

MODELING IN PRACTICE: THE LIFE CYCLE OF A MODELING PROJECT, FROM CONCEPTION TO PUBLICATION

- The example of Buruli ulcer in Cameroon -



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E²M² Workshop
Ranomafana, January 2019



Steps in a modeling project

- 1. Development of the study concept and question*
- 2. Literature review*
- 3. Data collection*
- 4. Construction of model framework*
- 5. Model analyses and selection*
- 6. Model validation*
- 7. Manuscript writing and submission*



Development of the study concept



- What is your question?
- Why is it interesting?
- Who is interested?
- Can it be narrowed down to a question about specific quantitative relationships?

- Who has tried to answer this before and how did they do it?
 - Empirical studies
 - Modeling studies
- What are these studies short-comings?
- Are there already parameter estimates or data sets to help you answer

Alegana et al. *International Journal of Health Geographics* 2012, 11:6
http://www.ij-healthgeographics.com/content/11/1/6



INTERNATIONAL JOURNAL
OF HEALTH GEOGRAPHICS

RESEARCH

Open Access

Spatial modelling of healthcare utilisation for treatment of fever in Namibia

Victor A Alegana^{1*}, Jim A Wright², Uusku Penttinen³, Abdalmonem M Noor^{1,4}, Robert W Snow^{1,4} and Peter M Atkinson⁵

Abstract

Background: Health care utilisation is affected by several factors including geographic accessibility. Empirical data on utilisation of health facilities is important to understanding geographic accessibility and defining health facility catchments at a national level. Accurately defining catchment population improves the analysis of gaps in access, commodity needs and interpretation of disease incidence. Here, empirical household survey data on treatment seeking for fever were used to model the utilisation of public health facilities and define their catchment area and populations in northern Namibia.

Methods: This study uses data from the Malaria Indicator Survey (MIS) of 2009 on treatment seeking for fever among children under the age of five years to characterise facility utilisation. Probability of attendance of public health facilities for fever treatment was modelled against a theoretical surface of travel times using a three parameter logistic model. The fitted model was then applied to a population surface to predict the number of children likely to use a public health facility during an episode of fever in northern Namibia.

Results: Overall, from the MIS survey, the prevalence of fever among children was 17.6% (CI 16.0-19.1) (401 of 2,283 children) while public health facility attendance for fever was 51.1% (95% CI 46.5-56.0). The coefficients of the logistic model of travel time against fever treatment at public health facilities were all significant ($p < 0.001$). From this model, probability of facility attendance remained relatively high up to 180 minutes (3 hours) and thereafter decreased steadily. Total public health facility catchment population of children under the age five was estimated to be 162,286 in northern Namibia, with an estimated fever burden of 24,820 children. Of the estimated fevers, 8,021 (32.3%) were within 30 minutes of travel time to the nearest health facility while 14,902 (60.0%) were within 1 hour.

Conclusion: This study demonstrates the potential of routine household surveys to empirically model health care utilisation for the treatment of childhood fever and define catchment populations enhancing the possibilities of accurate commodity needs assessment and calculation of disease incidence. These methods could be extended to other African countries where detailed mapping of health facilities exists.

Keywords: Namibia, Fever, Treatment, Spatial, Utilisation, Malaria

Background Understanding population health care utilisation and defining the catchment sizes of health providers are important for efficient planning and resource allocation [1,2]. Utilisation is a function of access to health services and is affected by geographical accessibility, alongside

many other factors [3-9]. In low income countries, such as those of the African continent where the burden of ill health is greatest [10-14], adequate information on the locations of populations, health services, facility workload, patient addresses and socio-demographic characteristics are rarely available to develop high resolution utilisation models nationally [15,16]. Available data on health care utilisation are mainly from routine national household surveys undertaken every 3 to 5 years [17], while few countries have a spatial database of health service providers [18,19]. Recent developments in

Health services modifies the effect of pneumococcal vaccine on risk among children less than 2 in Bohol, Philippines

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Health services and surveillance studies typically use passive surveillance study outcomes, which may lead to under-reporting of study outcomes to care. This distinction bias can have an adverse effect on estimates of pneumonia risk derived from vaccine trials. A secondary analysis of a randomized, placebo-controlled, double-blind trial examined the efficacy of an 11-valent pneumococcal vaccine in less than 2 years of age in Bohol, Philippines. Trial data were collected on each participant using a geographical information system using 11729 children who received three doses of any 13-valent pneumococcal vaccine. Multivariate Cox proportional hazards models were used to assess the relationship between pneumonia diagnosis and the relationship between

distance from the nearest health facility and vaccination with PCV with risk for pneumonia. Significant interaction effect between distance from BHH and vaccination was found. Among children living 12 km from BHH, vaccination was associated with a decreased hazard ratio for radiographic pneumonia, in both the study placebo (0.57, 95% confidence interval (CI) 0.33-0.97) and in children living 1 km from BHH, there was little difference in risk of pneumonia between children vaccinated with PCV11 and those given

International Journal of Epidemiology 2015, 44:1549

Physical access to maternal and child health services in rural Ethiopia

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Background: Physical access to maternal and child health services is a key determinant of service utilisation. The aim of this study was to explore risk factors for physical access to maternal and child health services among women of reproductive age (15-49 years) in rural Ethiopia.

Methods: A cross-sectional survey of 1,456 rural households was conducted. Data on household assets and socio-demographic characteristics were collected on 1,400 women of reproductive age. The aim of this study was to explore risk factors for physical access to maternal and child health services among women of reproductive age (15-49 years) in rural Ethiopia.

Results: A secondary analysis of a randomized, placebo-controlled, double-blind trial examined the efficacy of an 11-valent pneumococcal vaccine in less than 2 years of age in Bohol, Philippines. Trial data were collected on each participant using a geographical information system using 11729 children who received three doses of any 13-valent pneumococcal vaccine. Multivariate Cox proportional hazards models were used to assess the relationship between pneumonia diagnosis and the relationship between distance from the nearest health facility and vaccination with PCV with risk for pneumonia.

Conclusion: This study demonstrates the potential of routine household surveys to empirically model health care utilisation for the treatment of childhood fever and define catchment populations enhancing the possibilities of accurate commodity needs assessment and calculation of disease incidence. These methods could be extended to other African countries where detailed mapping of health facilities exists.

International Journal of Health Geographics 2010, 9:38
http://www.ij-healthgeographics.com/content/9/1/38

RESEARCH

Barriers and facilitators to health seeking behaviours in pregnant women of southern Mozambique

Khutia Mungumbel^{1*}, Helena Boone¹, Marianne Vidler², Cassimiro Prestige Tatenda Makanga³, Rahet Qureshi⁴, Eusebio Mazze⁵, and Esperança Severina⁶

Background: In countries such as Mozambique, where maternal and child health services are limited, understanding the barriers and facilitators to health seeking behaviours is important. The aim of this study was to explore risk factors for physical access to maternal and child health services among women of reproductive age (15-49 years) in rural Ethiopia.

Methods: A cross-sectional survey of 1,456 rural households was conducted. Data on household assets and socio-demographic characteristics were collected on 1,400 women of reproductive age. The aim of this study was to explore risk factors for physical access to maternal and child health services among women of reproductive age (15-49 years) in rural Ethiopia.

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Conclusion: This study demonstrates the potential of routine household surveys to empirically model health care utilisation for the treatment of childhood fever and define catchment populations enhancing the possibilities of accurate commodity needs assessment and calculation of disease incidence. These methods could be extended to other African countries where detailed mapping of health facilities exists.

Al-Tajer et al. *International Journal of Health Geographics* 2010, 9:38
http://www.ij-healthgeographics.com/content/9/1/38



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RESEARCH

Open Access

Physical accessibility and utilization of health services in Yemen

Abdullah Al-Tajer^{1,2}, Allan Clark³, Joseph C Longenecker¹ and Christopher JM Whitty⁴

Abstract

Background: Assessment of physical access to health services is extremely important for planning. Complex methods that incorporate data inputs from road networks and transport systems are used to assess physical access to health services in industrialised countries. However, such data inputs hardly exist in many developing countries. Straight-line distances between the service provider and resident population are easily obtained but their relationship with driving distance and travel time is unclear. This study aimed to investigate the relationship between different measures of physical access, including straight-line distances, road distances and travel time and the impact of these measures on the vaccination of children in Yemen.

Methods: Coordinates of houses and health facilities were determined by GPS machine in urban and rural areas in Taiz province, Yemen. Road distances were measured by an odometer of a vehicle driven from participants' houses to the nearest health centre. Driving time was measured using a stop-watch. Data on children's vaccination were collected by personal interview and verified by inspecting vaccination cards.

Results: There was a strong correlation between straight-line distances, driving distances and driving time (straight-line distances vs. driving distance: $r = 0.92$, $p < 0.001$; straight-line distances vs. driving time: $r = 0.75$, $p < 0.001$; driving distance vs. driving time: $r = 0.83$, $p < 0.001$). Each measure of physical accessibility showed strong association with vaccination of children after adjusting for socio-economic status.

Conclusion: Straight-line distances, driving distances and driving time are strongly linked and associated with vaccination uptake. Straight-line distances can be used to assess physical access to health services where data inputs on road networks and transport are lacking. Impact of physical access is clear in Yemen, highlighting the need for efforts to target vaccination and other preventive healthcare measures to children who live away from health facilities.

Background Access to health services is difficult to define. It is a multidimensional process that in addition to the quality of care, involves geographical accessibility, availability of the right type of care for those who need it, financial accessibility, and acceptability of service [1]. Geographic accessibility, the distance that must be traveled in order to use health facility, may present an important barrier of access to health services. Studies in developing countries have presented strong evidence that physical proximity of health service can play an important role in the use of primary healthcare [2-12]. In Yemen, we have demonstrated that driving distance and driving time are important predictors for developing severe malaria in comparison to

straight-line distance [13]. It is hypothesized that long distance can be a significant obstacle to reaching health facilities, and a disincentive even to trying to seek care [14]. The recent advances of Geographic Information Systems (GIS) have provided an important tool for health-care planning particularly in measuring access to health services. Major progress was made in industrialized countries where the detailed data inputs such as detailed road network are available [15]. For example, Brabyn and Skelly used cost path analysis in order to determine the minimum travel time and distance to the closest hospital via road network in New Zealand [16]. More recently there was an attempt to produce a single index for the overall access to health services from combined physical access to the resources and the amount of resources available [17]. Application of such methods in developing countries, however, remained constrained by the lack of

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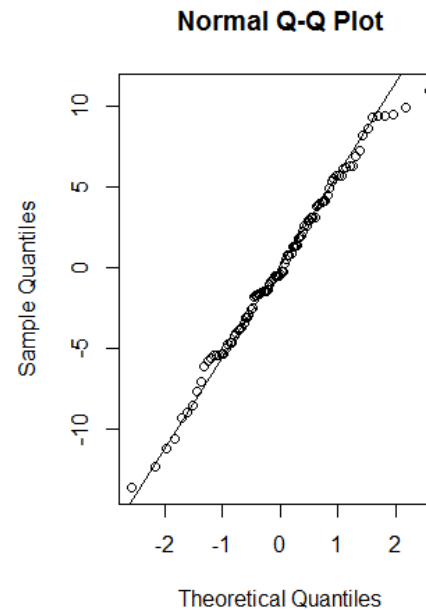
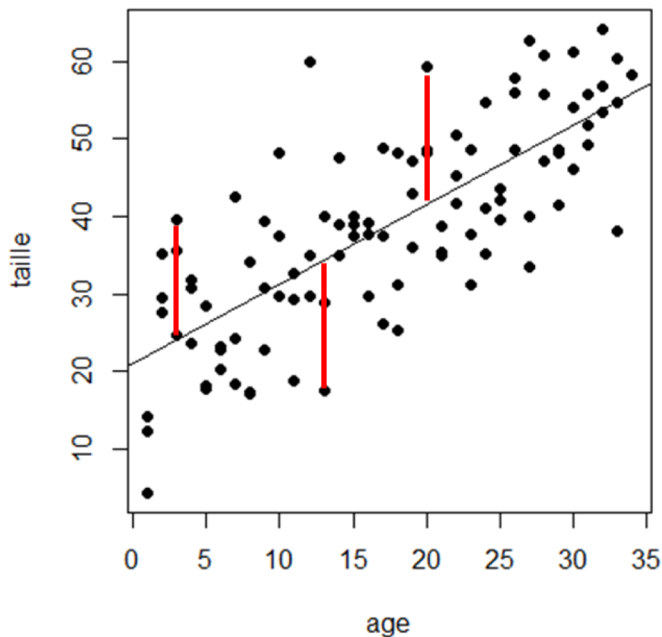
Construction of model framework

