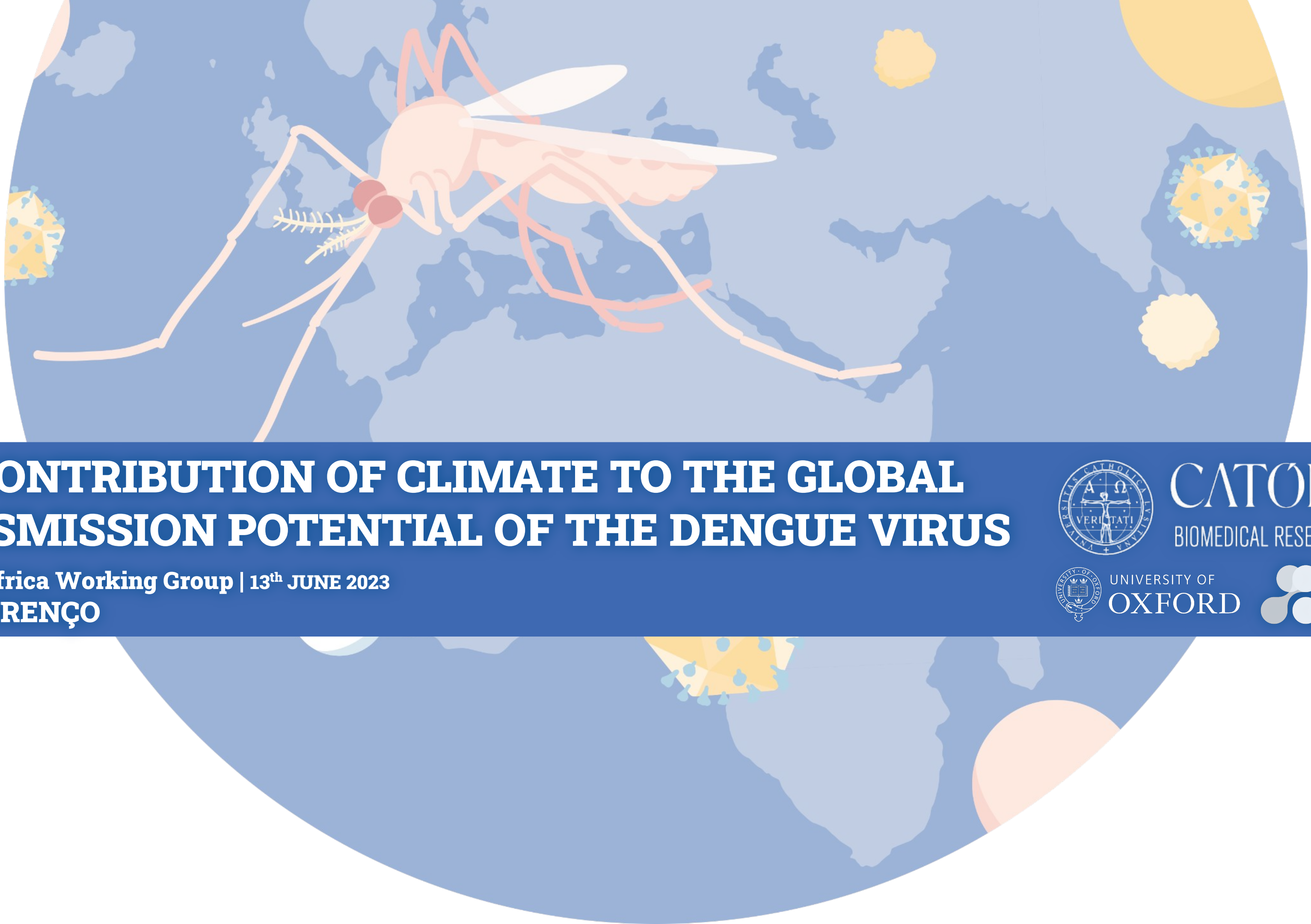

THE CONTRIBUTION OF CLIMATE TO THE GLOBAL TRANSMISSION POTENTIAL OF THE DENGUE VIRUS

CLIMADE Africa Working Group | 13th JUNE 2023

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CATÓLICA BIOMEDICAL RESEARCH CENTRE

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RESEARCH ON CLIMATE & MOSQUITO-BORNE VIRUSES

DENGUE

The 2012 madeira dengue outbreak: epidemiological determinants and future epidemic potential.
PLoS Neg Trop Dis 2014

Genomic and epidemiological characterisation of a dengue virus outbreak among blood donors in Brazil.
Nature Scientific Reports 2017

MVSE: An R-package that estimates a climate-driven mosquito-borne viral suitability index.
Methods in Ecology & Evolution 2019

Asynchronicity of endemic and emerging mosquito-borne disease outbreaks in the Dominican Republic.
Nature Communications 2021

Field and classroom initiatives for portable sequence-based monitoring of dengue virus in Brazil.
Nature Communications 2021

Global transmission suitability maps for dengue virus transmitted by Aedes aegypti from 1981 to 2019.
Nature Scientific Data 2023

ZIKA

Epidemiological and ecological determinants of Zika virus transmission in an urban setting.
eLIFE 2017

Measuring mosquito-borne viral suitability in Myanmar and implications for local zika virus transmission.
PLoS Currents 2018

MVSE: An R-package that estimates a climate-driven mosquito-borne viral suitability index.
Methods in Ecology & Evolution 2019

Genomic and epidemiological surveillance of zika virus in the amazon region.
Cell Reports 2020

Asynchronicity of endemic and emerging mosquito-borne disease outbreaks in the Dominican Republic.
Nature Communications 2021

CHIKUNGUNYA

MVSE: An R-package that estimates a climate-driven mosquito-borne viral suitability index.
Methods in Ecology & Evolution 2019

Return of the founder Chikungunya virus to its place of introduction into Brazil is revealed by genomic characterization of exanthematic disease cases.
Emerging Microbes & Infections 2019

Asynchronicity of endemic and emerging mosquito-borne disease outbreaks in the Dominican Republic.
Nature Communications 2021

WEST NILE

Characterising West Nile virus epidemiology in Israel using a transmission suitability index.
Eurosurveillance 2020

West nile virus in Brazil.
Pathogens 2021

West Nile virus transmission potential in Portugal.
Communications Biology 2022

Atypical weather is associated with the 2022 early start of West Nile virus transmission in Italy.
Eurosurveillance 2022

YELLOW FEVER

Genomic epidemiology sheds light on the recent spatio-temporal dynamics of Yellow Fever virus and the spatial corridor that fueled its ongoing emergence in southern Brazil.
Science Advances (review) 2023

NOT ZOONOTIC — ZOONOTIC

AEDES SPP. — CULEX SPP. — AEDES AEGYPTI

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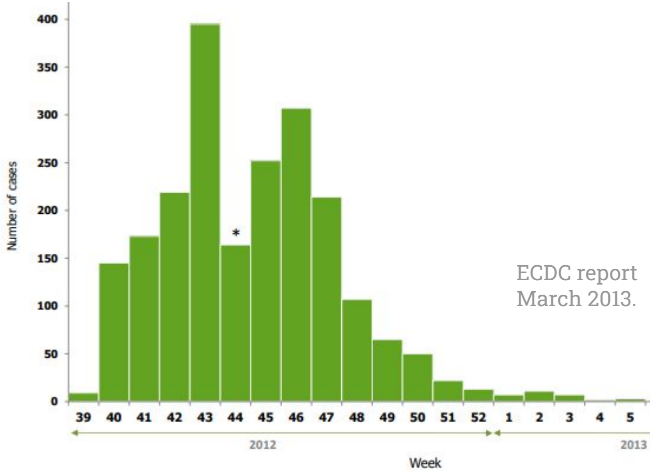
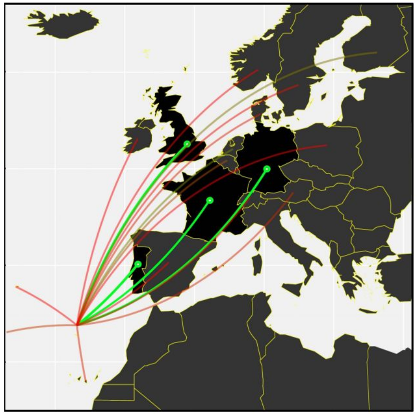
METHODOLOGY

STARTING POINT: THE DENGUE OUTBREAK IN MADEIRA 2012

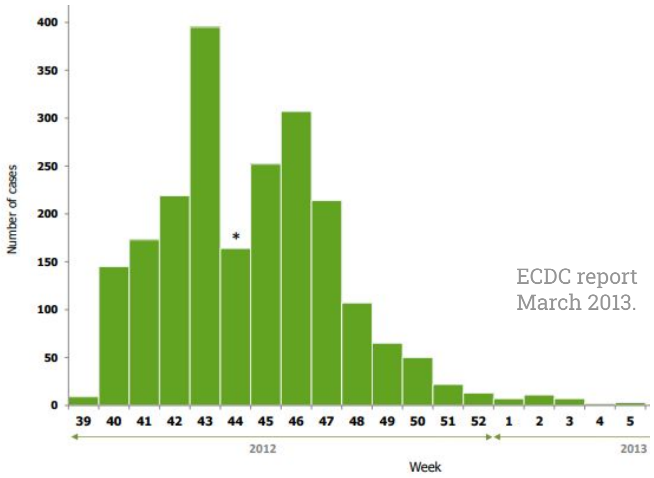


ECDC report
March 2013.



Lourenco et al PLoS NTDs 2014

STARTING POINT: THE DENGUE OUTBREAK IN MADEIRA 2012



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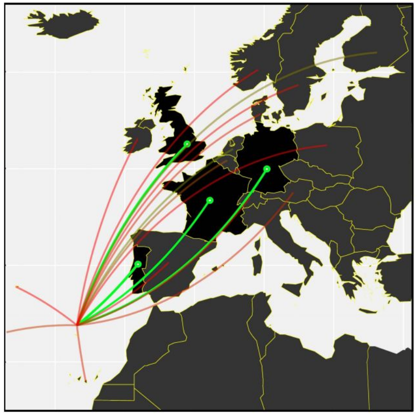
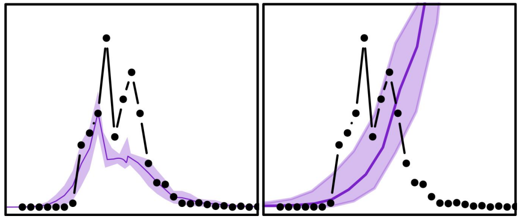
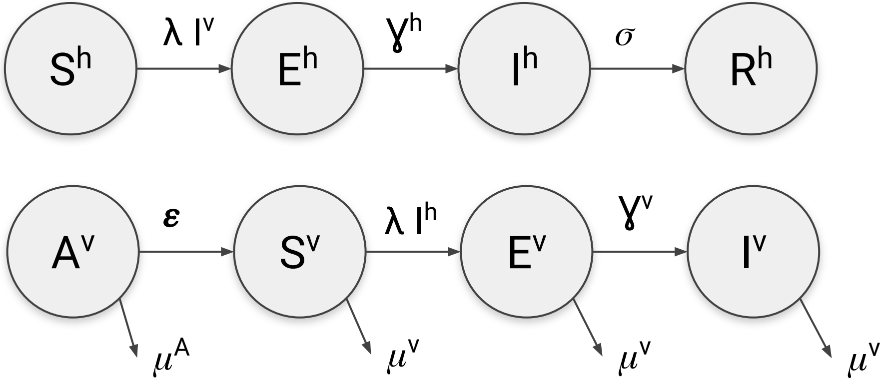


Lourenco et al PLoS NTDs 2014



We could not fit dengue transmission models to the observed outbreak dynamics.

Why?



$$\frac{dS^h}{dt} = -\lambda^{v\to h} \qquad \frac{dA}{dt} = cf\dot{\theta}^v_A\left(1-\frac{A}{K}\right)V-(\dot{\epsilon}^v_A+\dot{\mu}^v_A)A$$

$$\frac{dE^h}{dt} = \lambda^{v\to h}-\gamma^h E^h \qquad \frac{dS^v}{dt} = \dot{\epsilon}^v_A A-\lambda^{h\to v}-\dot{\mu}^v_V S^v$$

$$\frac{dI^h}{dt} = \gamma^h E^h-\sigma^h I^h \qquad \frac{dE^v}{dt} = \lambda^{h\to v}-\dot{\gamma}^v E^v-\dot{\mu}^v_V E^v$$

$$\frac{dR^h}{dt} = \sigma^h I^h \qquad \frac{dI^v}{dt} = \dot{\gamma}^v E^v-\dot{\mu}^v_V E^v$$

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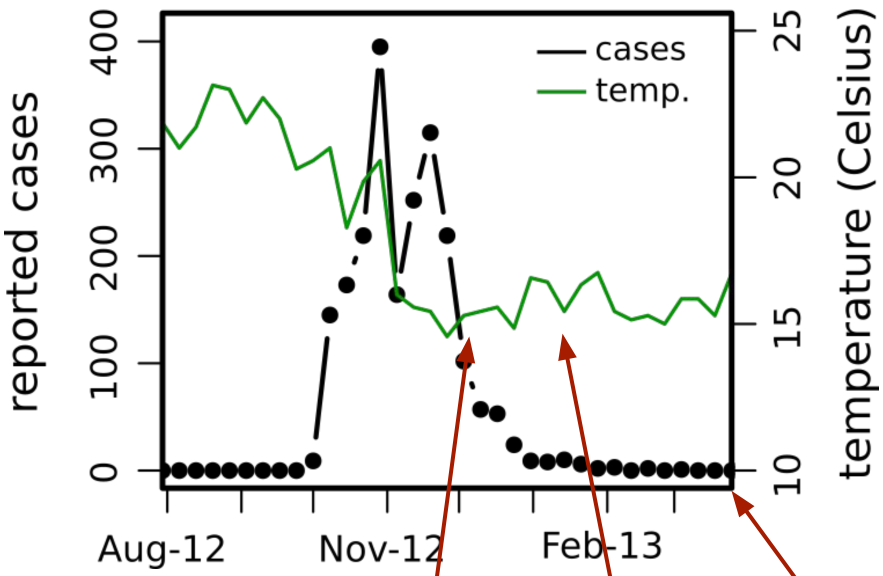
STARTING POINT: THE DENGUE OUTBREAK IN MADEIRA 2012



Lourenco et al PLoS NTDs 2014

December

January

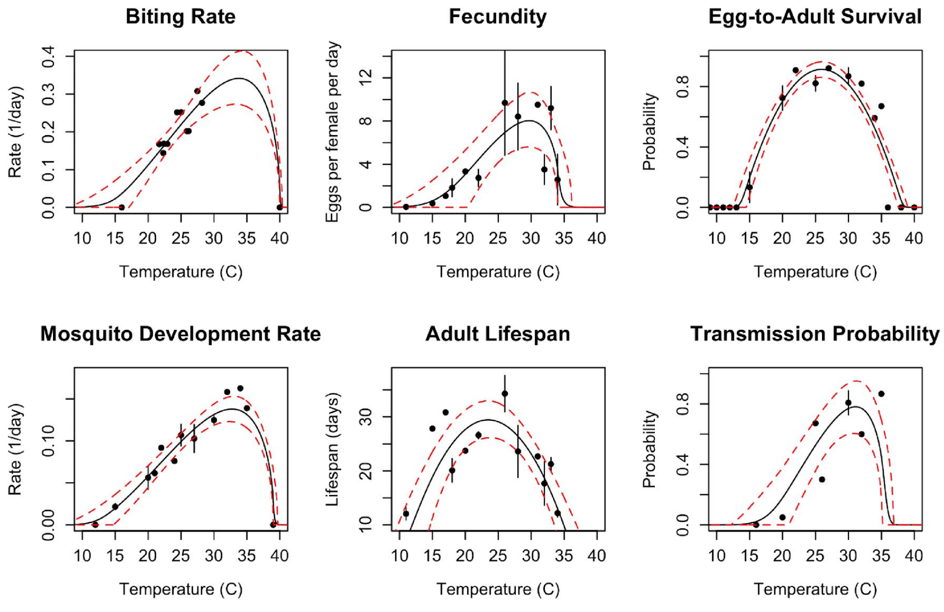
Extinction
before next season (spring)

HOW COULD CLIMATE AFFECT OUTBREAK DYNAMICS?

