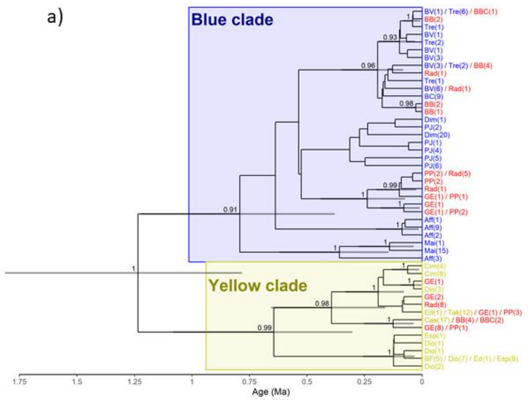
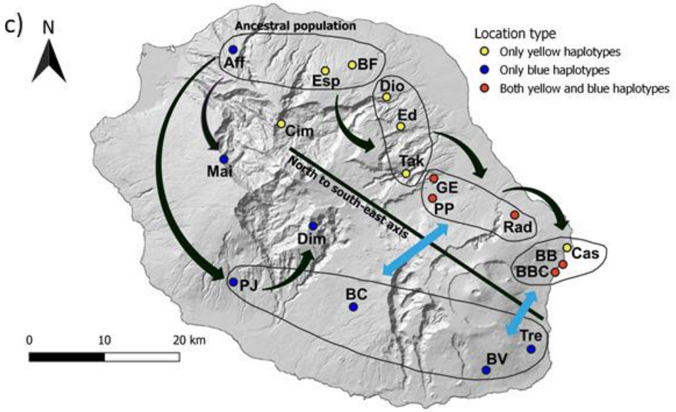
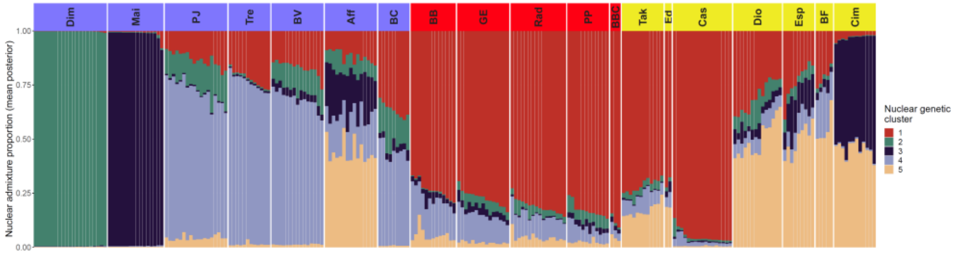
EMPIRICAL AND METHODOLOGICAL RESEARCH IN BIOGEOGRAPHY, POPULATION GENETICS, AND PHYLOGENETICS

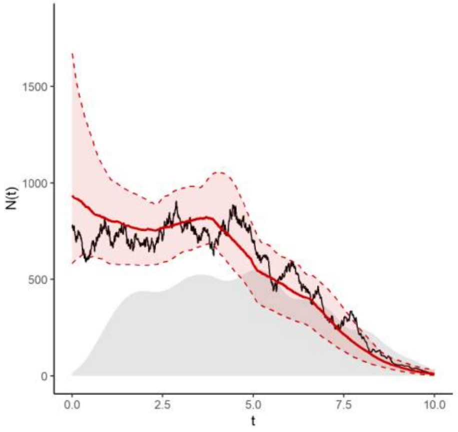
Josselin Cornuault, ISEM, Montpellier

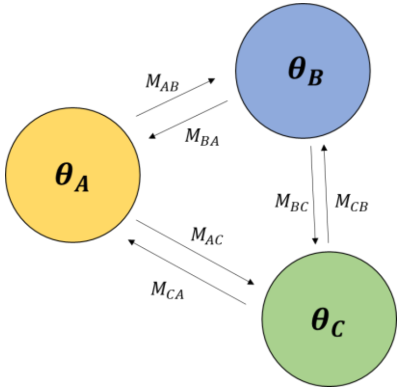
9 janvier 2024

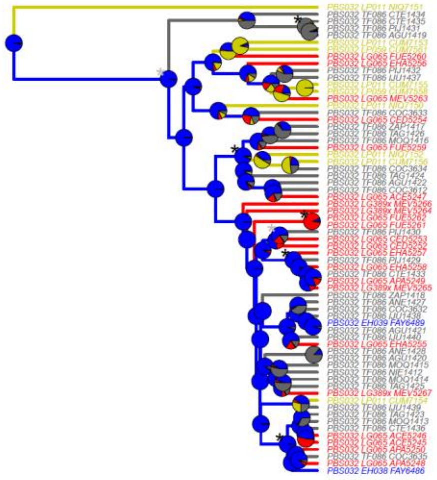








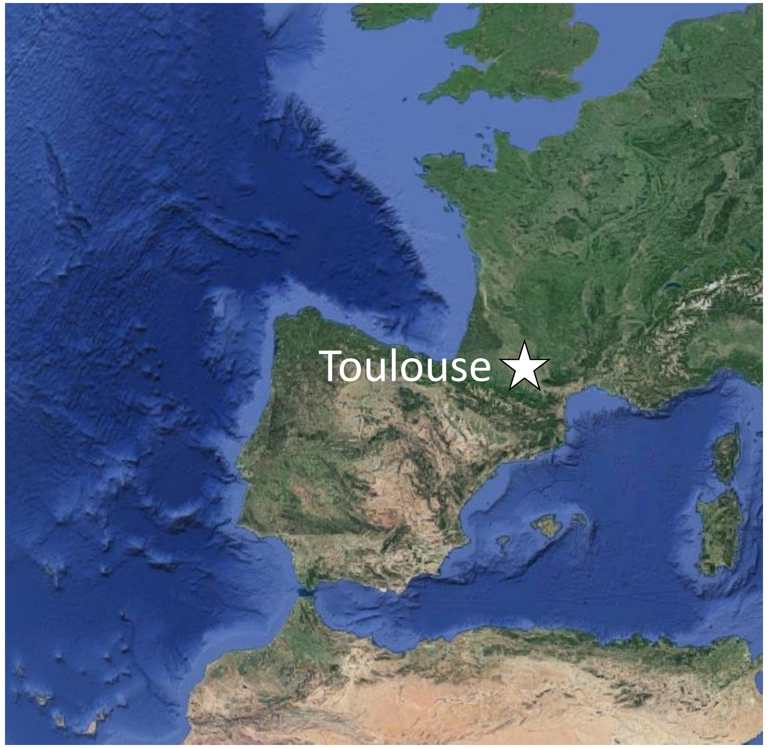


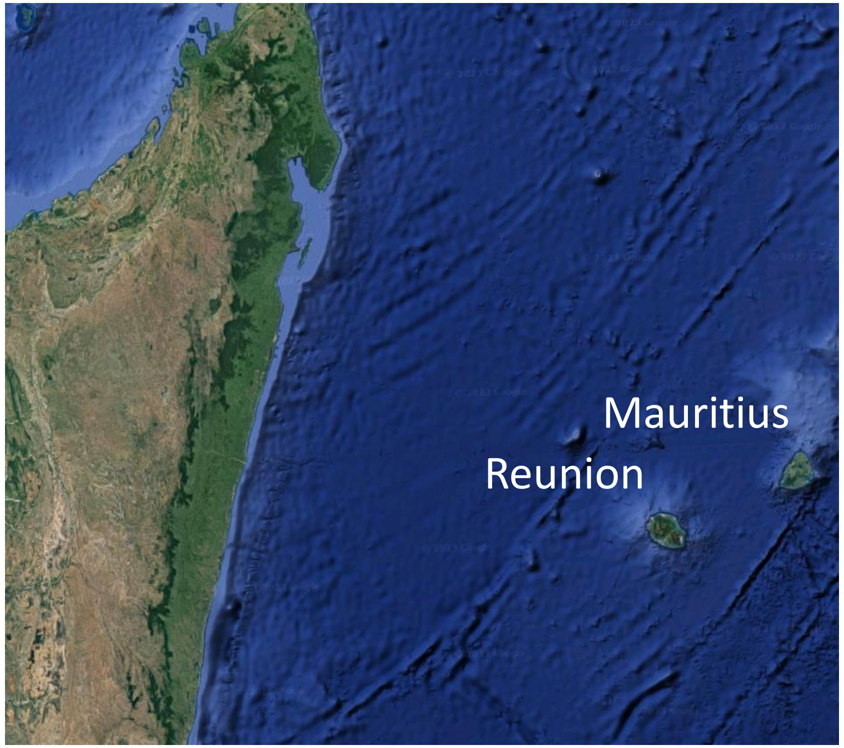


HEMOSPORIDIAN PARASITES
–
DIVERSITY IN THE MASCARENES

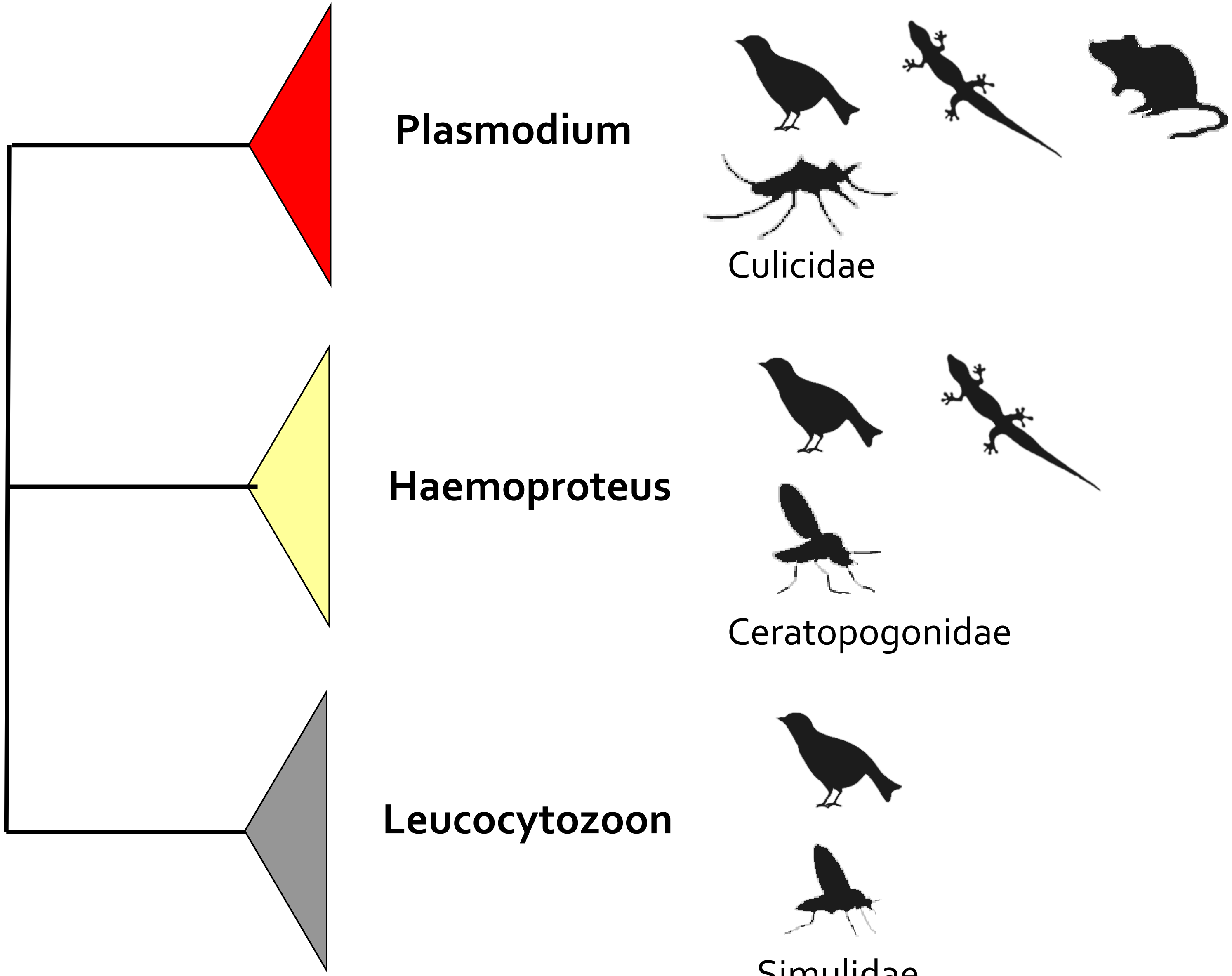
Josselin Cornuault, Christophe Thébaud, Philippe Heeb, Borja Mila, Ben Warren, Thomas Duval

Lab Evolution & Diversité Biologique





HEMOSPORIDIAN PARASITES – GENERALITIES



Plasmodium

Culicidae

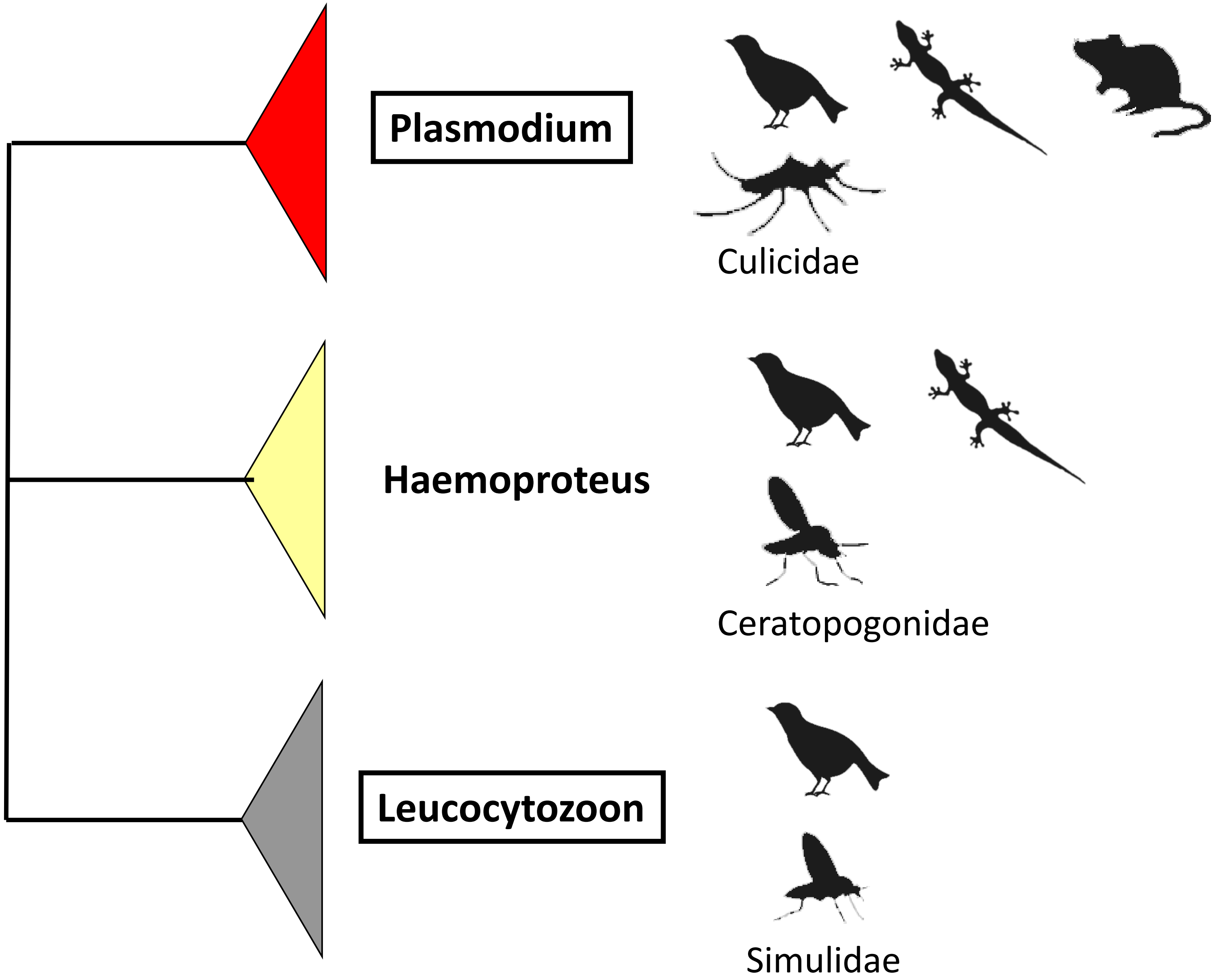
Haemoproteus

Ceratopogonidae

Leucocytozoon

Simulidae

HEMOSPORIDIAN PARASITES – GENERALITIES



Plasmodium

Culicidae

Haemoproteus

Ceratopogonidae

Leucocytozoon

Simulidae

HEMOSPORIDIAN PARASITES – DIVERISTY IN THE MASCARENES

Leucocytozoon

Plasmodium

26 lineages **>** 10 lineages

HEMOSPORIDIAN PARASITES – DIVERISTY IN THE MASCARENES

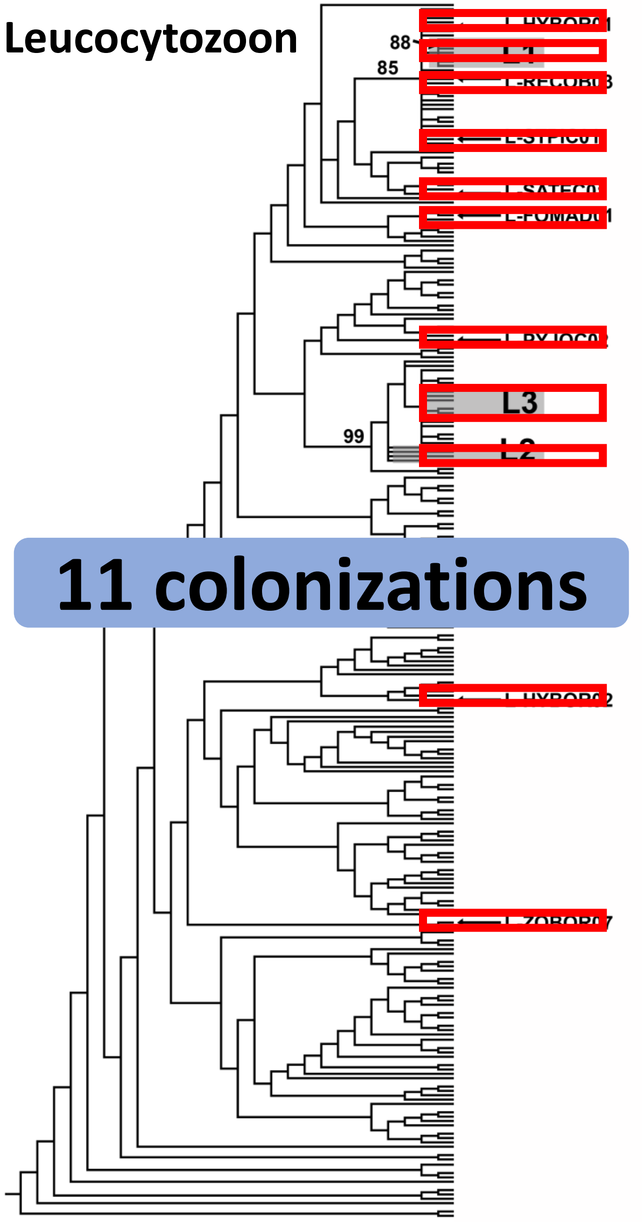
Leucocytozoon **Plasmodium**

26 lineages > 10 lineages

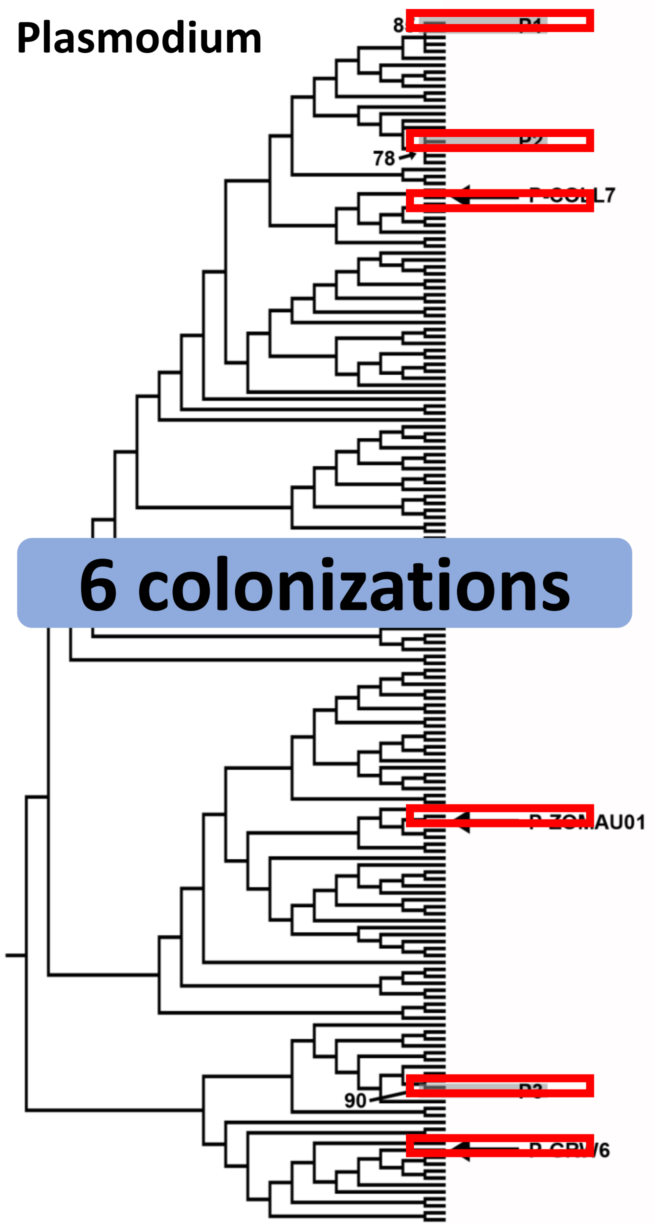
Proximal determinants of diversity:

- Number of colonizations
- Colonization time
- Diversification rate

HEMOSPORIDIAN PARASITES – DIVERISTY IN THE MASCARENES



Leucocytozoon



Plasmodium

11 colonizations > **6 colonizations**

Hemosporidian Parasites – Diveristy in the Mascarenes

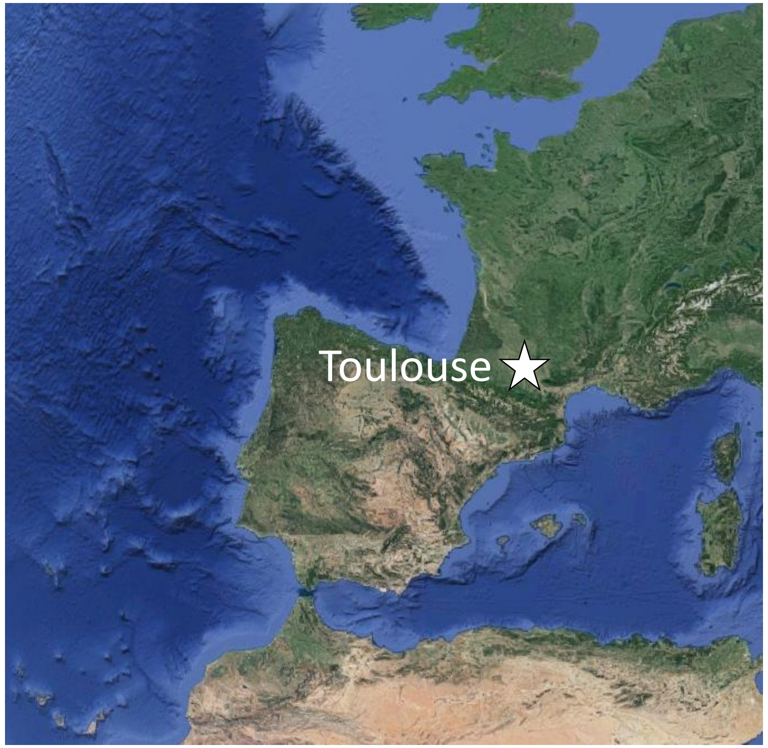
	Leucocytozoon	**Plasmodium**
Colonization #	+	-
Colonization times	+	-
Diversification rate	=	=

Greater diversity in Leucocytozoon

GENETIC STRUCTURE IN *PHELSUMA BORBONICA*
–
IMPLICATIONS FOR CONSERVATION

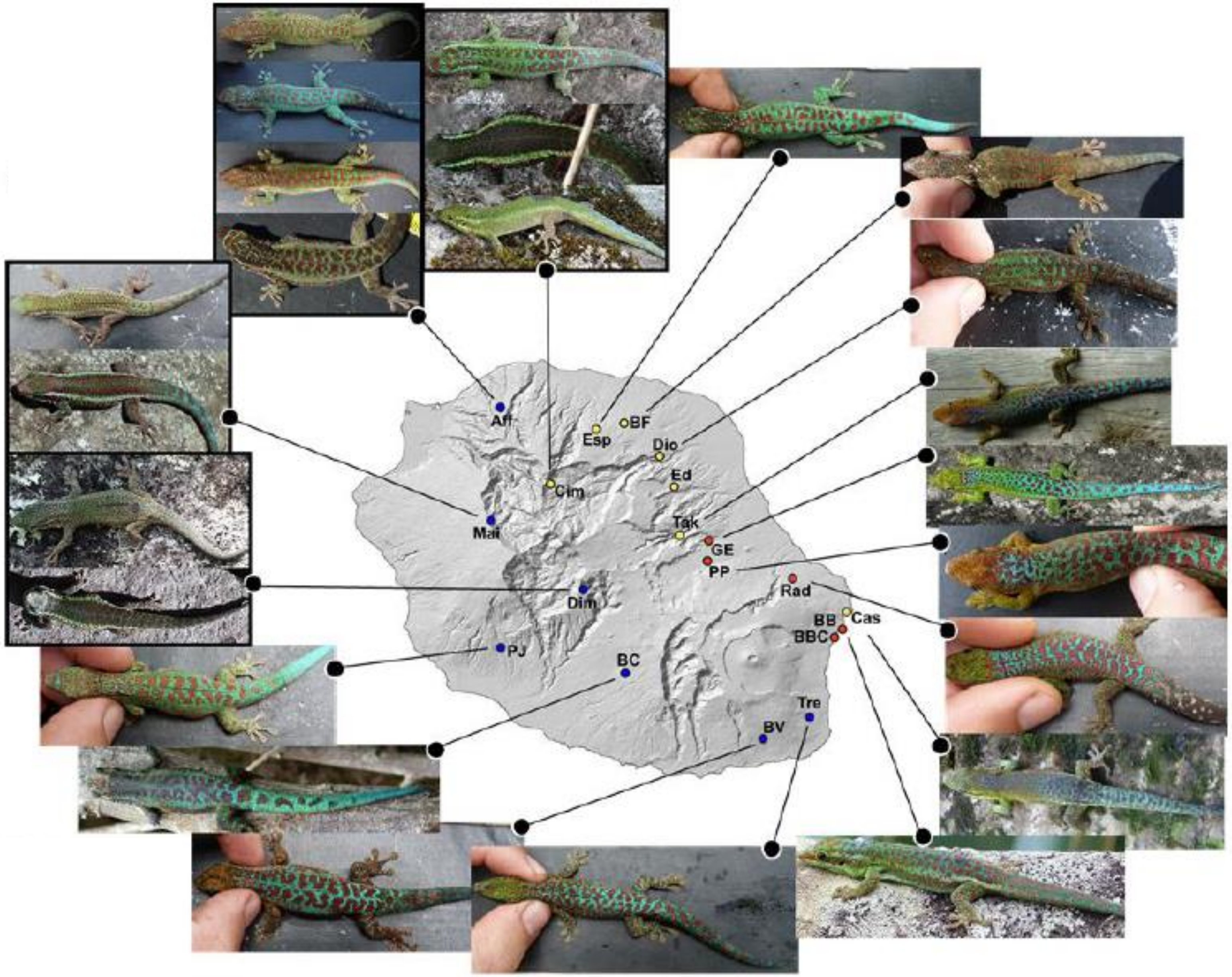
Josselin Cornuault, Mickaël Sanchez, Thomas Duval, Antoine Fouquet, Christophe Thébaud

Lab Evolution & Diversité Biologique



Phelsuma borbonica – Generalities

- Almost endemic to Reunion island
- Endangered species (IUCN)
- Human-altered habitat
- Geographically-structured color variation

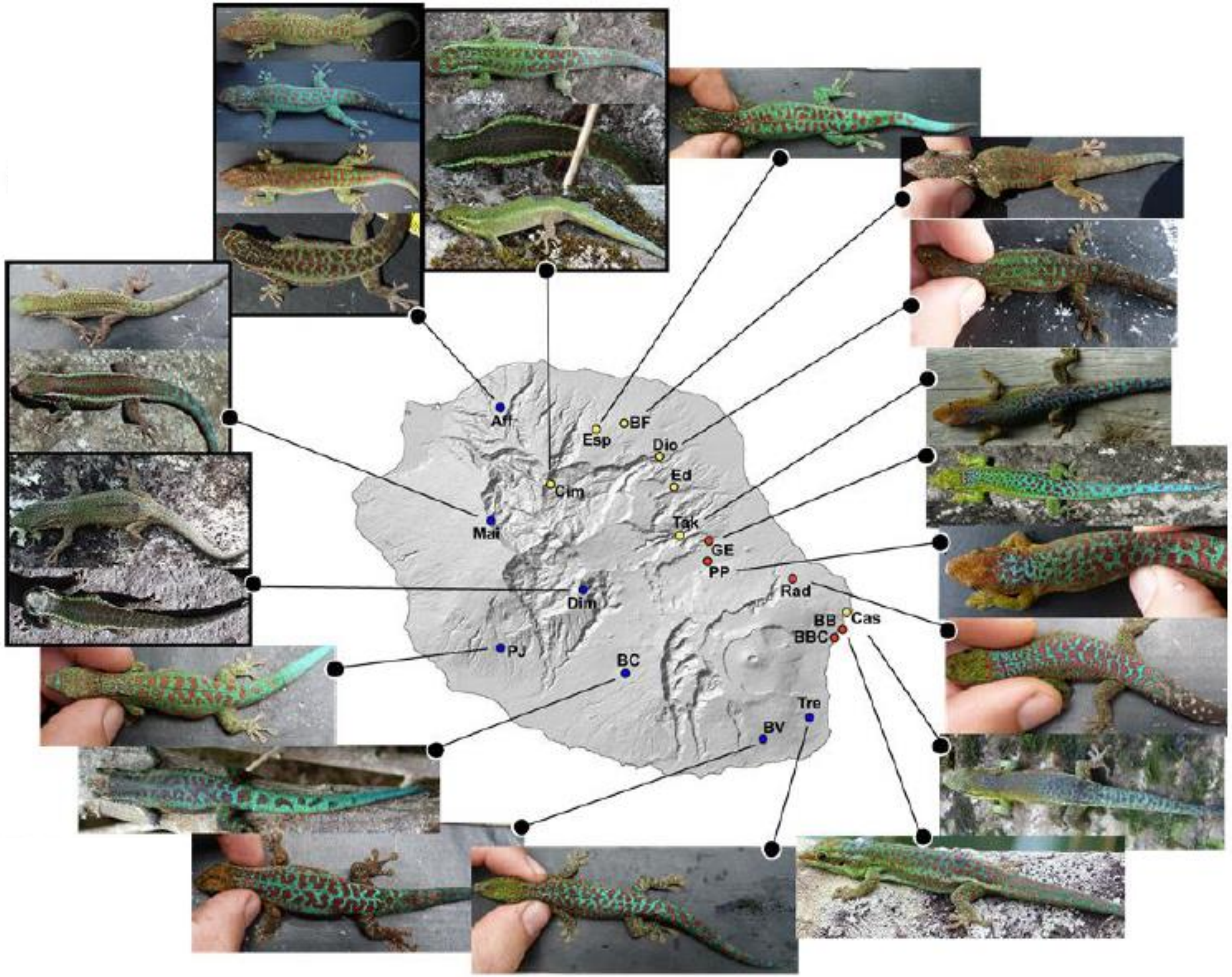


Phelsuma borbonica – GENERALITIES

- Almost endemic to Reunion island
- Endangered species (IUCN)
- Human-altered habitat
- Geographically-structured color variation

Genetic structure ?

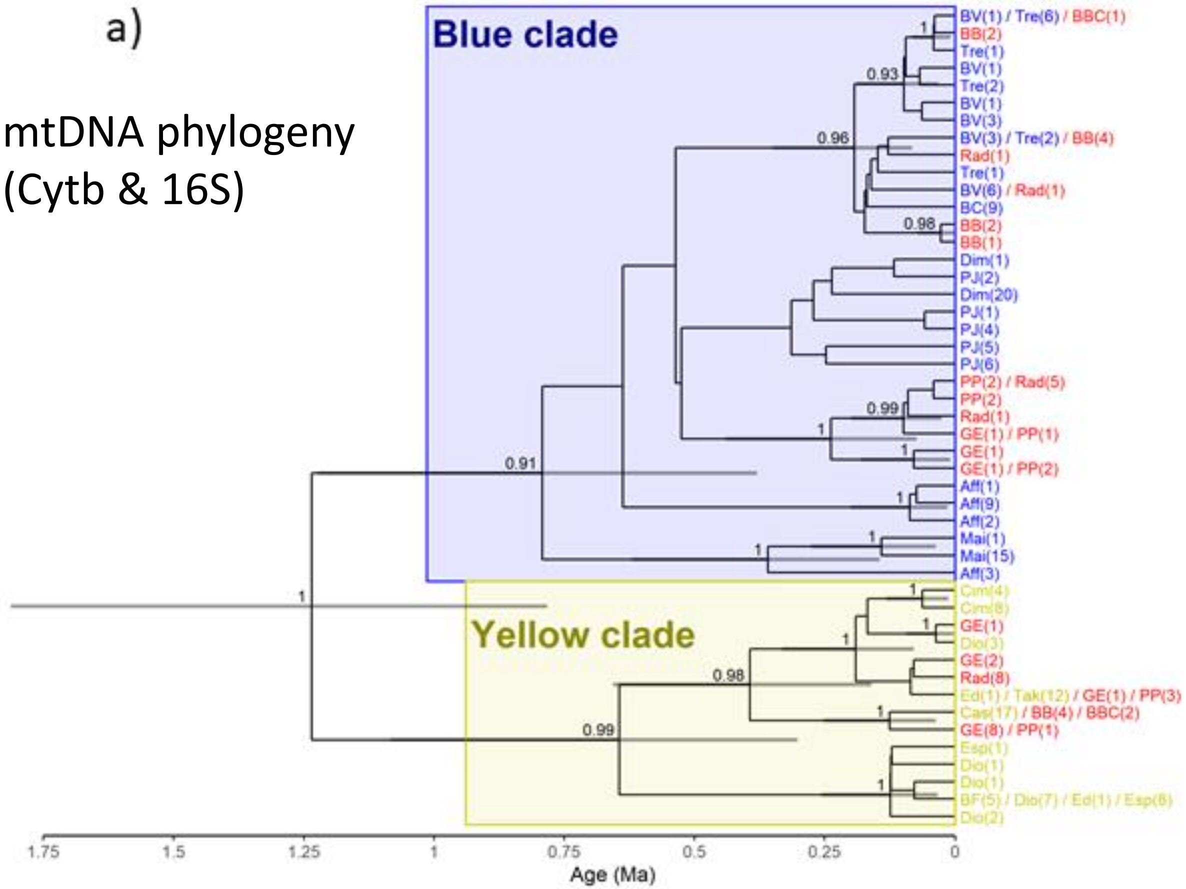
Different evolutionary significant units ?



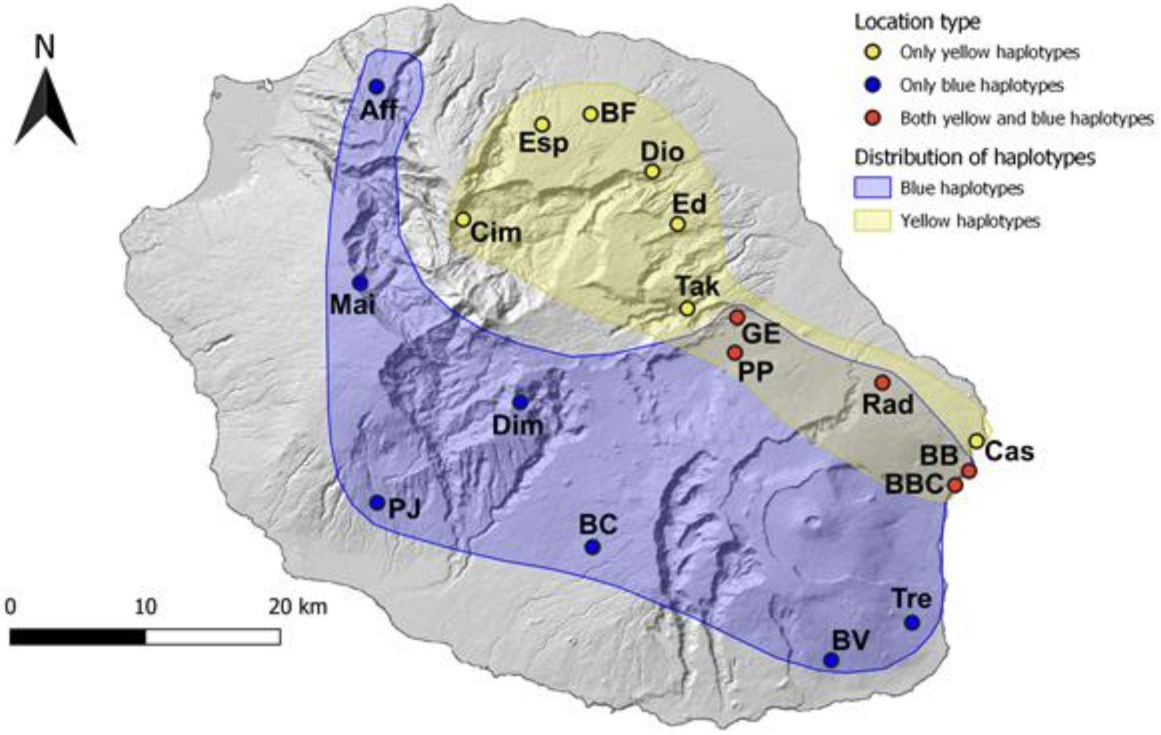
PHELSUMA BORBONICA – MTDNA STRUCTURE

mtDNA phylogeny
(Cytb & 16S)

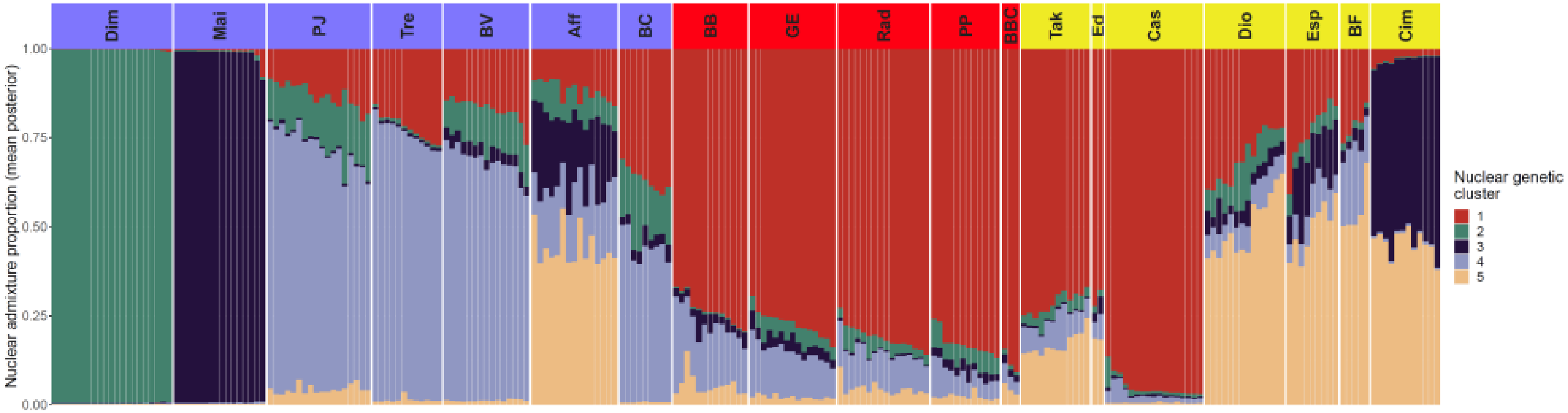
a)

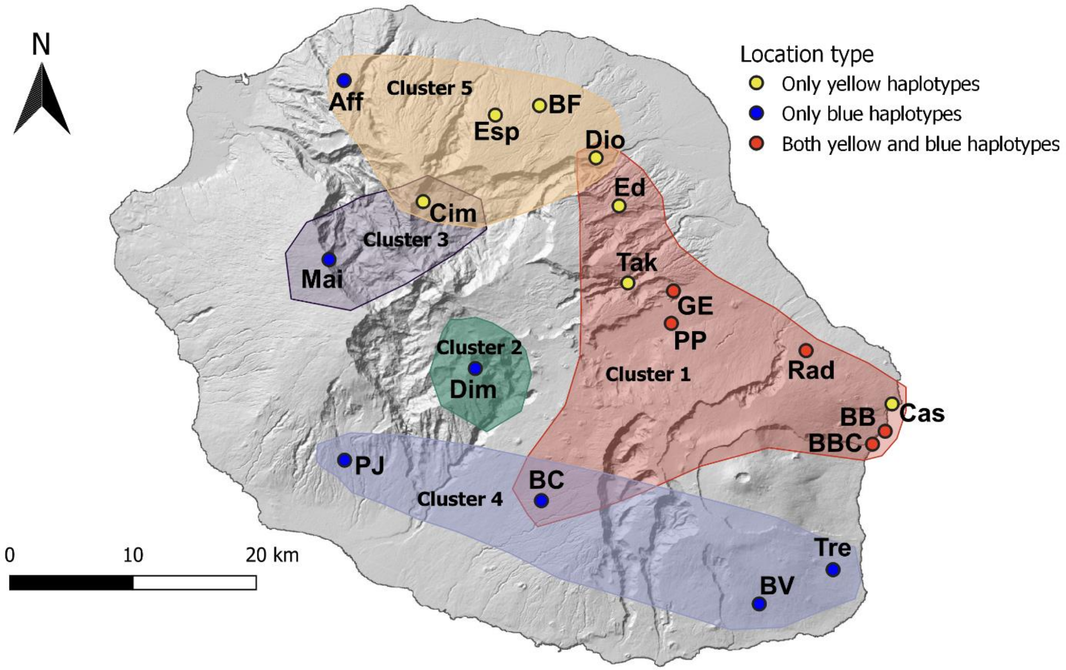


b)