- What drawbacks of previous studies can I mitigate?
- What type of modeling is necessary to answer my question?
 - Statistical: GLM, spatial, time-series, etc.
 - Mathematical: population based, individual based
- What modeling elements are necessary for my question?
 - Stochasticity
 - Compartments and complexity



Model analysis, selection and validation

- What model(s) best fit my data and explain my question?
 - Comparison of alternative models and application of selection procedures
- Does the selected model suffer from any substantial drawbacks?
 - Statistical models: verification of model assumptions
 - Mathematical models: sensitivity analyses and out-of-sample predictions





Types of modeling studies

Without data collection

1. Purely theoretical studies
2. Parametrization based on published studies
 - Systematic reviews and meta-analyses
 - Experimental and field studies

1. Development of the study concept
2. Literature Review
3. Data collection
4. Construction of model framework
 - Dynamic equations and code
 - Relationships between parameters
5. Model analyses and selection
 - Parametrization
 - Simulations and debugging
6. Model validation
 - Model validation
 - Sensitivity analyses
7. Manuscript writing and submission



Types of modeling studies

1. Development of the study concept
2. Literature Review
- 3. Data collection**
4. Construction of model framework
 - Statistical vs. Mathematical model
 - Model better adapted to our data
5. Model analyses and selection
 - Descriptive, univariate and multivariate
 - Parametrization and simulations
6. Model validation
 - Model validation, comparison
 - Sensitivity analyses
7. Manuscript writing and submission

With data collection

1. Data already collected for other purposes
 - Focus only on analyses
 - Need to understand data limitations and quality
 - Need to adapt modeling to the available data
2. Data collected for the modeling project
 - Very time consuming
 - Modeling is generally more straightforward

Buruli-ulcer
ecology
Malaria
infectious-diseases
populations
traps
health
Environmental-changes
modelling
M.ulcerans
public
Poverty
feedbacks
Deforestation
links
Disease-Prevalence

THE EXAMPLE OF BURULI ULCER IN CAMEROON



Buruli ulcer



Most affected : Children <15 years

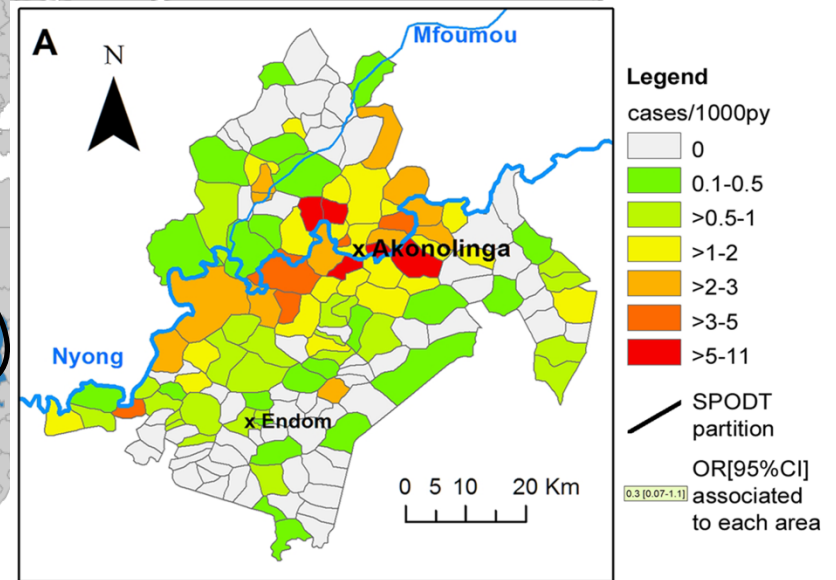
25% cases with functional limitations



Source of images: www.who.int (2014)



Buruli ulcer: an emergent and neglected disease



WHO meeting on BU control and research (2013)

Landier *et al.* (2014, *PLoS NTDs*)

Cases in more than 30 countries

Focal distribution

Around 5000 new cases each year

What is my question?

Why is it interesting?

Who has tried to answer this before and how?

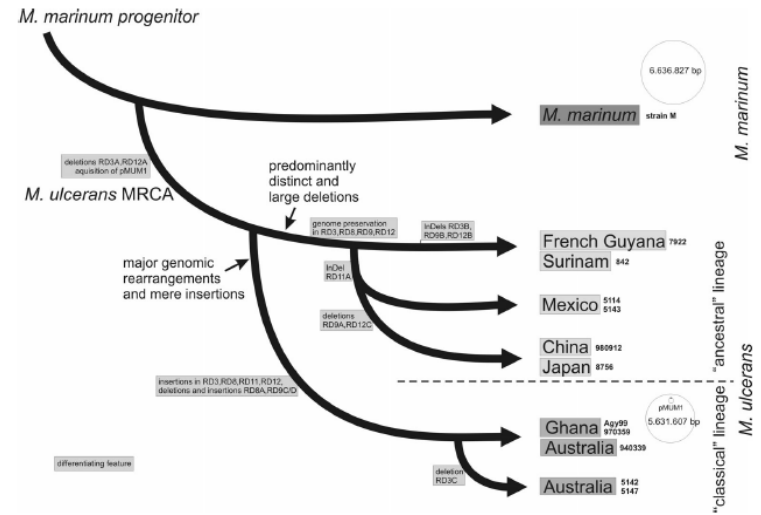
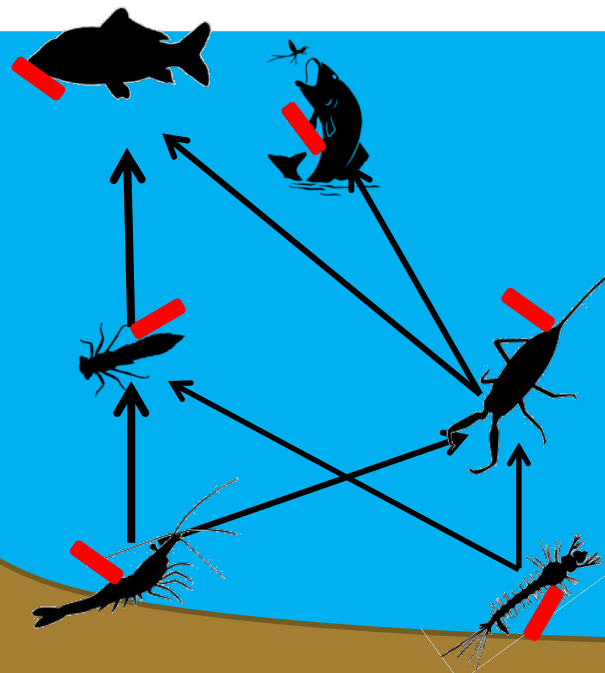
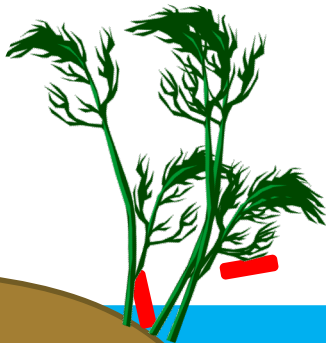
What are these studies short-comings?

1. LITERATURE REVIEW & IDENTIFICATION OF THE PROBLEM



Mycobacterium ulcerans: generalities

Multi-host
&
Environmentally persistent



Kaser *et al.* (2007, BMC Evolutionary Biology)



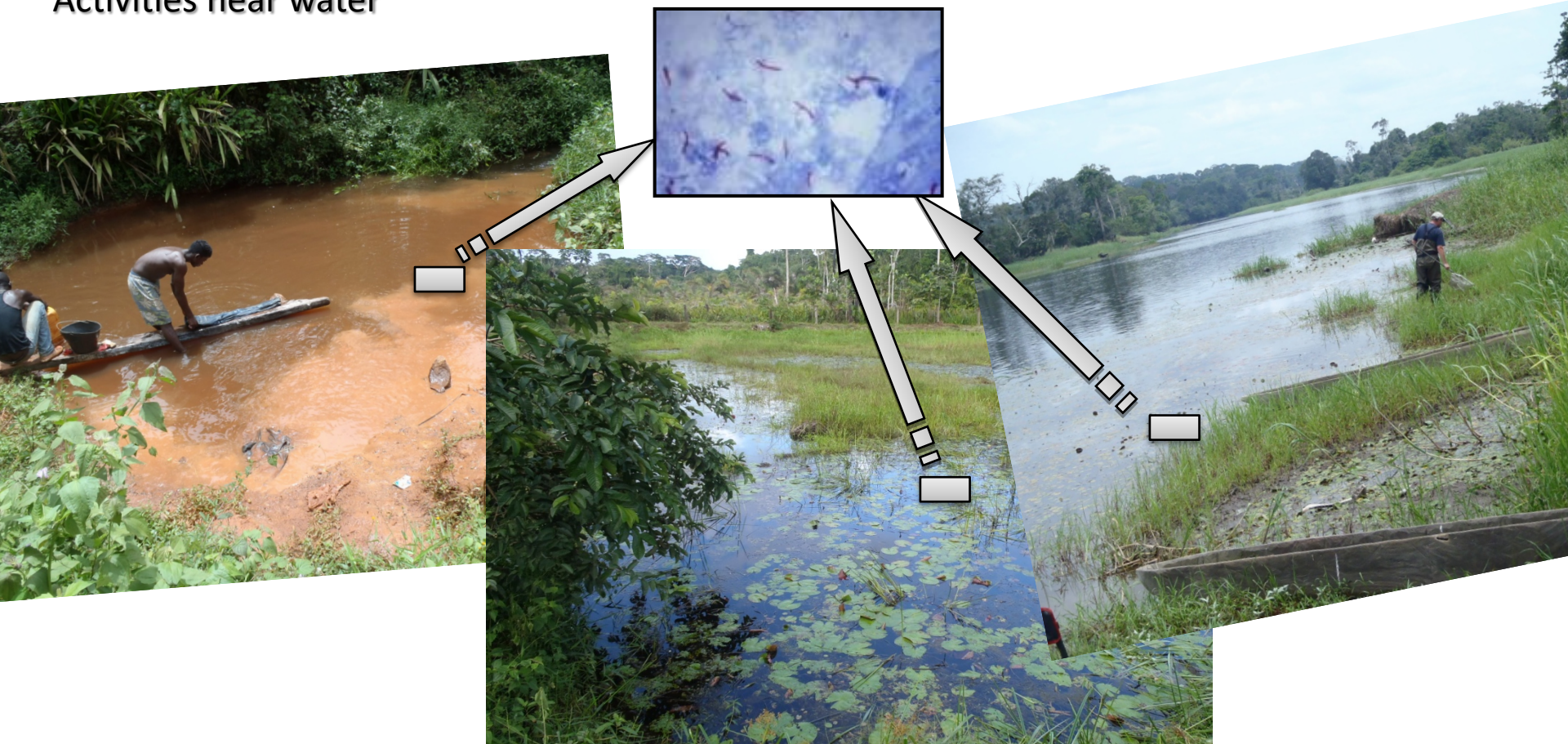
Buruli ulcer: a disease linked to aquatic ecosystems