COULD WE MODEL THE EFFECTS?

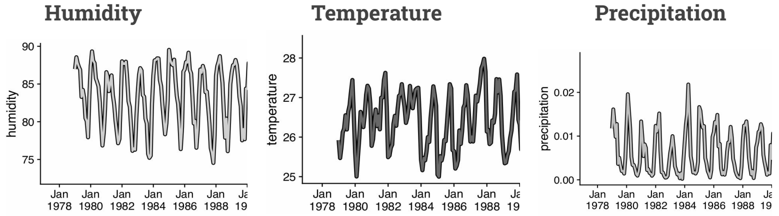
HOW DOES CLIMATE AFFECT MOSQUITO-VIRUS TRAITS ?

TRAITS VARY WITH TEMPERATURE, HUMIDITY, ETC

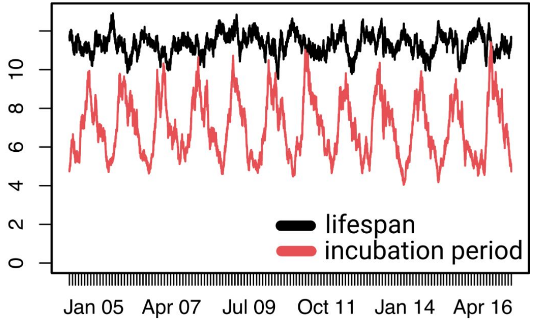


Mordecai et al. PLoS NTDs 2017

CLIMATE VARIES IN TIME (AND SPACE)



TRAITS VARY IN TIME (SPACE)



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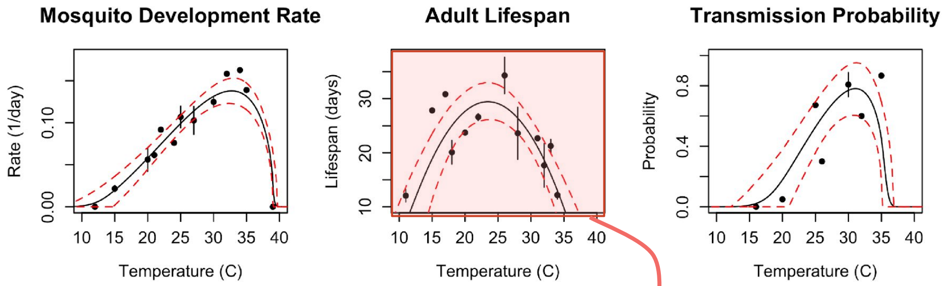
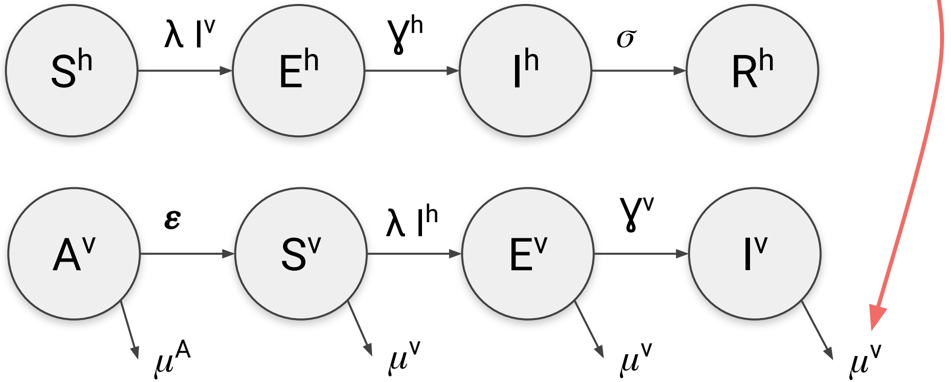
STARTING POINT: THE DENGUE OUTBREAK IN MADEIRA 2012



Fit mathematical expression to each trait & fed them into model parameters

$$\dot{\mu}_V^v = \mu_V^v(T) = 0.8692 - 0.1599T + 0.01116T^2 - 0.0003408T^3 + 0.000003809T^4$$



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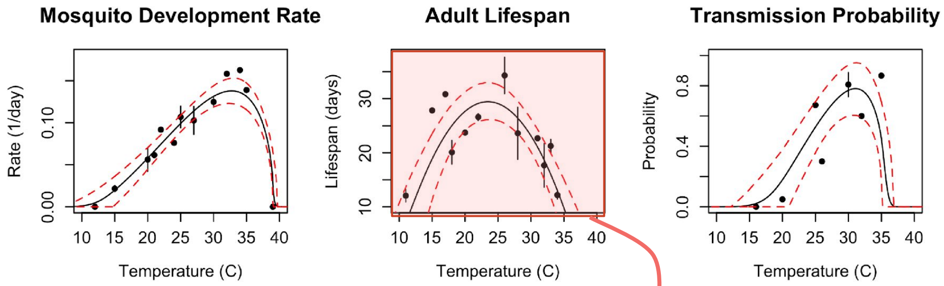
STARTING POINT: THE DENGUE OUTBREAK IN MADEIRA 2012



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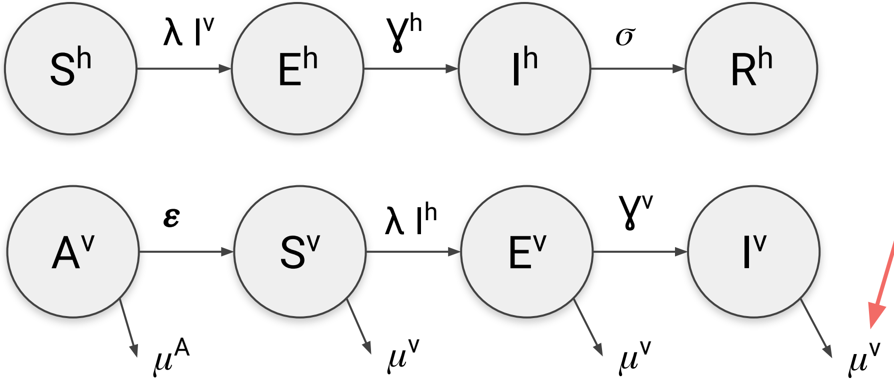
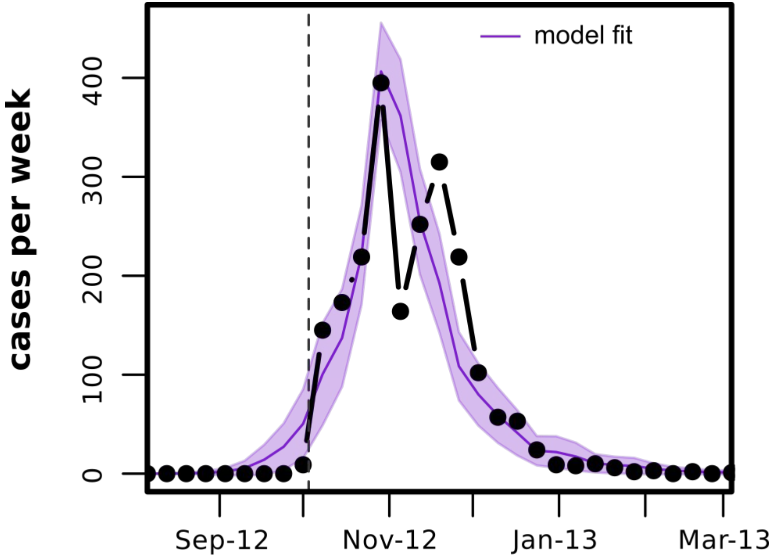
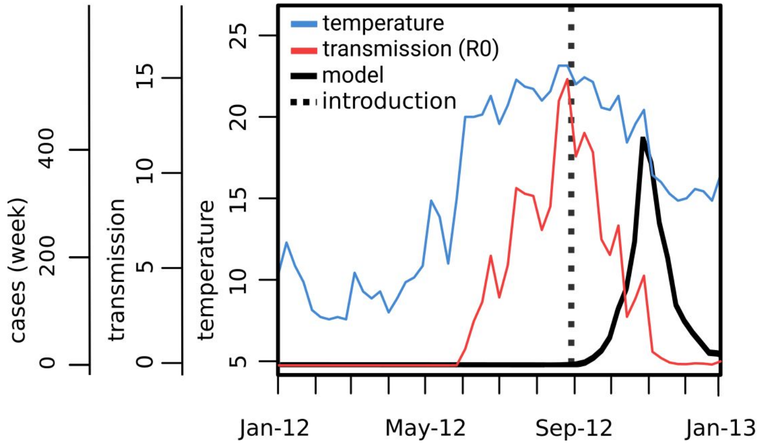


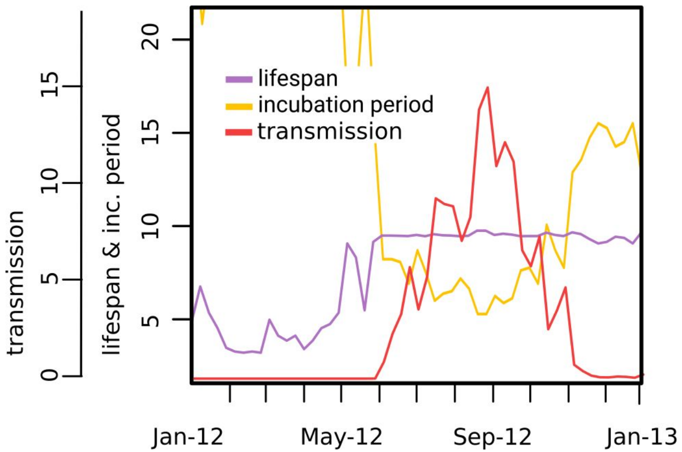


Lourenco et al PLoS NTDs 2014

STARTING POINT: THE DENGUE OUTBREAK IN MADEIRA 2012

Lourenco et al PLoS NTDs 2014

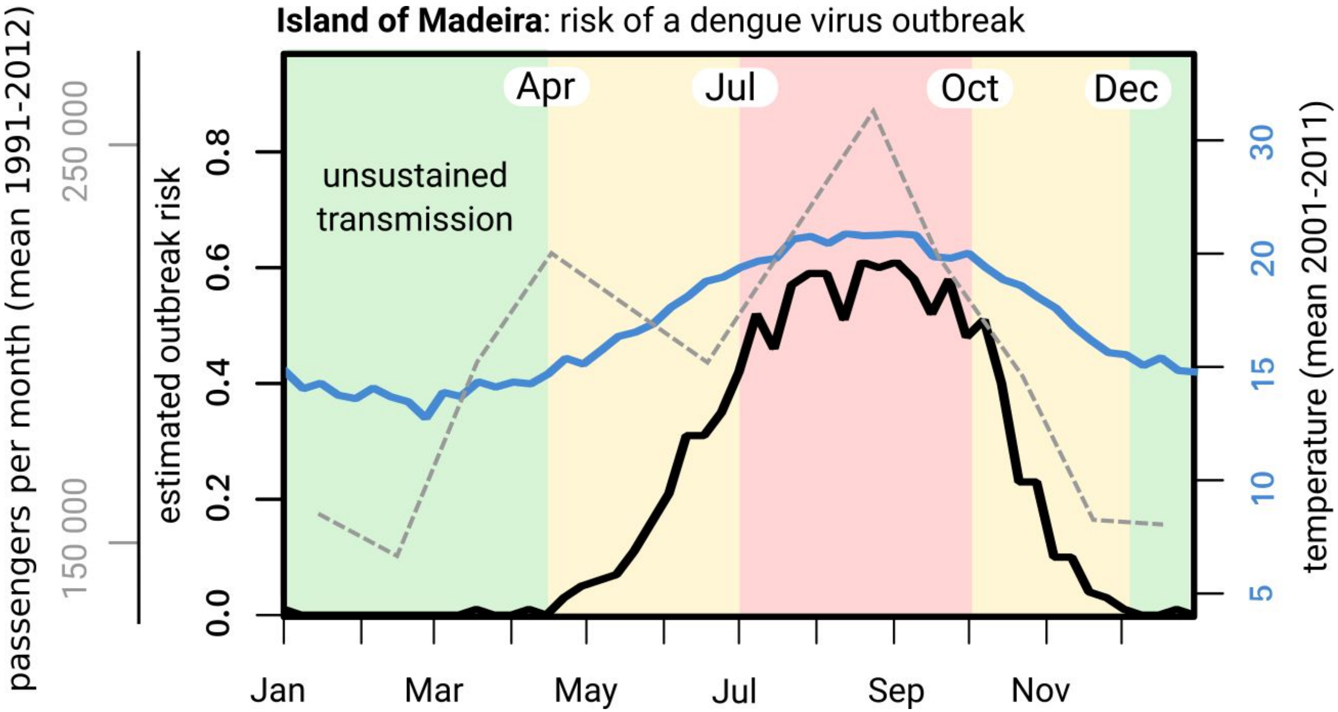


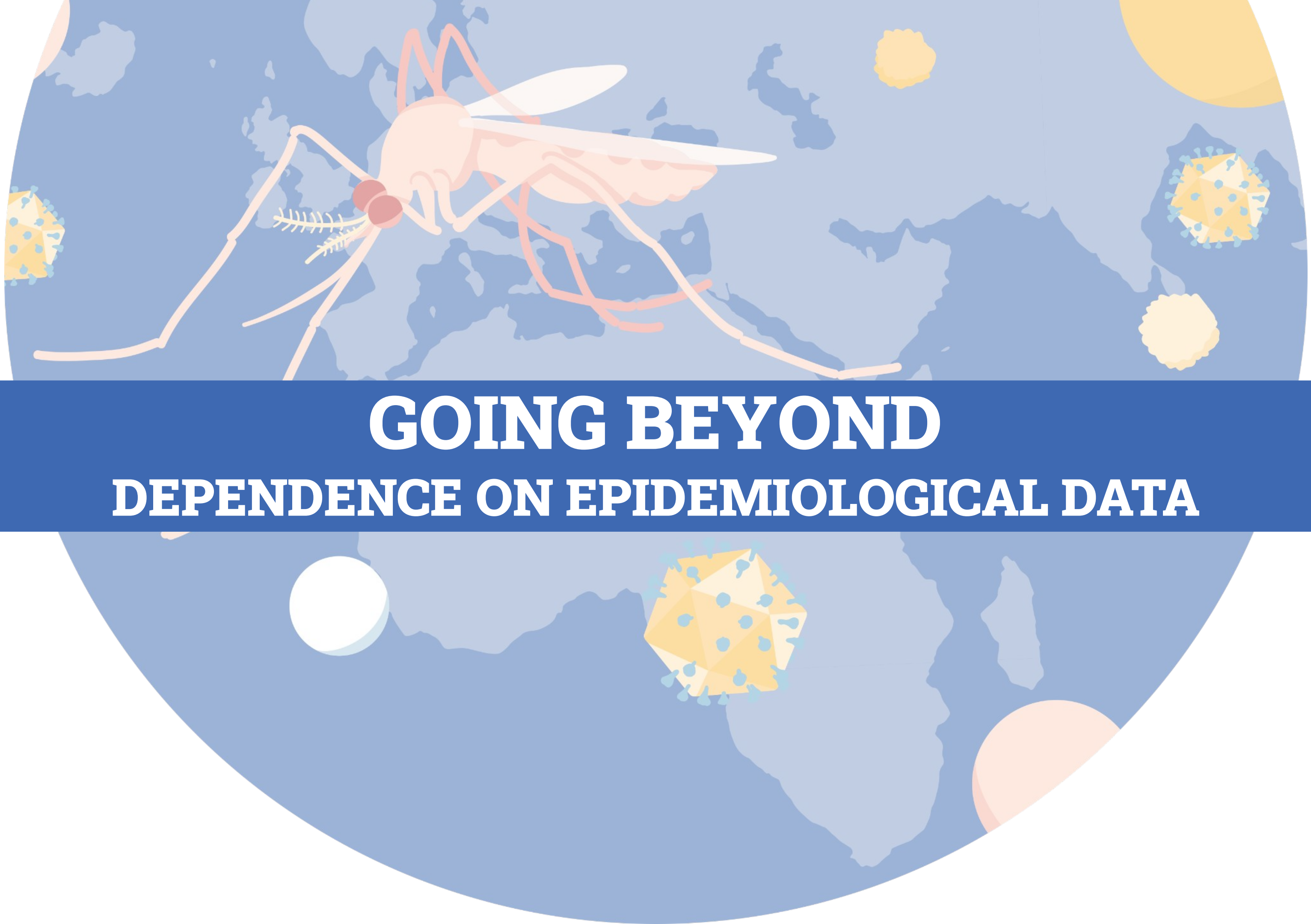


Transmission was possible while **temperature** was kept above 15C.