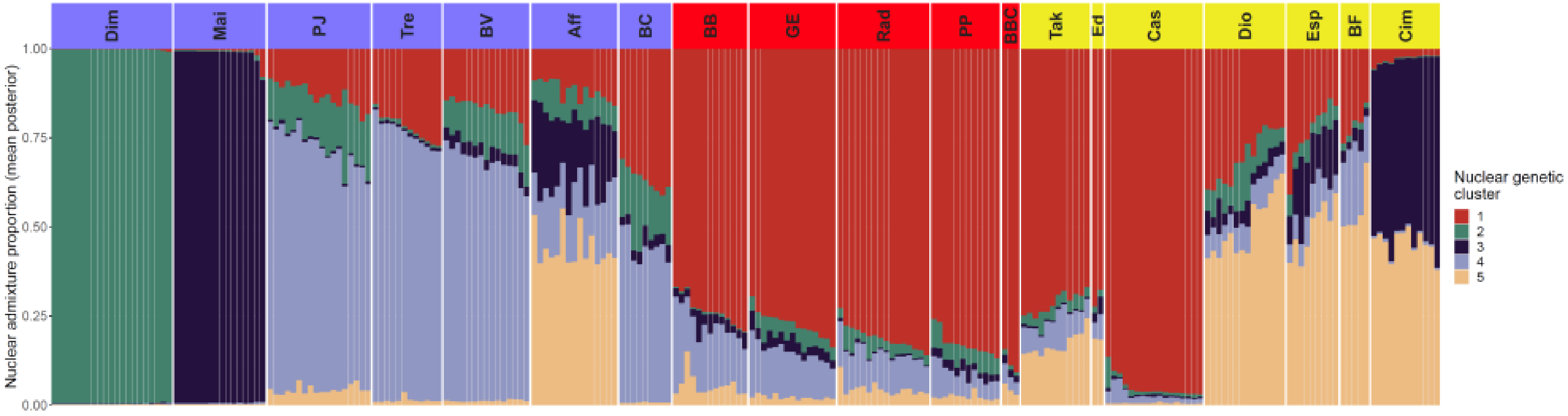


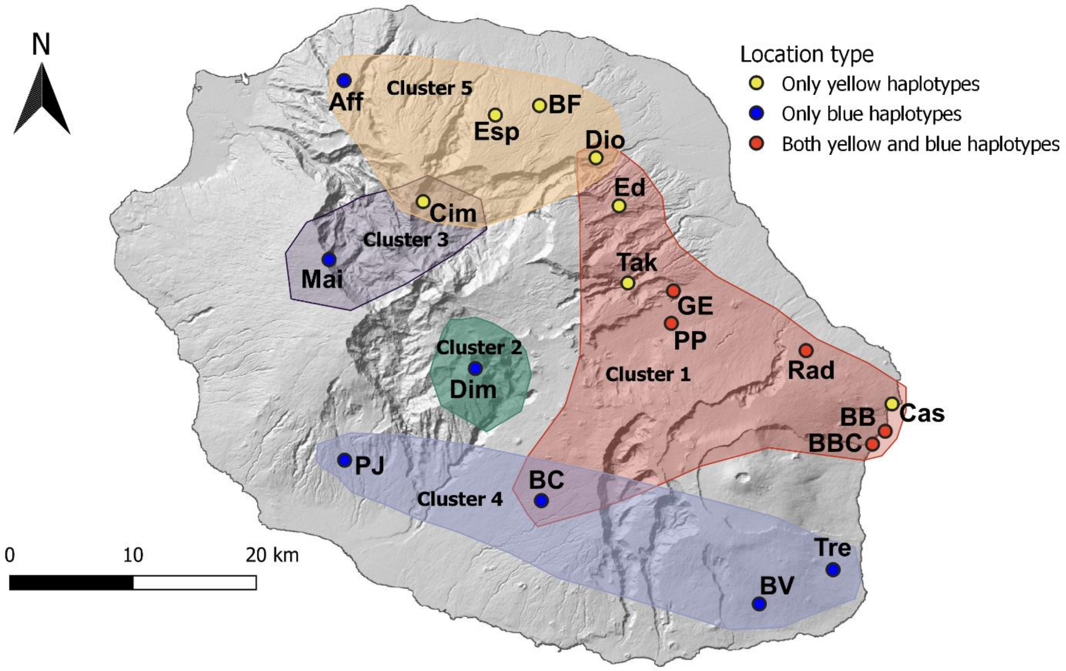
Phelsuma borbonica – Microsatellite structure





PHELSUMA BORBONICA – MICROSATELLITE STRUCTURE

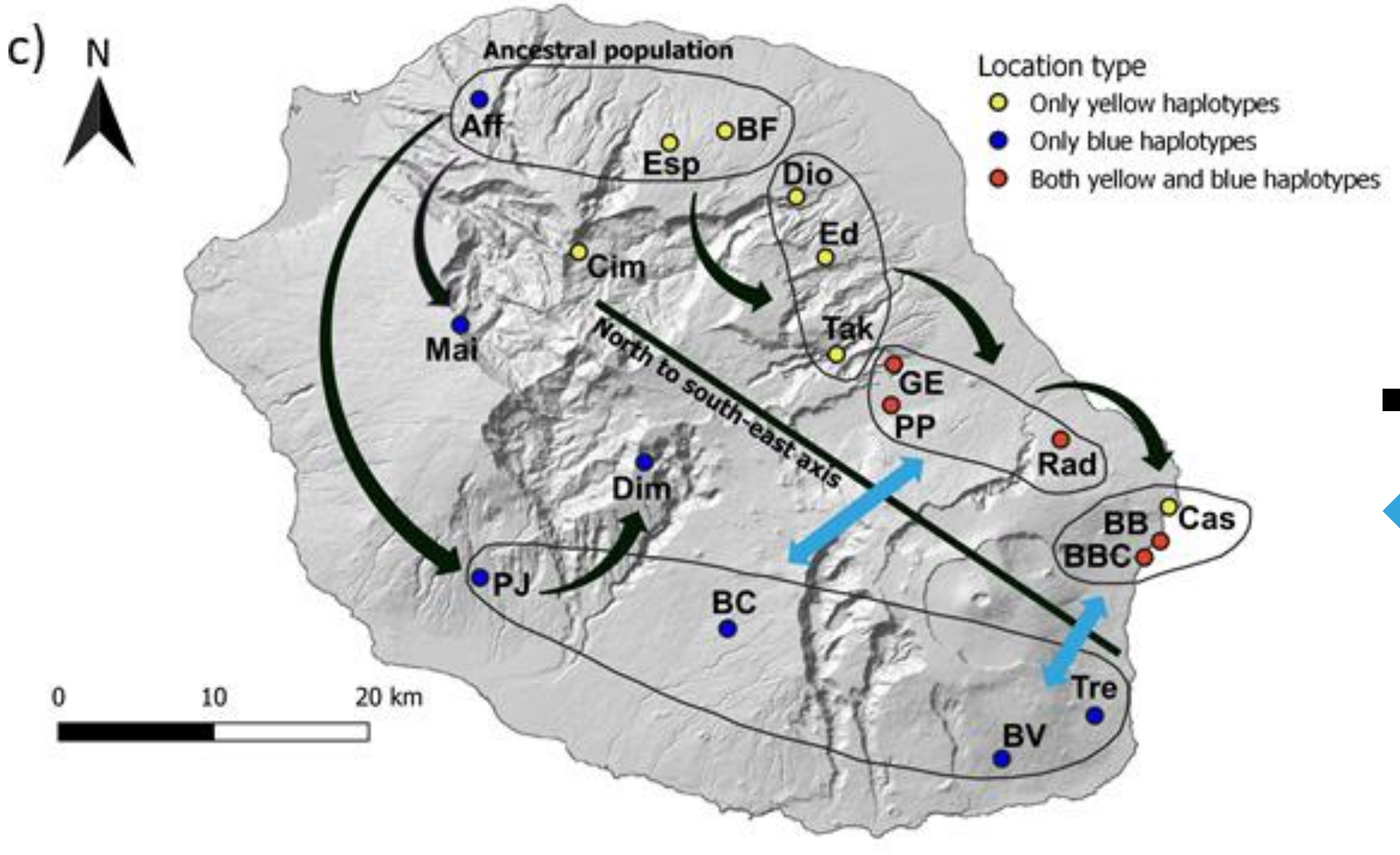




<u>High F_{st}'s for some populations:</u>

- Dimitile (Dim): F_{st}'s range from 0.38 to 0.63
- Maïdo (Mai): F_{st}'s range from 0.19 to 0.58

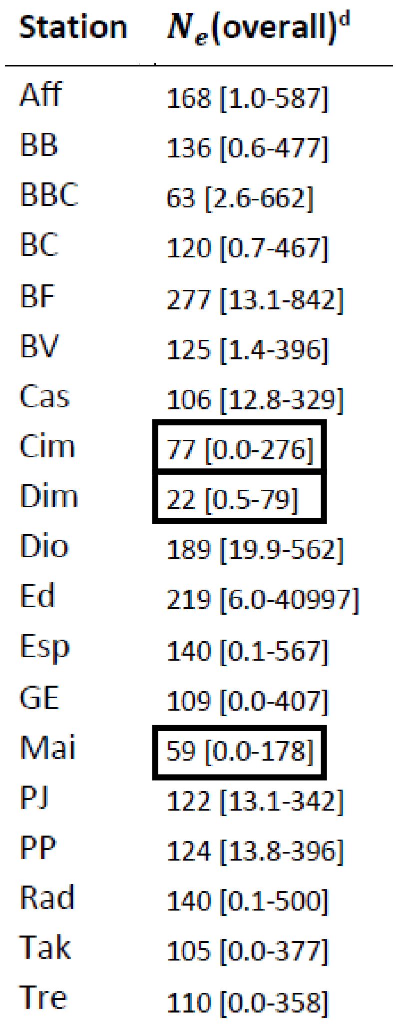
PHELSUMA BORBONICA – PHYLOGEOGRAPHY



➡ Range expansion

⬌ Gene flow

PHELSUMA BORBONICA – EFFECTIVE POPULATION SIZES



Station	N_e(overall)[d]
Aff	168 [1.0-587]
BB	136 [0.6-477]
BBC	63 [2.6-662]
BC	120 [0.7-467]
BF	277 [13.1-842]
BV	125 [1.4-396]
Cas	106 [12.8-329]
Cim	77 [0.0-276]
Dim	22 [0.5-79]
Dio	189 [19.9-562]
Ed	219 [6.0-40997]
Esp	140 [0.1-567]
GE	109 [0.0-407]
Mai	59 [0.0-178]
PJ	122 [13.1-342]
PP	124 [13.8-396]
Rad	140 [0.1-500]
Tak	105 [0.0-377]
Tre	110 [0.0-358]

Phelsuma borbonica – CONCLUSIONS

- Long-lasting isolation of populations (especially montane populations)
- Small effective sizes (especially for montane populations)

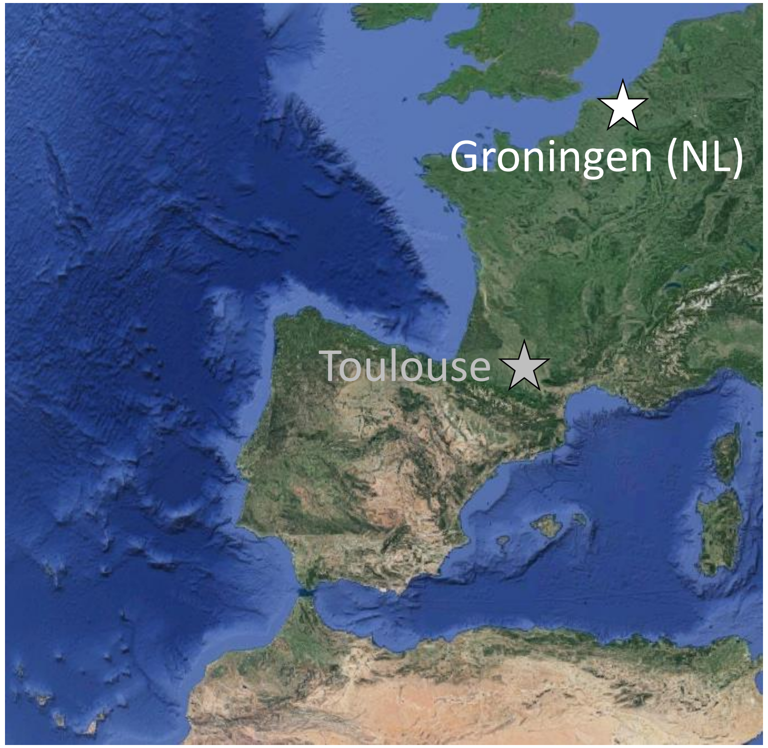
➡ **Take account of evolutionary history** in conservation practices (various ESUs)

➡ Especially for **montane populations**

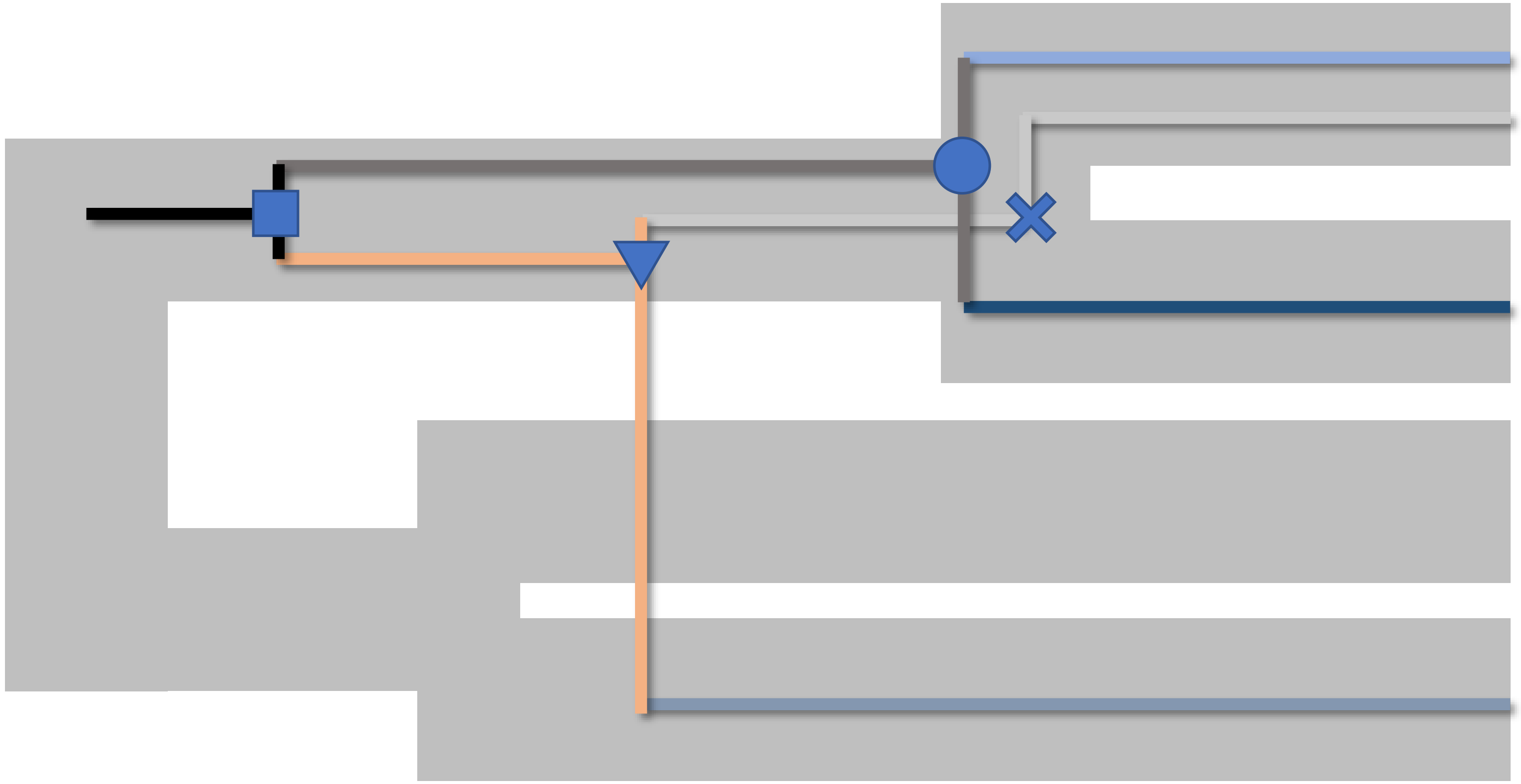
CO-PHYLOGENY
–
A LIKELIHOOD-BASED APPROACH

Josselin Cornuault, Rampal Etienne

Lab GELIFES (Univ. Groningen)



CO-PHYLOGENY – EVENTS



▬ Host

▬ Parasite

● Cospeciation

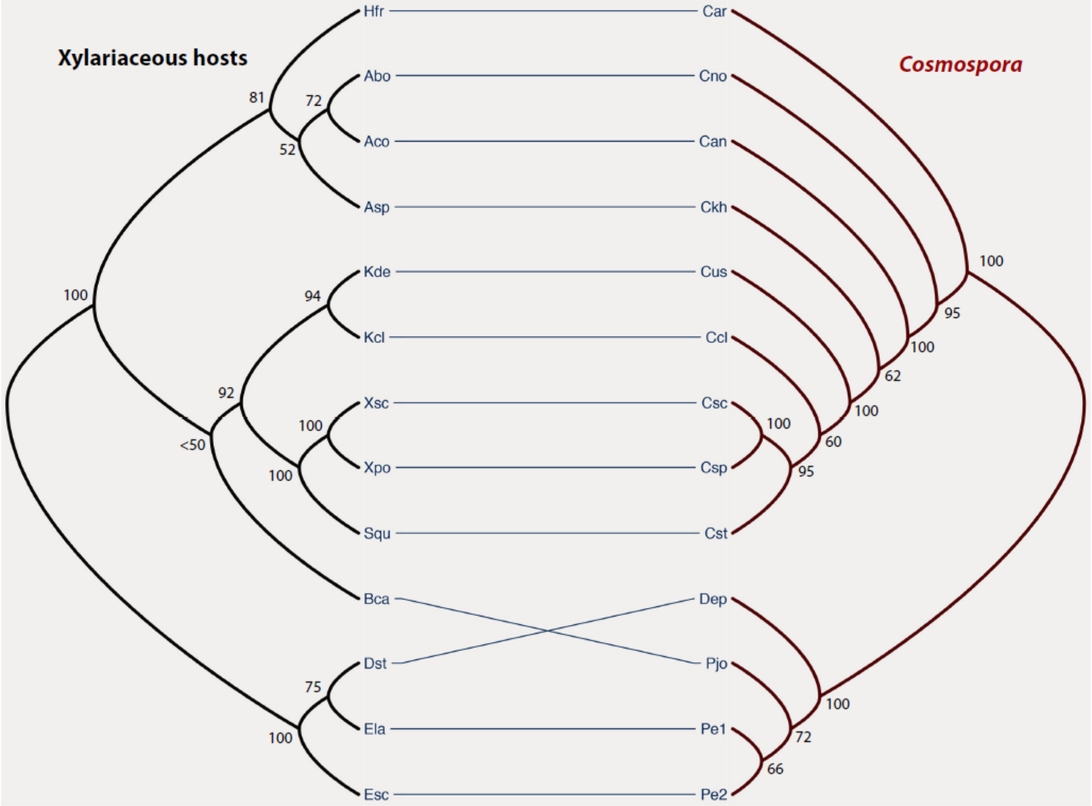
■ Duplication

✕ Loss

▼ Host switch

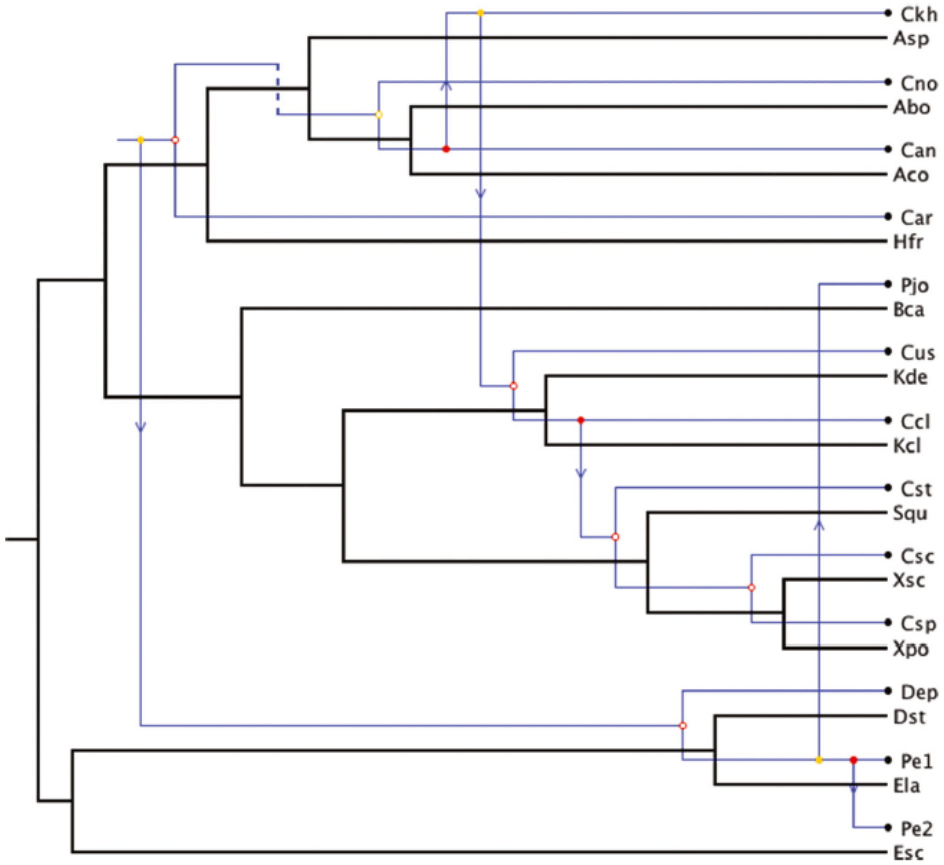
CO-PHYLOGENY – RECONCILIATION ANALYSIS

Tanglegram



Maximum parsimony

Reconciliation



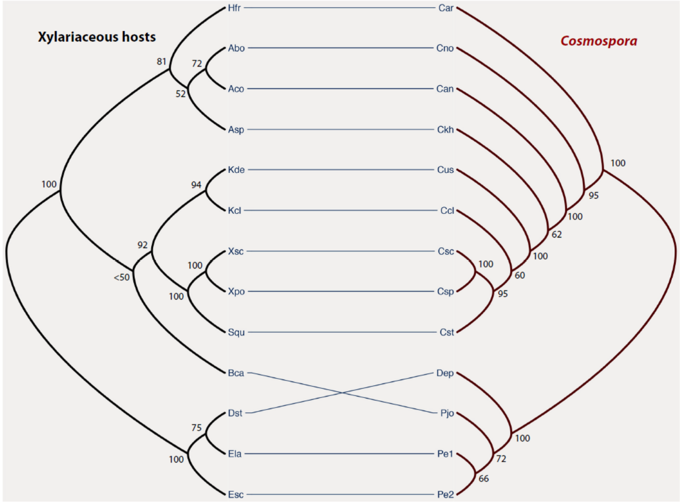
Most parsimonious reconciliation(s):