BU Risk factors

Proximity to stagnant or slow flowing waters

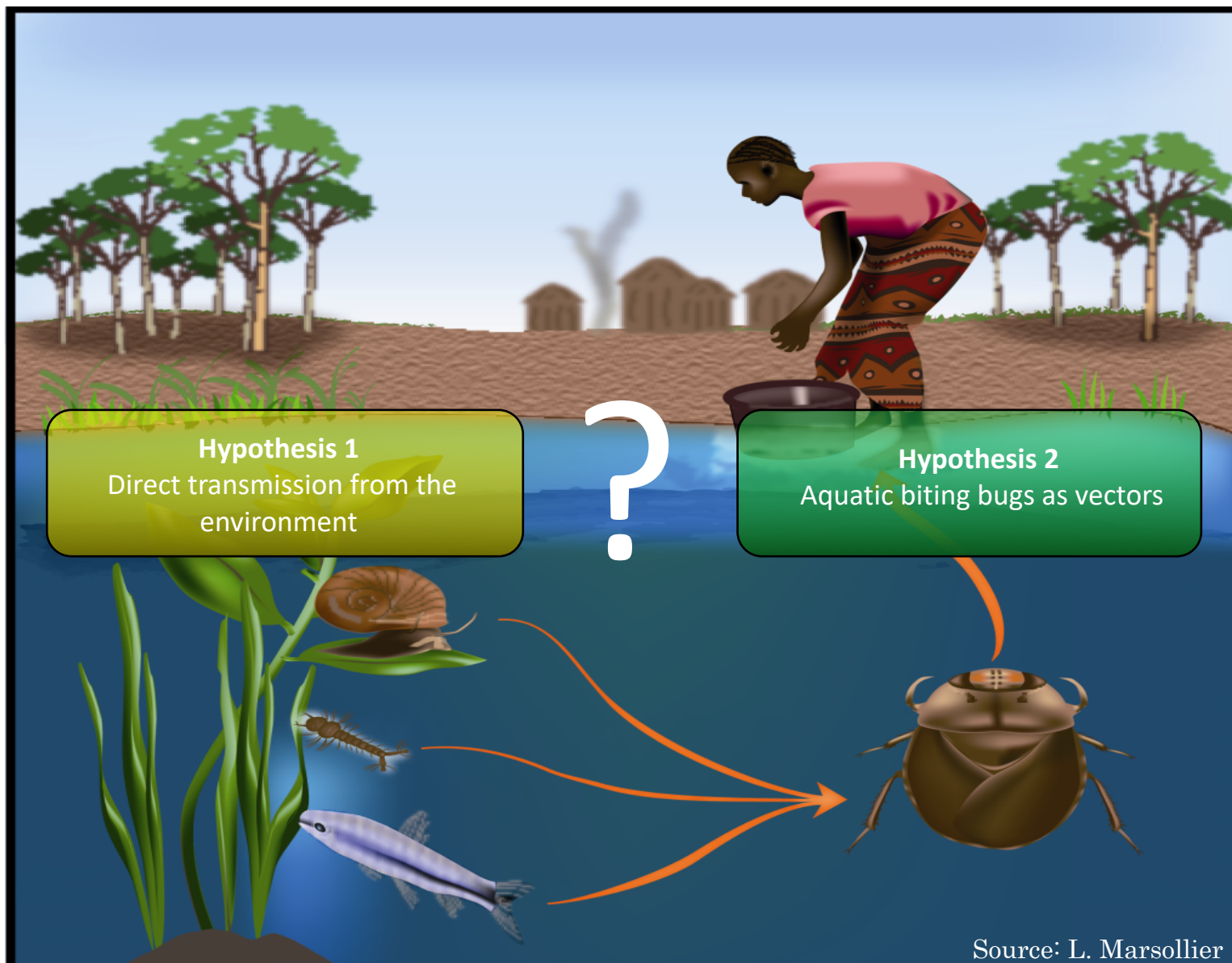
Activities near water

M. ulcerans





Buruli ulcer: a mysterious disease





Objectives of the project

General objective

To gain insights on the ecological determinants of Buruli ulcer disease.

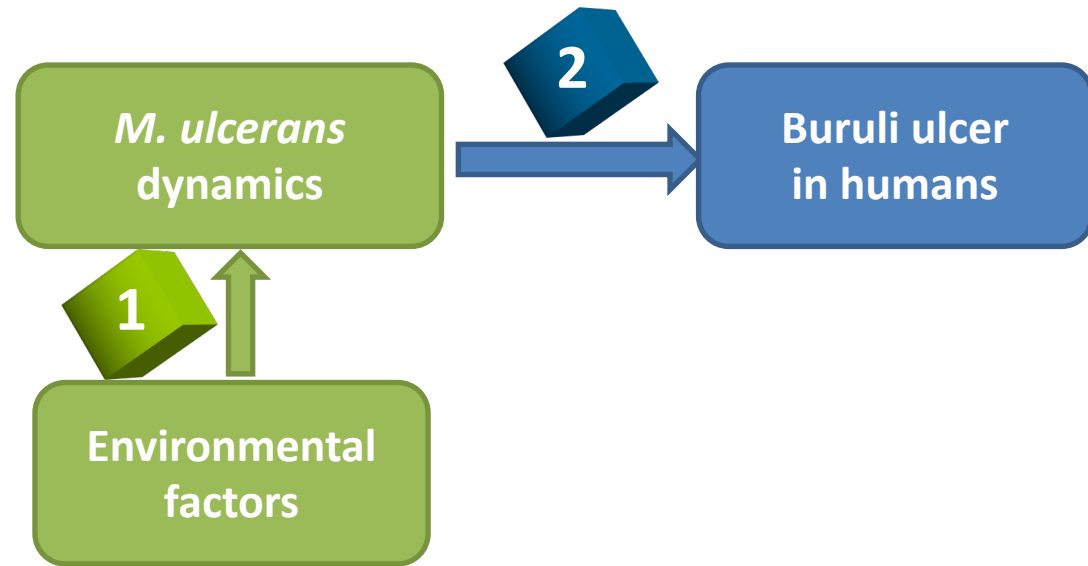
Specific objectives

1

To understand the effects of environmental factors on *M.ulcerans* ecology

2

To study the transmission of *M.ulcerans* from the aquatic environment to humans



What do I need to characterize?

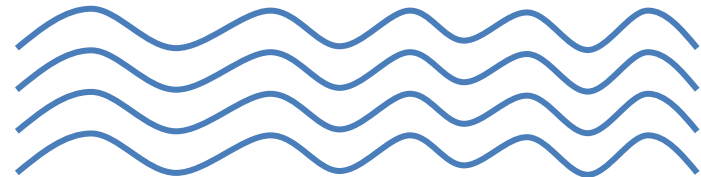
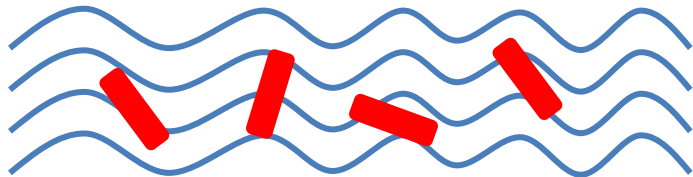
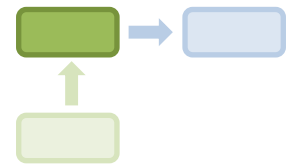
Spatial and/or temporal dynamics?

Relationships between parameters or systems?

DATA COLLECTION & DESCRIPTIVE ANALYSES

1

Introduction



Regions of study

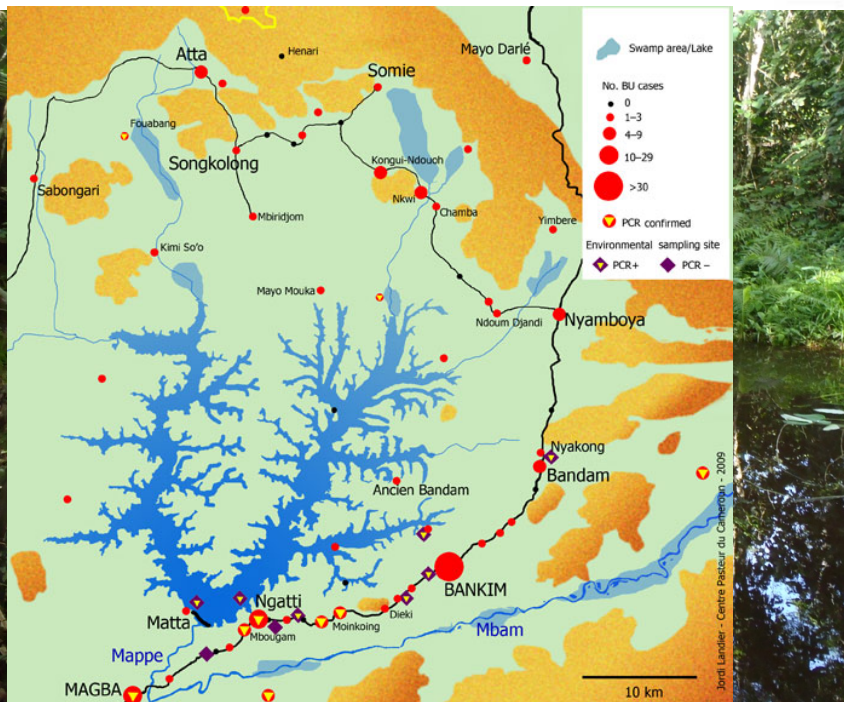
Akonolinga

- Landscape: Tropical rainforest
- Historically endemic area (>40 years)



Bankim

- Landscape: Savannah-Forest
- New endemic area (10 years)



Marion *et al.* (2011, *EID*)



Landier *et al.* (2014, *PLoS NTDs*)