That was the period in which the **incubation period of the virus** in mosquitoes was shorter than the **life-span of the mosquitoes**

STARTING POINT: THE DENGUE OUTBREAK IN MADEIRA 2012

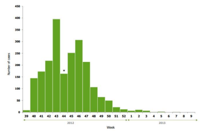


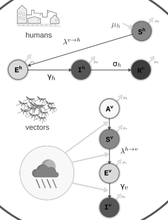


GOING BEYOND
DEPENDENCE ON EPIDEMIOLOGICAL DATA

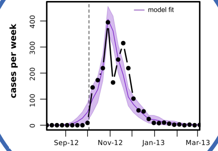
DEPENDENCE ON EPIDEMIOLOGICAL DATA

data on the
biological system



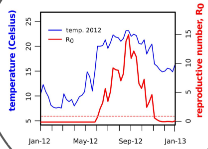


mathematical
model of the
biological system



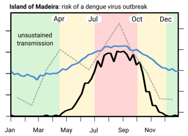
fit the model to
the data

outputs



prediction &
simulation of
unobserved
scenarios

inform and contribute
to public health



WITHOUT EPIDEMIOLOGICAL DATA, CALIBRATION CANNOT BE DONE

How to use models that we know work well without depending on epidemiological data?

INDEX P: A SUITABILITY MEASURE OF VIRAL TRANSMISSION

$$\frac{dS^h}{dt} = -\lambda^{v\to h}$$

$$\frac{dE^h}{dt} = \lambda^{v\to h} - \gamma^h E^h$$

$$\frac{dI^h}{dt} = \gamma^h E^h - \sigma^h I^h$$

$$\frac{dR^h}{dt} = \sigma^h I^h$$

$$\frac{dA}{dt} = cf\dot{\theta}^v_A\left(1-\frac{A}{K}\right)V - (\dot{\epsilon}^v_A + \dot{\mu}^v_A)A$$

$$\frac{dS^v}{dt} = \dot{\epsilon}^v_A A - \lambda^{h\to v} - \dot{\mu}^v_V S^v$$

$$\frac{dE^v}{dt} = \lambda^{h\to v} - \dot{\gamma}^v E^v - \dot{\mu}^v_V E^v$$

$$\frac{dI^v}{dt} = \dot{\gamma}^v E^v - \dot{\mu}^v_V E^v$$

human-to-vector transmission probability per infectious bite

vector-to-human transmission probability per infectious bite

number of female vectors per host

bitting rate

extrinsic incubation period

intrinsic incubation period

$$R_0 = \frac{(V/N) \quad a^v \quad a^v \quad \phi^{v\to h} \quad \phi^{h\to v} \quad \boxed{\gamma^v} \quad \boxed{\gamma^h}}{\mu^v_V(\sigma^h+\mu^h)(\gamma^h+\mu^h)(\gamma^v+\mu^v_V)}$$

vector life-span

host infectious period

host infectious life-span

$$R_0 = \boxed{(V/N)}\boxed{P}$$

(V/N) = NUMBER OF MOSQUITOES PER HUMAN

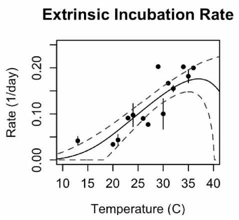
unknown

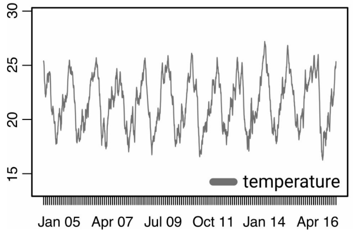
CLIMATE-DEPENDENT PARAMETERS

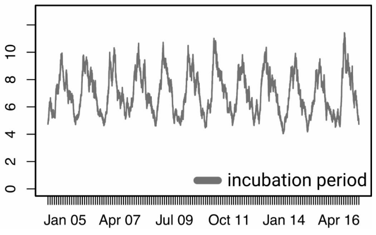
known

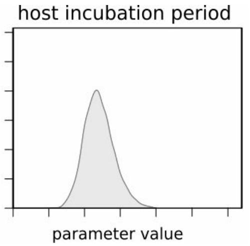
CLIMATE-INDEPENDENT PARAMETERS

known









INDEX P

Average number of new infections a single female mosquito can produce in a lifetime.

- Homogeneous mixing
- Susceptible population

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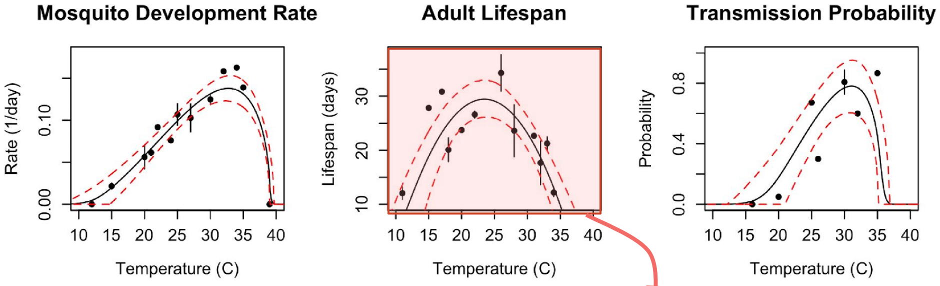
INDEX P: A SUITABILITY MEASURE OF VIRAL TRANSMISSION

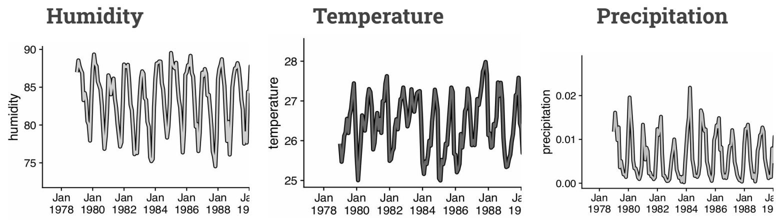
EMPIRICAL DATA



Mordecai et al. PLoS NTDs 2017

$$\mu_V^v = \mu_V^v(T) = 0.8692 - 0.1599T + 0.01116T^2 - 0.0003408T^3 + 0.000003809T^4$$

CLIMATE DATA



bitting rate
<humidity>

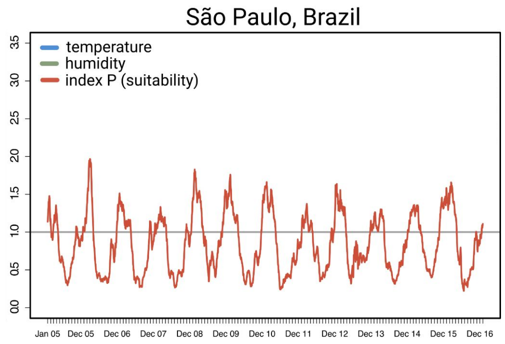
probability per infectious bite
<temperature>

extrinsic incubation period
<temperature>

$$P = \frac{a^v \; a^v \; \phi^{v\rightarrow h} \; \phi^{h\rightarrow v} \; \gamma^v \; \gamma^h}{\mu_V^v(\sigma^h + \mu^h)(\gamma^h + \mu^h)(\gamma^v + \mu_V^v)}$$

life-span
<humidity, temperature>

SIMULATION / QUANTIFICATION



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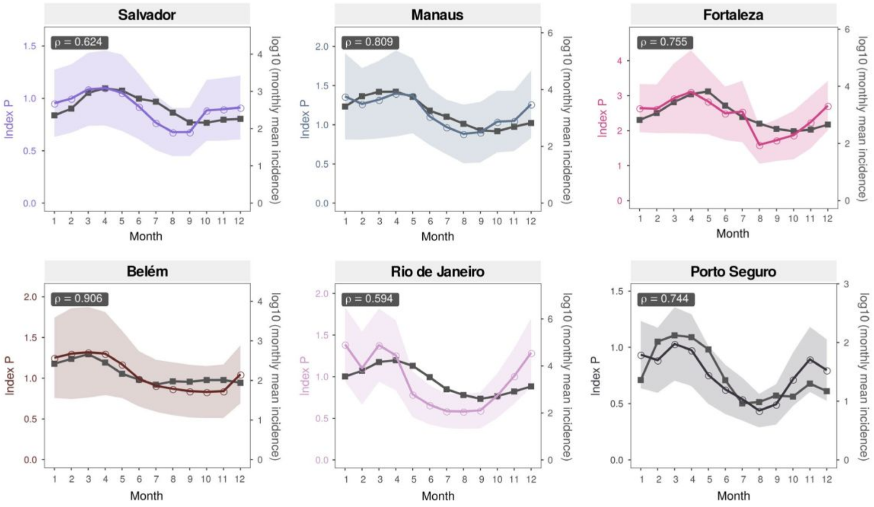
VALIDATION OF INDEX P: local scales

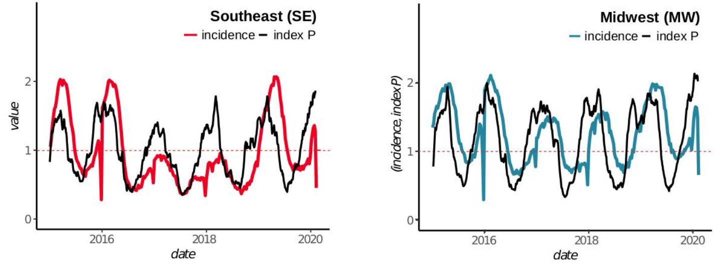
[DENGUE] CITY LEVEL

Obolski et al 2019 Met. Eco. Evo



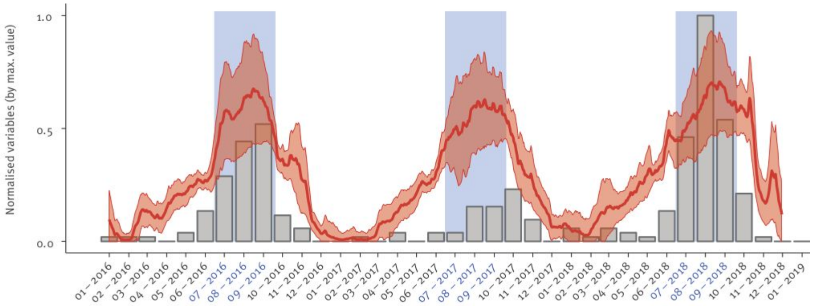
[DENGUE] REGIONAL LEVEL

Adelino et al 2021 Nat. Comms



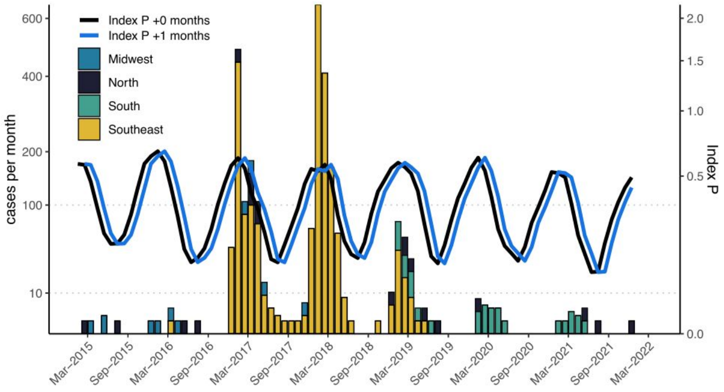
[WEST NILE] COUNTRY / REGIONAL LEVELS

Lourenco et al 2020 Euro Surveillance



[YELLOW FEVER] REGIONAL LEVELS

Giovanetti et al 2023 Science Advances



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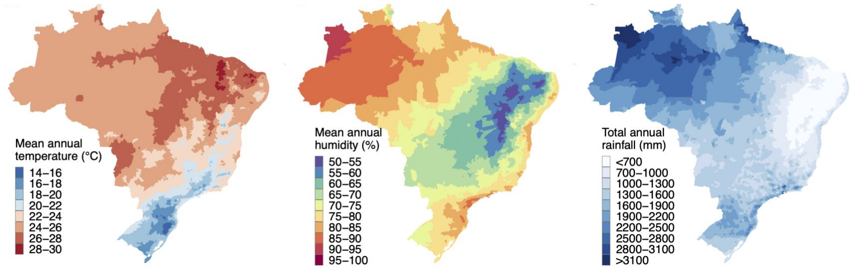
VALIDATION OF INDEX P

large time & space (Brazil, Thailand)

TAISHI
NAKASE
MSC

VALIDATION OF INDEX P: large time & space (Brazil, Thailand)

CLIMATE SATELLITE DATA TO INFORM INDEX P



bitting rate
<humidity>

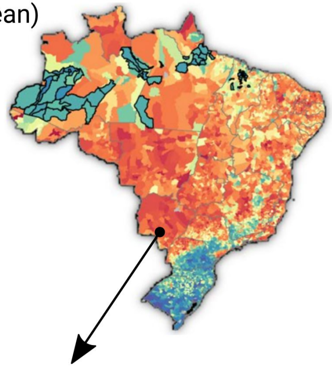
probability per infectious bite
<temperature>

extrinsic incubation period
<temperature>

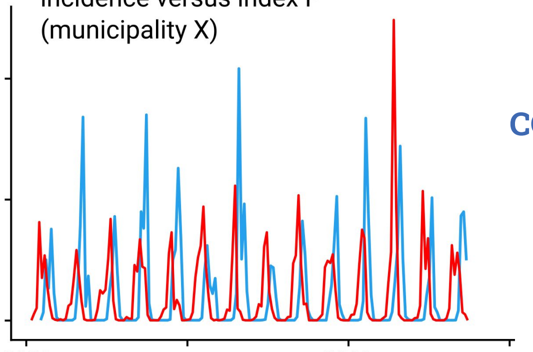
$$P = \frac{a^v \; a^v \; \phi^{v\to h} \; \phi^{h\to v} \; \gamma^v \; \gamma^h}{\mu_V^v(\sigma^h+\mu^h)(\gamma^h+\mu^h)(\gamma^v+\mu_V^v)}$$

life-span
<humidity, temperature>

dengue incidence 2000-2014 (mean)



incidence versus index P (municipality X)



CORRELATION?

