | 1968.0 |

In the table "$p$" denotes the number of parameters for each model. AIC is computed by the formula $\mathrm{AIC} = -2\ell + 2p$. The SARIMA model was fitted to the data on the log scale (see the supplement of [2] for a detailed description of this procedure).

## The rainfall-driven transmission model exhibits high prediction skill (retrospectively)

Prediction skill = 0.89 for Kutch (and 0.92 for Barmer)



## Prediction performance: 4 months

$$\text{skill} = 1 - \frac{\sum_{i=1987}^{2006}(y_i - \hat{y}_i)^2 w_i}{\sum_{i=1987}^{2006}(y_i - \mu)^2 w_i}$$

- $w_i$ inverse of the prediction variance for the year $i$
- $\hat{y}_i$ and $y_i$ are the predicted and observed cases, accumulated over September to December for the year $i$
- $\mu$ : 20 year mean of the observed cases accumulated between September and December

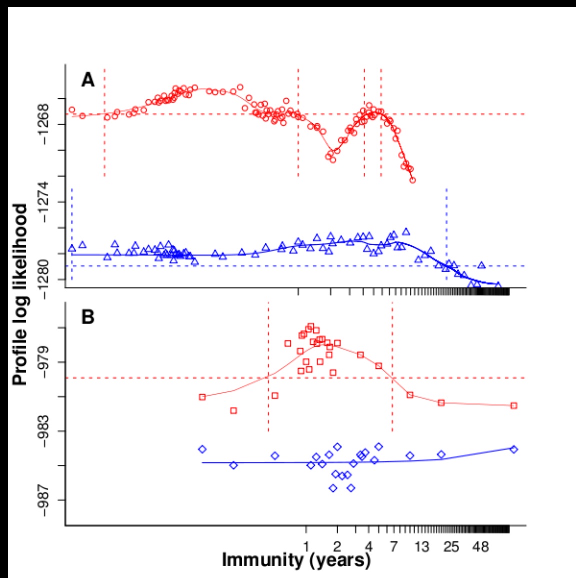
*skill* $\longrightarrow$ 1 Good Prediction
*skill* $\longrightarrow$ 0 Bad Prediction

## Prediction performance:

| | Kutch | | | Barmer | | |
|---|---|---|---|---|---|---|
| | $\text{skill}_1$ | $\text{skill}_3$ | $\ell$ | $\text{skill}_1$ | $\text{skill}_3$ | $\ell$ |
| 1. VSEIRS with rainfall | 0.899 | 0.798 | −161.3 | 0.928 | 0.887 | −141.0 |
| 2. VSEIRS without rainfall | 0.545 | −0.921 | −176.2 | 0.747 | 0.596 | −150.0 |
| 3. Linear model | 0.787 | 0.619 | −176.7 | −0.004 | 0.405 | −181.9 |
| 4. Mixture negative binomial model | 0.753 | 0.409 | −167.3 | 0.826 | 0.613 | −147.6 |

Subscripts 1 and 3 denote the model whose variances were used for the calculation of the skill measure. $\ell$ is the prediction log likelihood as defined in Text S1.
doi:10.1371/journal.pcbi.1000898.t002

Duration of Immunity




Simulation model with rainfall (MLE parameters)