- No quantification of uncertainty
- No hypothesis testing

Herrera et al. (2016) Ecol. Evol. 6:1504-1514

CO-PHYLOGENY – LIKELIHOOD-BASED ANALYSIS

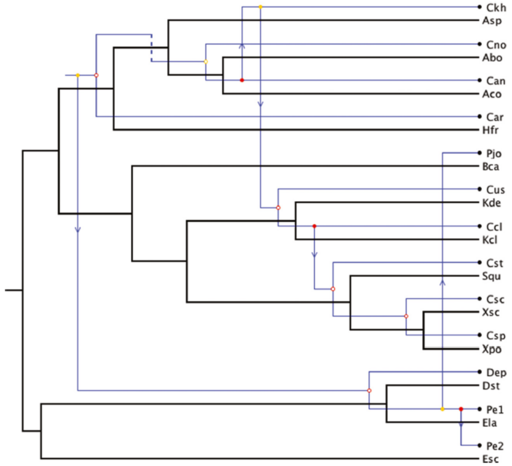
Tanglegram (T)



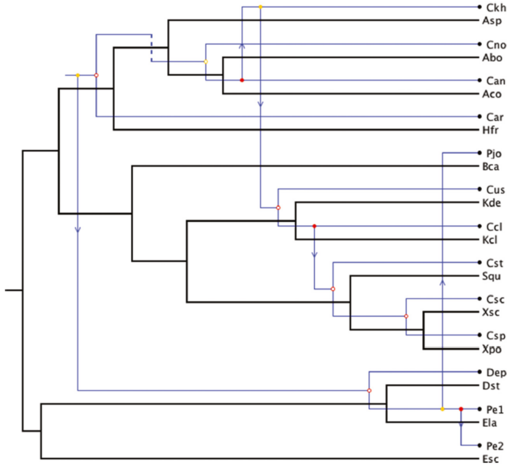
Reconciliations

$P(T \mid R_1, \theta)$

$P(T \mid R_2, \theta)$



R_1



R_2

Parameters:

$\theta = \{d, s, l\}$

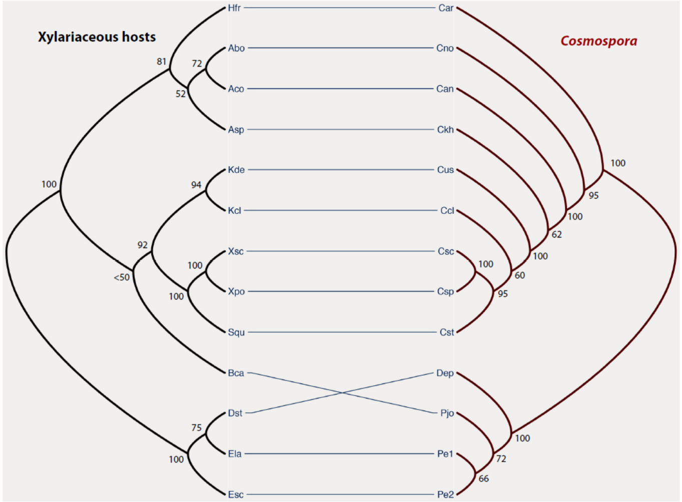
d = duplication rate

s = host-switch rate

l = loss rate

CO-PHYLOGENY – LIKELIHOOD-BASED ANALYSIS

Tanglegram (T)



$$P(T|\theta) = \sum_i P(T \mid R_i, \theta)$$

Reconciliations are marginalized out

Parameters:

$\theta = \{d, s, l\}$

d = duplication rate

s = host-switch rate

l = loss rate

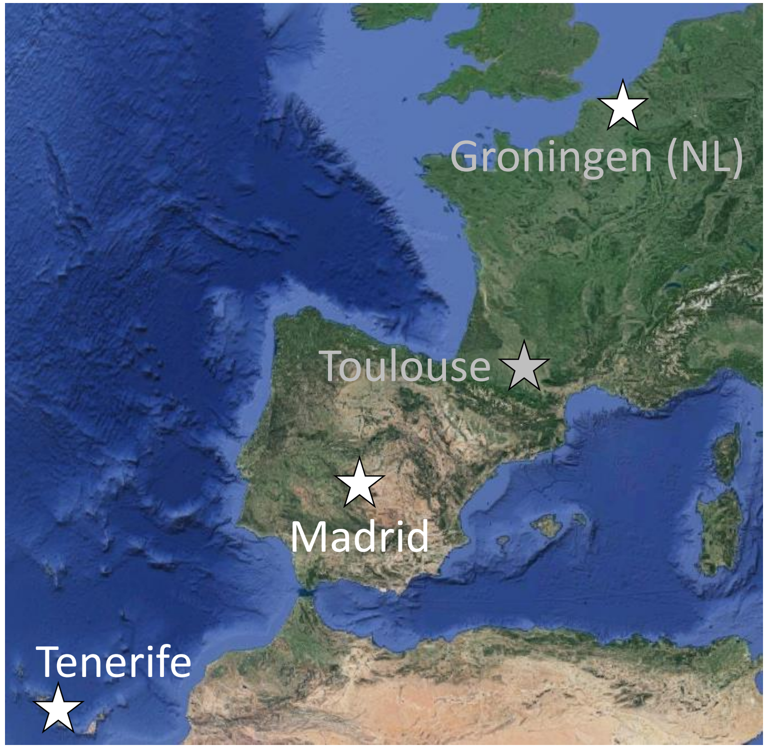
Marginal likelihood approach:

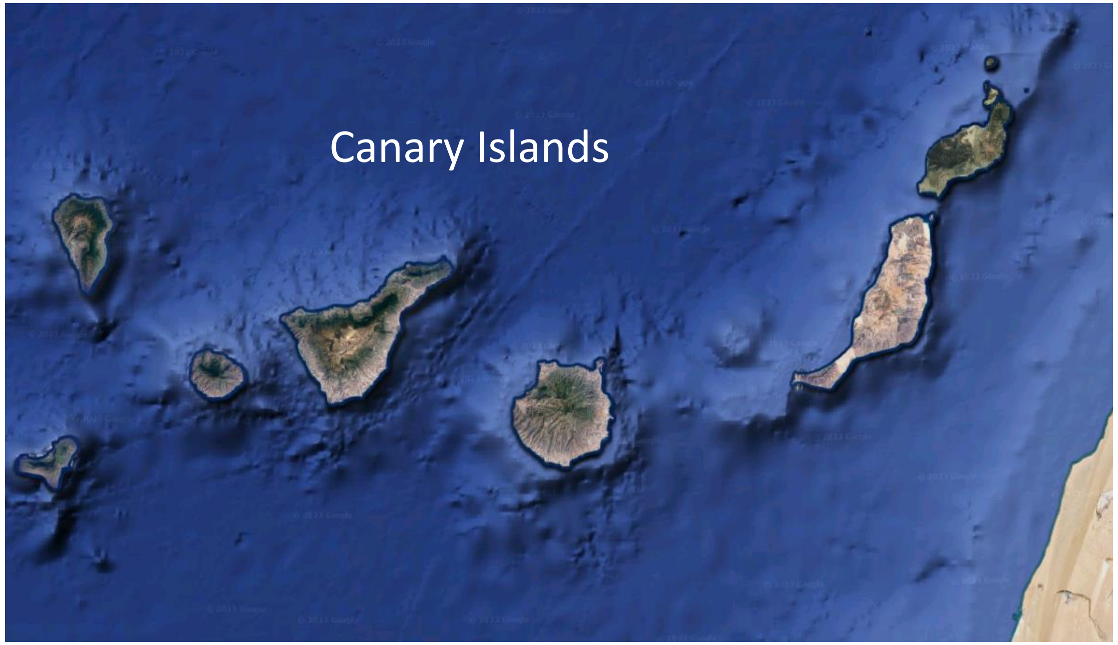
- Focus on estimating evolutionary rates (not reconciliations)
- Uncertainty quantified
- Hypothesis testing possible
- Multiple hosts per parasites and multiple parasites per hosts
- Current drawbacks:
  - Co-speciation not included
  - Hardly computable for more than 10 hosts

STRUCTURED COALESCENT

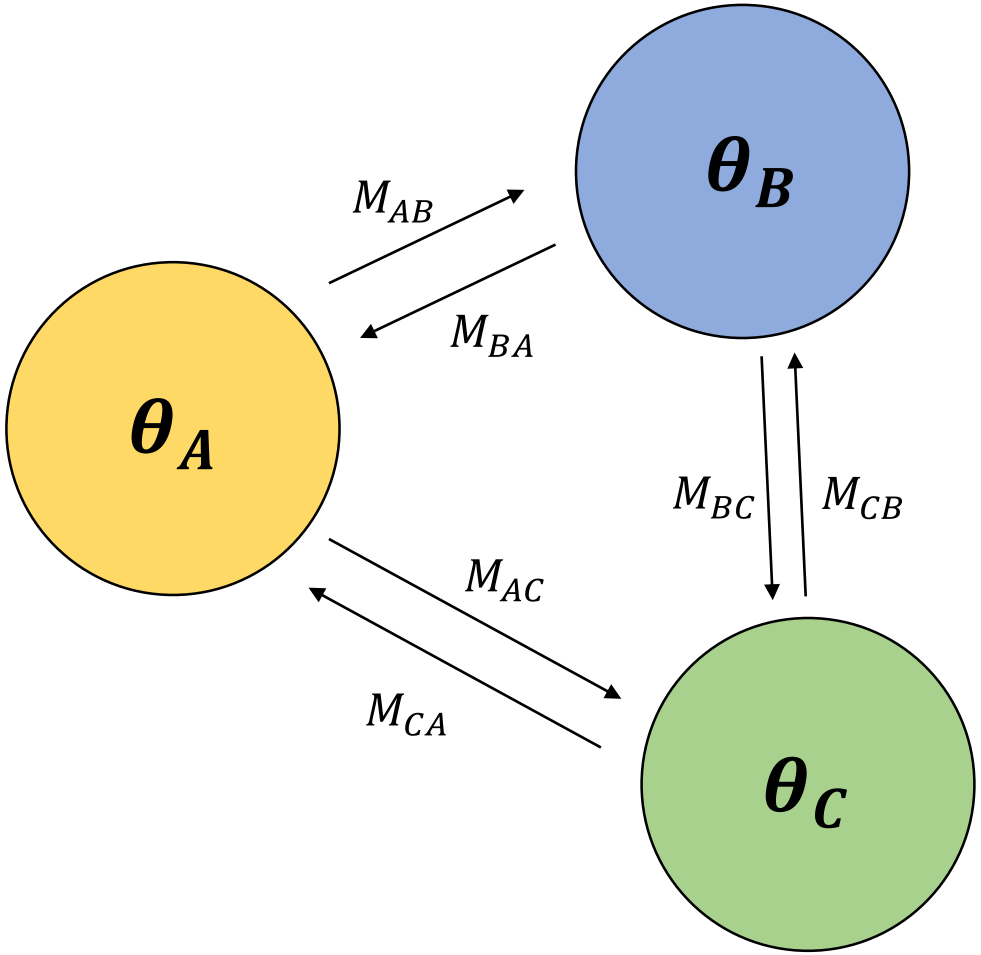
Josselin Cornuault, Antonia Salces Castellano, Brent Emerson, Isabel Sanmartin

Real jardin Botanico – CSIC – Madrid
Island Ecology and Evolution – IPNA/CSIC – Tenerife





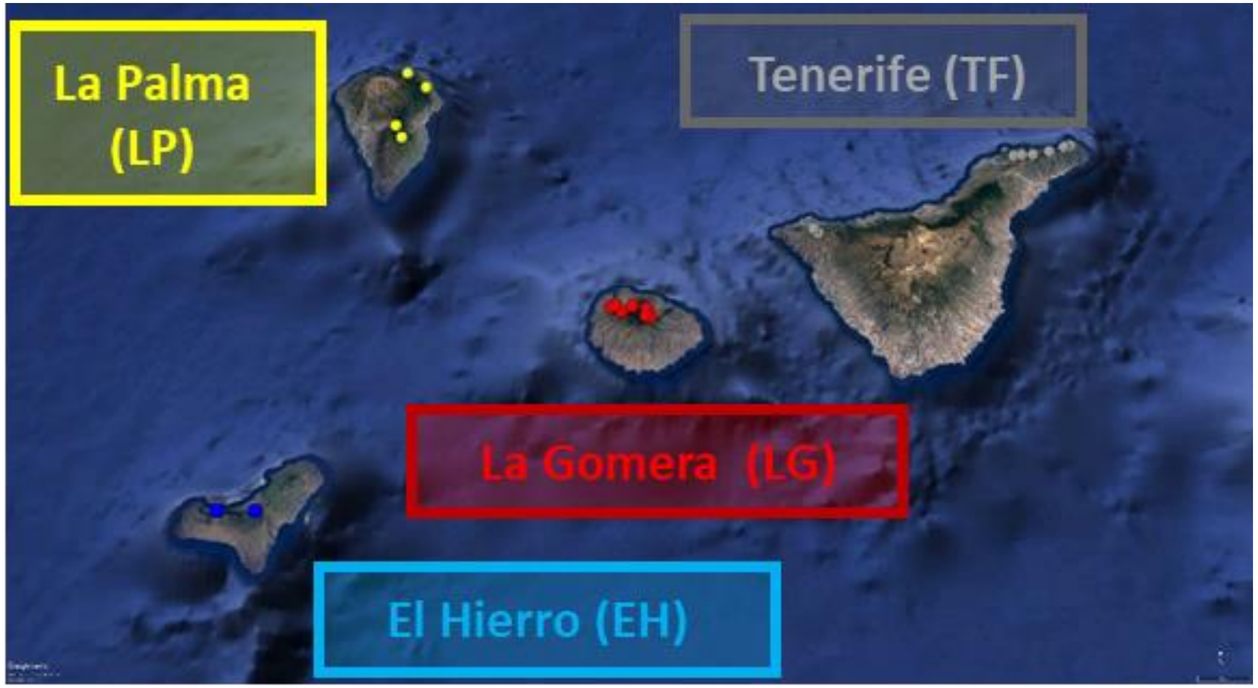
STRUCTURED COALESCENT – GENERALITIES



Coalescent model extended to multiple populations:

- Own effective population sizes (θ_A, θ_B …)
- Migration rates (M_{AB}, M_{BC} …)

STRUCTURED COALESCENT – CANARY ISLANDS

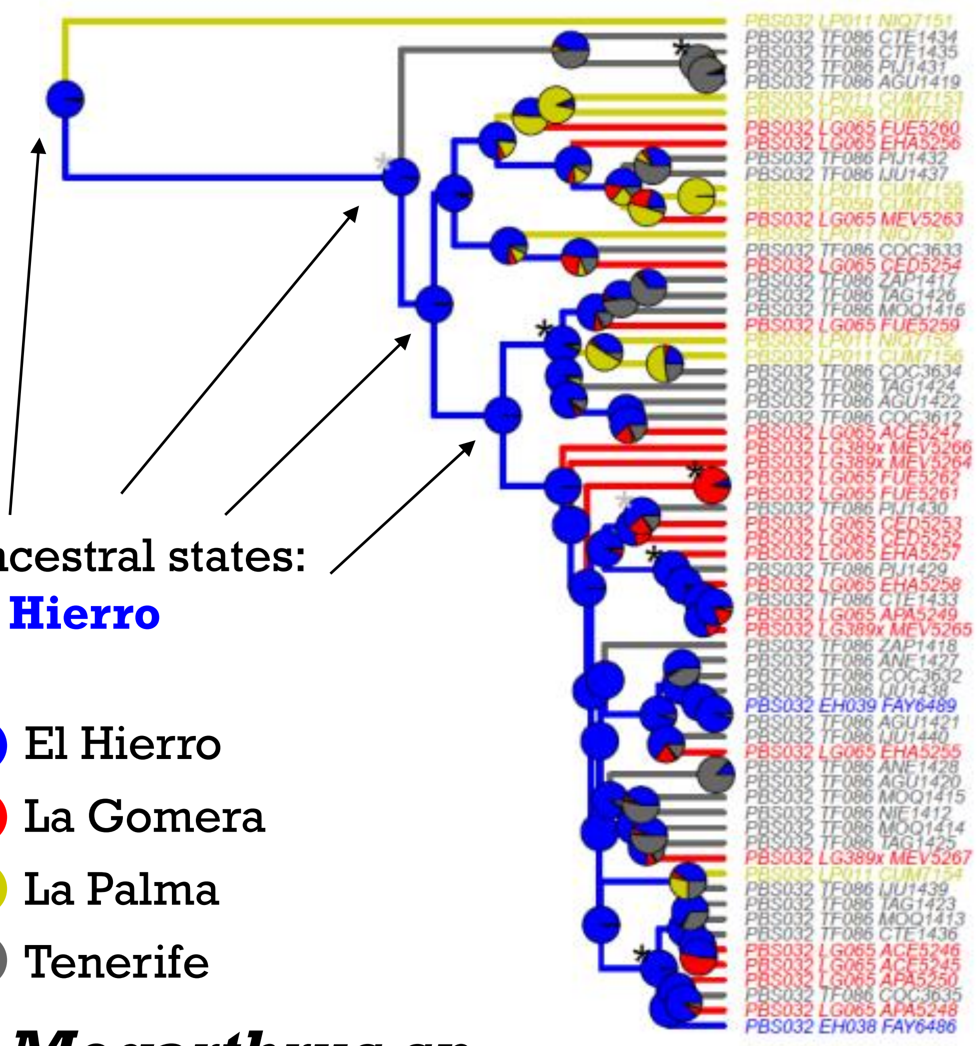


Genetic data for 200 Coleopteran species

➡ Estimate migration rates among islands for each species

➡ Determine main migration routes

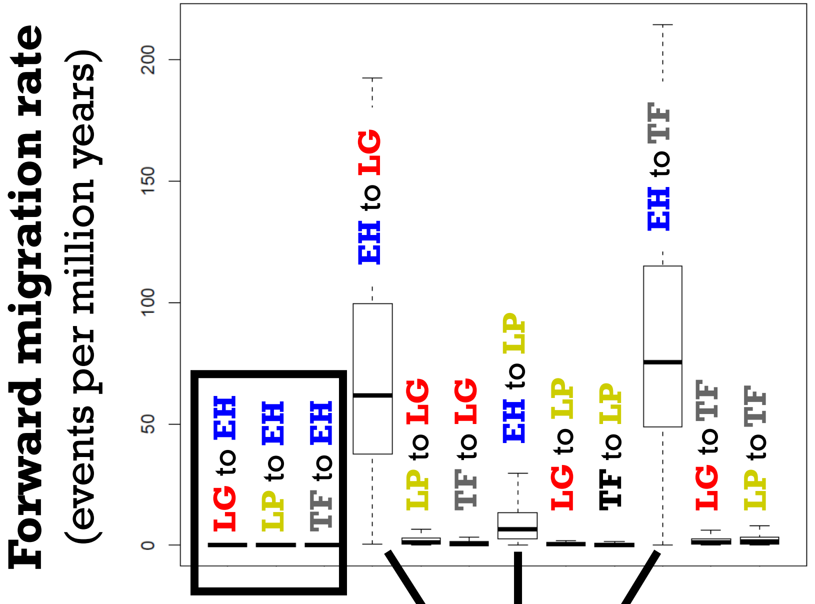
STRUCTURED COALESCENT – NONSENSICAL RESULTS