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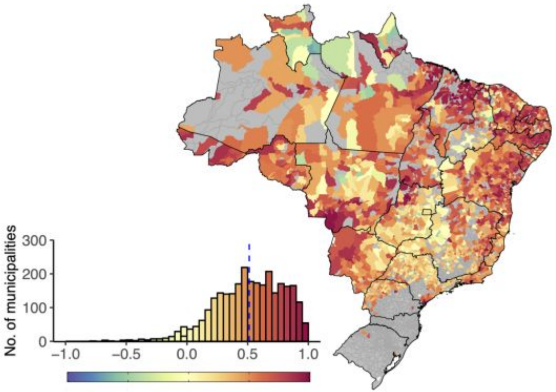
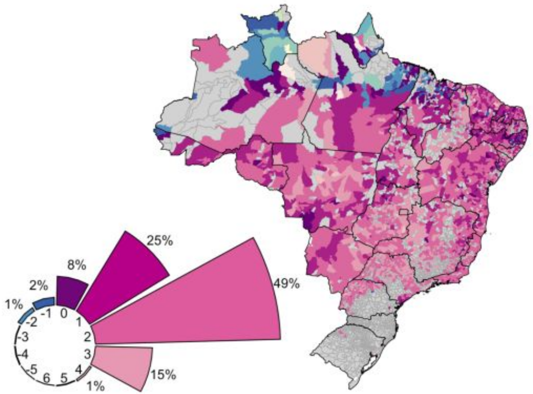
VALIDATION OF INDEX P: large time & space (Brazil, Thailand)

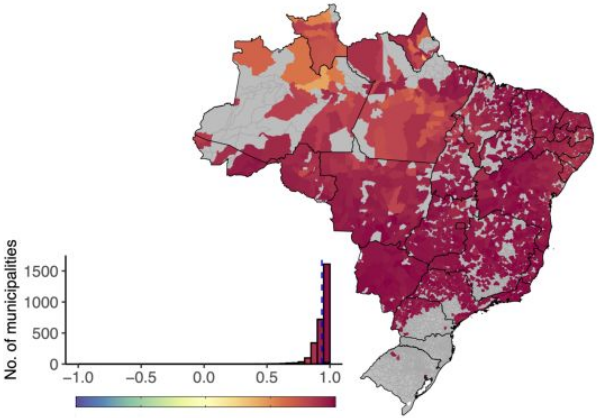
RAW CORRELATION



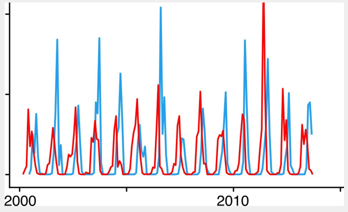
PHASE SHIFT (MONTHS)



PHASE SHIFTED CORRELATION



Many municipalities had low correlation



The index P preceded incidence.

We quantified the optimal lag (months) that maximized correlations.

The optimal lag varied spatially.

About 75% of localities had 1-2 months optimal lag.

Applying the optimal lag locally resulted in >95 correlation coefficients.

Climate is a major driver of the spatio-temporal incidence dynamics of dengue.

The index P captures the dynamics of dengue seasons.

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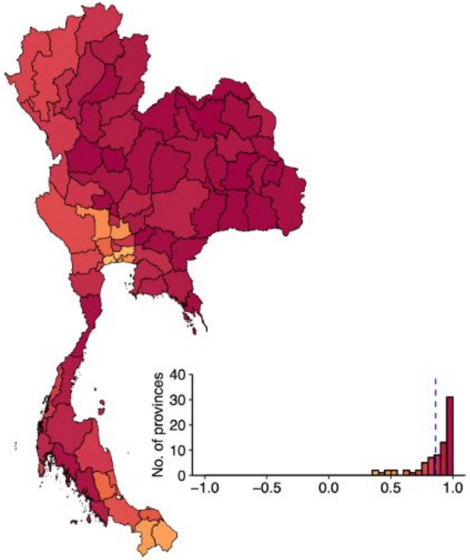
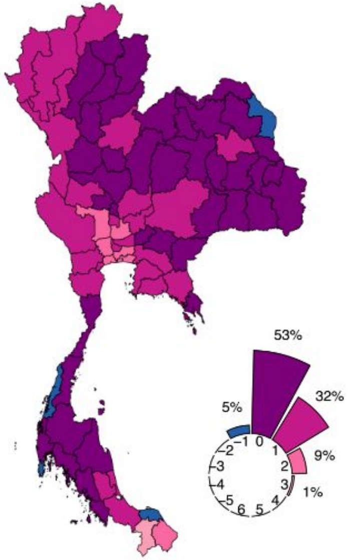
VALIDATION OF INDEX P: large time & space (Brazil, Thailand)

RAW CORRELATION



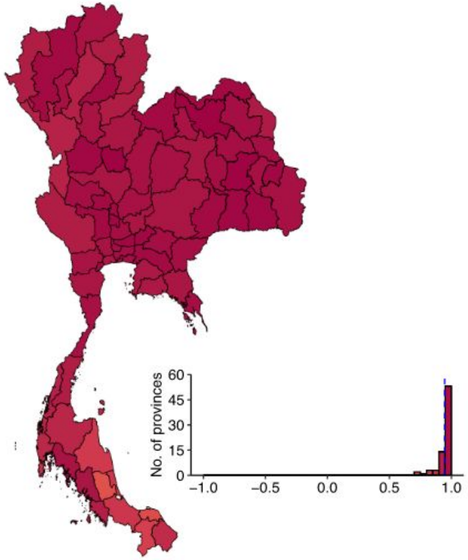
Correlation was higher than that obtained across Brazilian localities.

PHASE SHIFT (MONTHS)



~85 % of localities had 0-1 months of optimal lag.

PHASE SHIFTED CORRELATION

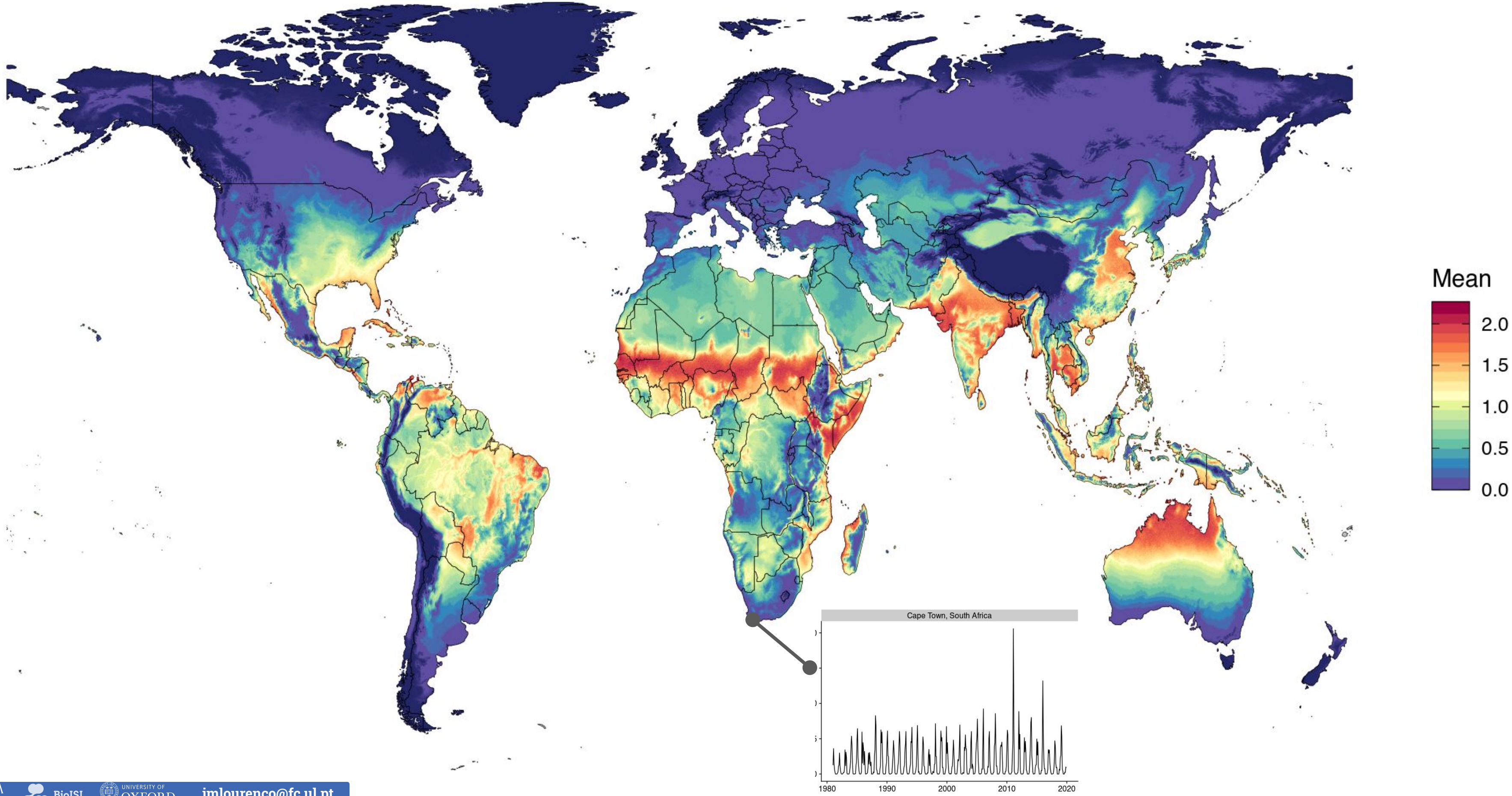


Applying the optimal lag locally resulted in >95 correlation coefficients.

THE GLOBAL DATASET 1981-2019

TAISHI
NAKASE
MSC

GLOBAL MEAN 1981-2019



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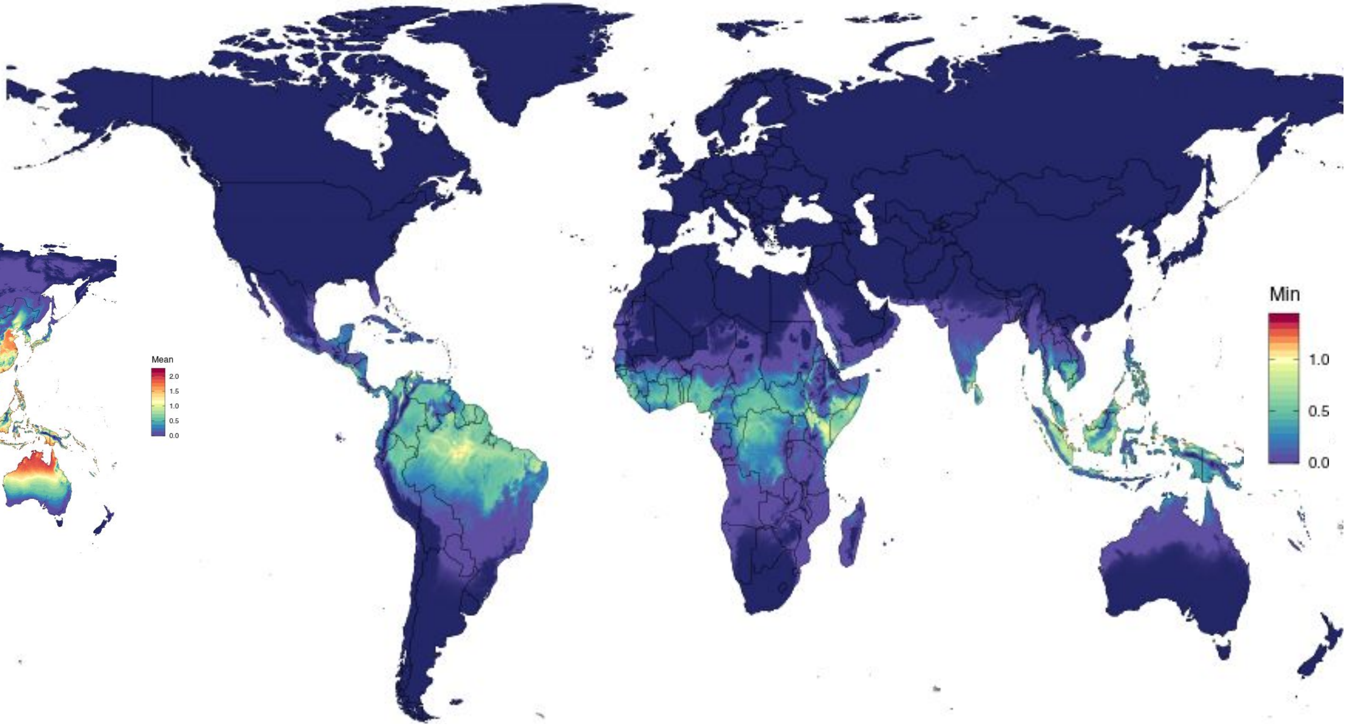
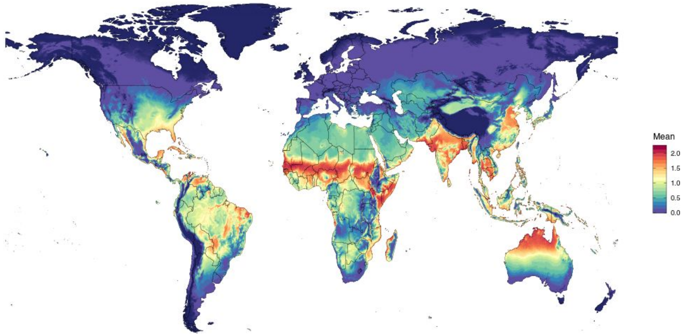
GLOBAL PATTERNS OF INTEREST 1981-2019