Observed cases

Rainfall

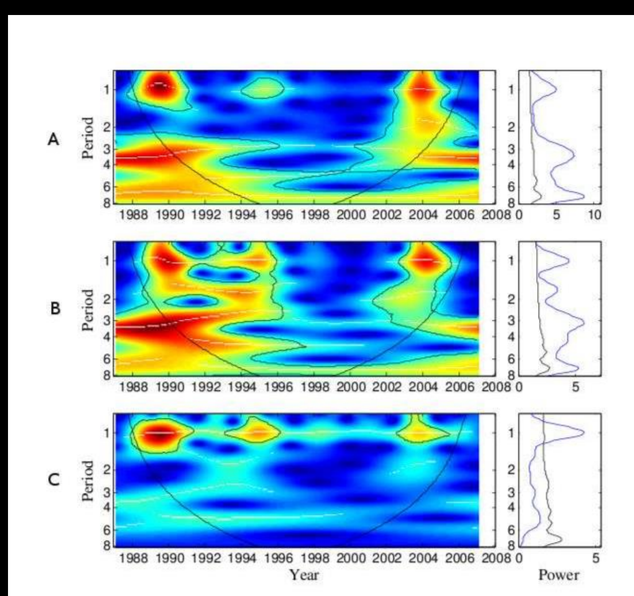
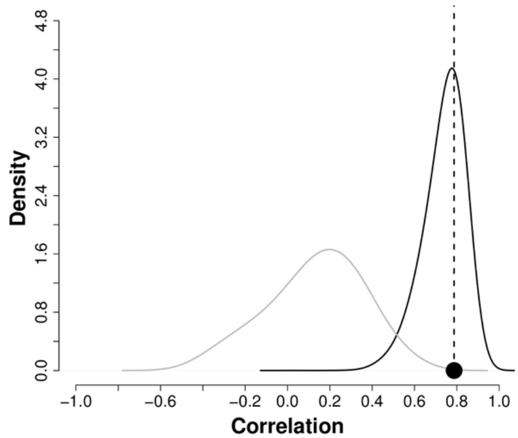


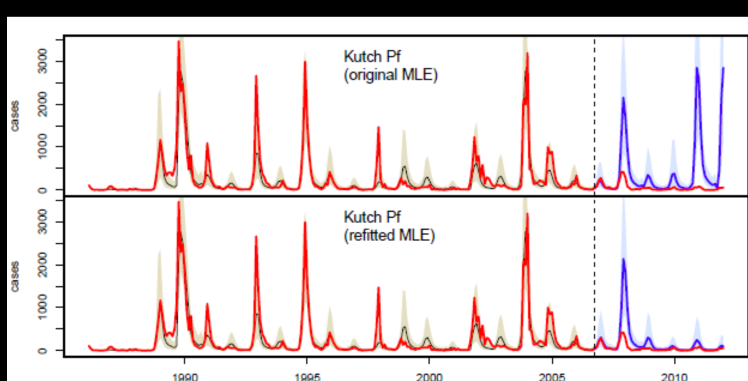
**Figure 5. Density plot of correlation between the accumulated rainfall from May to August and the accumulated cases from September to December in 10,000 simulations from a set of 2,000 solutions for the model with rainfall (black) and without rainfall (gray).**



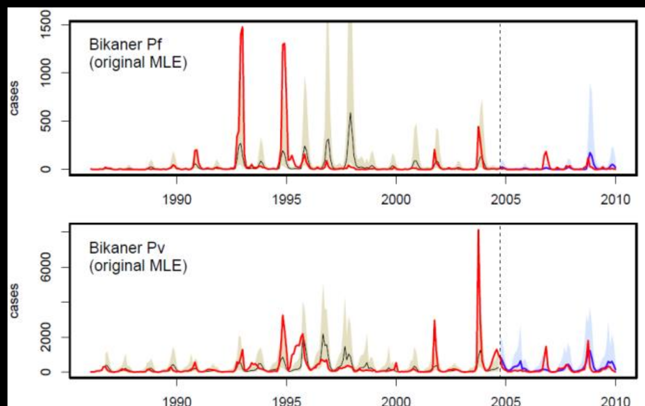

Laneri K, Bhadra A, Ionides EL, Bouma M, Dhiman RC, et al. (2010) Forcing Versus Feedback: Epidemic Malaria and Monsoon Rains in Northwest India. PLoS Comput Biol 6(9): e1000898. doi:10.1371/journal.pcbi.1000898
http://127.0.0.1:8081/ploscompbiol/article?id=info:doi/10.1371/journal.pcbi.1000898

PLOS | COMPUTATIONAL BIOLOGY

## ’Prediction’ in the presence of non-stationarity



In this other district, we can see that the recent decrease in cases can completely be explained by the lack of rains

