Detecting climate drivers of malaria using a causality criterion

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- wanted to investigate (causal) factors affecting malaria cases
- used a causality test based on attractor reconstruction
- can extract more than "causal or not": time lags, and sign and strength of the effect
- interpret these results in terms of processes involved in the infection

Attractor reconstruction and Causality

Causality in time series

Spurious correlations: correlation does not imply causality

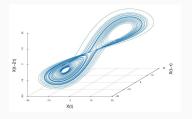




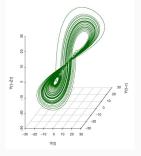


More commonly, *confounding variables* are an important issue.

Takens's theorem: it's possible to reconstruct the attractor (of a multi-dimensional system) using a single variable!





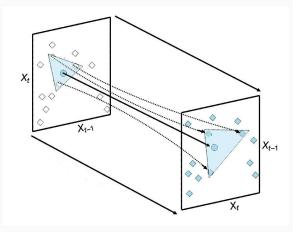


Reconstruction using variable y

The reconstructed attractor is not equal to the original, but there's a local mapping between them at each point.

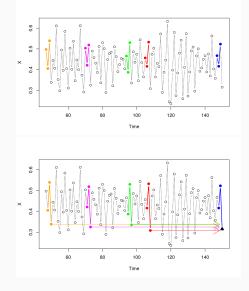
Projection using the reconstructed attractor

Looking for nearby points in the attractor (in the phase space, not in time), we can predict the next point (in time). It's a weighted average (simplex or S-map methods).



Source: Liu et al. (2012).

Projection using the reconstructed attractor



We take close points in the attractor and follow them.

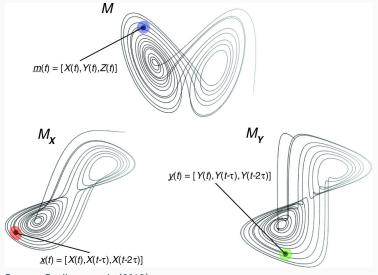
This gives us some power of prediction.

 $\rho =$ "prediction skill": the correlation between predicted and observed values over the whole series gives a measure of how good is this prediction

Two variables are causally related if they are part of the same dynamical system, and at least one affects the other.

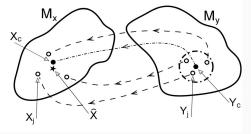
If two variables belong to the same dynamical system, they map onto the same attractor!

Equivalent attractors



Source: Sugihara et al. (2012).

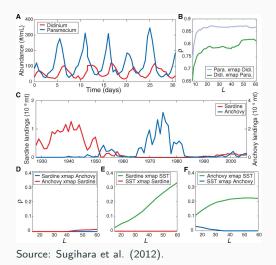
We use the reconstructed attractor from variable Y to predict the value of variable X at the same time – \hat{X} .



Source: Sugihara et al. (2012).

Again, we repeat the procedure for every point, and look at the correlation between predicted and actual values – ρ – "cross-mapping prediction skill"

Convergent cross-mapping (CCM)



If there is causality, prediction skill should:

- be higher than correlation between time series
- increase as the amount of data used for reconstruction increases

False negatives are common: too much noise can quickly blur the reconstructed attractors

False positives are very rare, but they do occur in a particular situation: strongly seasonal patterns. Oops!

What can we do? We separate the effect of the seasonal pattern from the effect of the variation around that pattern, by building *surrogate* time series: the residues of the seasonal pattern are scrambled.

We test thousands of surrogate series to find a statistical distribution of ρ ; then we check if the original series has a significant value of ρ . (Deyle et al. 2016)

Climate drivers of malaria



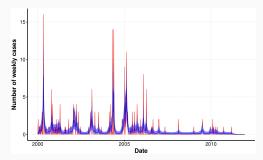
Tartagal, in the region of Salta in Argentina

Southernmost region of malaria incidence in the Americas Probably regulated more strongly by climate than by (human) epidemiology? Data: 12 years of weekly malaria *P. vivax* cases, relative humidity and

temperature time series

Series from Jan 2000 – Dec 2011: total of 266 cases of malaria *vivax*

Typically from November to April (summer season), during winter (July to September) they drop to zero.

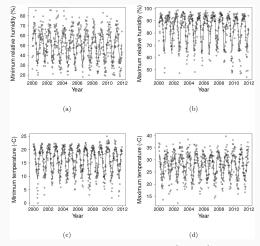


Red line: number of cases of malaria in Tartagal (Argentina). Blue: estimated mean weekly number of cases with its 95% credibility interval. Source: Laneri et al. (2019)

Potential climate drivers

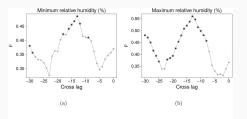
What are the climatic factors driving number of cases?

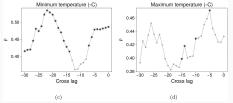
We tested maximum and minimum relative humidity and minimum and maximum temperature.



Weekly values of climate variables (points) and their seasonal trends, fitted by spline regressions. Source: Laneri et al. (2019)

Causal factors influencing malaria cases





Significant causal factors against time lag. Laneri et al. (2019)

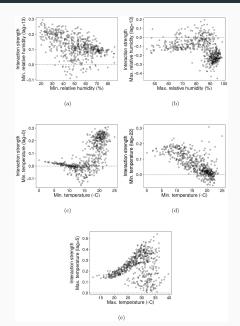
Temperature and humidity are causal factors - with *lags*.

Each time lag can be associated to different processes!?

- at short (below 5 weeks) time delays, effects of parasite cycle (EIP)
- at long (over 12 weeks) time delays, effects related to mosquito population dynamics

Interaction strength of each variable on malaria cases

- Minimum humidity has a positive effect on cases; maximum humidity above 85% has a negative effect
- Temperature has always a positive non-linear effect on cases, with maximum temperature effects more pronounced above 25°C and minimum above 17°C



- CCM is a useful model-free tool to unravel causal factors
- the relevant time lags and patterns in interaction strength also can yield important biological information
- Climate drivers do drive malaria vivax cases in Tartagal
- The features of the interactions are consistent with temperature and humidity affecting both vector population dynamics and *Plasmodium* development

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Brenno Cabella (former post-doc at IFT-Unesp)



Paulo Inácio Prado (IB-USP)





Thanks for your attention!





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