Ancestral states:
El Hierro

- ● El Hierro
- ● La Gomera
- ● La Palma
- ● Tenerife

Megarthrus sp

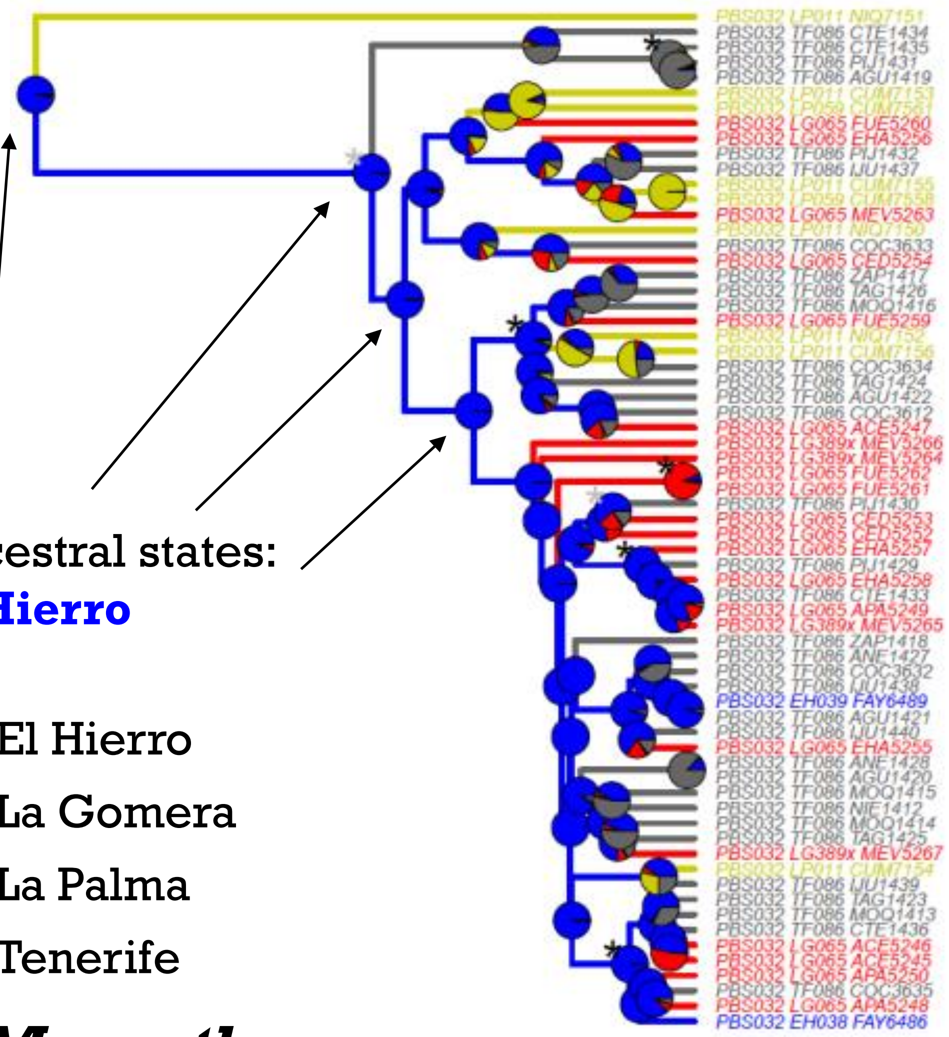


LOW migration
to **El Hierro**

HIGH migration
from **El Hierro**

El Hierro is a
SOURCE

STRUCTURED COALESCENT – NONSENSICAL RESULTS



Ancestral states:
El Hierro

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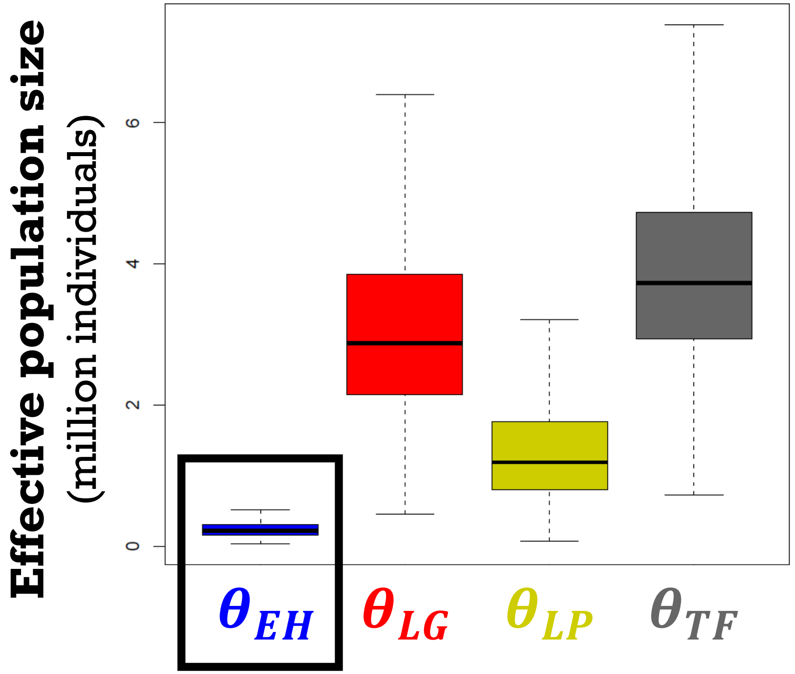
Megarthrus sp



LOWER θ_{EH} (**El Hierro** population size)

STRUCTURED COALESCENT – FUTURE WORK

Multimodal likelihood function (as many modes as there are populations)

➡ Possible to get the MCMC to get stuck in any of the following modes:

1) **<u>El Hierro (EH) mode</u>**: Ancestral locations = EH, low population size for EH, EH source of migration
2) **<u>La Gomera (LG) mode</u>**: Ancestral locations = LG, low population size for LG, LG source of migration
3) **<u>Tenerife mode</u>**: idem
4) **<u>La Palma mode</u>**: idem

What type of datasets is more prone to the problem?

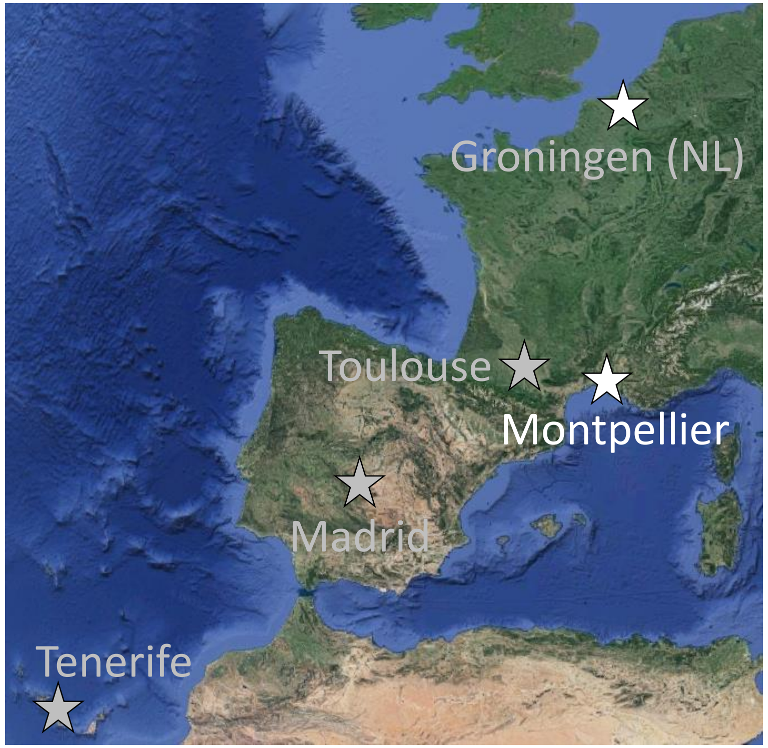
Can the problem be solved by using appropriate priors?

Is the model mathematically correctly defined?

PHYLODYNAMICS
–
PHYLOGENETIC EPIDEMIOLOGY

Josselin Cornuault, Fabio Pardi, Celine Scornavacca

ISEM Montpellier



PHYLODYNAMICS – CLASSICAL MODELS

1) **Birth-Death-Sampling (BDS) model**

2) **Kingman coalescent model**
    - a) **Skyline approach**
    - b) **Mechanistic approach**

PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

Parameters:

- $\lambda(t)$ (transmission rate)
- $\mu(t)$ (loss rate)
- $\psi(t)$ (sampling rate)

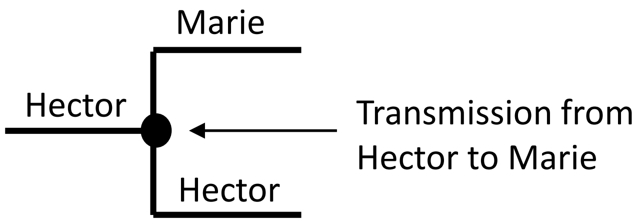
PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

Parameters:

- $\lambda(t)$ (transmission rate)
- $\mu(t)$ (loss rate)
- $\psi(t)$ (sampling rate)

Transmissions occur at rate $\lambda(t)$



Transmission from Hector to Marie

PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

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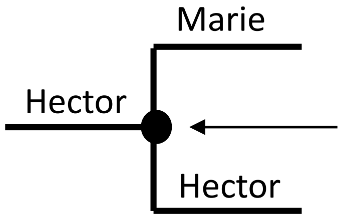
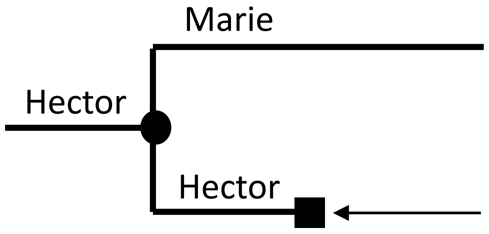


Transmission from Hector to Marie

Infections are lost at rate $\mu(t)$



End of Hector’s infection (ie. Hector recovered or died)

PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

Parameters:

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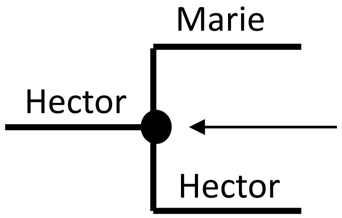
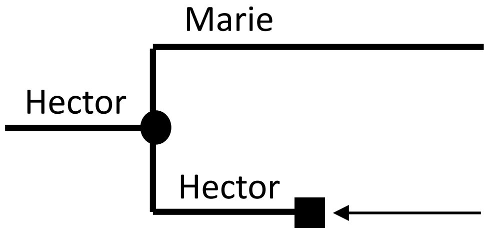


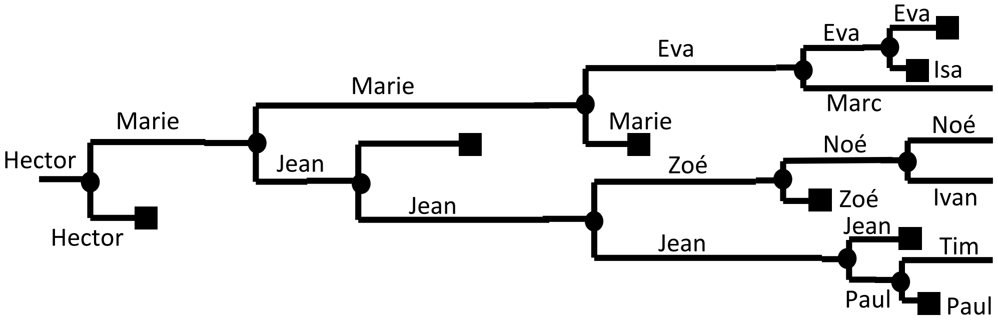
Transmission from Hector to Marie

Infections are lost at rate $\mu(t)$



End of Hector's infection (ie. Hector recovered or died)

Complete transmission tree



PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

Parameters:

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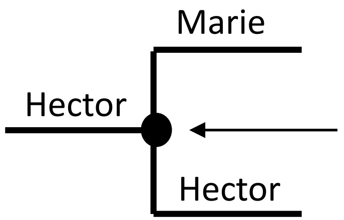
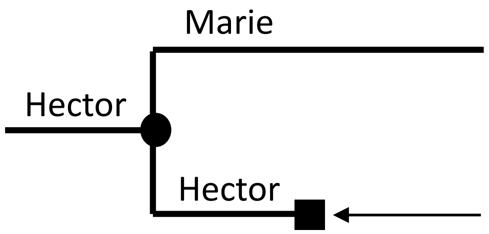
Transmissions occur at rate $\lambda(t)$



Transmission from Hector to Marie

Infections are lost at rate $\mu(t)$



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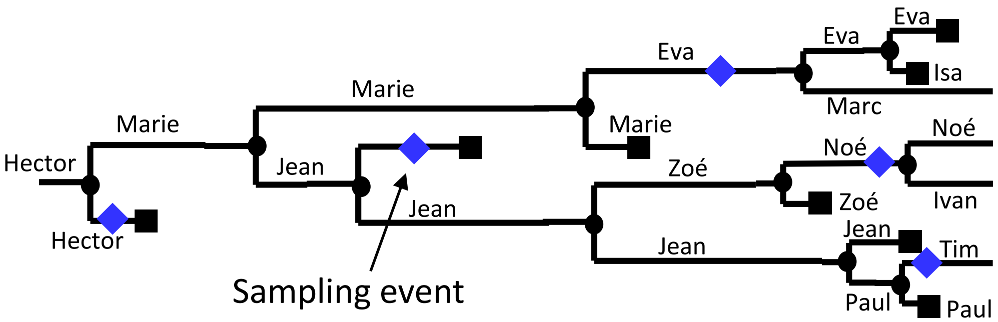


Sampling event

Sampling events occur at rate $\psi(t)$

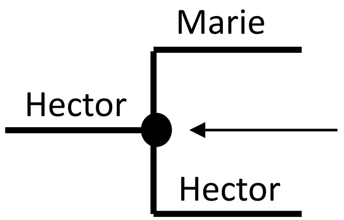
PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

Parameters:

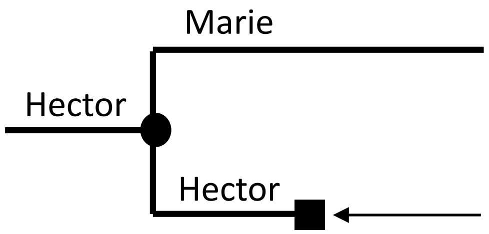
- $\lambda(t)$ (transmission rate)
- $\mu(t)$ (loss rate)
- $\psi(t)$ (sampling rate)

Transmissions occur at rate $\lambda(t)$



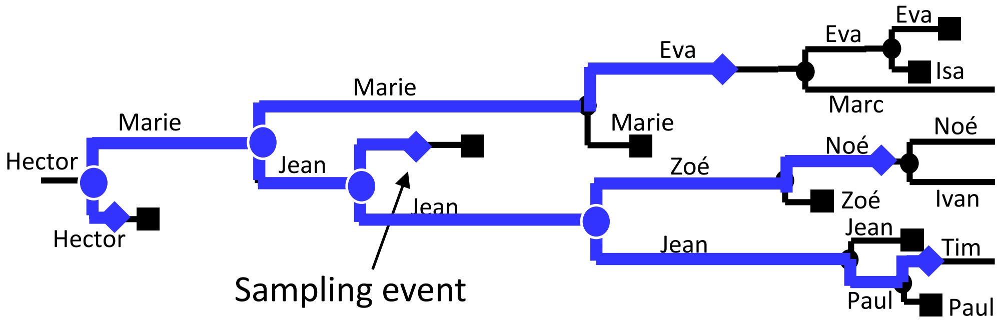
Transmission from Hector to Marie

Infections are lost at rate $\mu(t)$



End of Hector's infection (ie. Hector recovered or died)

Complete transmission tree



Sampling event

Sampling events occur at rate $\psi(t)$

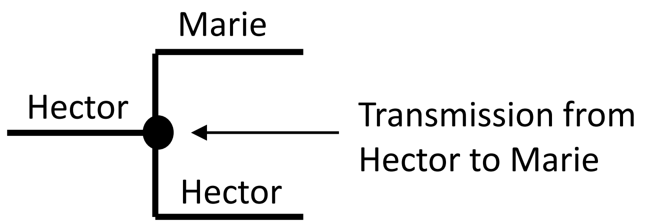
Phylodynamics – Classical Models

1) Birth-Death-Sampling (BDS) model

Parameters:

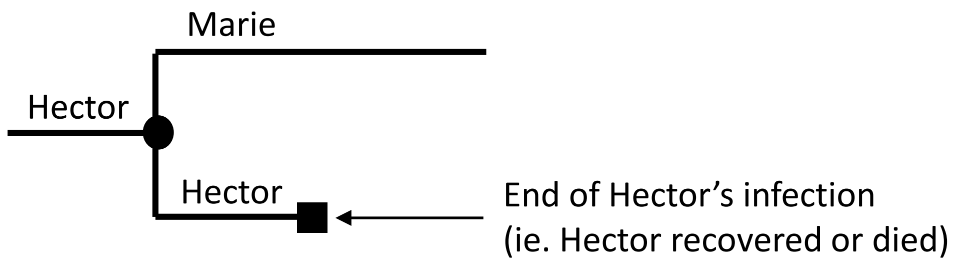
- $\lambda(t)$ (transmission rate)
- $\mu(t)$ (loss rate)
- $\psi(t)$ (sampling rate)

Transmissions occur at rate $\lambda(t)$



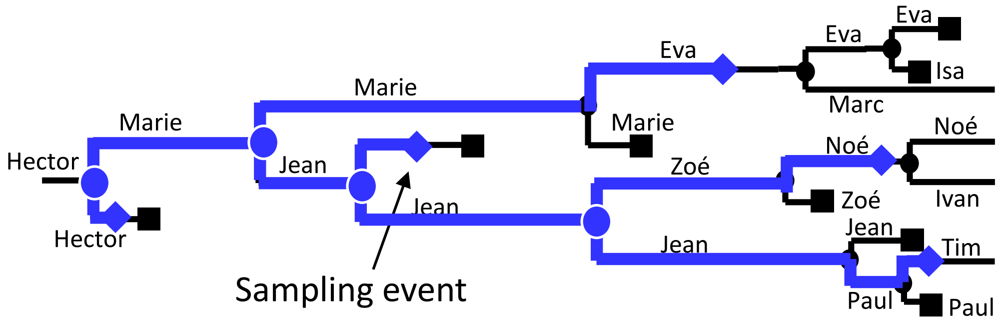
Transmission from Hector to Marie

Infections are lost at rate $\mu(t)$



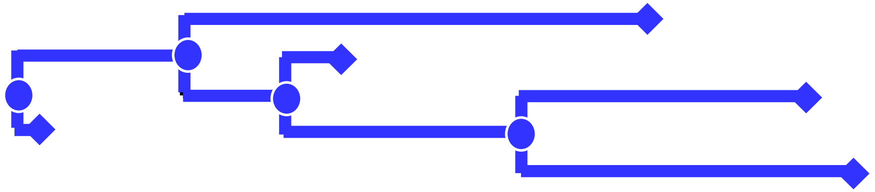
End of Hector's infection (ie. Hector recovered or died)

Complete transmission tree



Sampling event

Sampled transmission tree



Sampling events occur at rate $\psi(t)$

PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

Advantages

Drawbacks

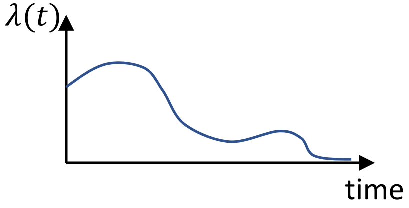
PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

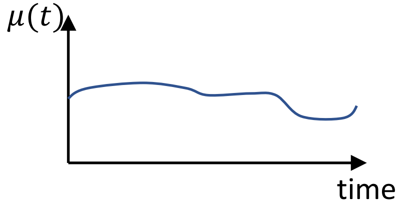
Advantages

- Interesting epidemiological parameters can be estimated:

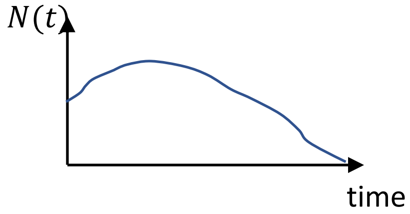
Transmission rate



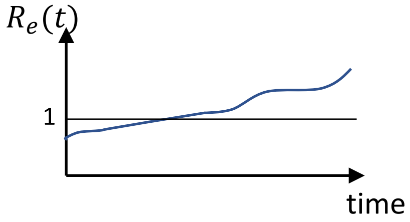
Loss rate



Prevalence



Reproduction number



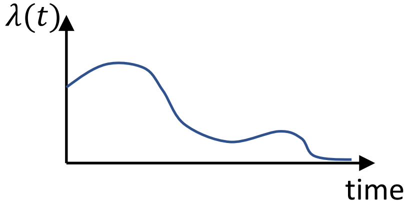
Drawbacks

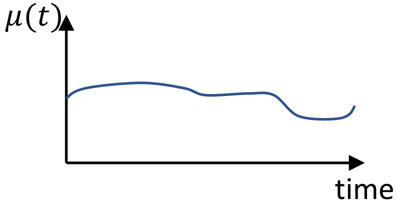
PHYLODYNAMICS – CLASSICAL MODELS

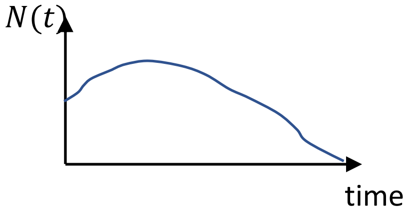
1) Birth-Death-Sampling (BDS) model

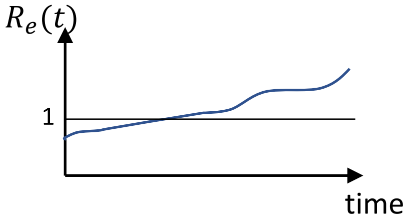
Advantages

- Interesting epidemiological parameters can be estimated:


Transmission rate


Loss rate


Prevalence


Reproduction number

Drawbacks

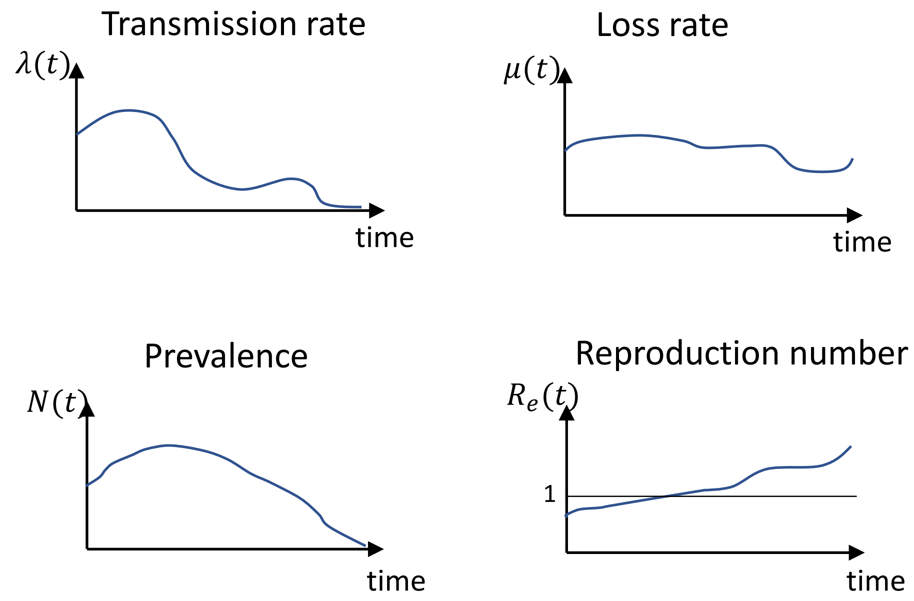
- Sampling procedure needs be assumed ($\psi(t)$)

PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

Advantages

- Interesting epidemiological parameters can be estimated:


Transmission rate

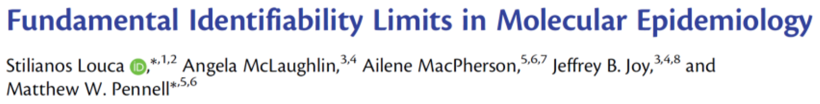
Loss rate

Prevalence

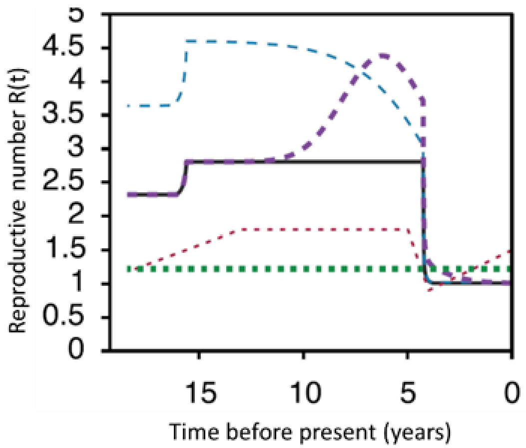
Reproduction number

Drawbacks

- Sampling procedure needs be assumed ($\psi(t)$)
- Parameters are not identifiable


Fundamental Identifiability Limits in Molecular Epidemiology

Stilianos Louca ,*,1,2 Angela McLaughlin,3,4 Ailene MacPherson,5,6,7 Jeffrey B. Joy,3,4,8 and Matthew W. Pennell*,5,6



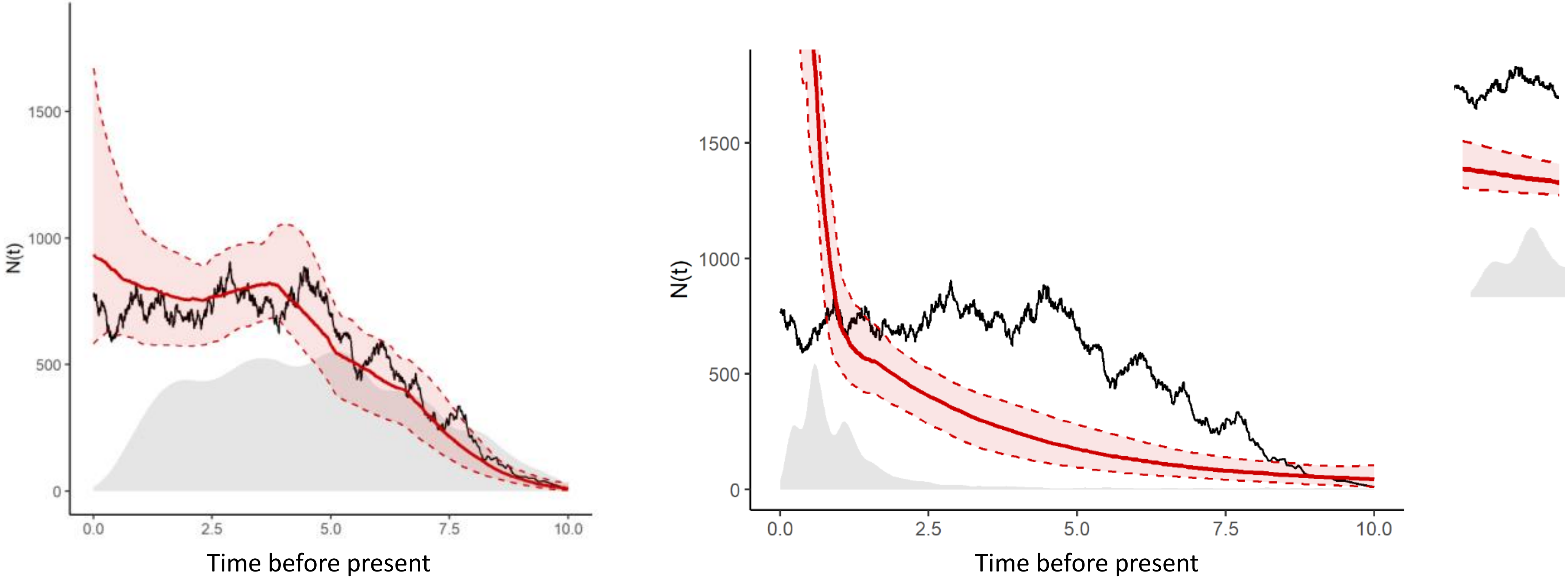
PHYLODYNAMICS – CLASSICAL MODELS

1) Birth-Death-Sampling (BDS) model

BDS inference with **<u>correct</u>** $\psi(t)$

Simulation: $\psi(t) = \psi$
Inference: $\psi(t) = \psi$

1) Birth-Death-Sampling (BDS) model



BDS inference with **correct** $\psi(t)$

Simulation: $\psi(t) = \psi$
Inference: $\psi(t) = \psi$

BDS inference with **incorrect** $\psi(t)$

Simulation: $\boldsymbol{\psi(t) \neq \psi}$
Inference: $\psi(t) = \psi$

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

Parameters:

- $\theta(t)$ (instantaneous effective population size)

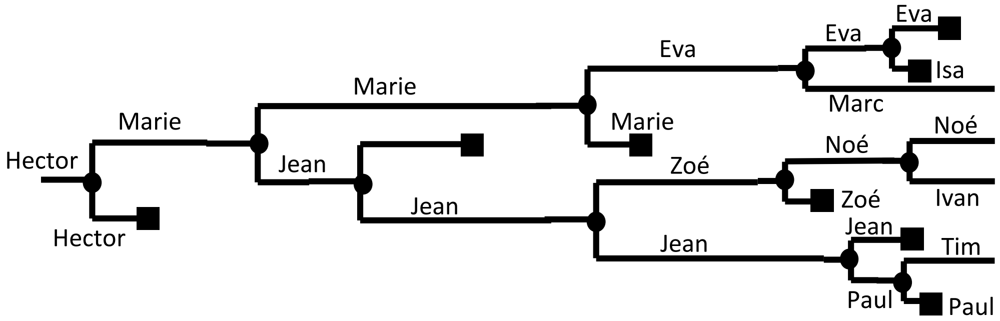
PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

Parameters:

- $\theta(t)$ (instantaneous effective population size)

Complete transmission tree



- Few assumptions about the model that generated the complete transmisison tree

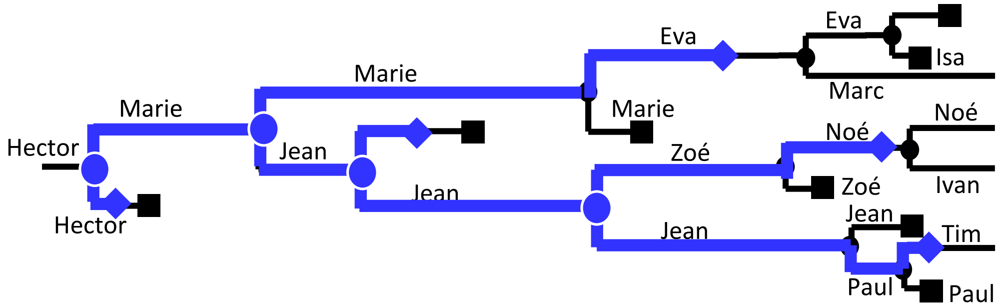
PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

Parameters:

- $\theta(t)$ (instantaneous effective population size)

Complete transmission tree



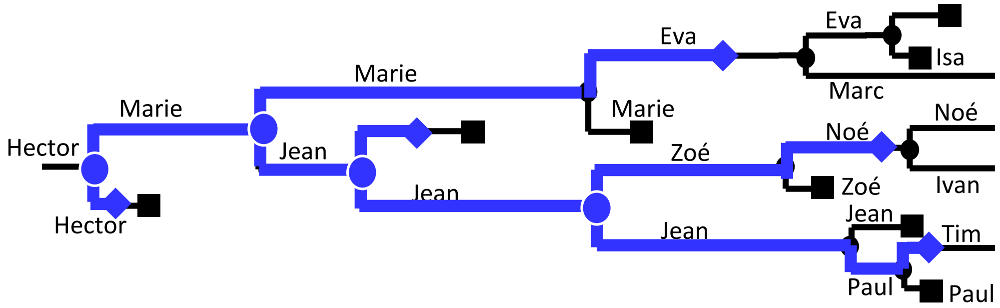
- Few assumptions about the model that generated the complete transmisison tree
- No assumptions about the sampling procedure

2) Kingman Coalescent (KC) model

Parameters:

- $\theta(t)$ (instantaneous effective population size)

Complete transmission tree



- Few assumptions about the model that generated the complete transmisison tree
- No assumptions about the sampling procedure

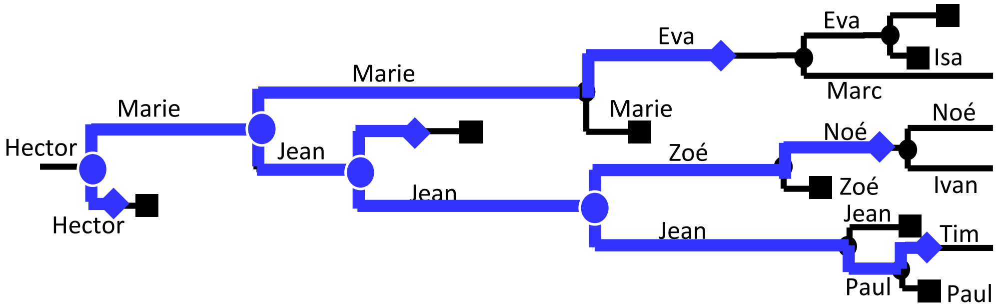
Coalescence of two lineages occurs at rate $\frac{1}{\theta(t)}$

2) Kingman Coalescent (KC) model

Parameters:

- $\theta(t)$ (instantaneous effective population size)

Complete transmission tree



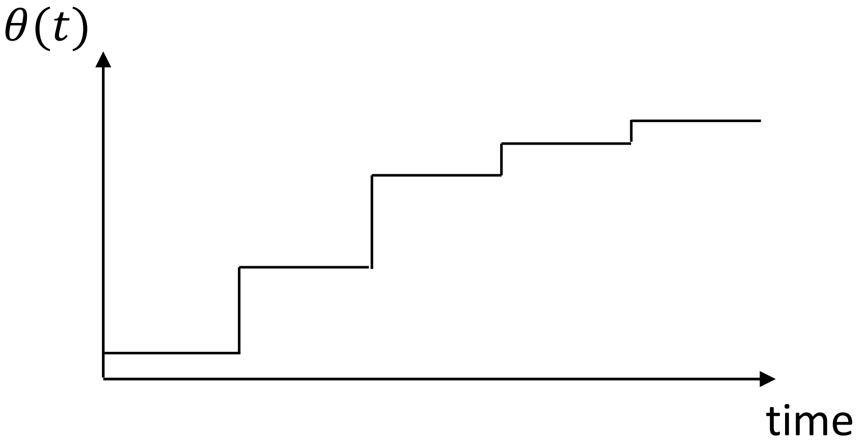
- Few assumptions about the model that generated the complete transmisison tree
- No assumptions about the sampling procedure

Coalescence of two lineages occurs at rate $\frac{1}{\theta(t)}$

Two approaches for parametrizing $\theta(t)$: $\left\{ \begin{array}{l} \textbf{Skyline approach} \\ \textbf{Mechanistic approach} \end{array} \right.$

2) Kingman Coalescent (KC) model

a) Skyline approach

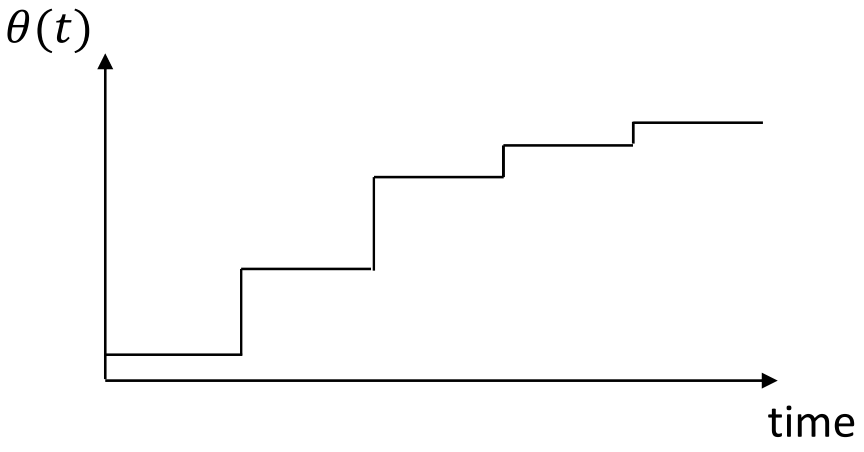


$\theta(t)$ is represented phenomenologically by a piecewise function

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

a) Skyline approach



$\theta(t)$ is represented phenomenologically by a piecewise function

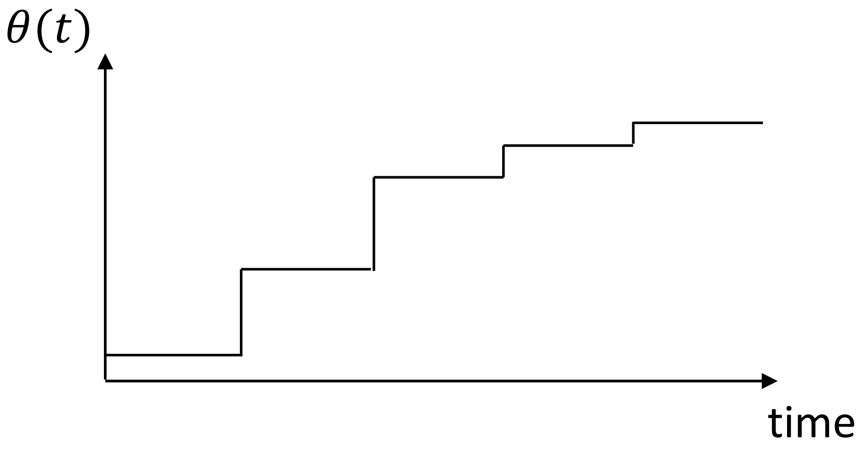
Advantages

Drawbacks

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

a) Skyline approach



$\theta(t)$ is represented phenomenologically by a piecewise function

Advantages

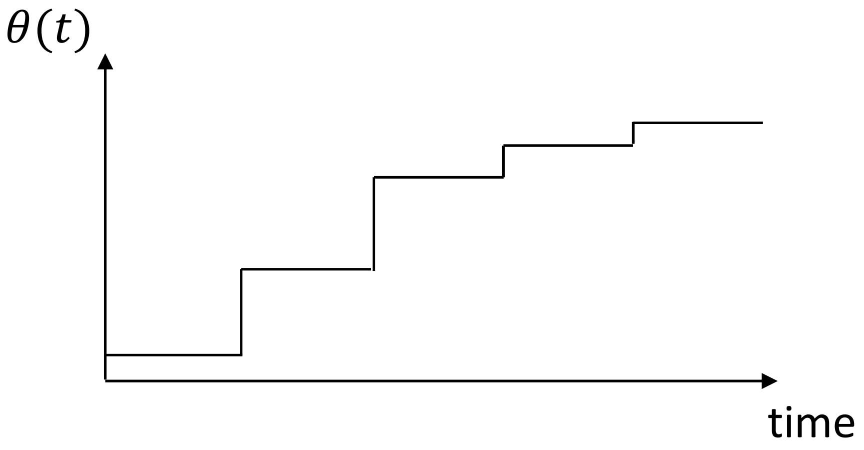
- No assumption on the sampling procedure (the KC conditions on sampling times)

Drawbacks

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

a) Skyline approach



$\theta(t)$ is represented phenomenologically by a piecewise function

Advantages

- No assumption on the sampling procedure (the KC conditions on sampling times)

Drawbacks

- Interesting epidemiological parameters **cannot** be estimated:

➡ $\lambda(t)$, $\mu(t)$, $N(t)$, $R_e(t)$ are not parameters

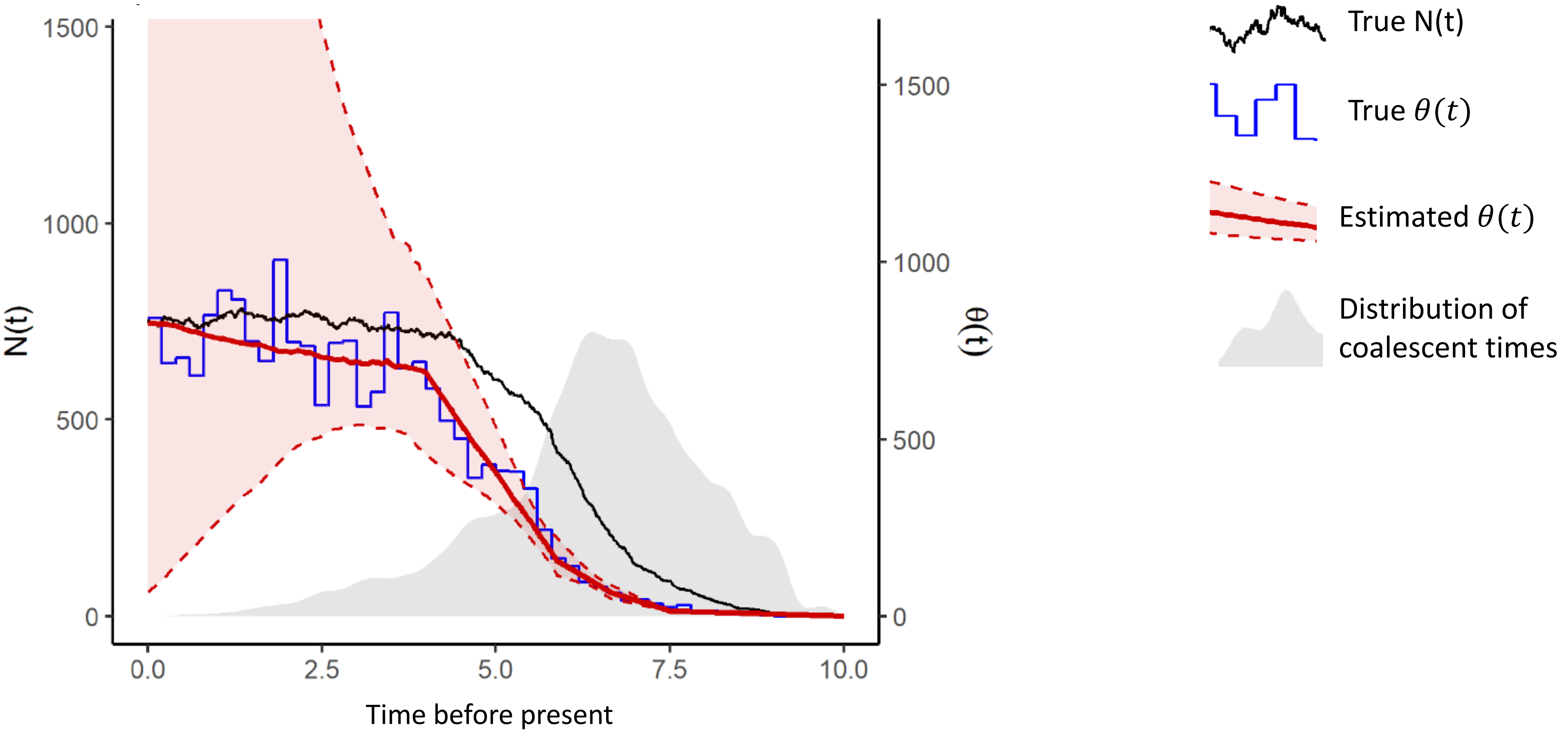
➡ $\theta(t)$ is not necessarily proportional to the prevalence $N(t)$