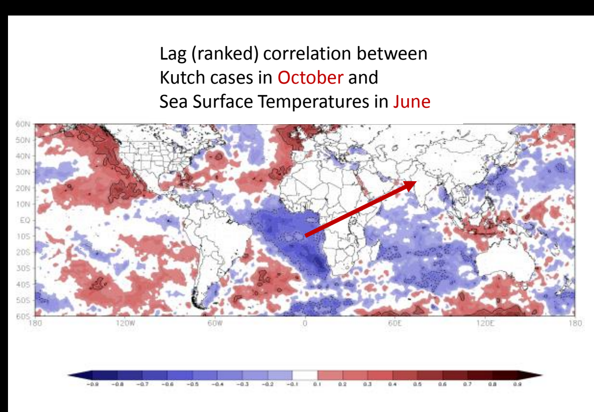



Ocean temperatures in the Tropical South Atlantic influence malaria epidemics in NW India

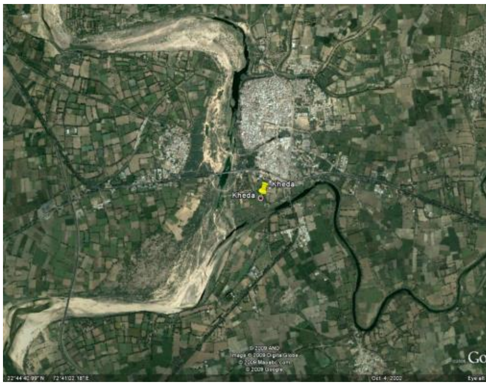
Sea Surface Temperatures (Atlantic)

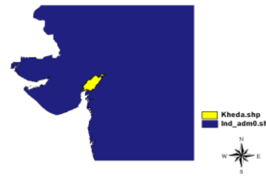
Rainfall NW India

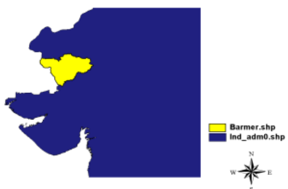
Malaria risk

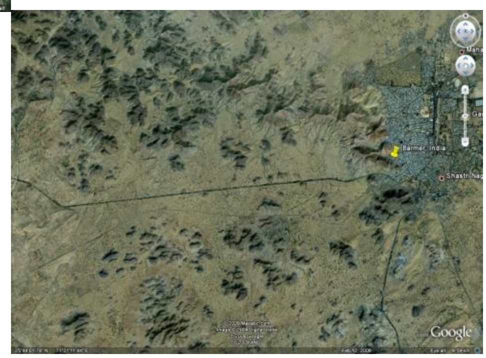



Cash *et al.* Nature Climate Change 2013



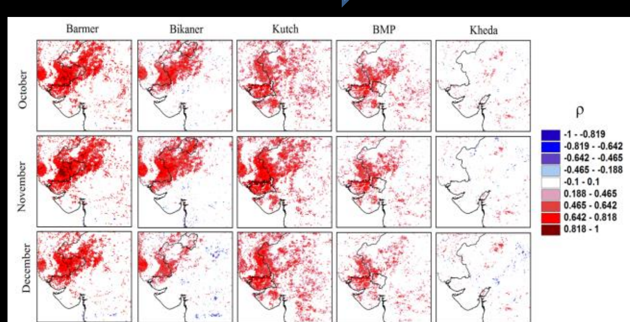




## Association with climate breaks down along an irrigation gradient

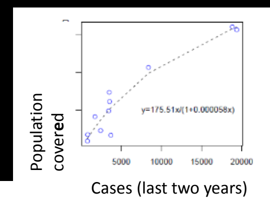
More irrigated land (more mosquito habitat / more wealth)