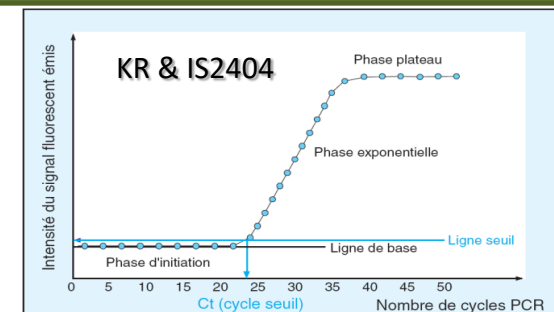
1. Fieldwork: Environmental sampling



2. Laboratory (CPC): Taxonomic identification & Pool composition

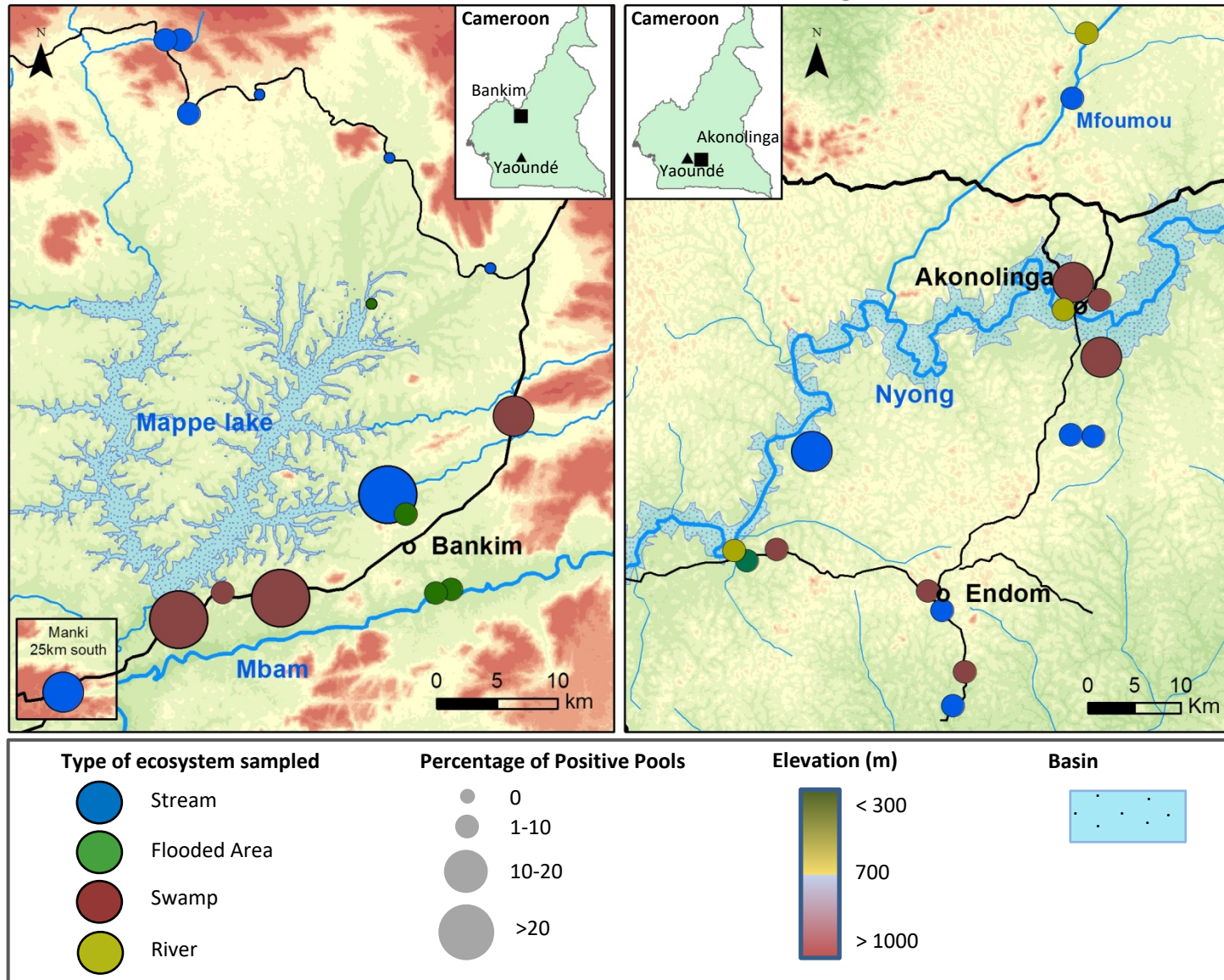


3. Laboratory (Angers): DNA extraction & Amplification



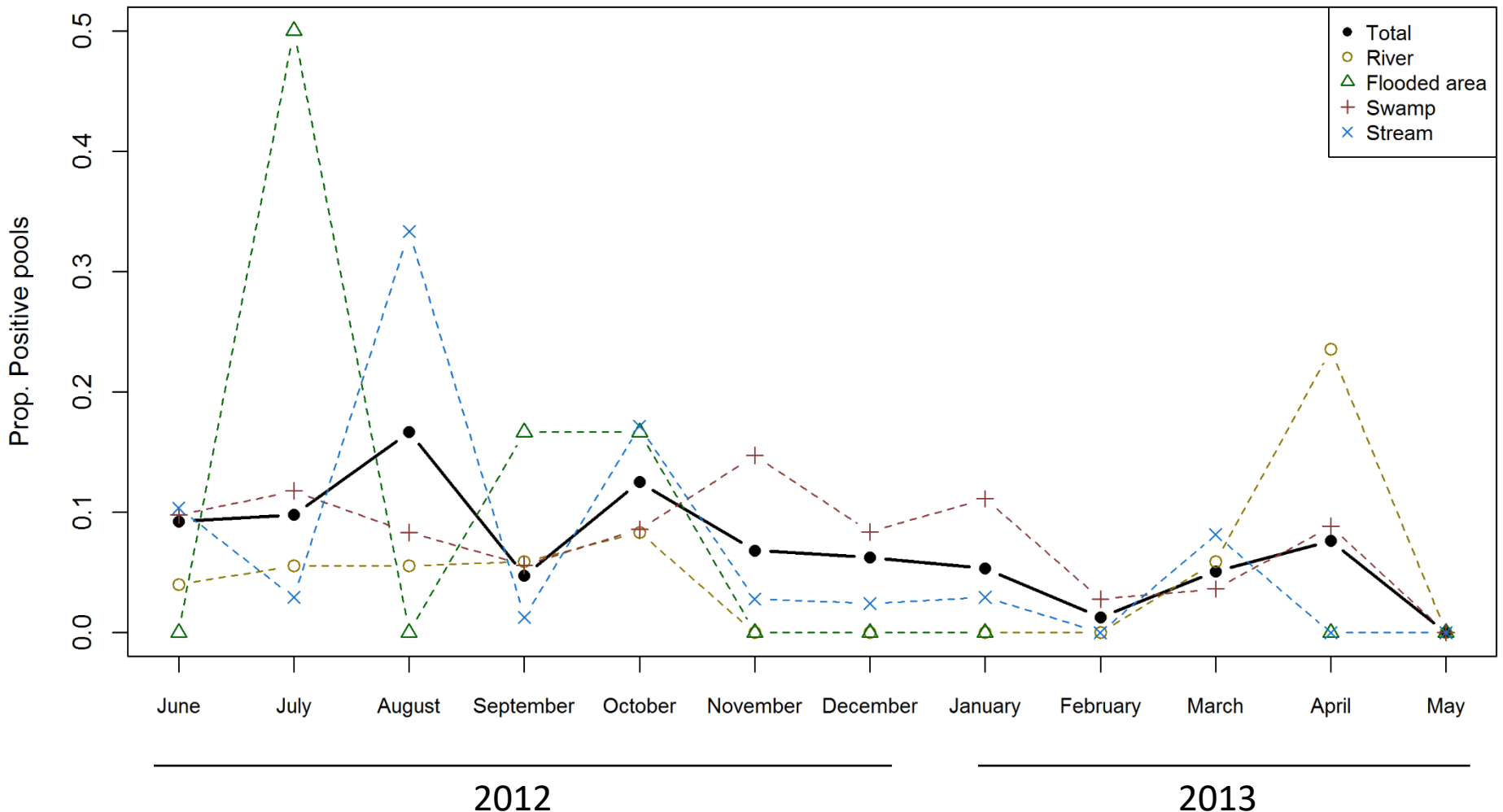
Characterization of MU in the environment

1 *M. ulcerans* geographical distribution



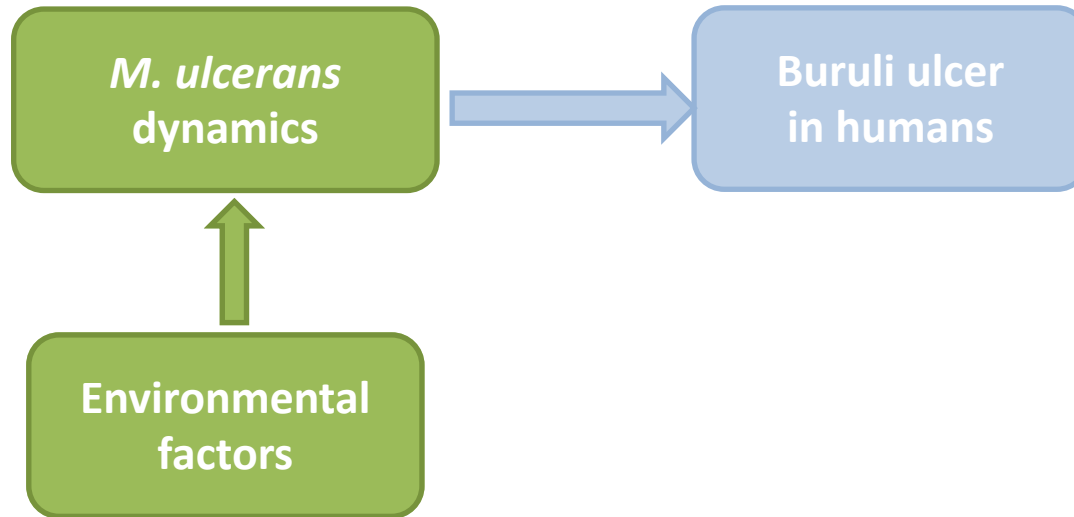
Garchitorena *et al.* (2014, *PLoS NTDs*)

Seasonal fluctuations of *M. ulcerans* in freshwater ecosystems



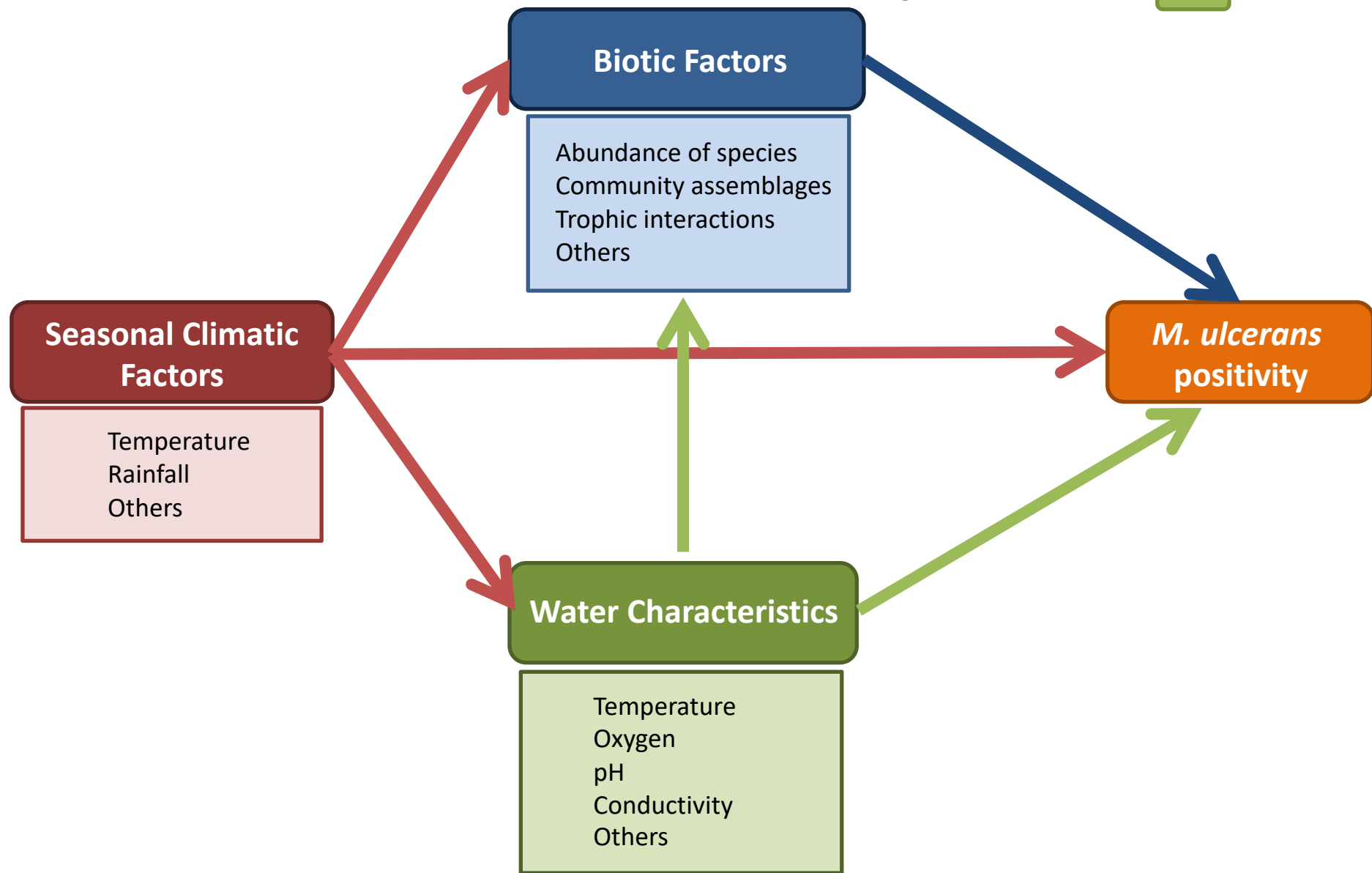
Garchitorena *et al.* (2014, *PloS NTDs*)

What type of modeling is necessary to answer my question?