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

a) Skyline approach

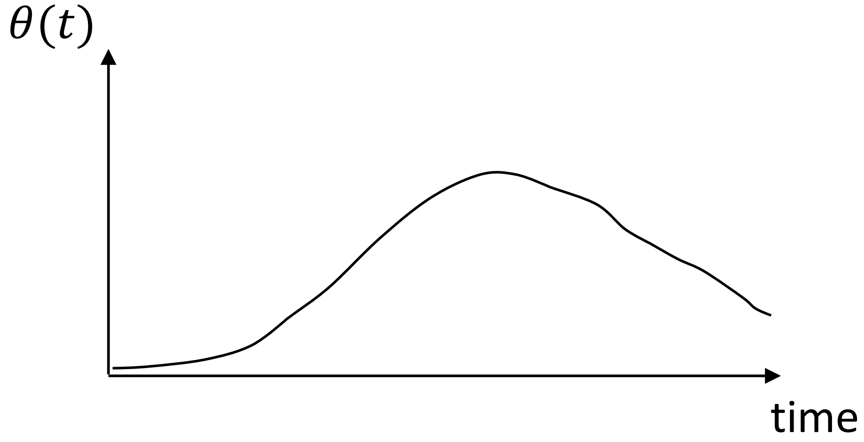
Skyline KC inference when $\theta(t)$ is **<u>not propotional</u>** to $N(t)$



PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

b) Mechanistic approach



$\theta(t) = k\, N(t)$ with $N(t)$ the population size as predicted by an **epidemiological model**

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

b) Mechanistic approach

Example: SIR epidemiological model

S(t) = # susceptible individuals

I(t) = # infected individuals

R(t) = # removed individuals (ie. immunised or dead)

K = S(t) + I(t) + R(t) = total population size (constant)

2) Kingman Coalescent (KC) model

b) Mechanistic approach

Example: SIR epidemiological model

S(t) = # susceptible individuals
I(t) = # infected individuals
R(t) = # removed individuals (ie. immunised or dead)
K = S(t) + I(t) + R(t) = total population size (constant)

$$I'(t) = \frac{\beta S(t)}{K}\, I(t) - \mu\, I(t)$$

$$S'(t) = -\frac{\beta S(t)}{K}\, I(t)$$

$$R'(t) = -\mu\, I(t)$$

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

b) Mechanistic approach

<u>Example:</u> SIR epidemiological model

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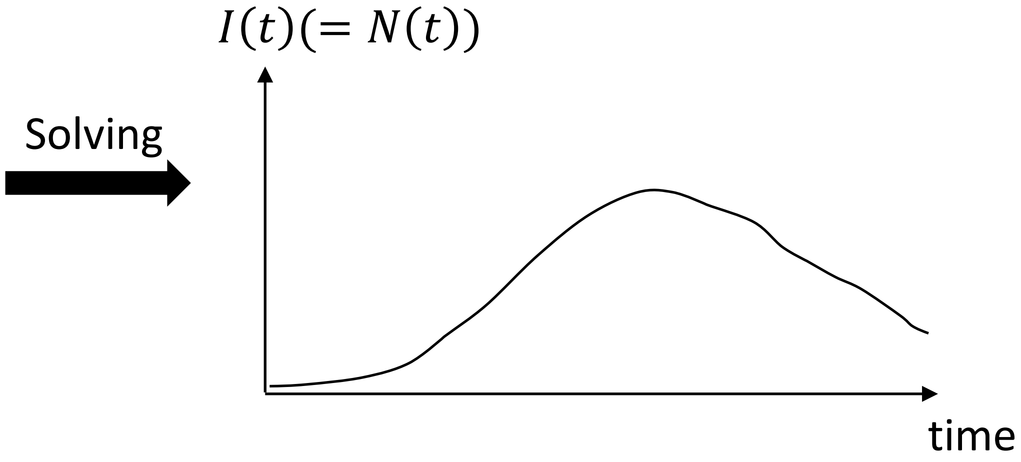
K = S(t) + I(t) + R(t) = total population size (constant)

$$\left.\begin{aligned}
I'(t) &= \frac{\beta S(t)}{K}\, I(t) - \mu\, I(t) \\
S'(t) &= -\frac{\beta S(t)}{K}\, I(t) \\
R'(t) &= -\mu\, I(t)
\end{aligned}\right\}$$



PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

b) Mechanistic approach

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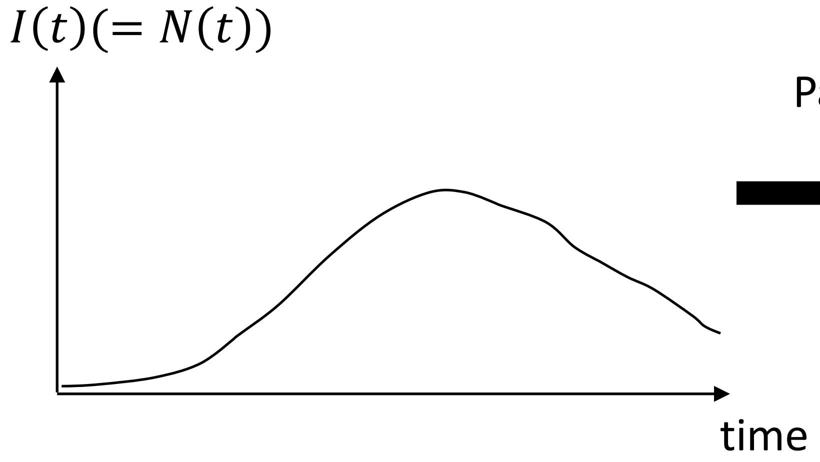
$$\left.\begin{aligned} I'(t) &= \frac{\beta S(t)}{K}\, I(t) - \mu\, I(t) \\ S'(t) &= -\frac{\beta S(t)}{K}\, I(t) \\ R'(t) &= -\mu\, I(t) \end{aligned}\right\} \xrightarrow{\text{Solving}}$$



$$\xrightarrow{\text{Parametrizing the KC}} \theta(t) = k\, I(t)$$

2) Kingman Coalescent (KC) model

b) Mechanistic approach

Advantages	Drawbacks

2) Kingman Coalescent (KC) model

b) Mechanistic approach

Advantages	Drawbacks
No assumption on the sampling procedure (the KC conditions on sampling times)	

2) Kingman Coalescent (KC) model

b) Mechanistic approach

Advantages	Drawbacks
- No assumption on the sampling procedure (the KC conditions on sampling times) - Interesting epidemiological parameters may be estimated	

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

b) Mechanistic approach

Advantages

- No assumption on the sampling procedure (the KC conditions on sampling times)
- Interesting epidemiological parameters may be estimated

Drawbacks

- $\theta(t)$ is not necessarily proportional to the prevalence $N(t)$

2) Kingman Coalescent (KC) model

b) Mechanistic approach

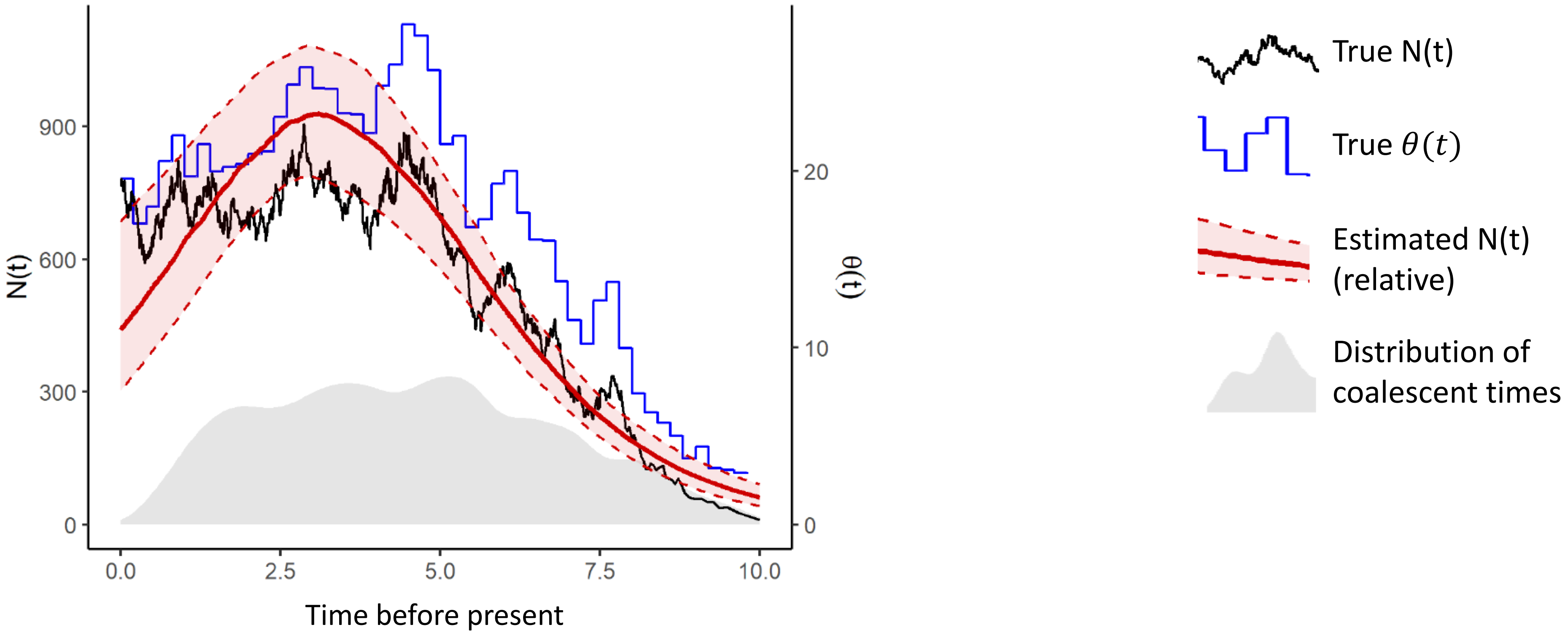
Advantages	Drawbacks
No assumption on the sampling procedure (the KC conditions on sampling times)	$\theta(t)$ is not necessarily proportional to the prevalence $N(t)$
Interesting epidemiological parameters may be estimated	Sensitive to model choice

PHYLODYNAMICS – CLASSICAL MODELS

2) Kingman Coalescent (KC) model

b) Mechanistic approach

Mechanistic KC inference with **incorrect** model



Simulation: SIS model (N(t) reaches a plateau)
Inference: SIR model (N(t) reaches a maximum and decreases)

PHYLODYNAMICS – A NEW METHOD

PHYLODYNAMICS – A NEW METHOD

Advantages

Drawbacks

PHYLODYNAMICS – A NEW METHOD

Advantages

- No assumption on the sampling procedure (based on the KC)

Drawbacks

PHYLODYNAMICS – A NEW METHOD

Advantages

- No assumption on the sampling procedure (based on the KC)
- No need to specify the model that generated the transmission tree

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- Interesting epidemiological parameters can be estimated

Drawbacks

PHYLODYNAMICS – A NEW METHOD

Advantages

- No assumption on the sampling procedure (based on the KC)
- No need to specify the model that generated the transmission tree
- Interesting epidemiological parameters can be estimated

Drawbacks

- The sampled tree is not enough information to identify the parameters

➡ Requires <u>auxilliary data</u>

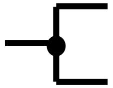
Phylodynamics – A New Method

1) Mathematical foundation

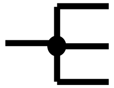
<u>Assumptions</u>:

- The epidemic unraveled according to a **BD-type model** (ie. multiple simultaneous births are not allowed)

Allowed



Not allowed



PHYLODYNAMICS – A NEW METHOD

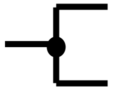
1) Mathematical foundation

Assumptions:

- The epidemic unraveled according to a **BD-type model** (ie. multiple simultaneous births are not allowed)

- Individuals are **exchangeable** (same transmission/recovery rates for all individuals and no geographic structure)

Allowed



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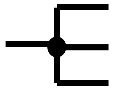

PHYLODYNAMICS – A NEW METHOD

1) Mathematical foundation

Assumptions:

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Result:

In the limit of large population size, the probability distribution of the sampled tree under a BD-type model converges to that of a Kingman coalescent with parameter

$$\theta(t) = \frac{N(t)}{2\lambda(t)}$$

PHYLODYNAMICS – A NEW METHOD

1) Mathematical foundation

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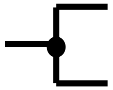

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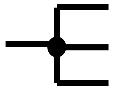

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$$\theta(t) = \frac{N(t)}{2\lambda(t)} = \frac{N_0 \exp \int_0^t \big(\mu(s) - \lambda(s)\big) ds}{2\lambda(t)}$$

PHYLODYNAMICS – A NEW METHOD

1) Mathematical foundation

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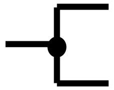
Allowed



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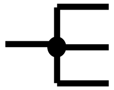

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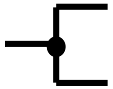
➡ The three parameters $\lambda(t)$, $\mu(t)$ and N_0 are not separately identifiable

1) Mathematical foundation

Assumptions:

- The epidemic unraveled according to a **BD-type model** (ie. multiple simultaneous births are not allowed)
- Individuals are **exchangeable** (same transmission/recovery rates for all individuals and no geographic structure)

Allowed



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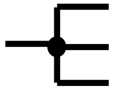


Result:

In the limit of large population size, the probability distribution of the sampled tree under a BD-type model converges to that of a Kingman coalescent with parameter

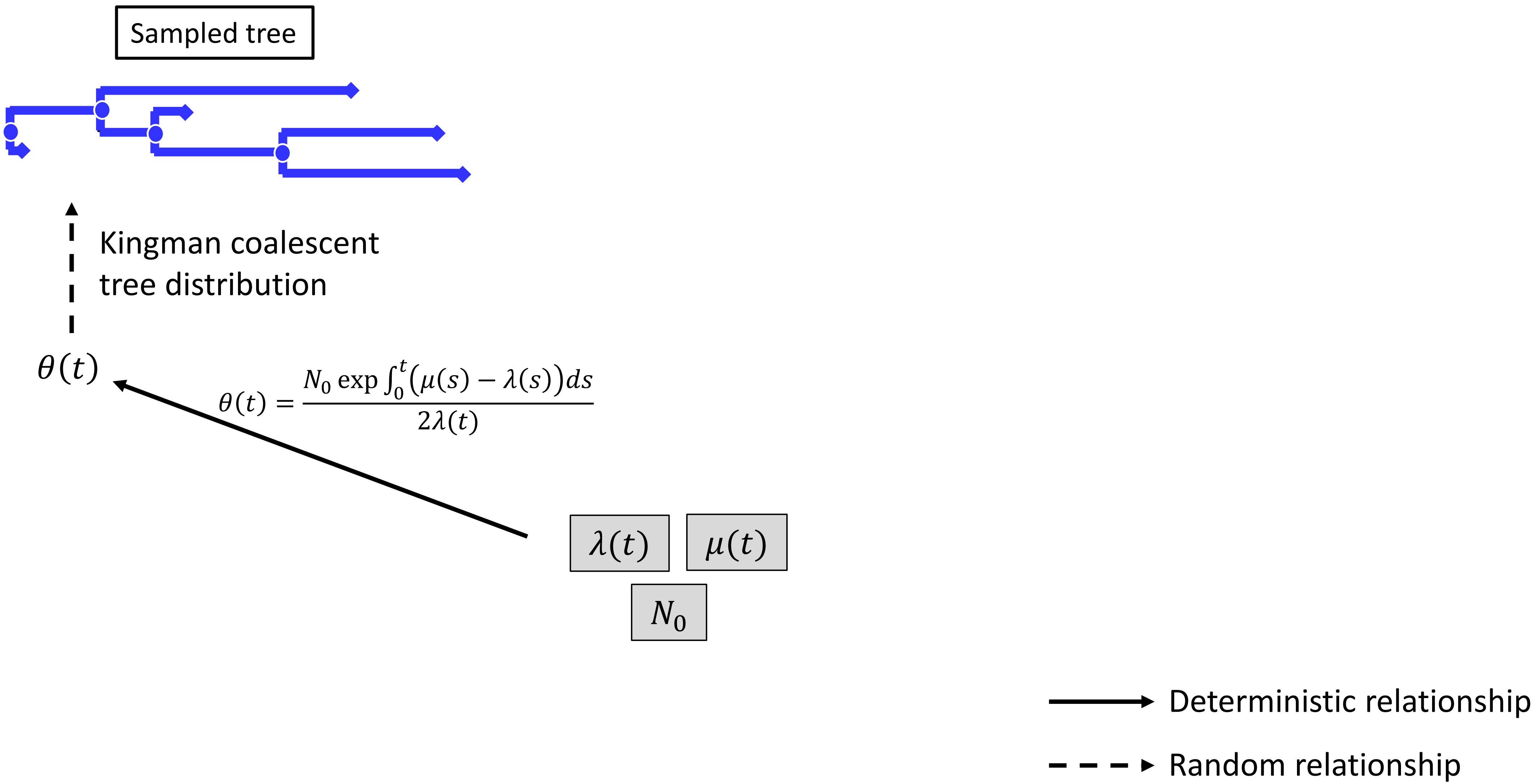
$$\theta(t) = \frac{N(t)}{2\lambda(t)} = \frac{N_0 \exp \int_0^t \big(\mu(s) - \lambda(s)\big) ds}{2\lambda(t)}$$

➡ The three parameters $\lambda(t)$, $\mu(t)$ and N_0 are not separately identifiable

➡ Auxilliary data required

PHYLODYNAMICS – A NEW METHOD

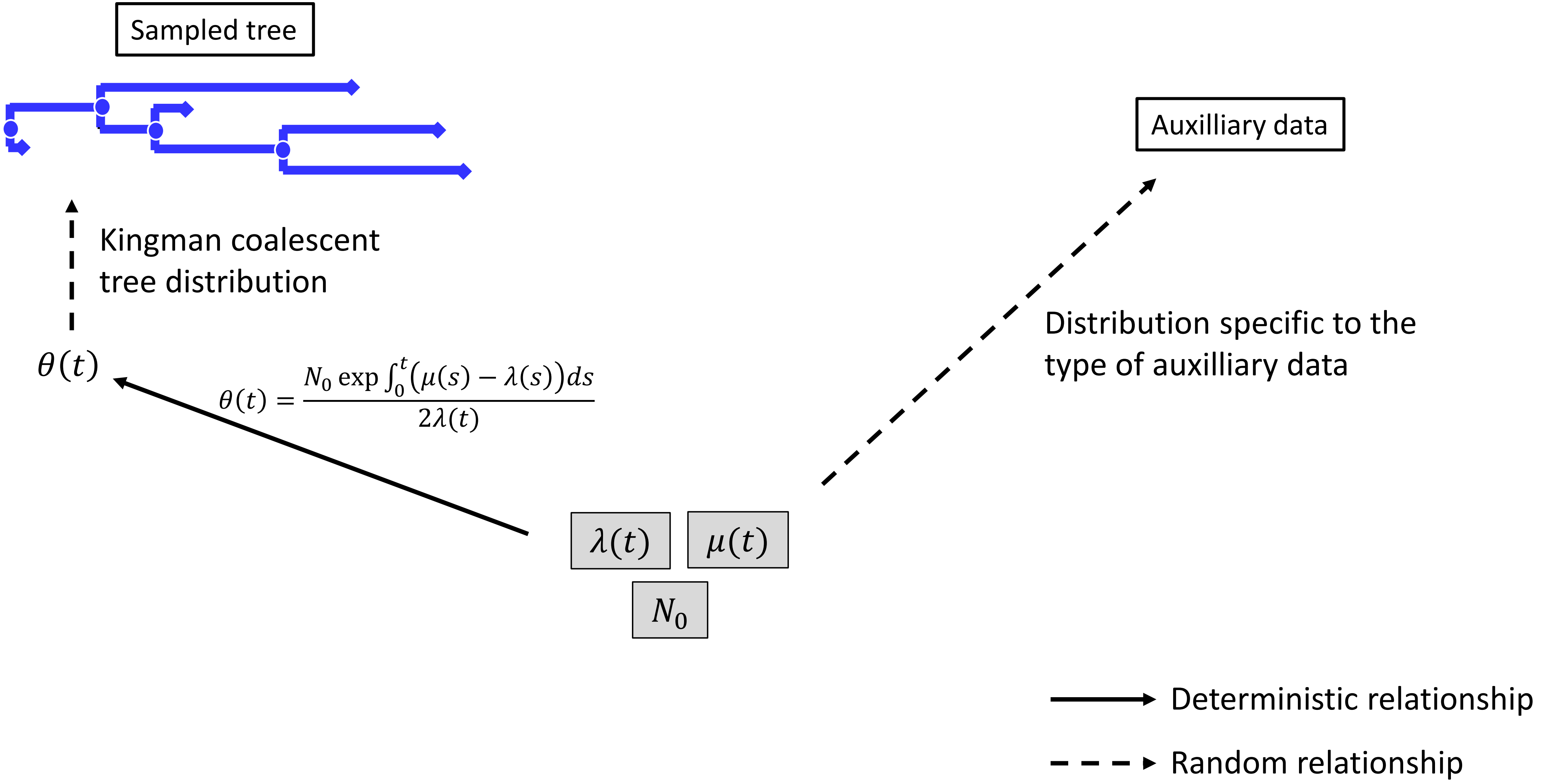
2) Statistical inference



$$\theta(t) = \frac{N_0 \exp \int_0^t \left(\mu(s) - \lambda(s)\right) ds}{2\lambda(t)}$$