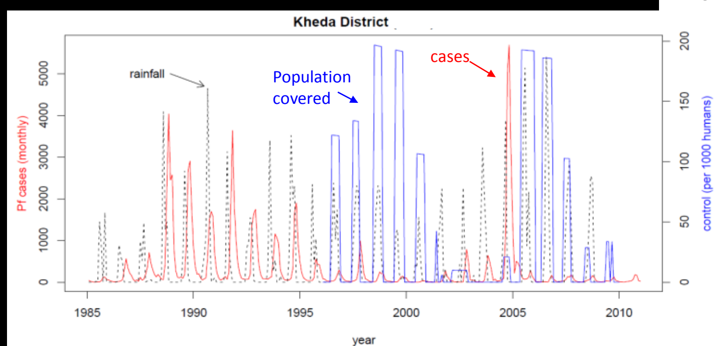



Rank correlation maps with vegetation index from remote sensing

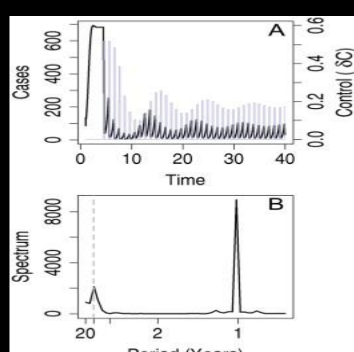
Baeza *et al.*, Malaria Journal 2011

## “Reactive” control policy generates cycles and unexpected epidemics, precluding elimination



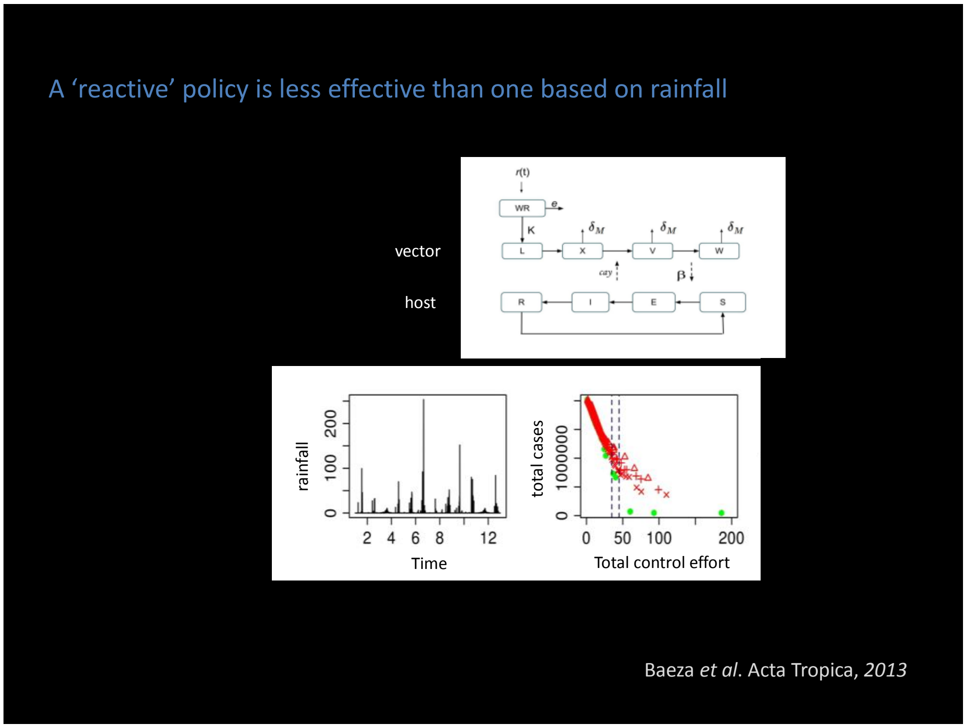

Baeza *et al.* Acta Tropica 2013
Baeza *et al.*, PNAS 2013

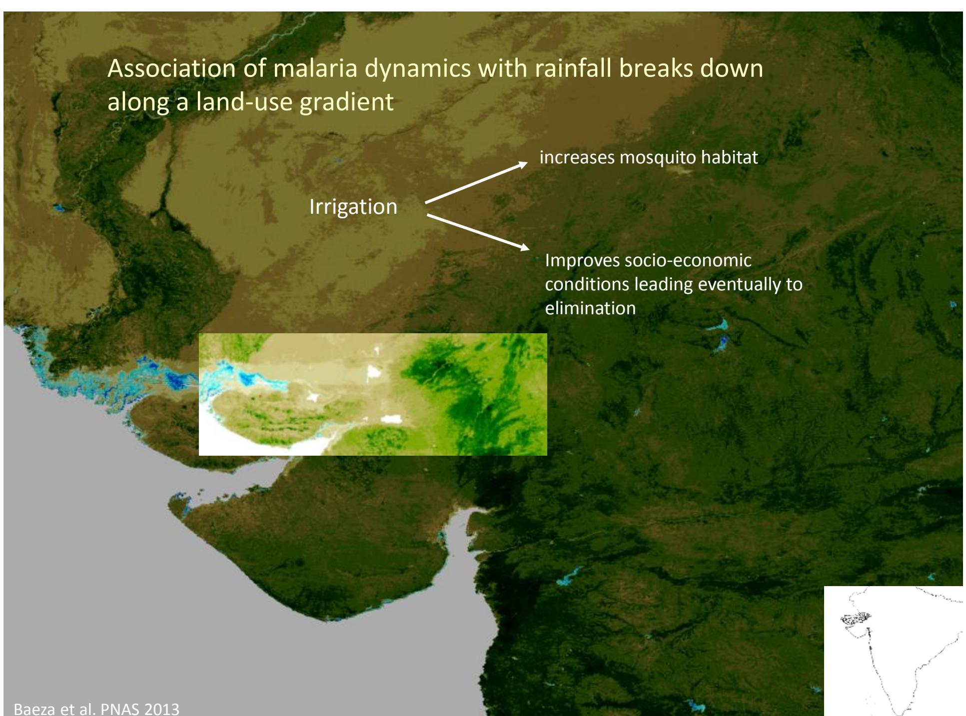


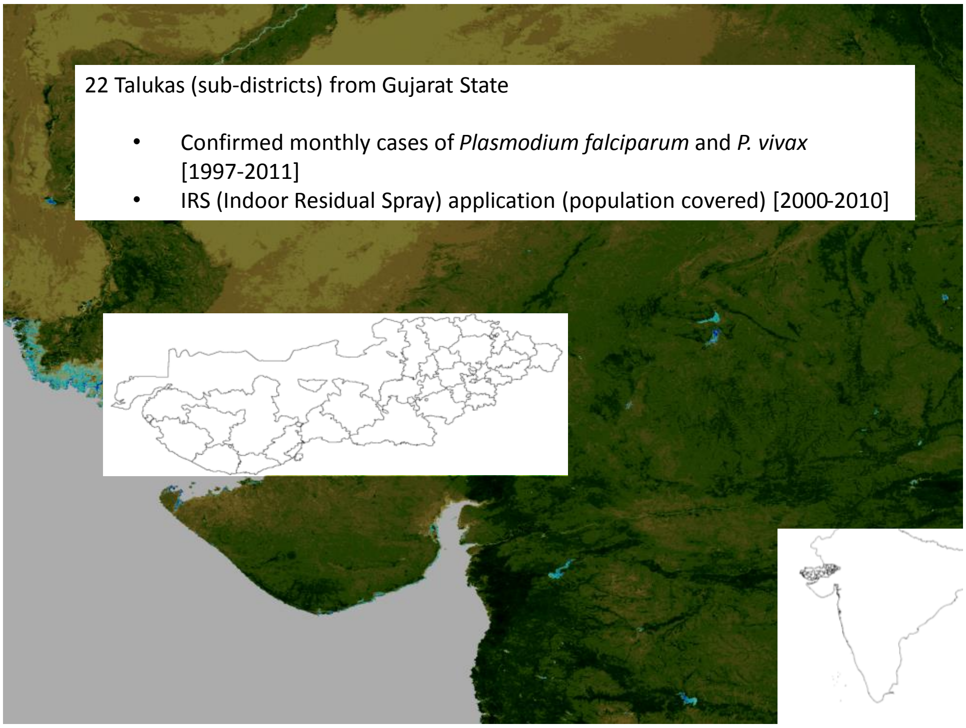

Malaria and control dynamics without environmental variability. The top panel shows the time series of new infected individuals

Andres Baeza , Menno J. Bouma , Ramesh Dhiman , Mercedes Pascual. Acta Tropica 2013

**Malaria control under unstable dynamics: Reactive vs. climate-based strategies**


A 'reactive' policy is less effective than one based on rainfall
vector
host
r(t)
WR
e
K
L
X
V
W
R
I
E
S
β
rainfall
Time
total cases
Total control effort
Baeza et al. Acta Tropica, 2013