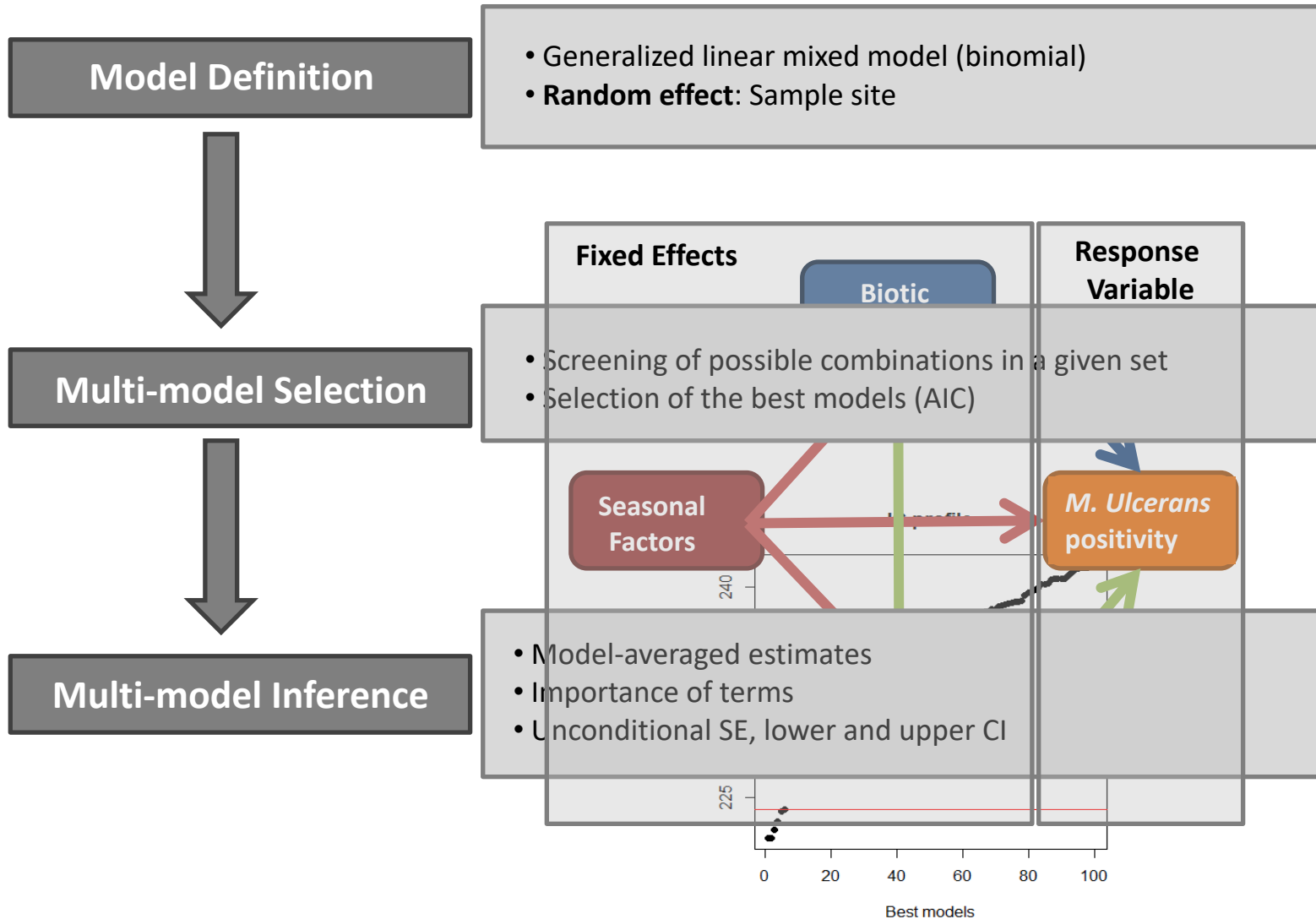
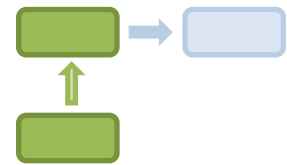


**STATISTICAL ANALYSES TO UNDERSTAND
M. ULCERANS ECOLOGY**

2 Environmental drivers of *M. ulcerans*

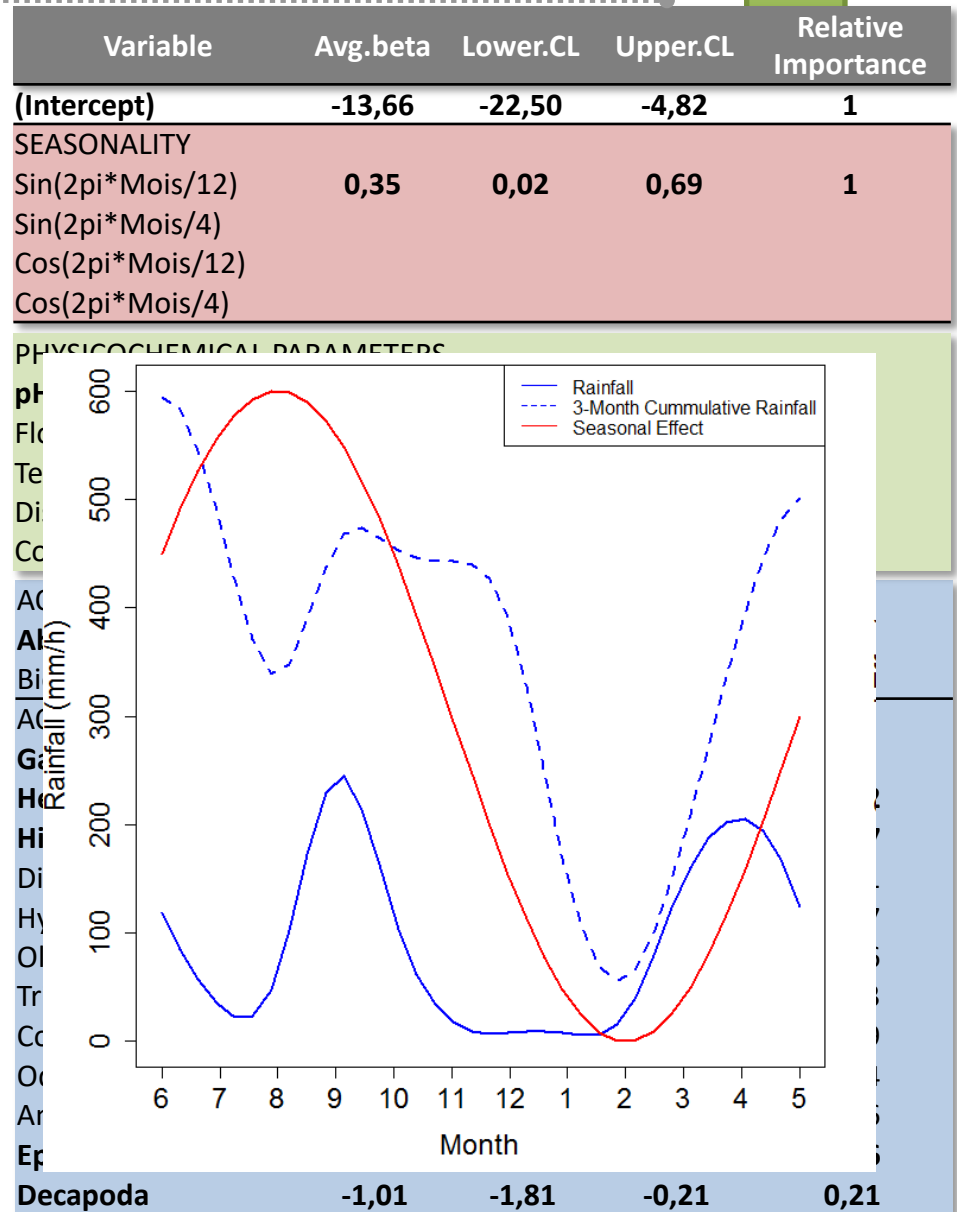
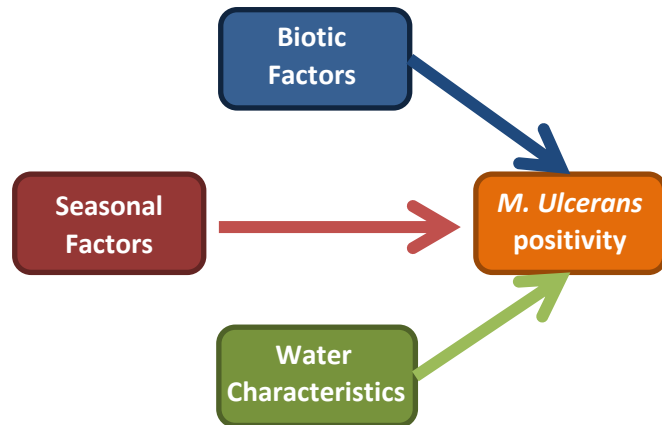


2 Methodology: Multi-model approach



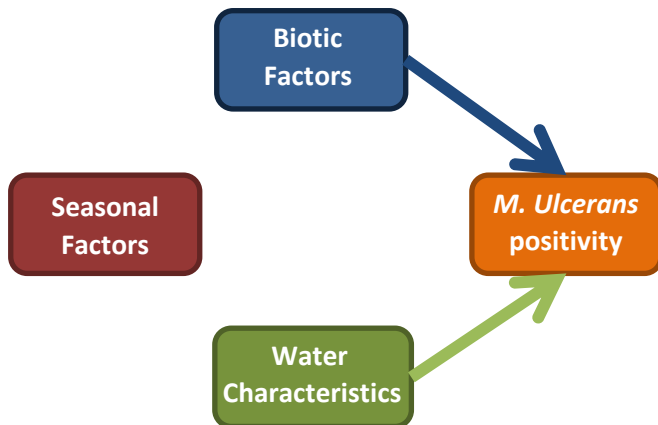
2

Environmental drivers of *M. ulcerans*: Akonolinga



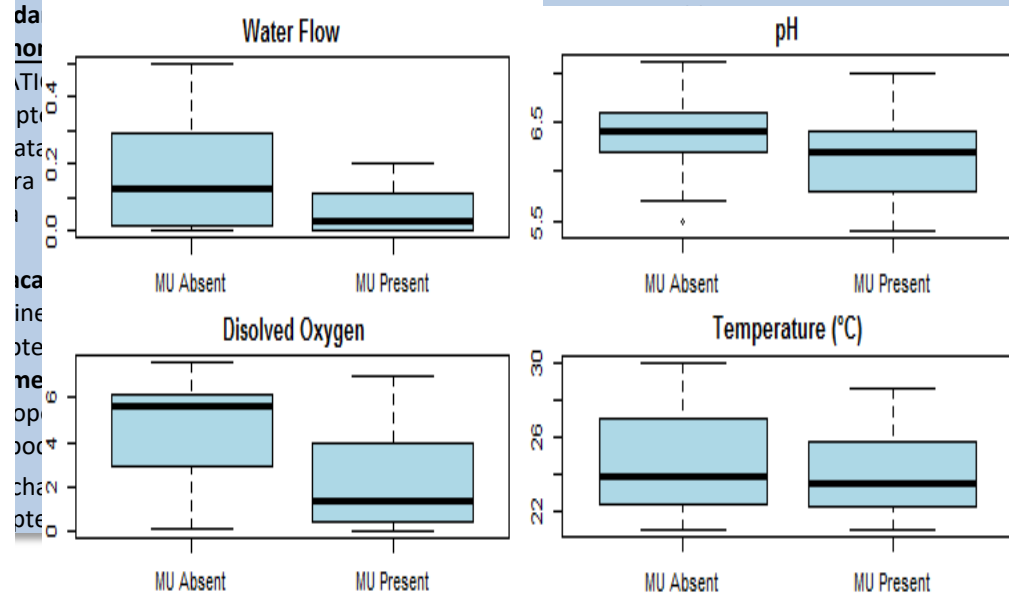
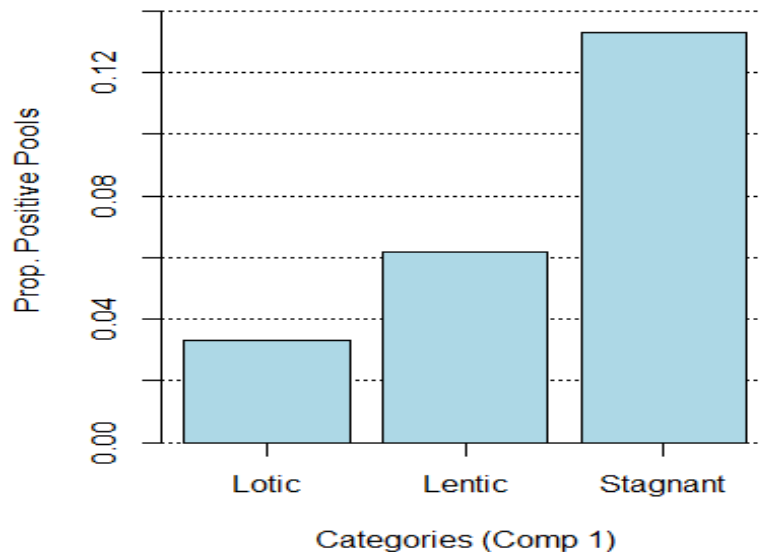
Environmental drivers of MU