MINIMUM



MEAN



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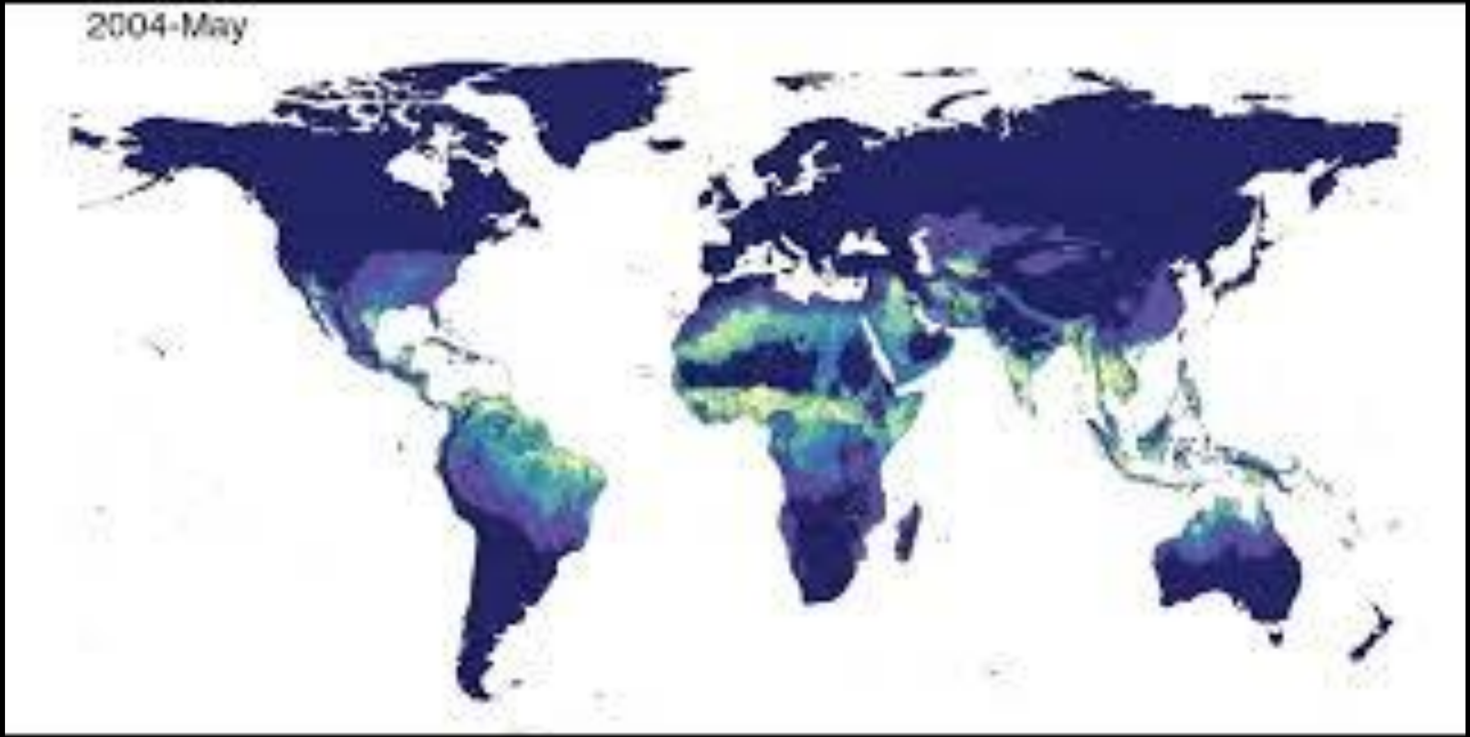
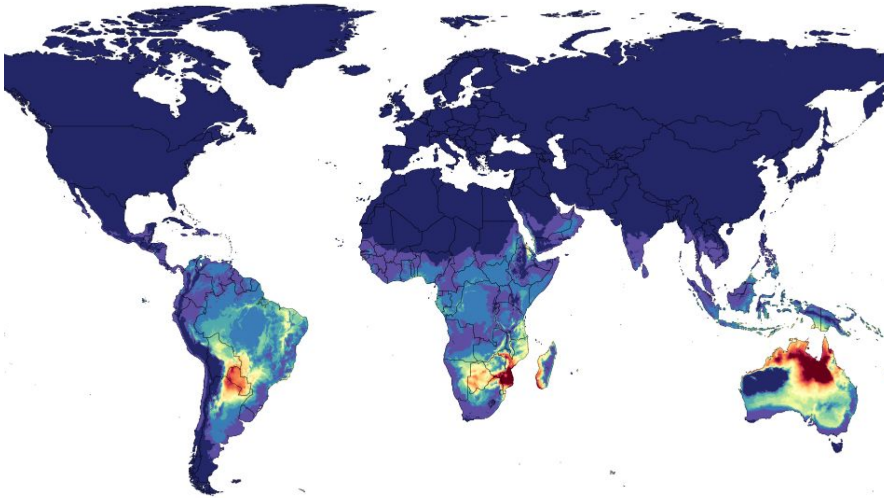
HISTORICAL TRENDS 1981-2019

SOUTH-NORTH SEASONALITY: ESTIMATION PER MONTH 1981-2019

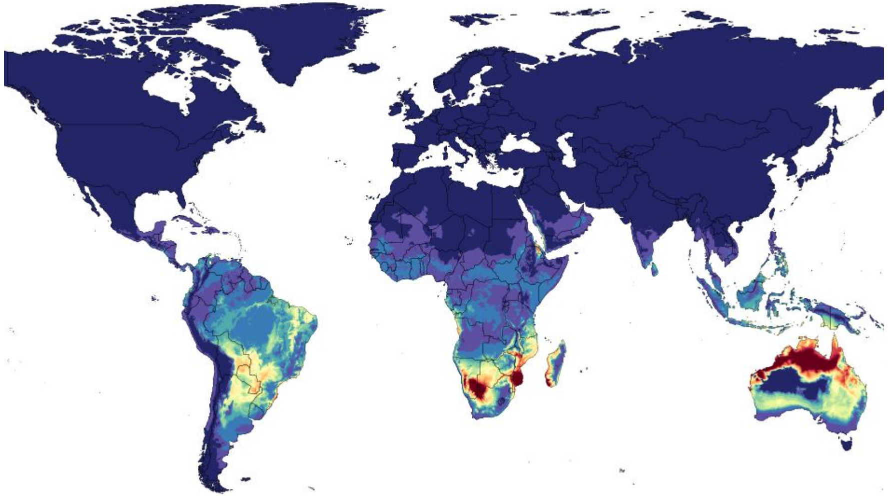


QUANTIFYING HISTORICAL TRENDS 1981-2019

JANUARY 1981



JANUARY 2011



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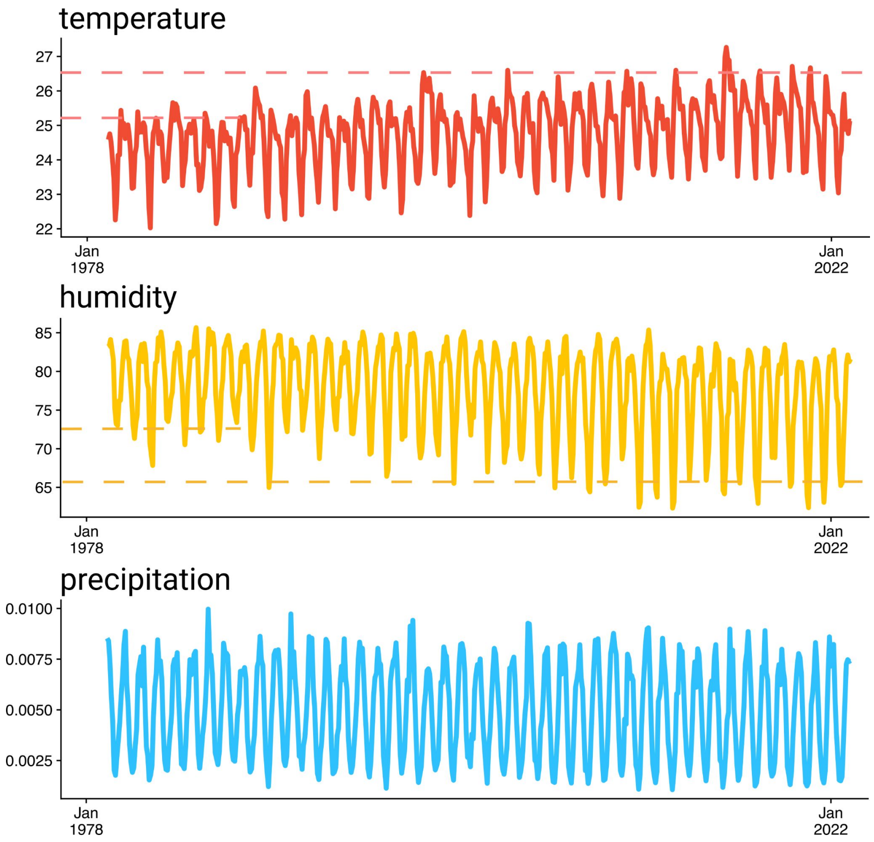
QUANTIFYING HISTORICAL TRENDS 1981-2019

BRAZIL 1978-2023

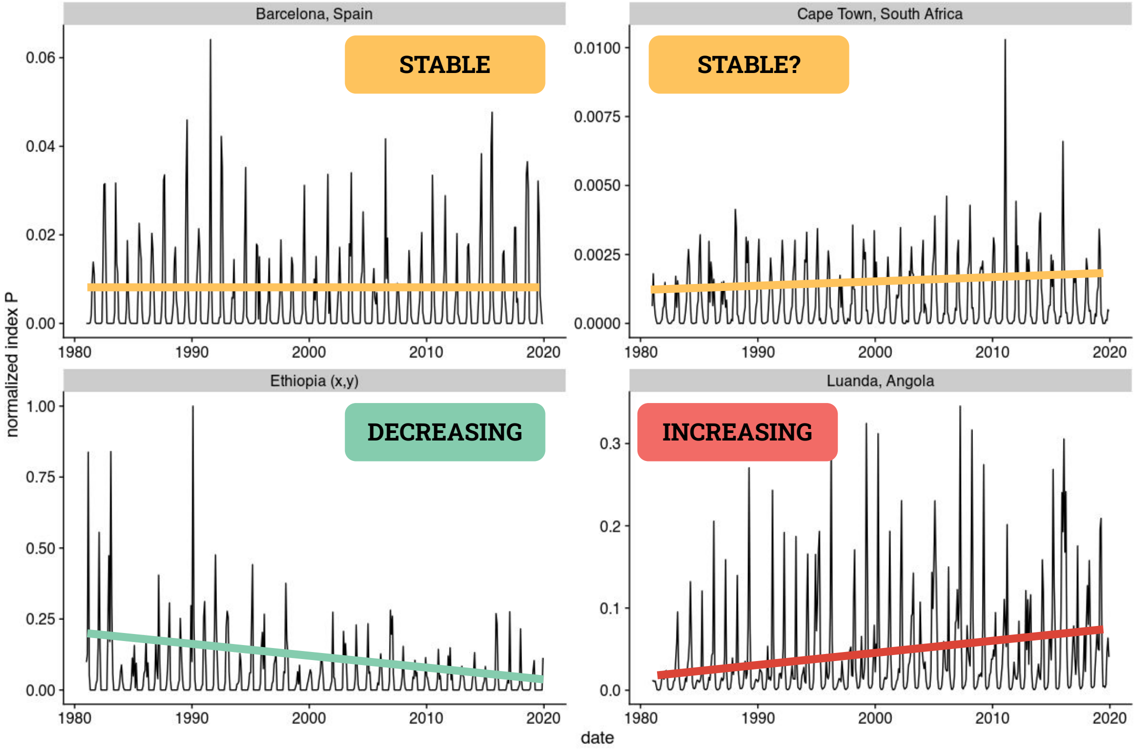
AVERAGE CLIMATIC VARIABLES



QUANTIFYING HISTORICAL TRENDS 1981-2019

EXAMPLES

INDEX P TIMESERIES



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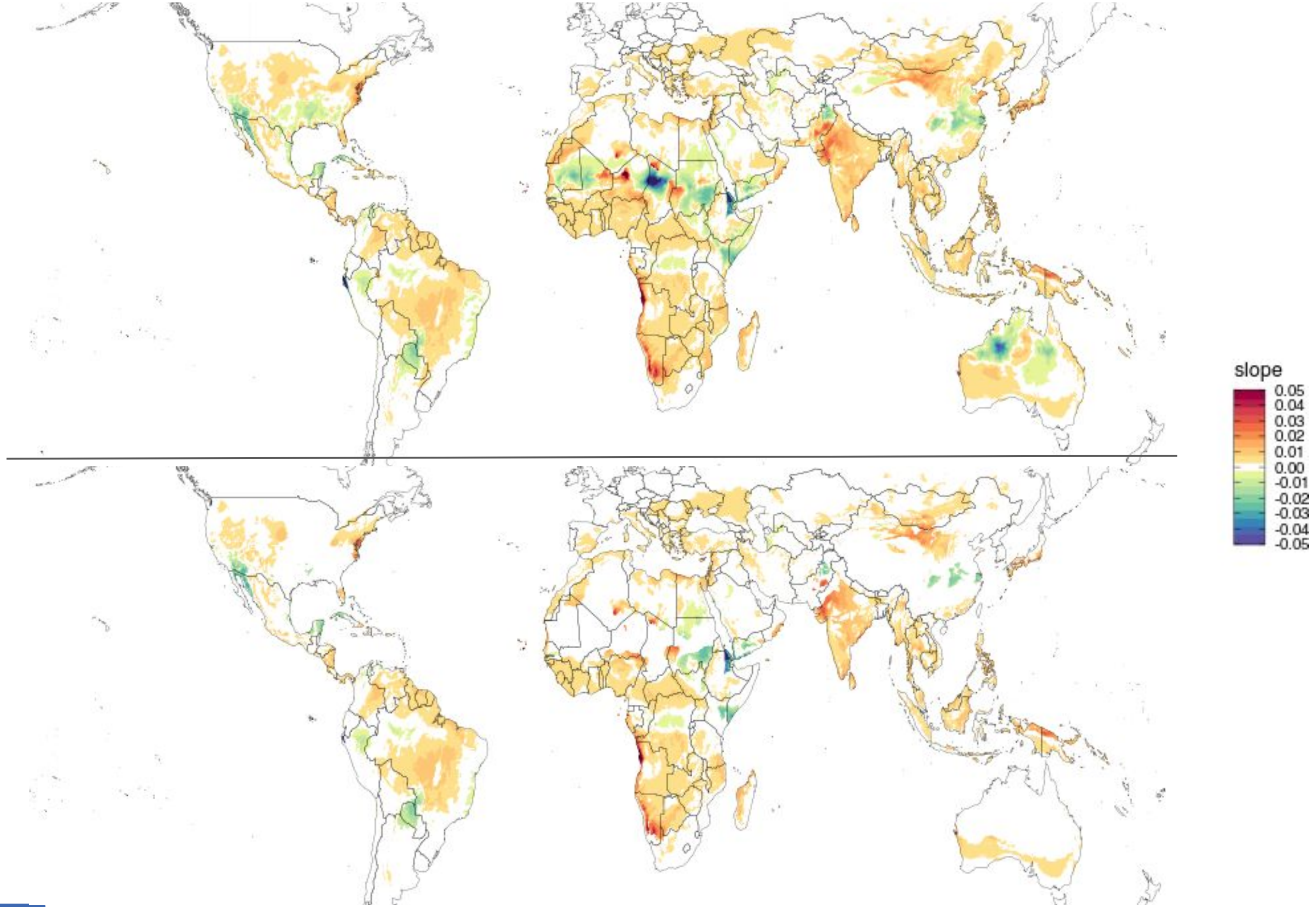
QUANTIFYING HISTORICAL TRENDS 1981-2019