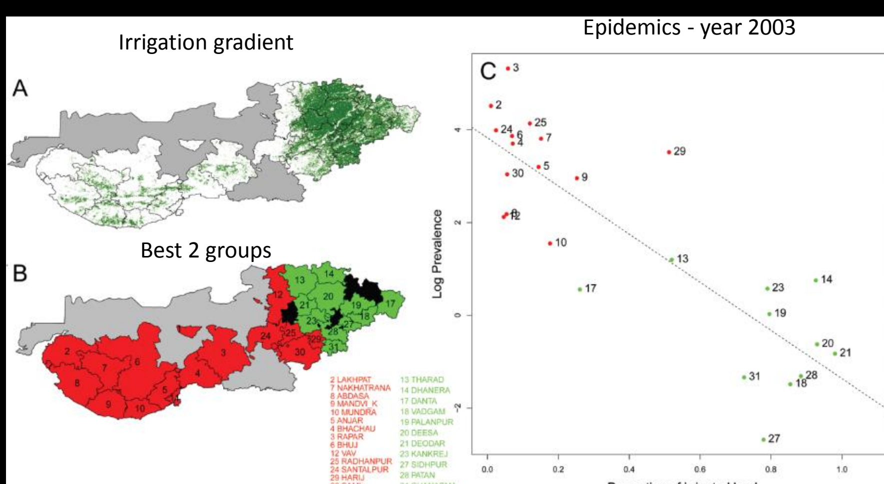

Association of malaria dynamics with rainfall breaks down along a land-use gradient
Irrigation
increases mosquito habitat
Improves socio-economic conditions leading eventually to elimination
Baeza et al. PNAS 2013



22 Talukas (sub-districts) from Gujarat State

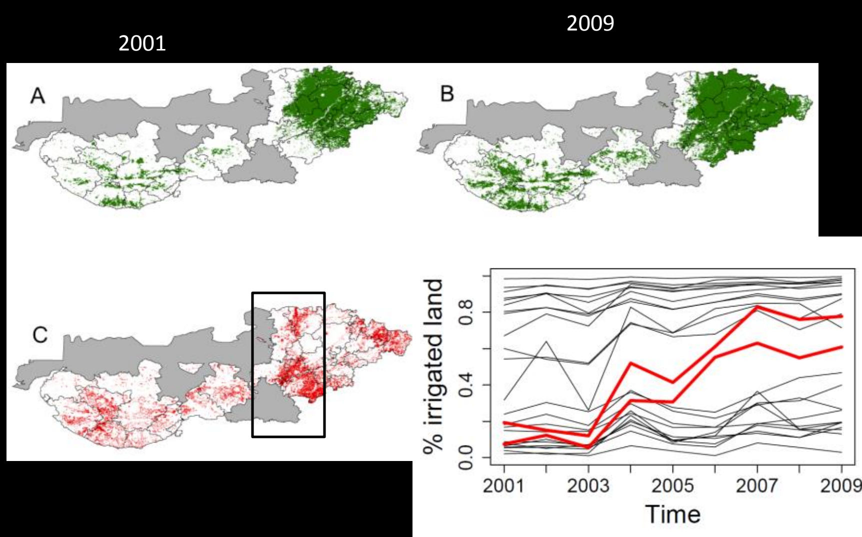
- Confirmed monthly cases of *Plasmodium falciparum* and *P. vivax* [1997-2011]
- IRS (Indoor Residual Spray) application (population covered) [2000-2010]

# Two groups and irrigation

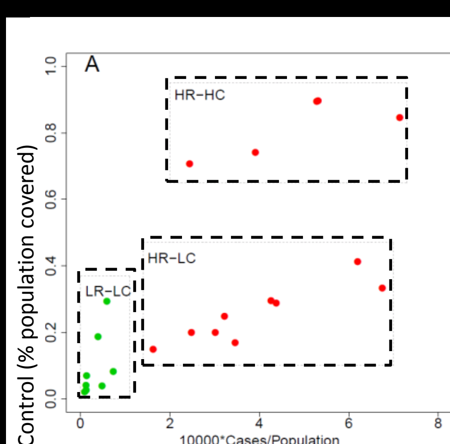



Baeza *et al. PNAS 2013*

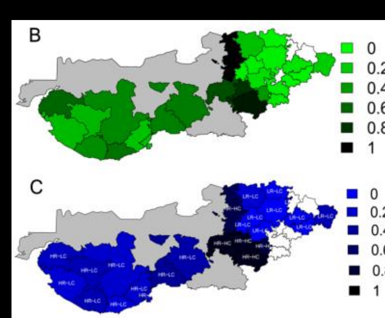
## Temporal change in vegetation (NDVI) outside monsoon season (i.e. irrigated agriculture)