Environmental drivers of *M. ulcerans*: Bankim

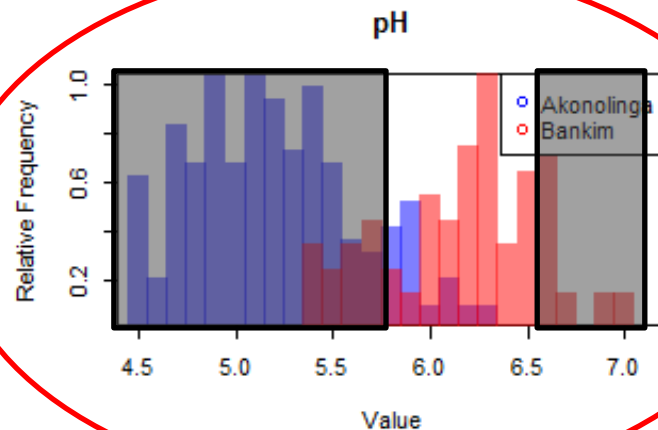
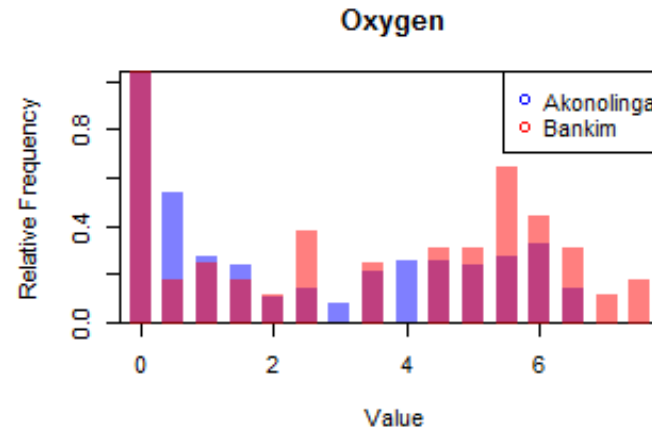
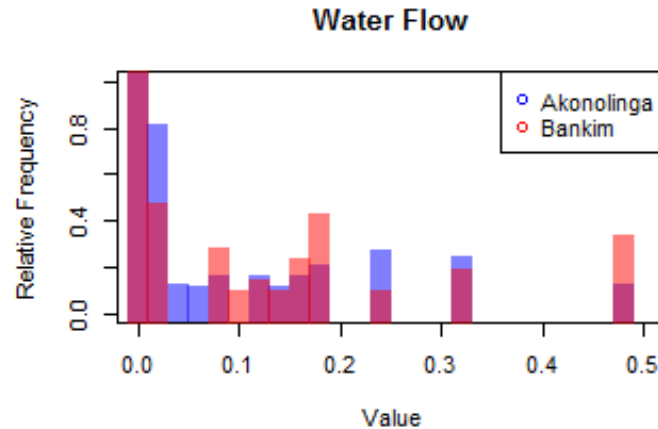
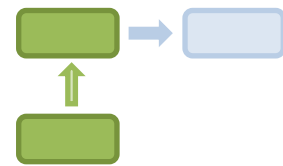


Variable	Avg.beta	Lower.CL	Upper.CL	Relative.Importance
(Intercept)	-10,13	-18,94	-1,32	1
PHYSICO-CHEMICAL PARAMETERS				
Water Flow (lentic)	-1,91	-3,25	-0,57	1
Water Flow (lotic)	-2,86	-4,38	-1,33	1
pH	-5,52	-15,64	4,61	0,02
Temperature				
Dissolved Oxygen				
Conductivity				
Comp3	0,24	-0,57	1,06	0,05
Comp1	0,34	-0,24	0,92	0,02
Comp2	-0,16	-0,85	0,53	0,01
COMMUNITY				

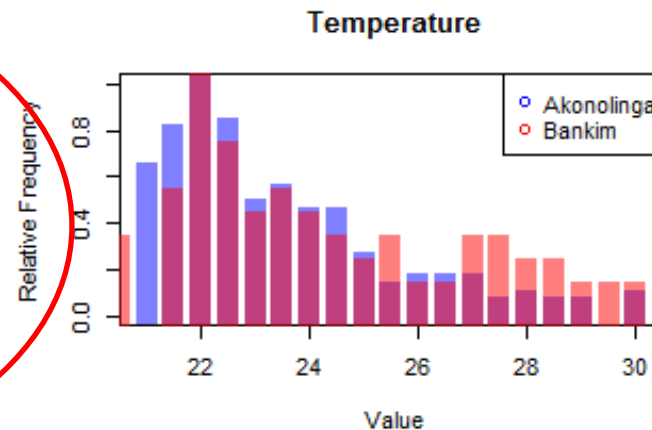
MU Positivity in Ecosystems

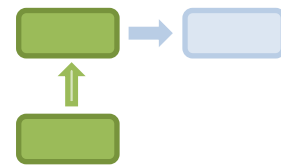


2 Why the two regions are so different?



Optimal *pH* for *MU* [5.8-6.5]



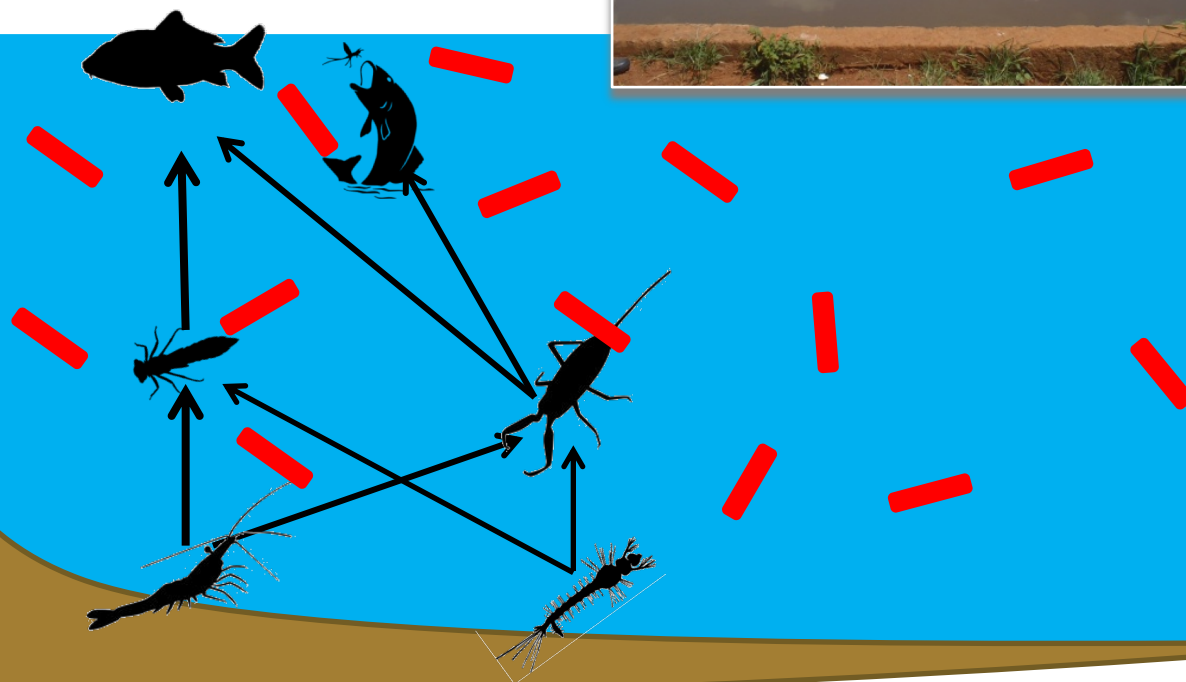


Scenario 1: Favourable physico-chemical conditions

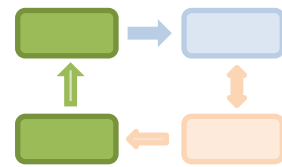
Free living stages
&
Environmental transmission to aquatic organisms



↓ Water flow
↓ O₂
↓ pH (optimal)

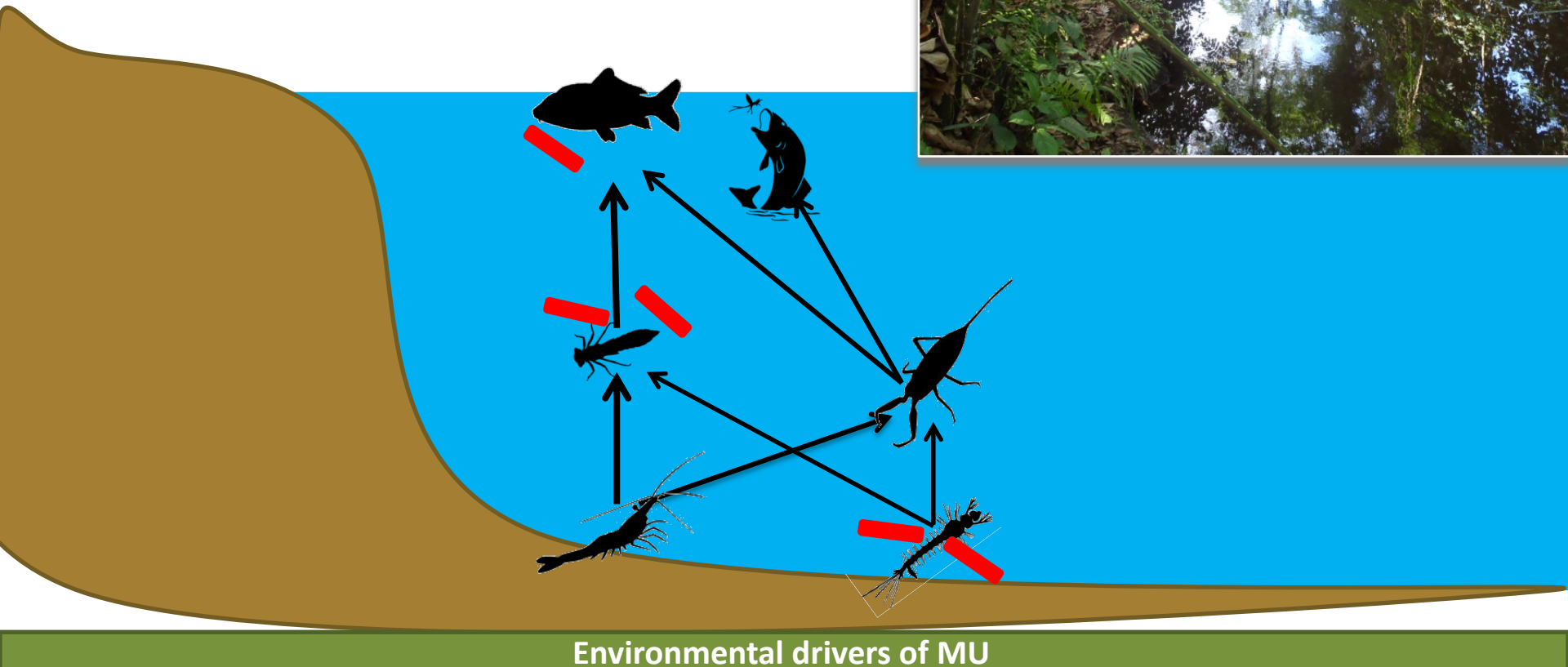


Environmental drivers of MU

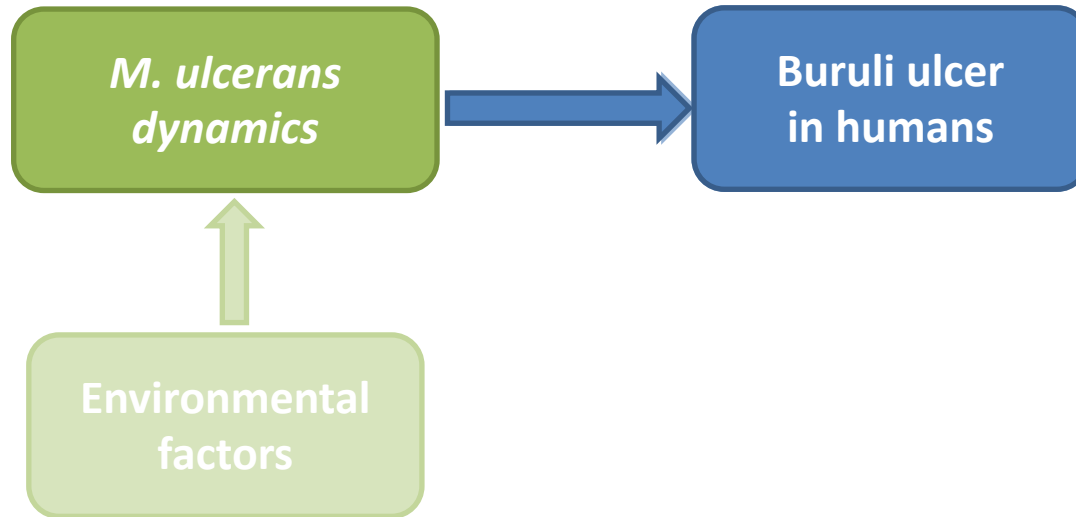


Scenario 2: Adverse physico-chemical conditions

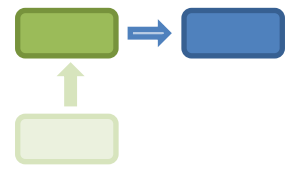
Mostly intra-host
&
Trophic transmission