SLOPES

STATISTICALLY SIGNIFICANT SLOPES



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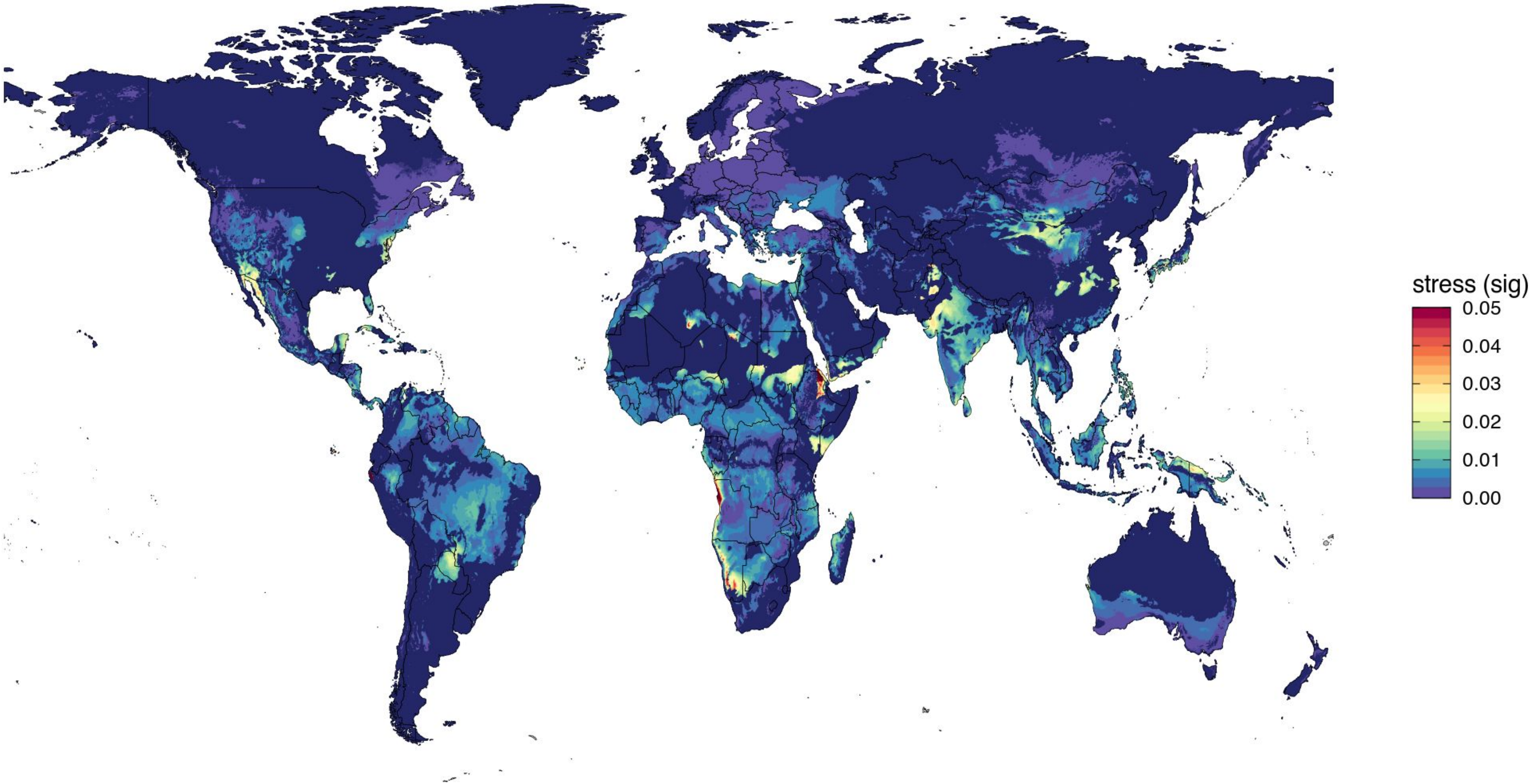
QUANTIFYING HISTORICAL TRENDS 1981-2019

SPATIAL DISTRIBUTION OF CLIMATE-DRIVEN STRESS

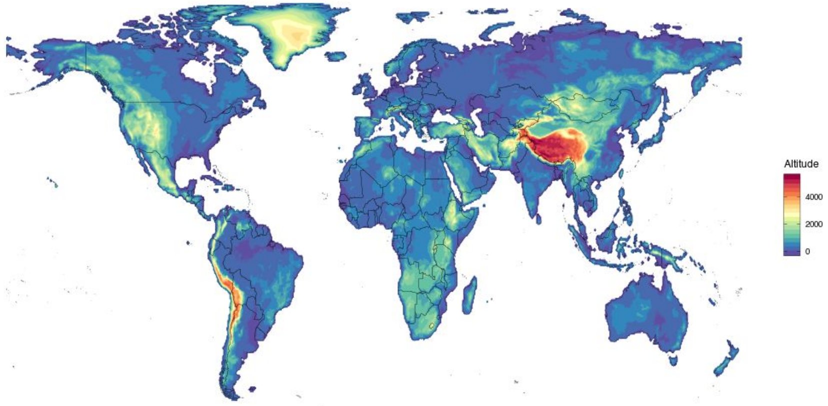


ECO-BACKGROUNDS

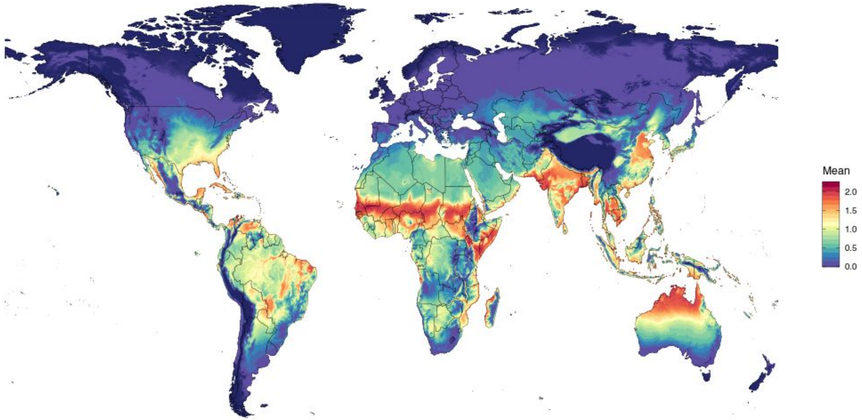
ALTITUDE

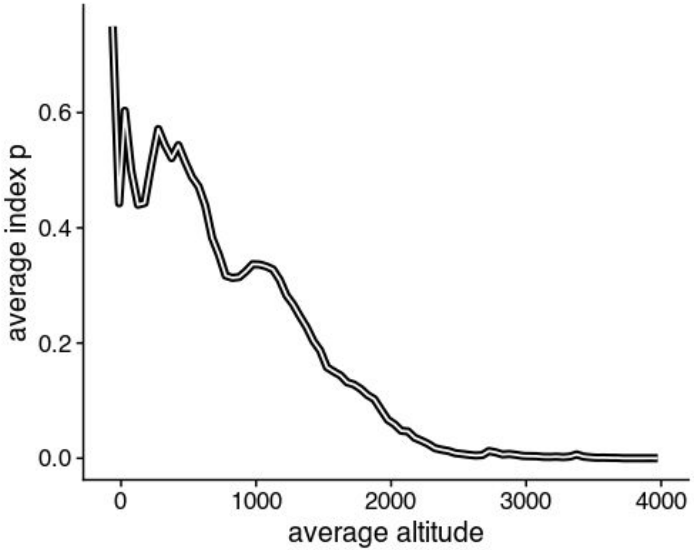
ECO-BACKGROUND: ALTITUDE

ALTITUDE

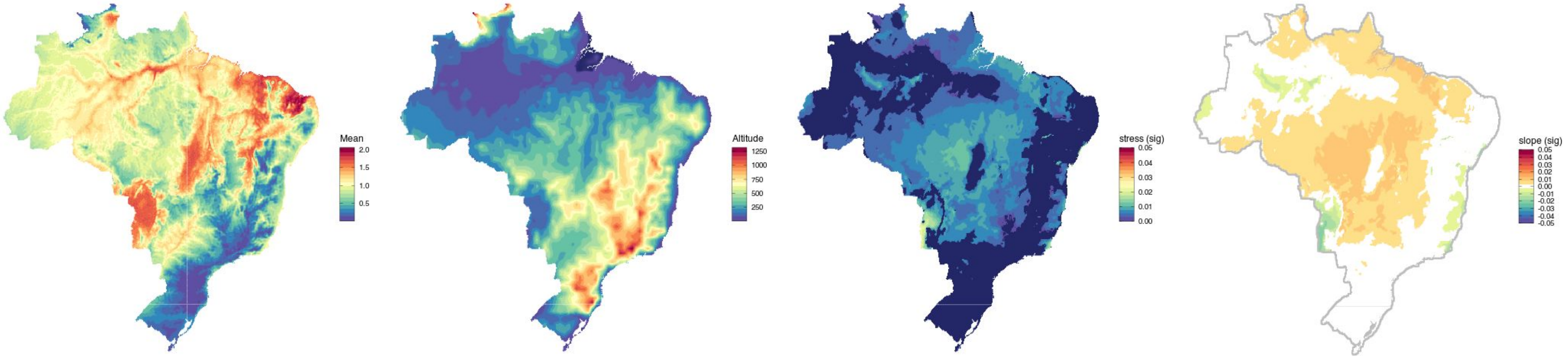


INDEX P

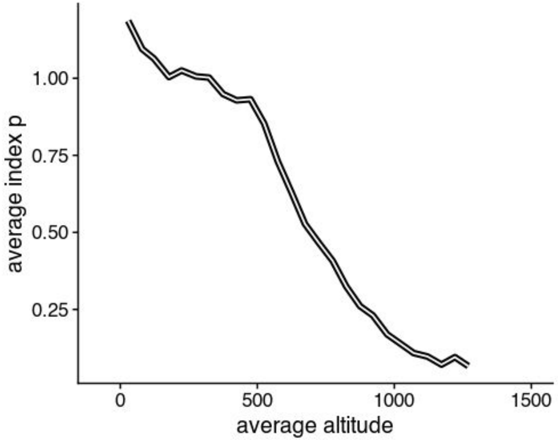




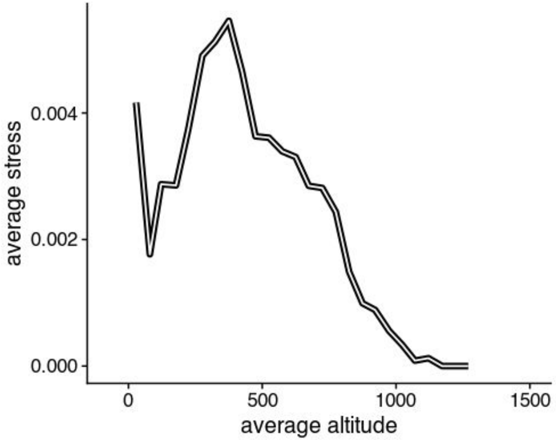
ECO-BACKGROUND: ALTITUDE



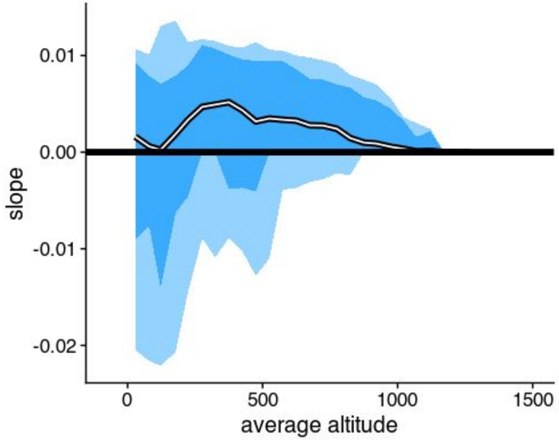
INDEX P



CLIMATE-STRESS



CHANGE (SLOPE)



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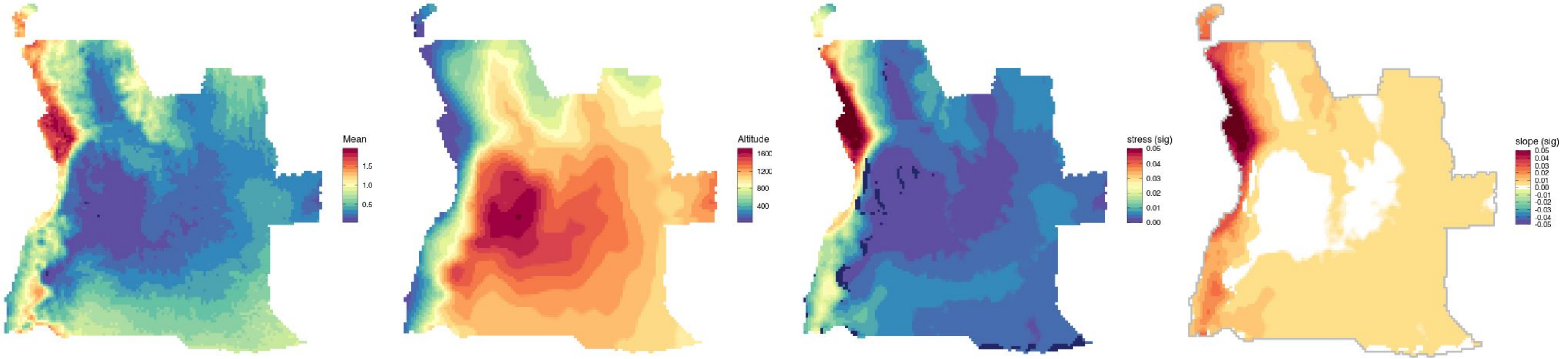
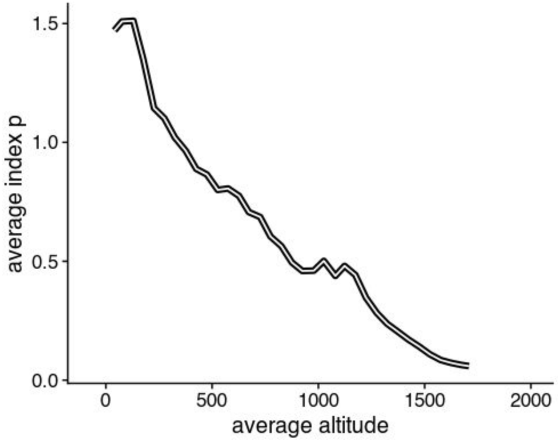
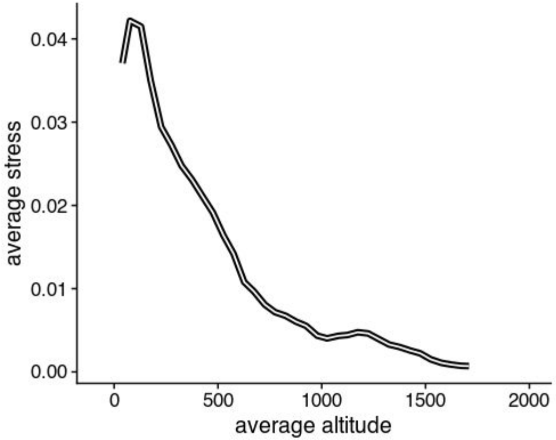
ECO-BACKGROUND: ALTITUDE