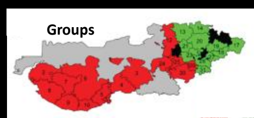

## patterns of risk and IRS control

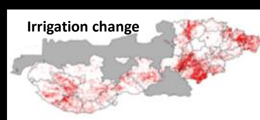



**LR-LC**: Low Risk-Low Control
**HR-LC**: High Risk-Low Control
**HR-HC**: High Risk-High Control

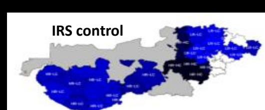


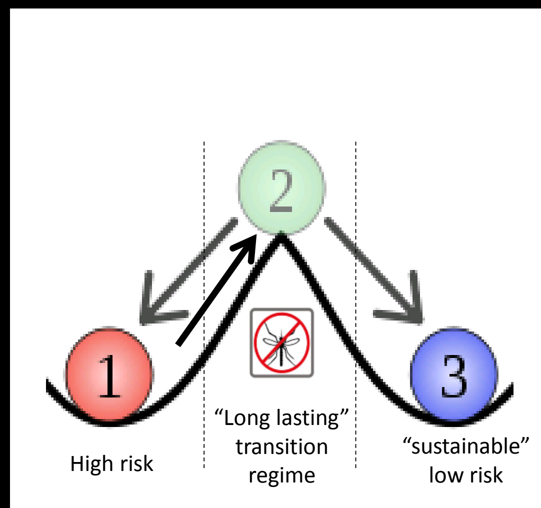
## Transitional phase can be long-lasting



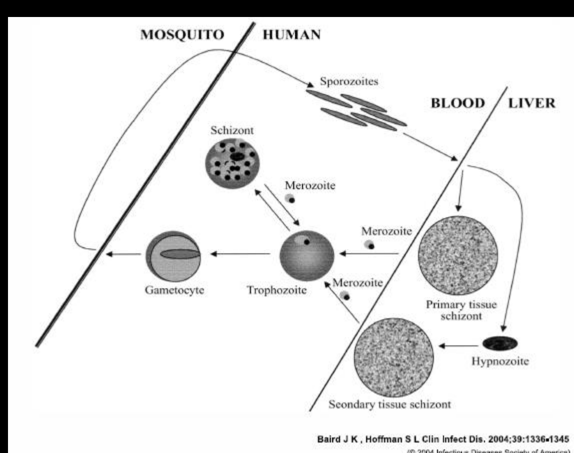







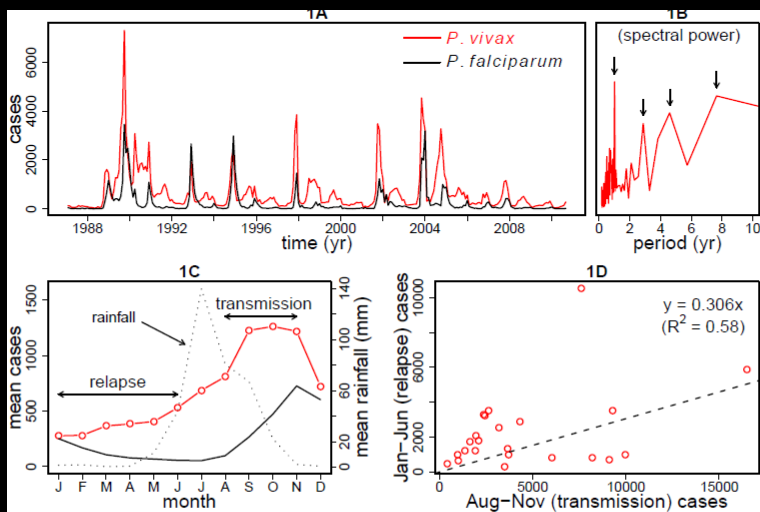




## *P. vivax* malaria : relapses, rainfall and treatment

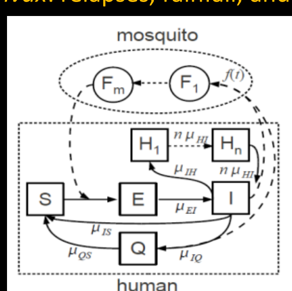


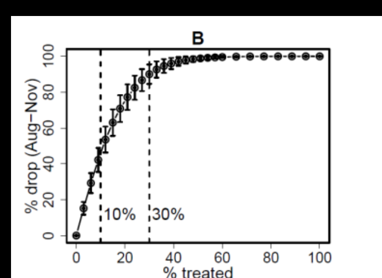

Inference on importance and duration of relapses from the population dynamics of the disease?