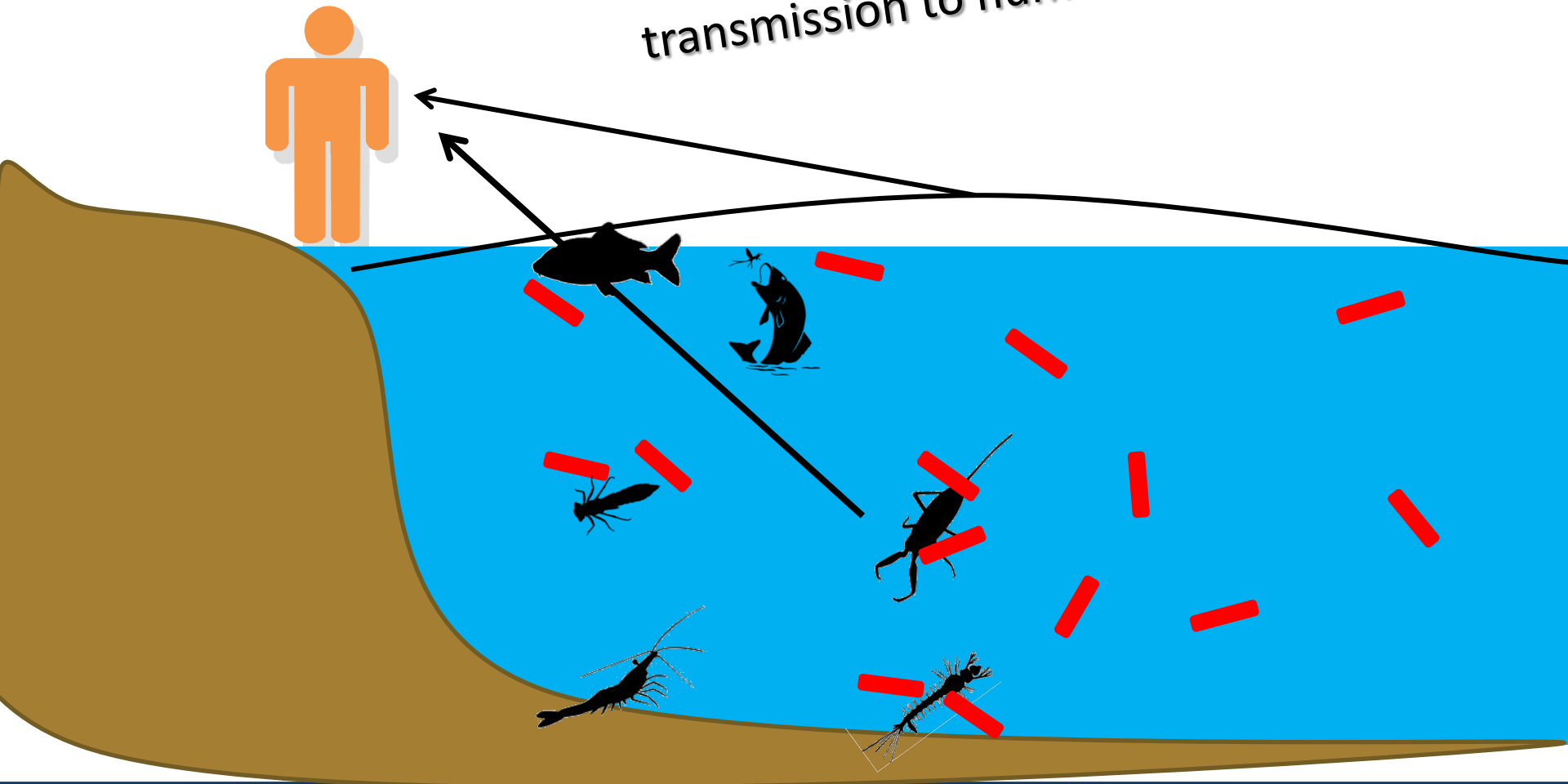
What type of modeling is necessary to answer my question?



**MATHEMATICAL MODELING TO
UNDERSTAND BU TRANSMISSION**

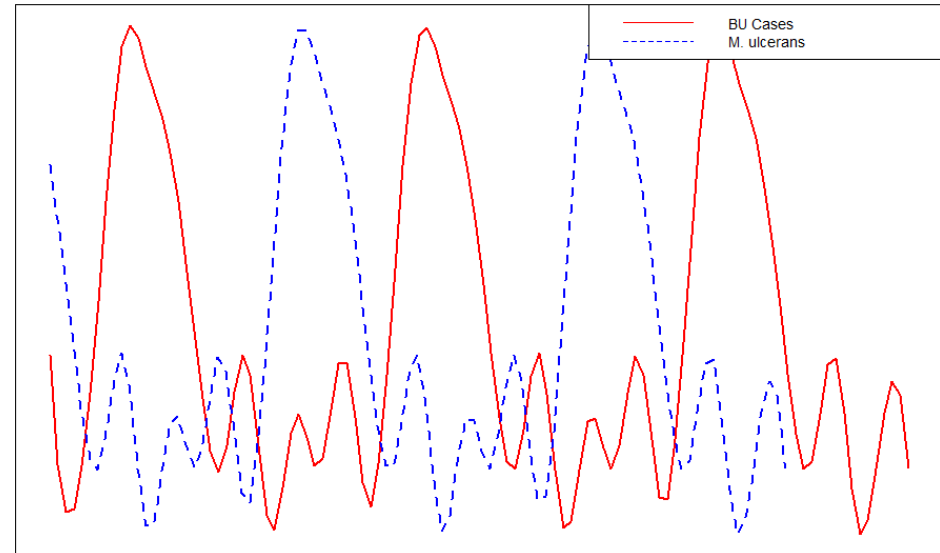


2 possible routes of transmission to humans

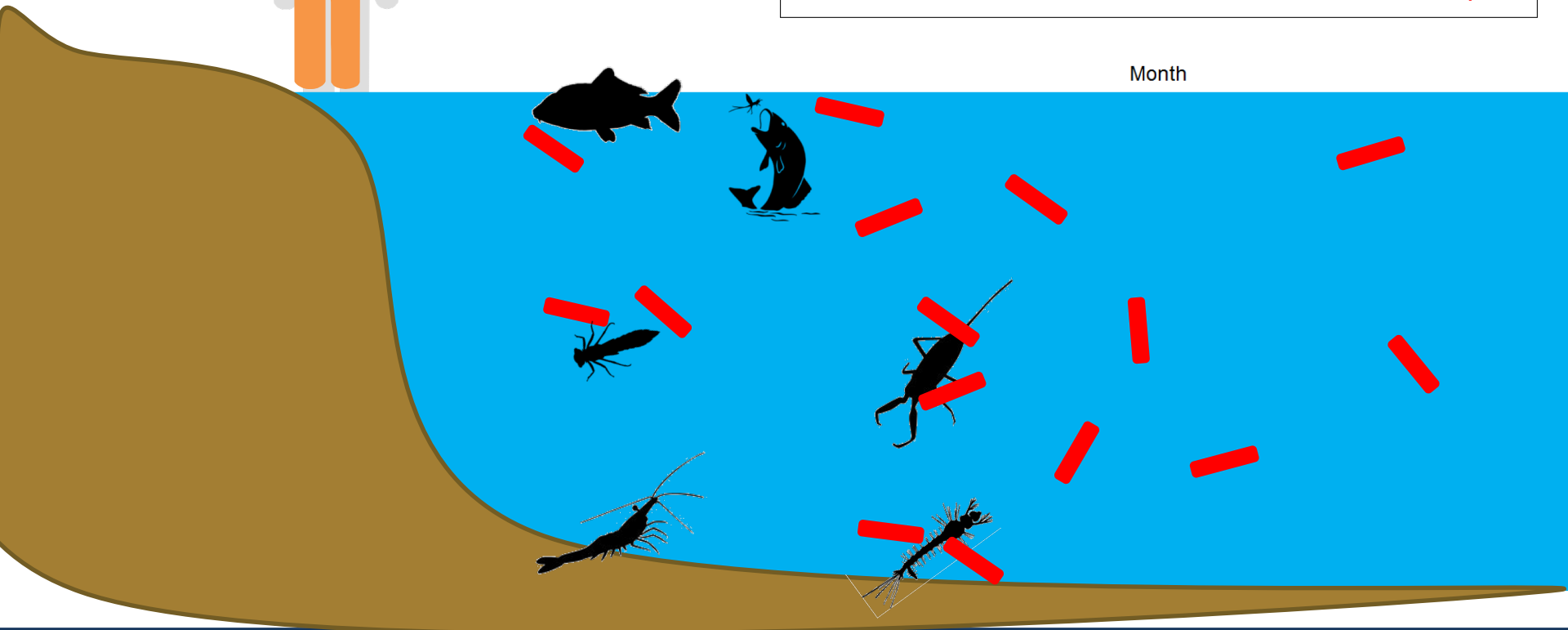


Transmission of MU to humans

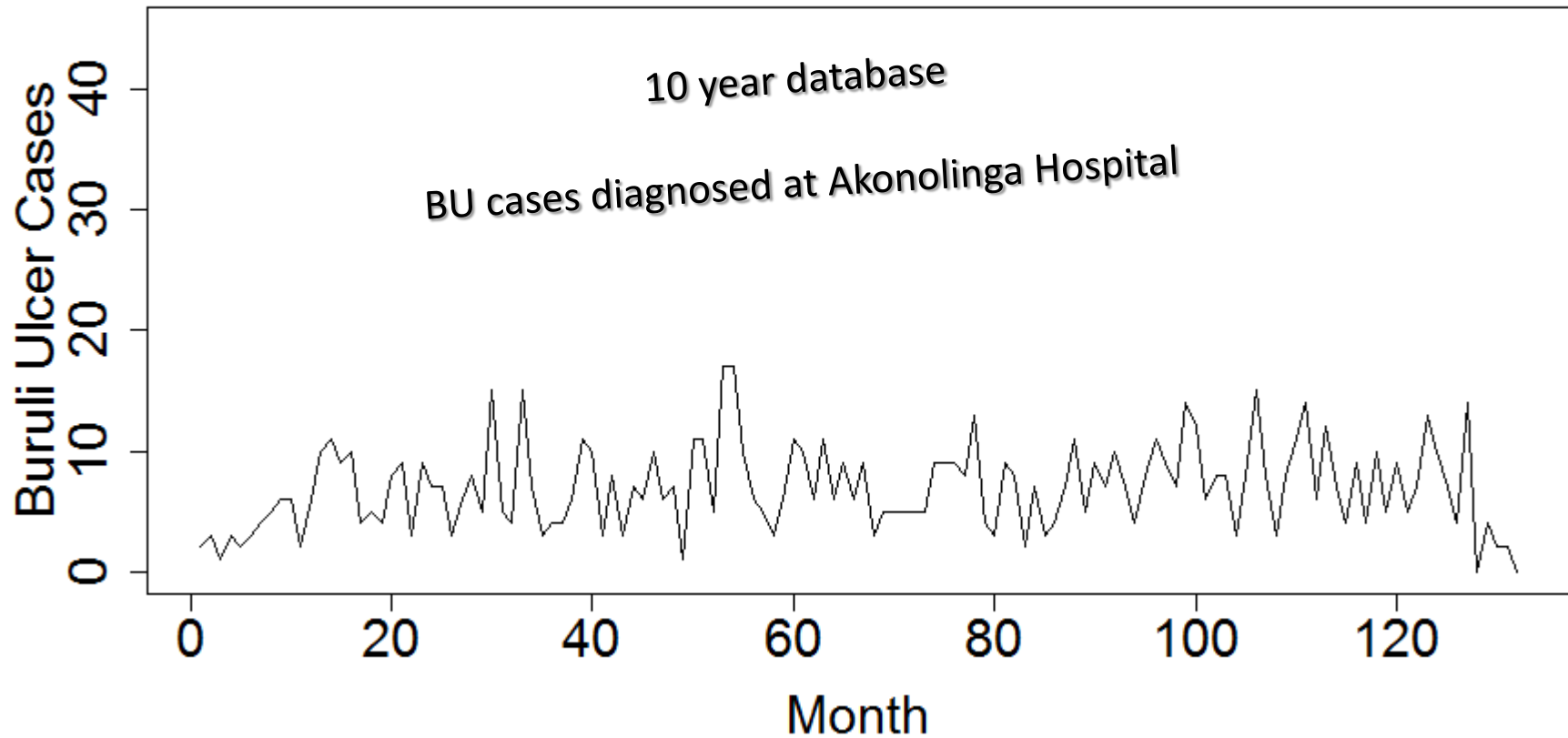
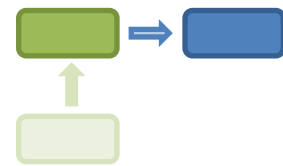
Dynamic model