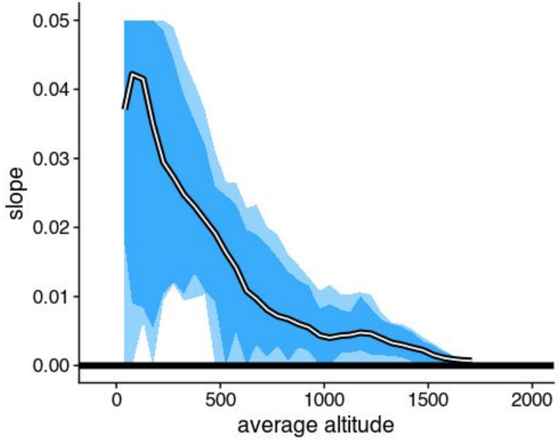
INDEX P



CLIMATE-STRESS



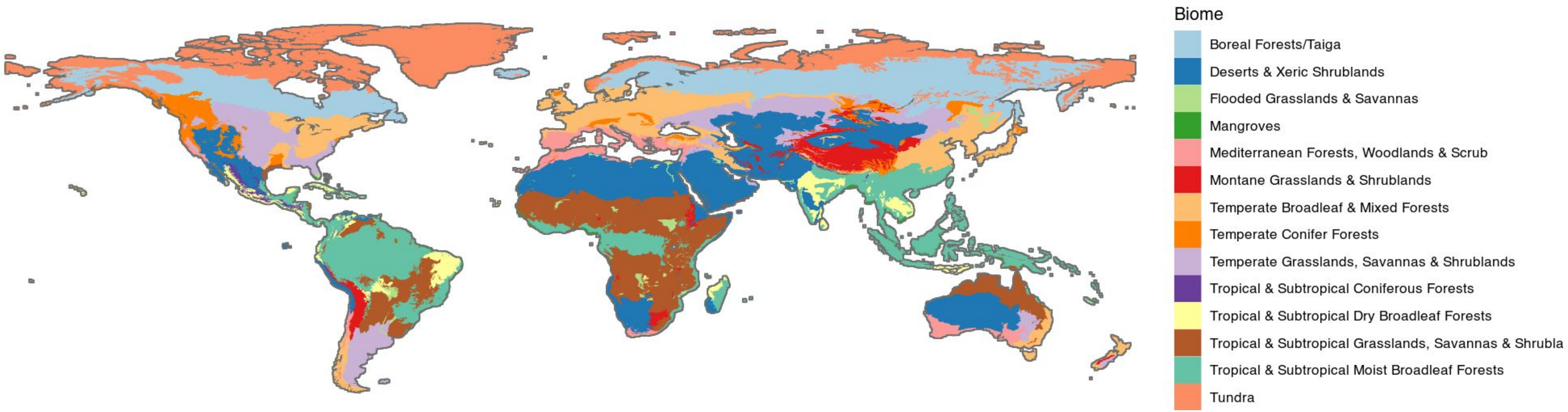
CHANGE (SLOPE)

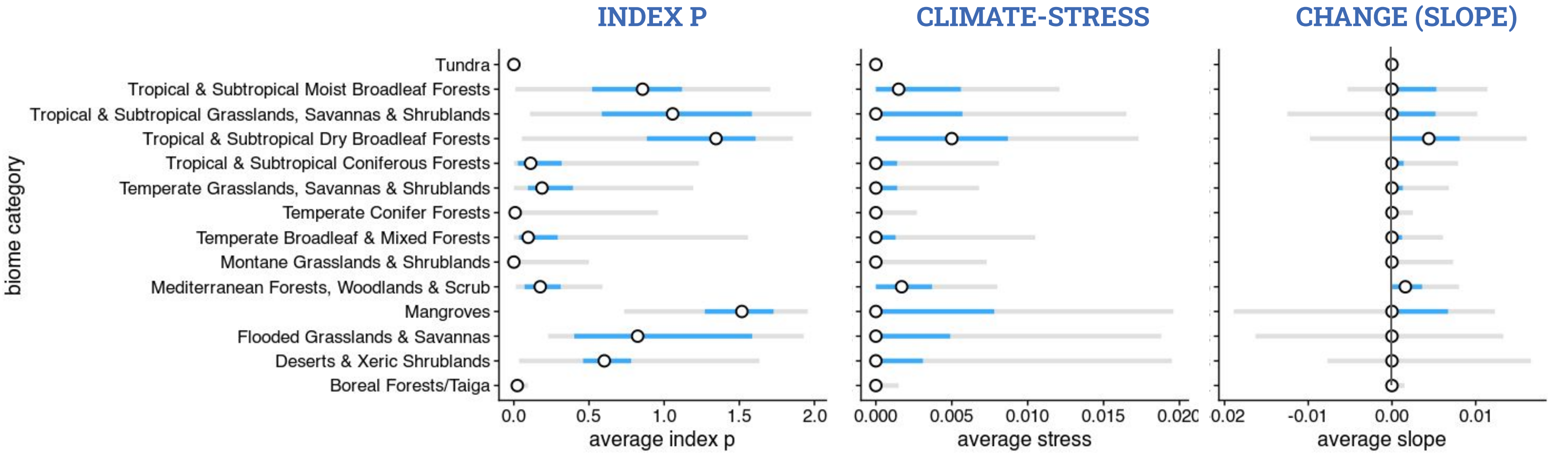


ECO-BACKGROUNDS

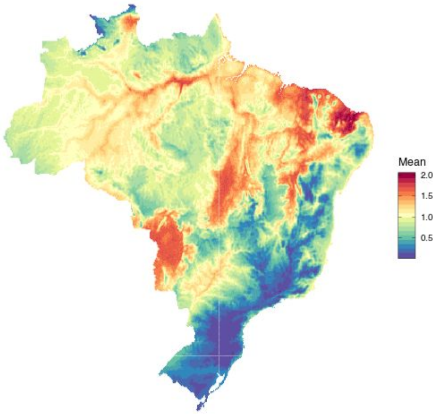
BIOME

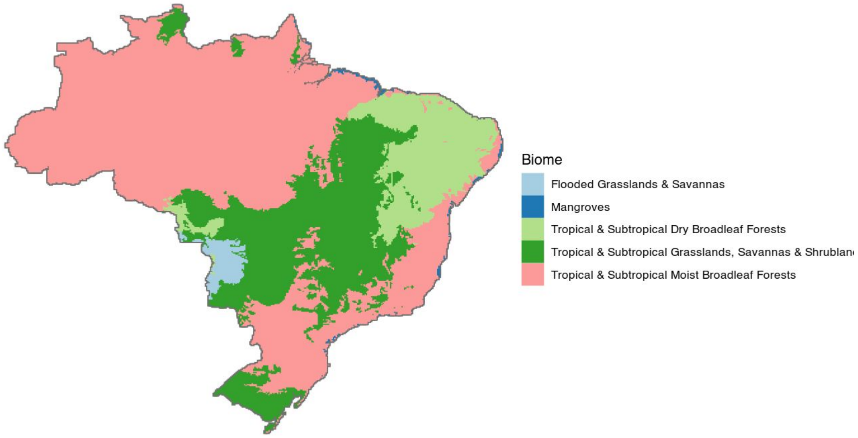
ECO-BACKGROUND: BIOME

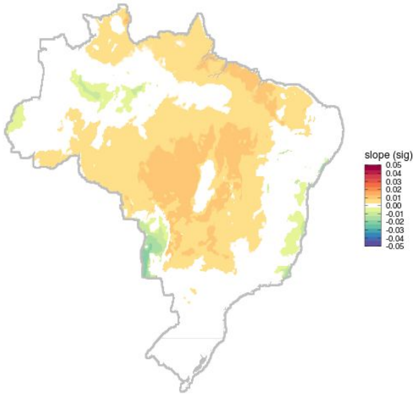


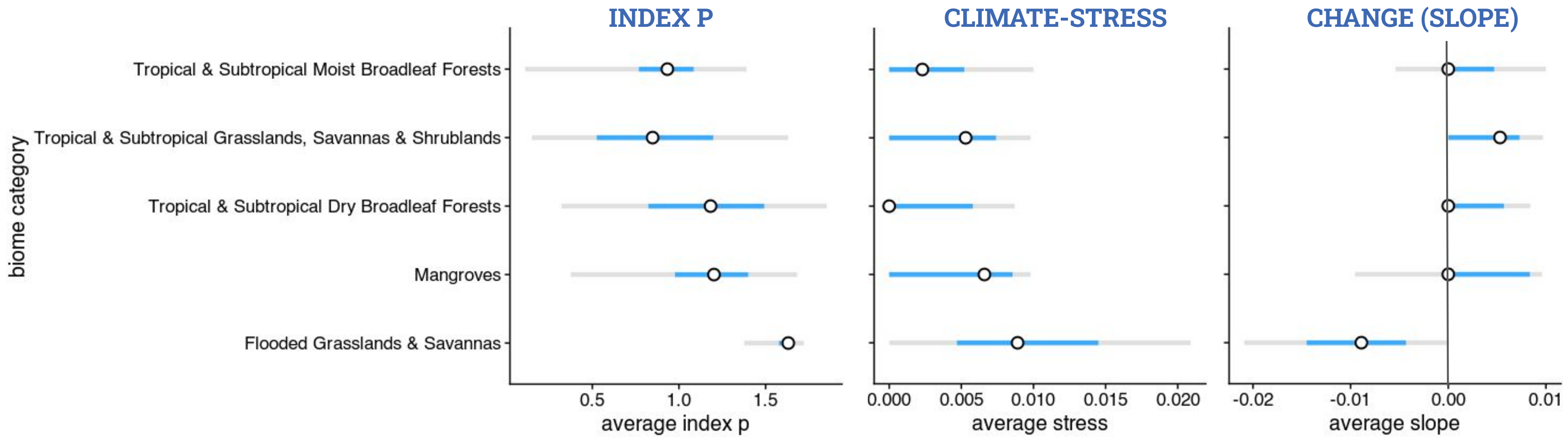


ECO-BACKGROUND: BIOME









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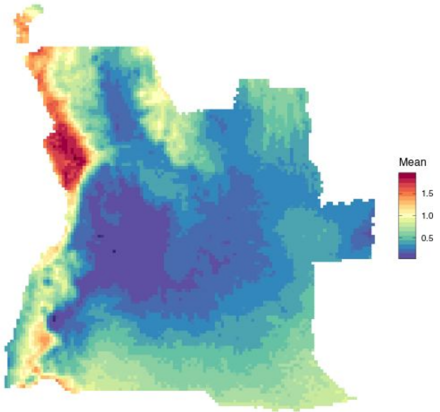
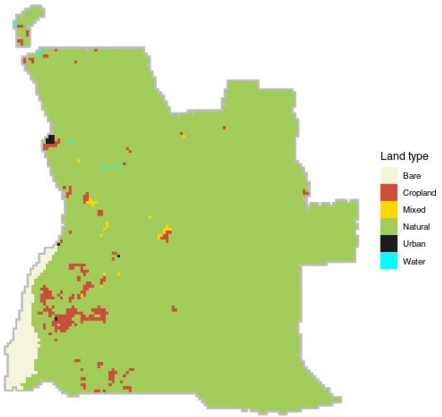
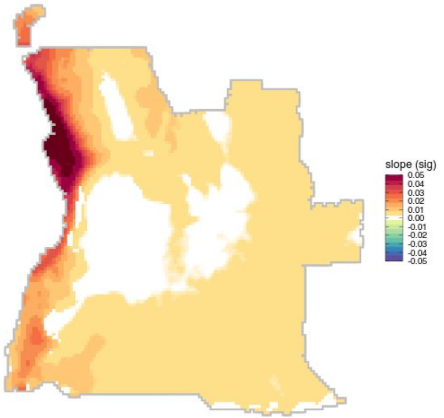
ECO-BACKGROUNDS

LAND TYPE

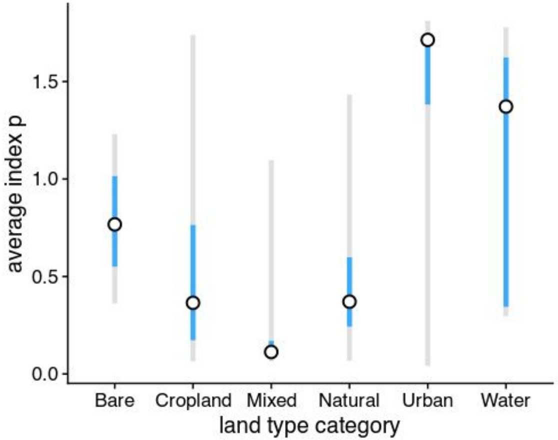
ECO-BACKGROUND: LAND TYPE



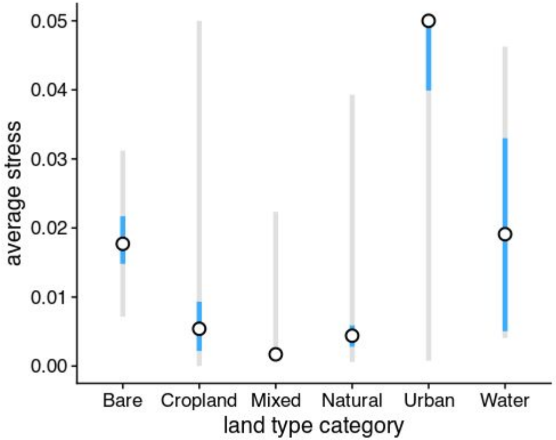




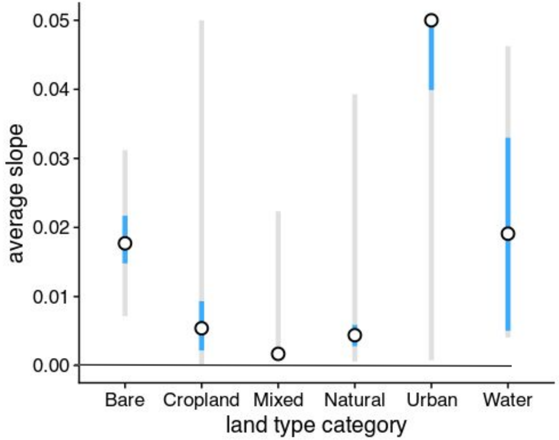
INDEX P



CLIMATE-STRESS



CHANGE (SLOPE)



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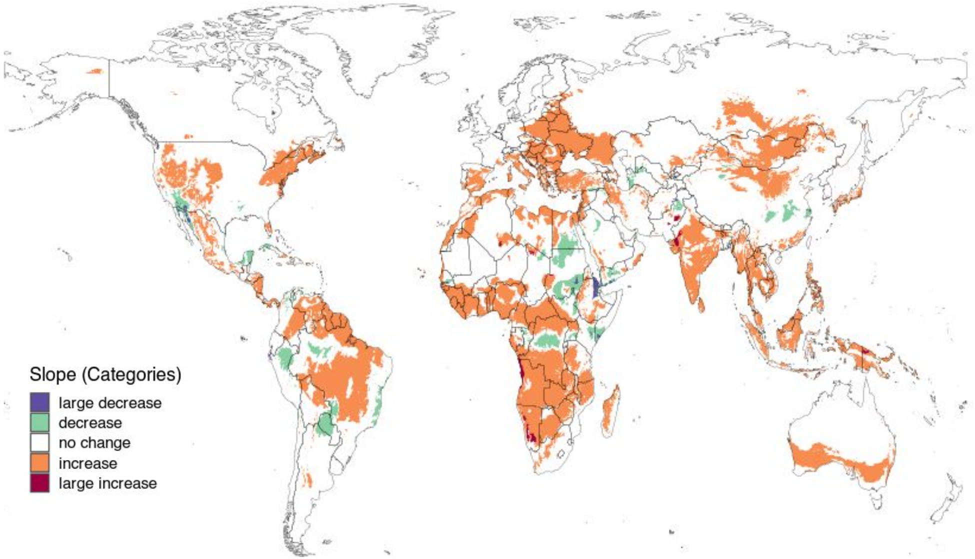
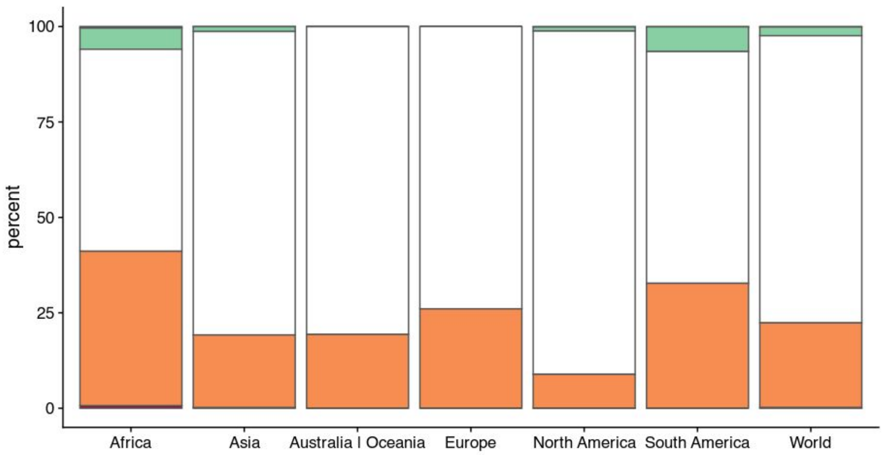
SUMMARIZING HISTORICAL TRENDS 1981-2019

SUMMARIZING HISTORICAL TRENDS 1981-2019

SPATIAL DISTRIBUTION OF SIGNIFICANT SLOPES (IN CATEGORIES)





No change for the majority of the globe.