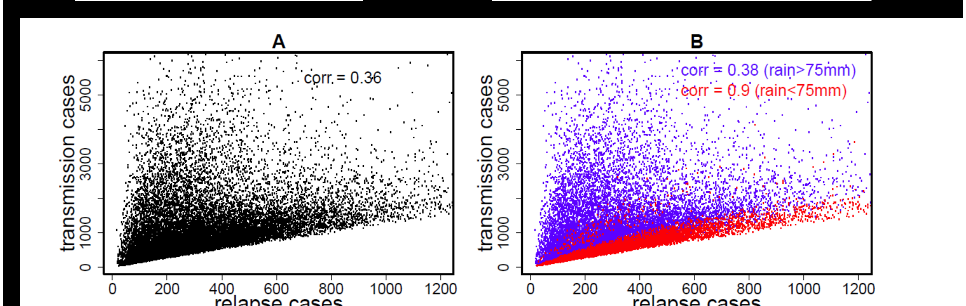
Potential implications for treatment that focuses on this stage of the disease?




## *P. vivax*: relapses, rainfall, and treatment



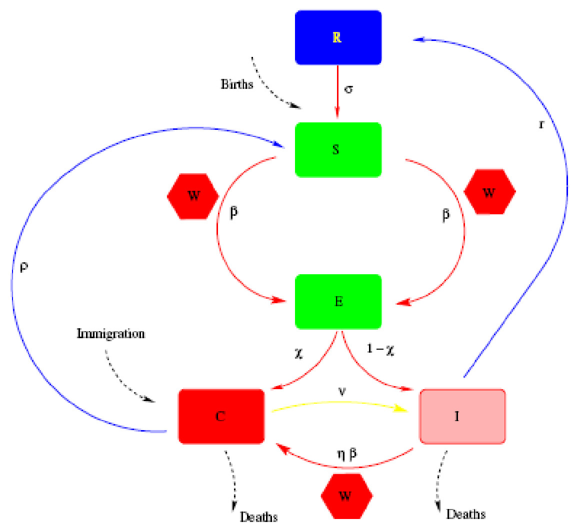




Roy *et al,* PloS Neglected Tropical Diseases, *PloS NTD*

# Coupled mosquito-human transmission model

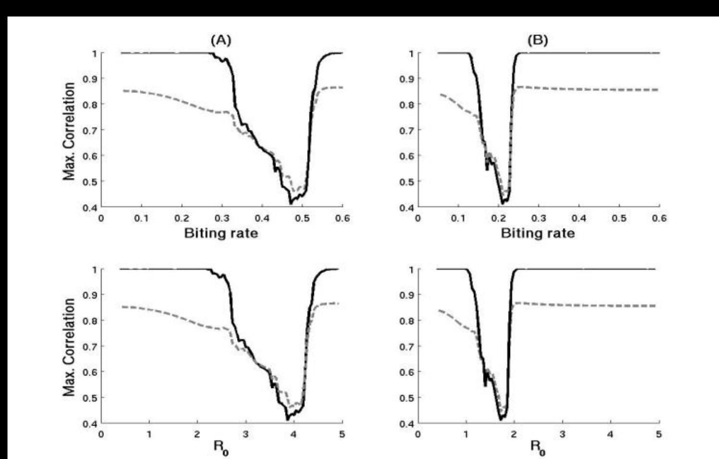
- Larvae
- Adults in three classes:
  - uninfected
  - exposed
  - infectious




## Correlation between simulated cases and forcing (seasonal and interannual)

Low carrying capacity for mosquito larvae
Prevalence in humans from 0.01 to 0.07

High carrying capacity
Prevalence in humans from 0.1 to 0.9




From Rodo *et al.* (Review on climate and disease in Climatic Change 2012)

# Gracias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