Month

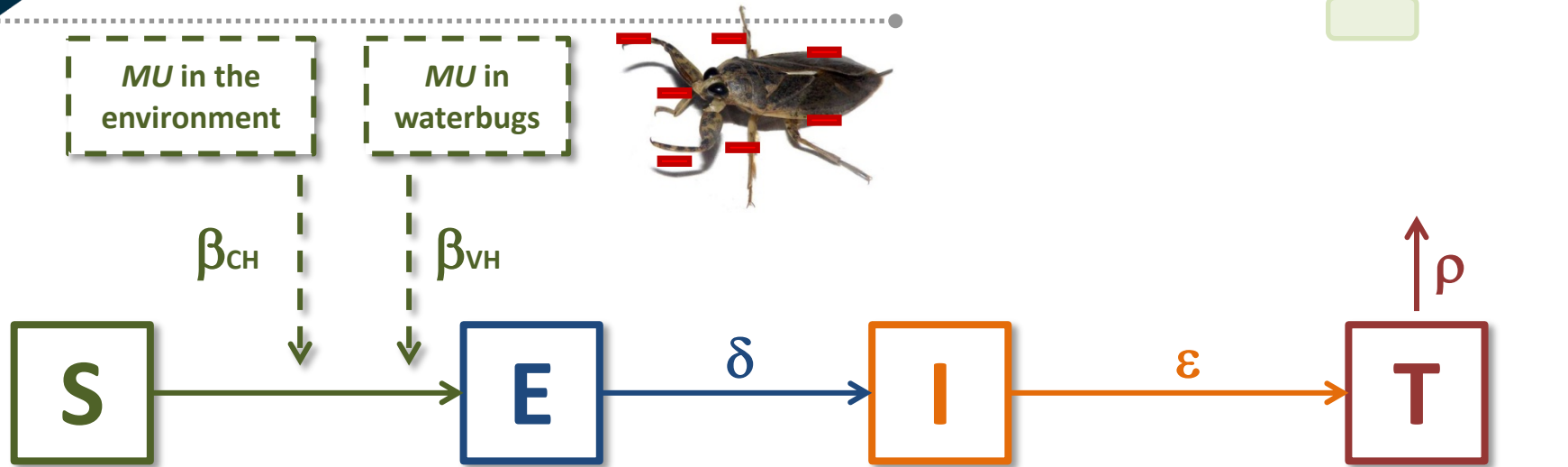


Transmission of MU to humans



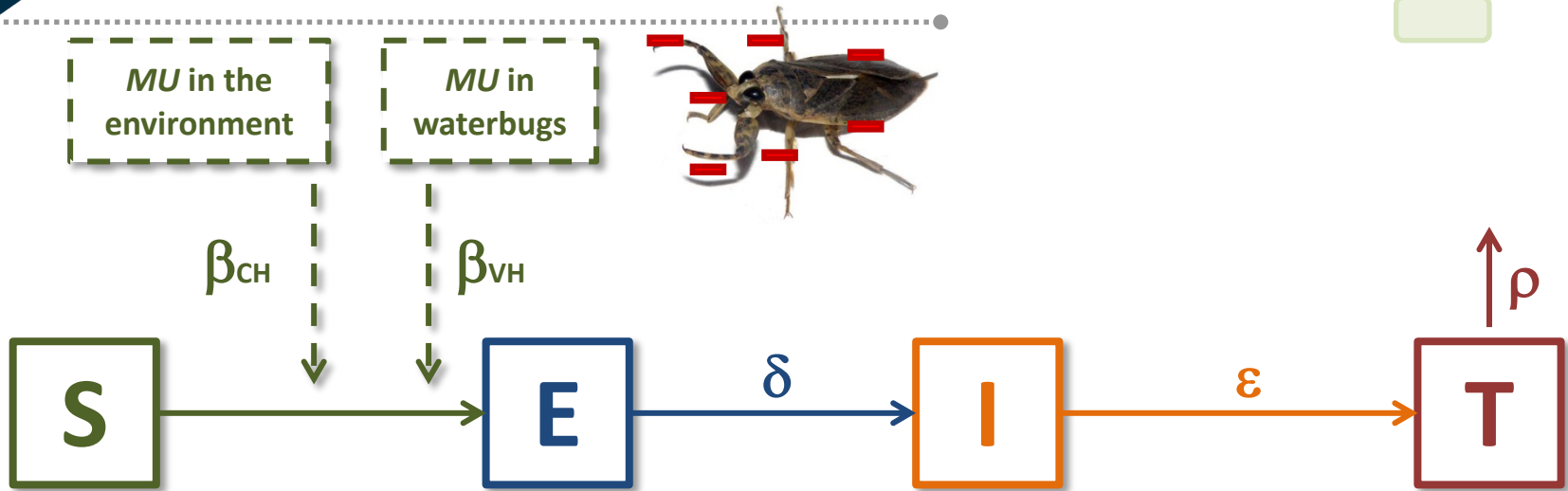
3

Mathematical model framework



3

Mathematical model framework



Mathematical Model

$$\frac{dS}{dt} = \mu N - \lambda_{CH}(Month_i) S - \lambda_{VH}(Month_i) S - \mu S$$

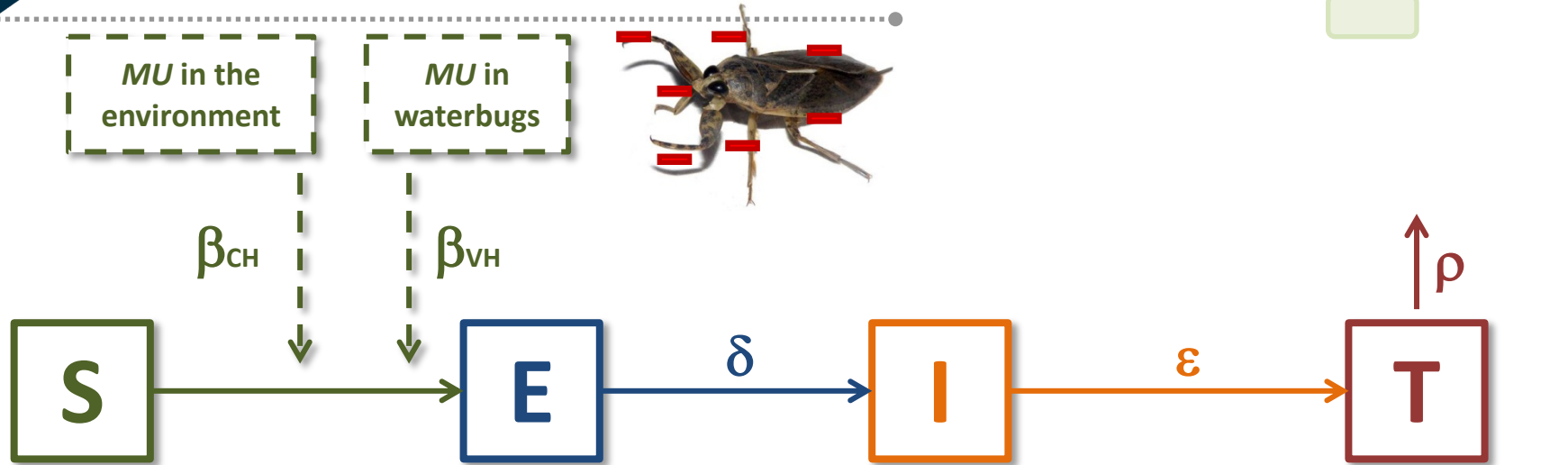
$$\frac{dE}{dt} = \lambda_{CH}(Month_i) S + \lambda_{VH}(Month_i) S - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \epsilon I - \mu I$$

$$\frac{dT}{dt} = \epsilon I - \gamma T - \mu T$$

3

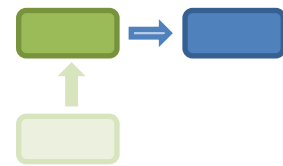
Mathematical model framework



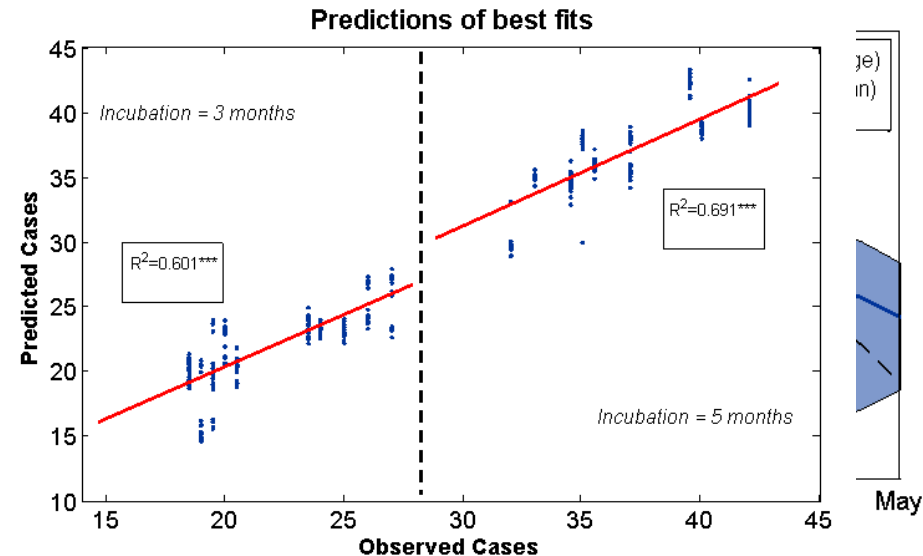
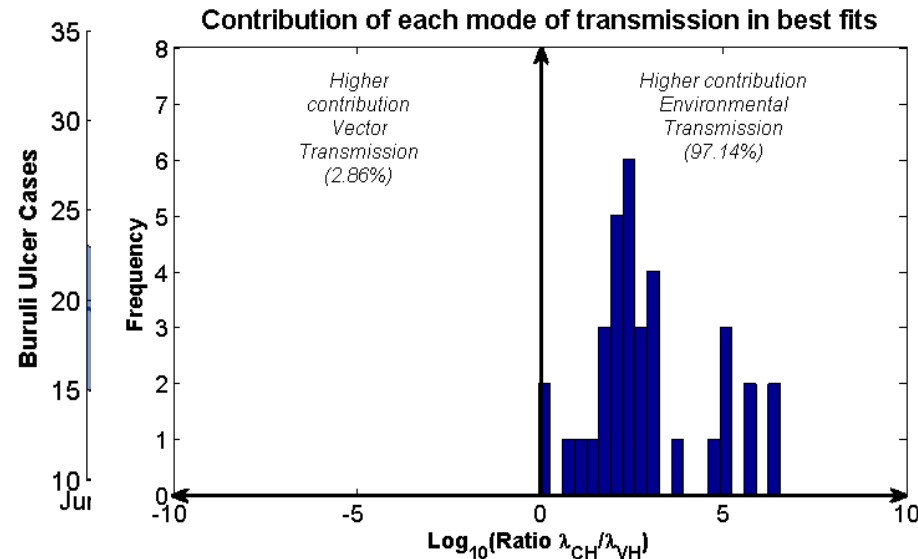
Model simulations to account for:

- A range of initial parameters
- Uncertainties in rates of incubation (δ) and seeking treatment (ϵ)
- Different proxies of waterbug transmission and environmental transmission
- Linear risks or thresholds in the relationship MU-BU

Comparison of model fit using AIC and selection of best performing (2 AIC)



Best temporal fit



Environmental transmission >>>> water bug transmission

MU environmental concentration as linear predictor of BU cases

AT THIS STAGE WE ARE ALMOST DONE...



Manuscript writing and submission

- What are the main results that provide the answer to my question?
 - 1 to 3 graphs
 - 1 to 3 tables
- What is the journal that best fits my study?
 - Scope, audience, impact factor, math focus
- How do I present my manuscript?
 - Introduction: set the stage to your question
 - Methodology: describe explicitly all steps for replicability
 - Results: clear and concise
 - Discussion: explain how your study improves previous knowledge

MODELING IN PRACTICE: THE LIFE CYCLE OF A MODELING PROJECT, FROM CONCEPTION TO PUBLICATION

- The example of Buruli ulcer in Cameroon -



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E²M² Workshop
Ranomafana, January 2019