Change towards higher transmission is more common than to towards lower transmission.

Extreme change is rare.

About 20% of the world with change towards higher transmission.

South America and Africa have more than 30% of the territory with change towards higher transmission.

Europe, Australia & Oceania have had only change towards higher transmission.

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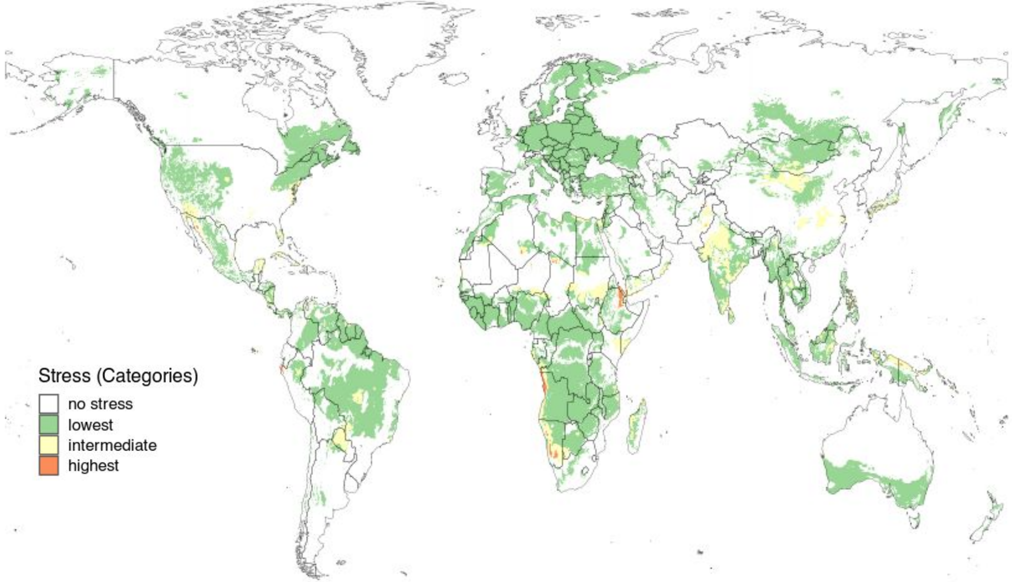
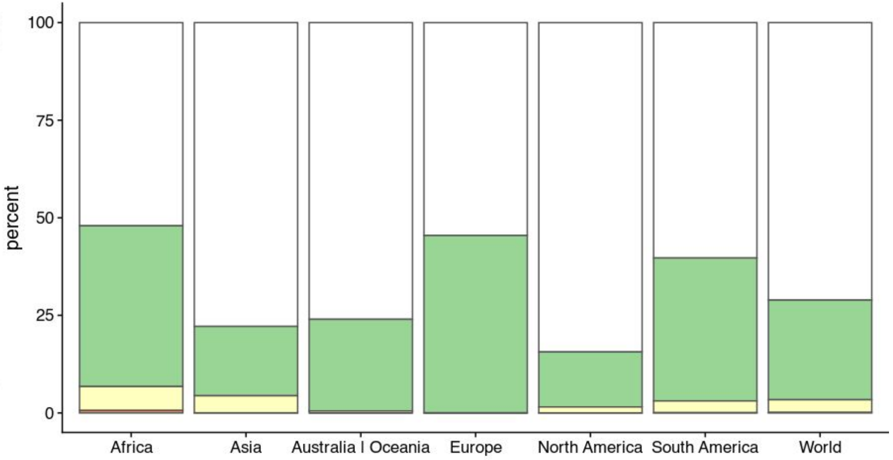
SUMMARIZING HISTORICAL TRENDS 1981-2019

SPATIAL DISTRIBUTION OF CLIMATE-DRIVEN STRESS (IN CATEGORIES)





Majority of the globe has not had climate-stress.

Extreme climate-stress is rare BUT highly localised.

About 30% of the world has had climate-stress.

Europe, Africa & South America have had between 40-50% of their territory under climate-stress.

Africa is leading in climate-stress.

GOING BEYOND

MOSQUITO PRESENCE / ABUNDANCE

TAREK ALREFAE
MSC

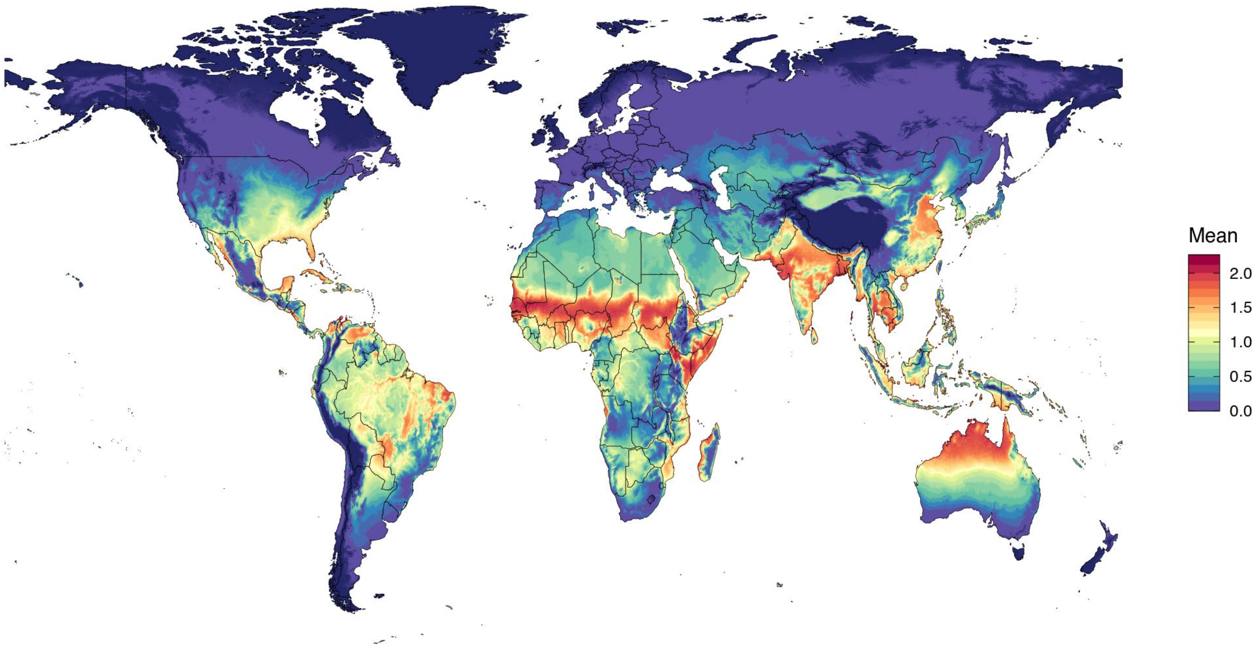
TRANSMISSION & MOSQUITO SUITABILITY ARE NOT THE SAME

INDEX P IS A MEASURE OF TRANSMISSION SUITABILITY

It quantifies suitability as informed by climate.

It does not address, e.g. host & viral presence.

Host: mosquito presence and/or abundance?



INDEX Q: MOSQUITO REPRODUCTION POTENTIAL

HOW MANY FEMALE ADULT MOSQUITOES CAN A FEMALE ADULT PRODUCE IN ITS LIFETIME

$$\frac{dA}{dt} = cf\dot{\theta}^v_A\left(1-\frac{A}{K}\right)V - (\dot{\epsilon}^v_A + \dot{\mu}^v_A)A$$

$$\frac{dS^v}{dt} = \dot{\epsilon}^v_A A - \lambda^{h\to v} - \dot{\mu}^v_V S^v$$

$$\frac{dE^v}{dt} = \lambda^{h\to v} - \dot{\gamma}^v E^v - \dot{\mu}^v_V E^v$$

$$\frac{dI^v}{dt} = \dot{\gamma}^v E^v - \dot{\mu}^v_V E^v$$

developmental rate

egg success rate

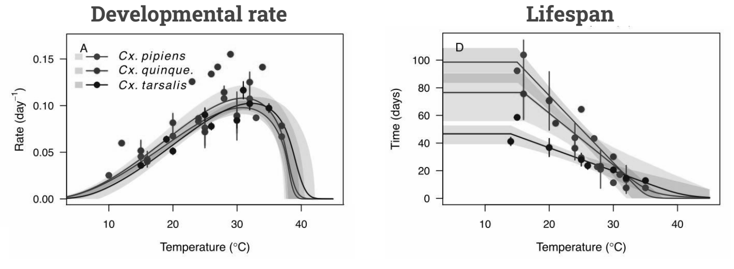
gender ratio

$$Q = \frac{\dot{\epsilon}^v_A}{\dot{\epsilon}^v_A + \dot{\mu}^v_A}\,\frac{\dot{c}f\dot{\theta}^v}{\dot{\mu}^v_V}$$

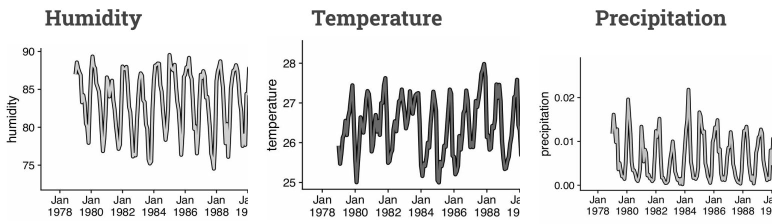
oviposition rate

aquatic mortality

adult mortality



Shocket et al eLIFE 2020



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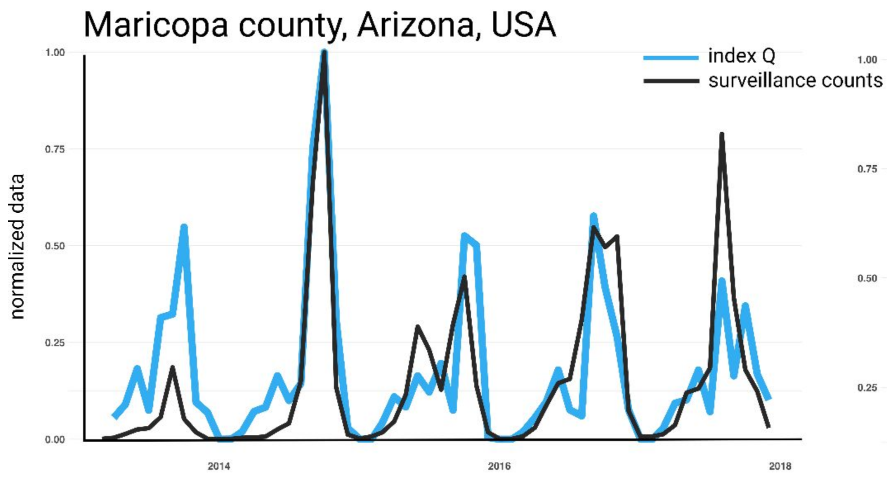
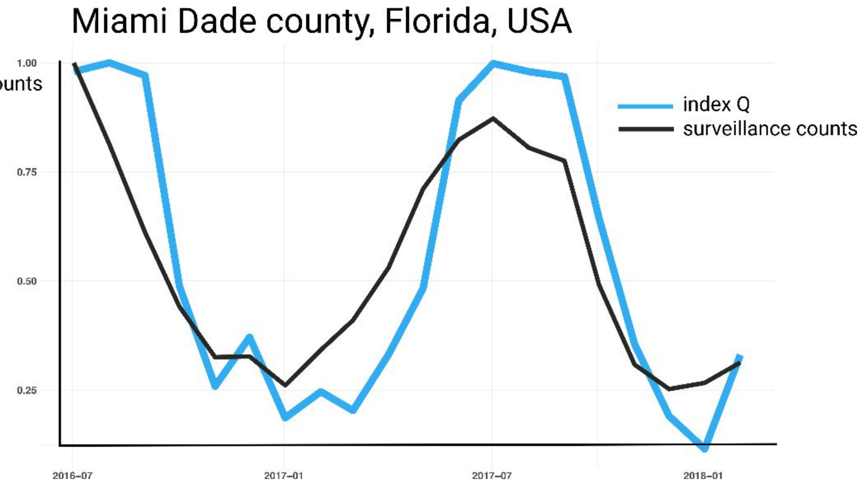
INDEX Q: MOSQUITO REPRODUCTION POTENTIAL

AEDES AEGYPTI SURVEILLANCE VS INDEX Q





Method is working well, but we need more mosquito surveillance data to calibrate the model.

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WRAPPING UP

COLLABORATING INSTITUTIONS

FCT
Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

wellcome

blue water vaccines

CTROP

Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

CLIMADE

parsuk
portuguese association of researchers and students in the uk

BILL & MELINDA GATES foundation

Stellenbosch
UNIVERSITY
IYUNIVESITHI
UNIVERSITEIT

BioISI

Stanford University

THE FRANCIS CRICK INSTITUTE

TEL AVIV UNIVERSITY

Department of BIOLOGY
UNIVERSITY OF OXFORD

cE3c
centre for ecology, evolution and environmental changes

dgav
Direção Geral de Alimentação e Veterinária

Ciências ULisboa

UNIVERSITY OF EXETER

UFMG

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

UCL

KENYA MEDICAL RESEARCH INSTITUTE
KEMRI

Ministério da Saúde
FIOCRUZ
Fundação Oswaldo Cruz

TAKE HOME MESSAGES

INDEX P

- Is a climate-driven transmission suitability measure highly correlated with dengue seasonal incidence
- Can be parameterized to specific mosquito-virus-host combinations
- Caveats: e.g. suitability precedes incidence

WHAT IS NEXT

- Transfer experience into measures of mosquito presence / abundance (index Q)
- Use climate-projections to explore climate-stress into the future

PRELIMINARY, GENERAL CONCLUSIONS (DENGUE)

- Transmission suitability is associated with particular eco-backgrounds
- Historical climate-stress is associated with particular eco-backgrounds
- The global south dominates in historical climate-stress on transmission suitability
- Not all climate-stress is bad news, but most is

R-PACKAGE

MVSE R-package v1.01r

scientific **data**

OPEN

DATA DESCRIPTOR

Global transmission suitability maps for dengue virus transmitted by *Aedes aegypti* from 1981 to 2019

Taishi Nakase[1], Marta Giovanetti[2,3], Uri Obolski[4,5] & José Lourenço[6]

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