PHYLODYNAMICS – A NEW METHOD

2) Statistical inference



Sampled tree

Kingman coalescent tree distribution

$\theta(t)$

$$\theta(t) = \frac{N_0 \exp \int_0^t (\mu(s) - \lambda(s))ds}{2\lambda(t)}$$

$\lambda(t)$ $\mu(t)$

N_0

Auxilliary data

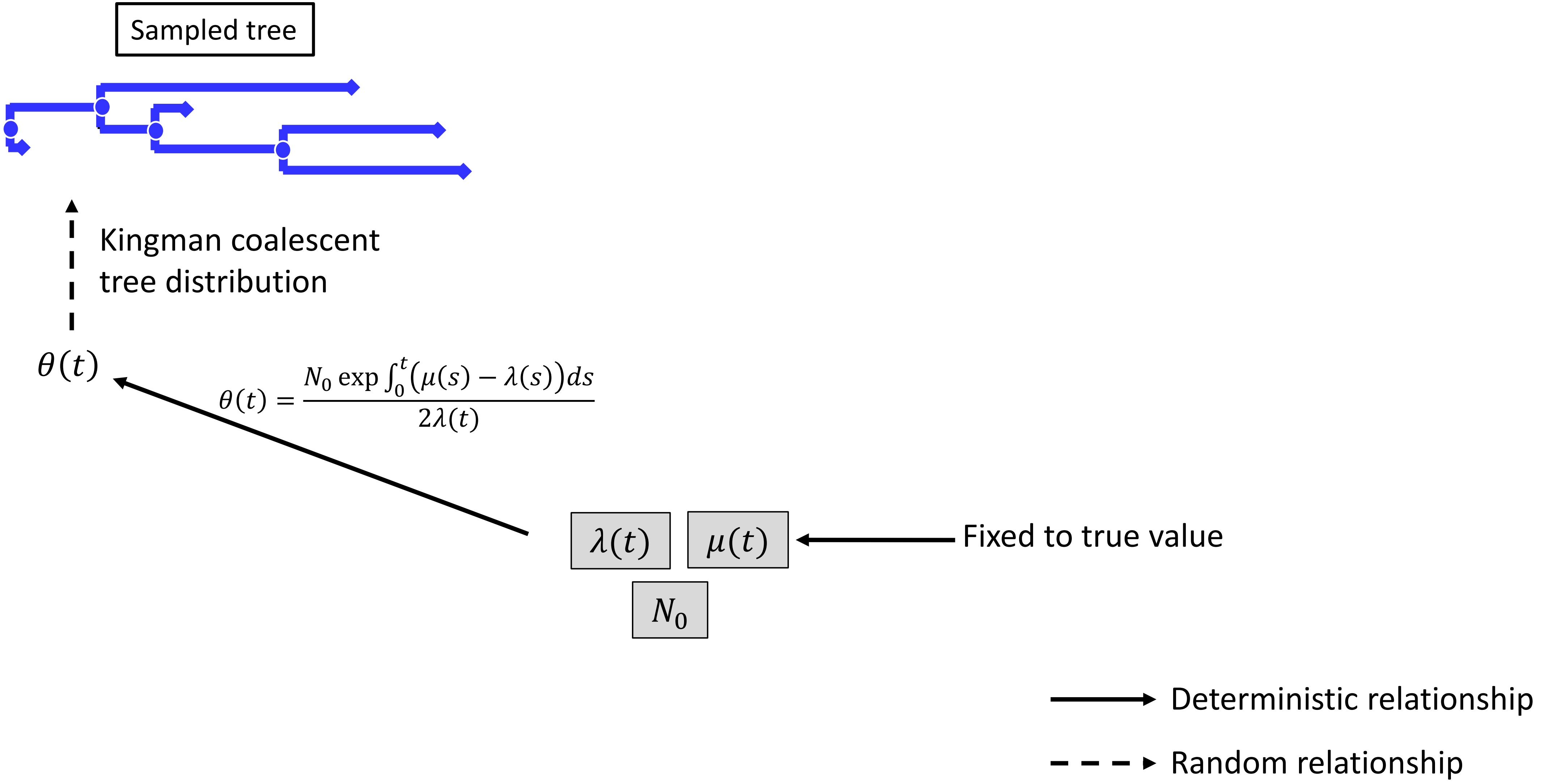
Distribution specific to the type of auxilliary data

Deterministic relationship

Random relationship

PHYLODYNAMICS – A NEW METHOD

2) Statistical inference



Sampled tree

Kingman coalescent tree distribution

$\theta(t)$

$$\theta(t) = \frac{N_0 \exp \int_0^t \big(\mu(s) - \lambda(s)\big) ds}{2\lambda(t)}$$

$\lambda(t)$ $\mu(t)$ N_0

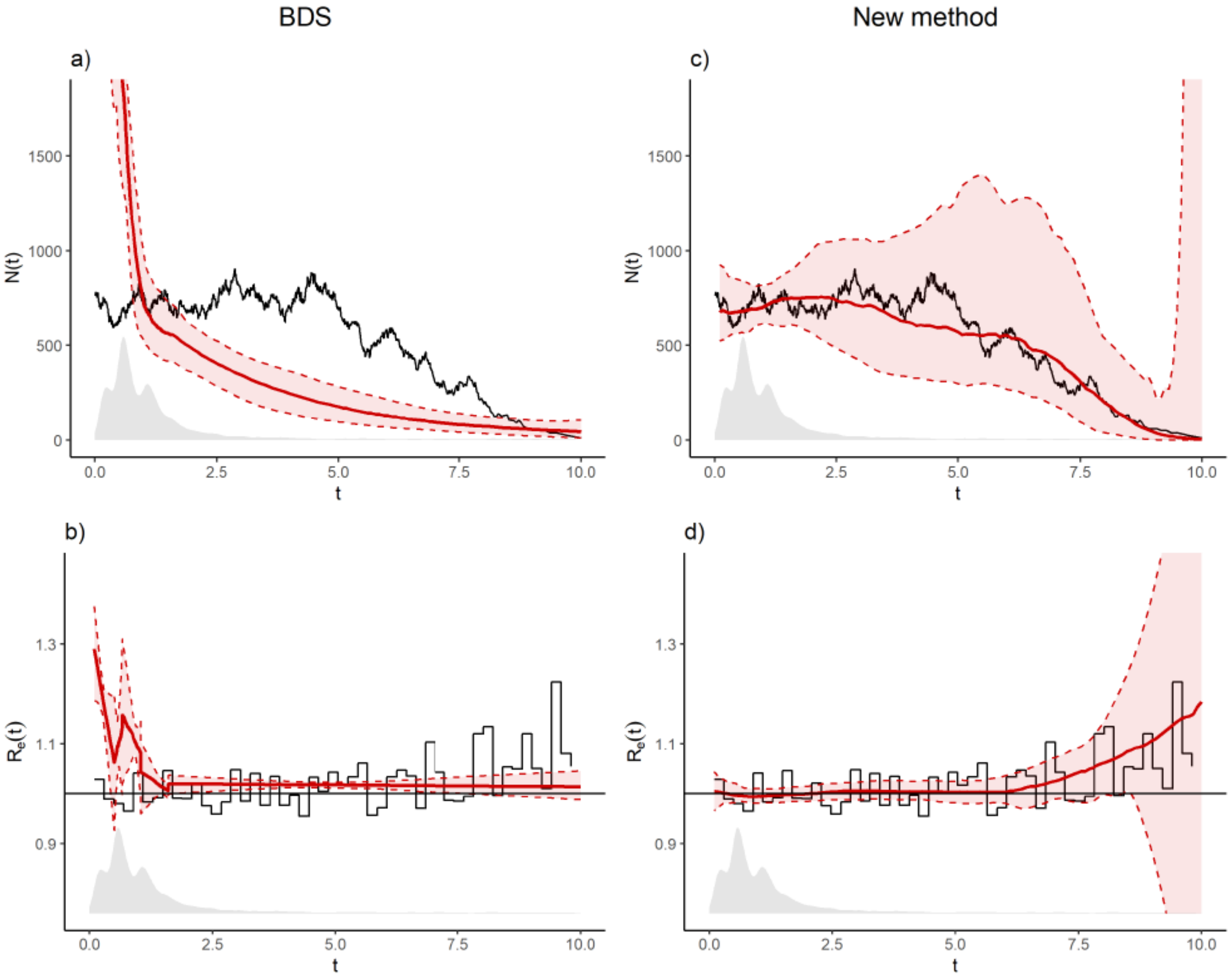
Fixed to true value

→ Deterministic relationship

- - → Random relationship

PHYLODYNAMICS – A NEW METHOD

3) Comparison with other methods

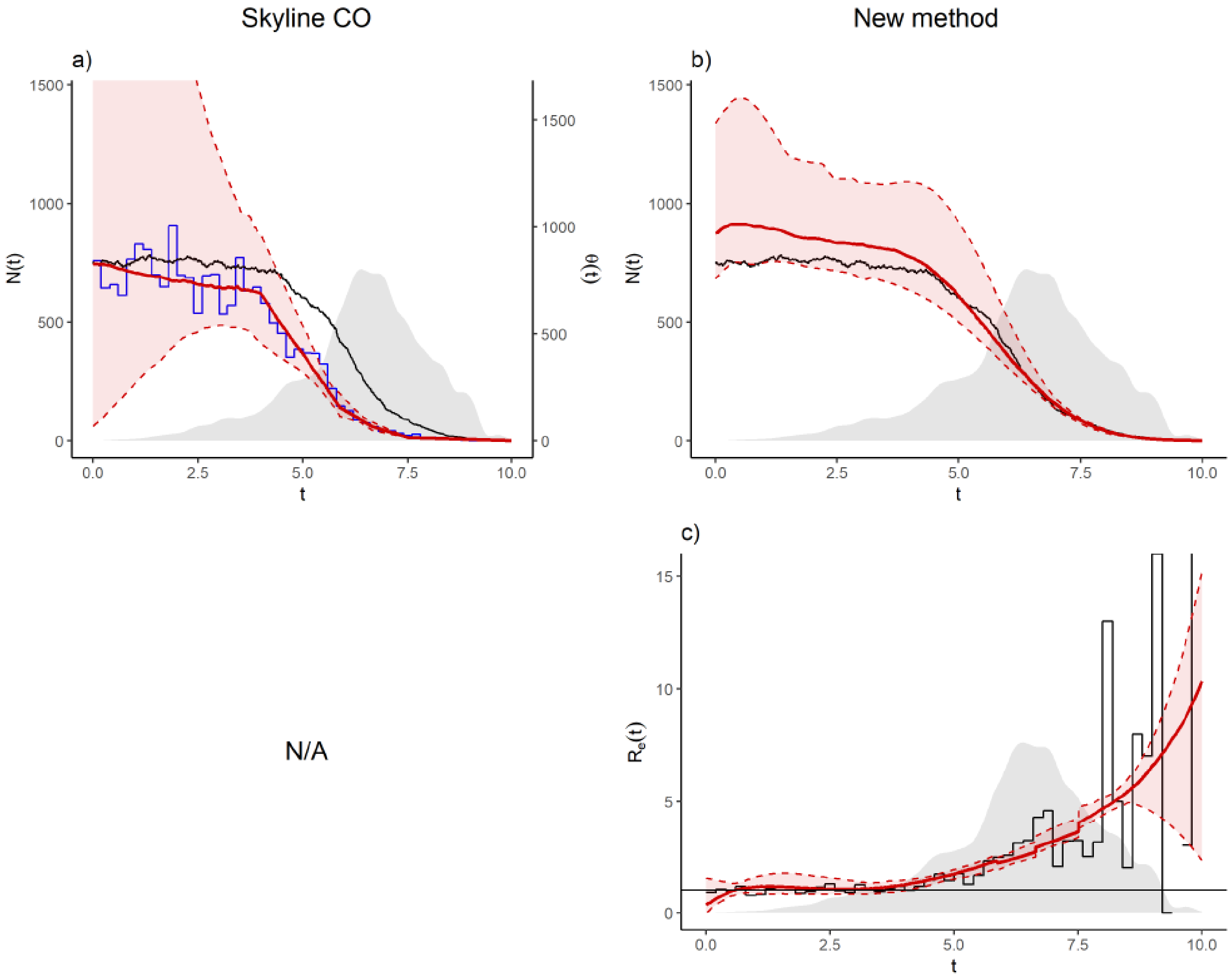


$\mu(t)$ fixed to true value

$\mu(t)$ fixed to true value

PHYLODYNAMICS – A NEW METHOD

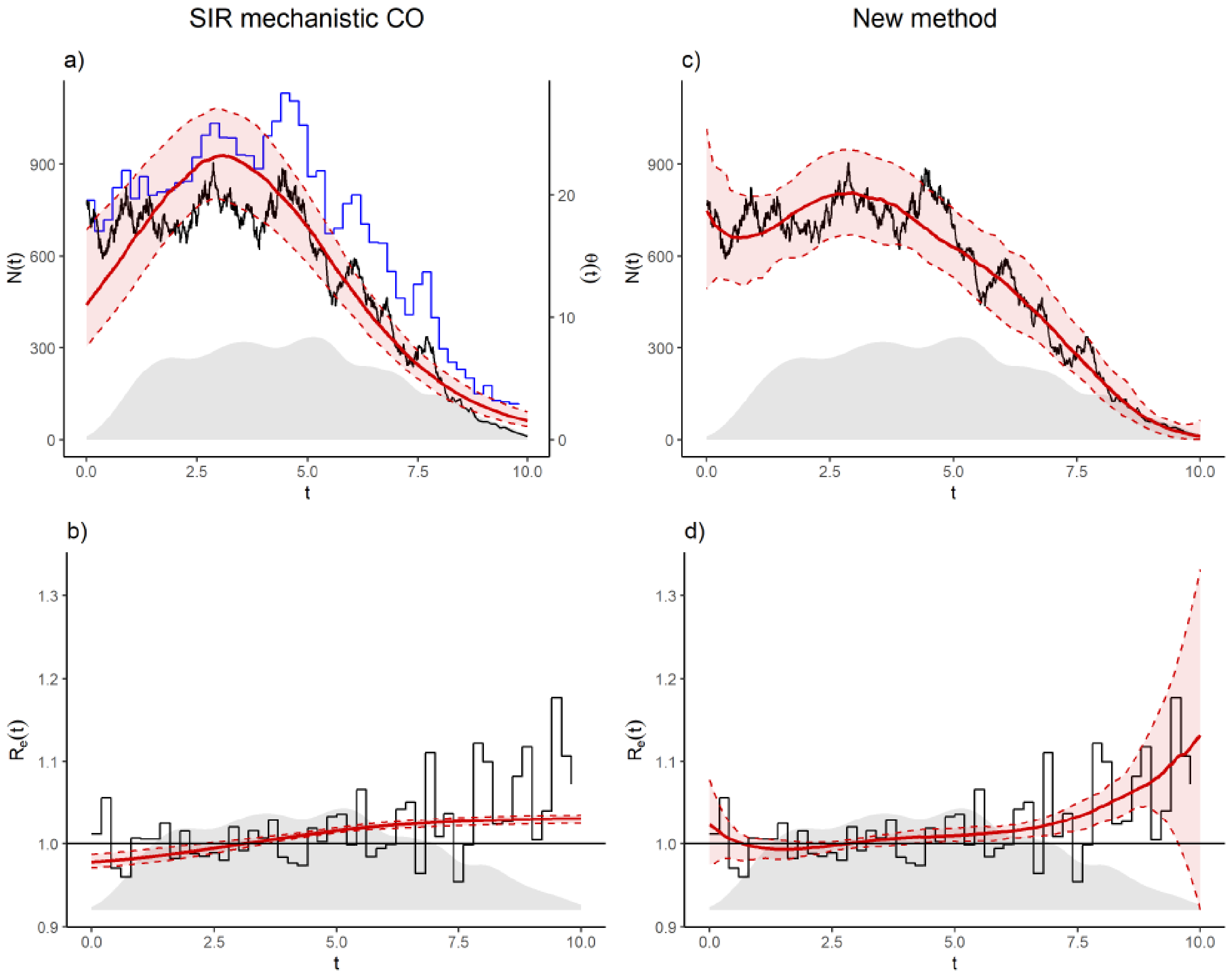
3) Comparison with other methods



$\mu(t)$ fixed to true value

PHYLODYNAMICS – A NEW METHOD

3) Comparison with other methods



μ fixed to true value

$\mu(t)$ fixed to true value

PHYLODYNAMICS – A NEW METHOD

4) Test of the method

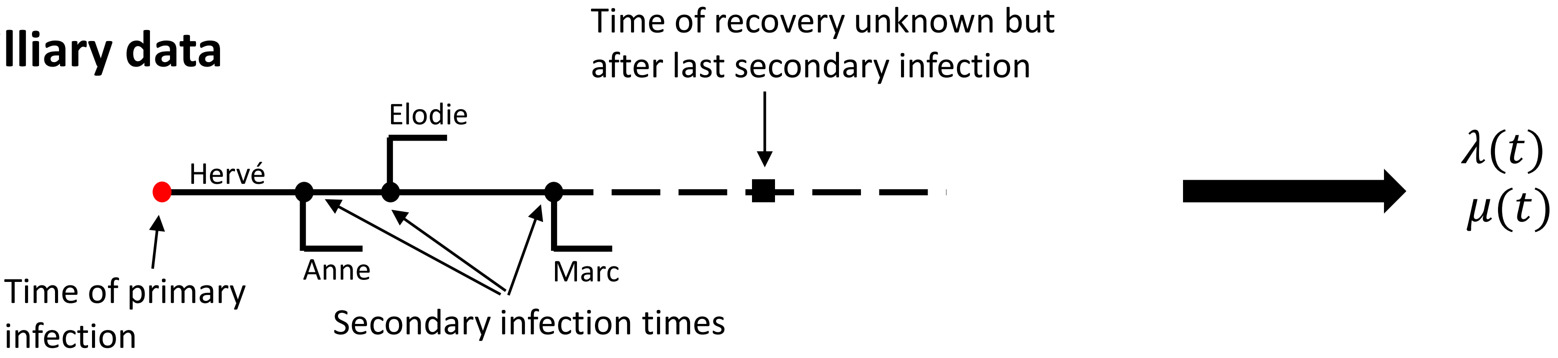
a) With various types of auxilliary data

PHYLODYNAMICS – A NEW METHOD

4) Test of the method

a) With various types of auxilliary data

- Transmission chains



Time of recovery unknown but after last secondary infection

Time of primary infection

Secondary infection times

$\lambda(t)$

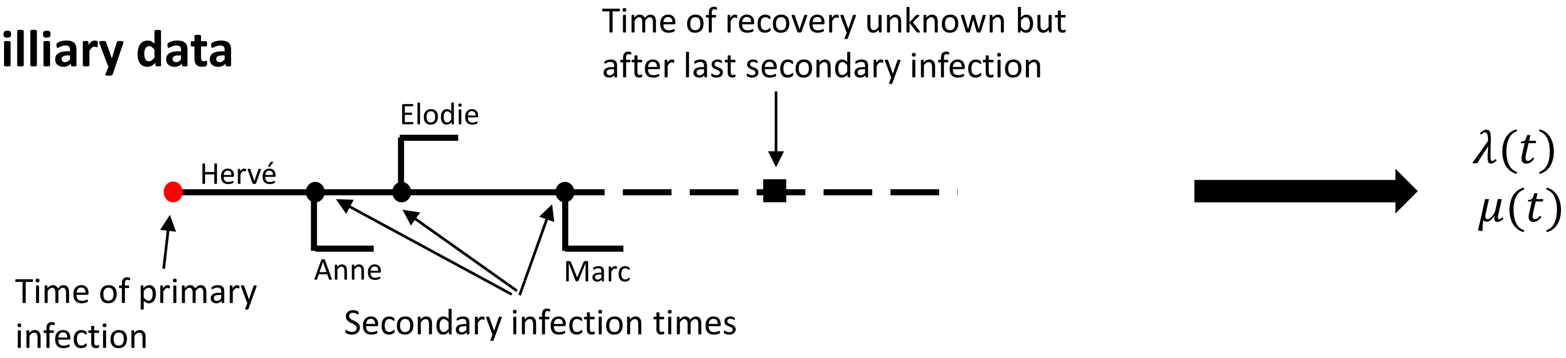
$\mu(t)$

PHYLODYNAMICS – A NEW METHOD

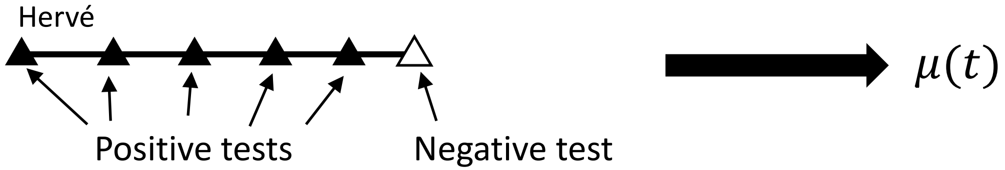
4) Test of the method

a) With various types of auxilliary data

- Transmission chains



- Duration of infection



PHYLODYNAMICS – A NEW METHOD

4) Test of the method

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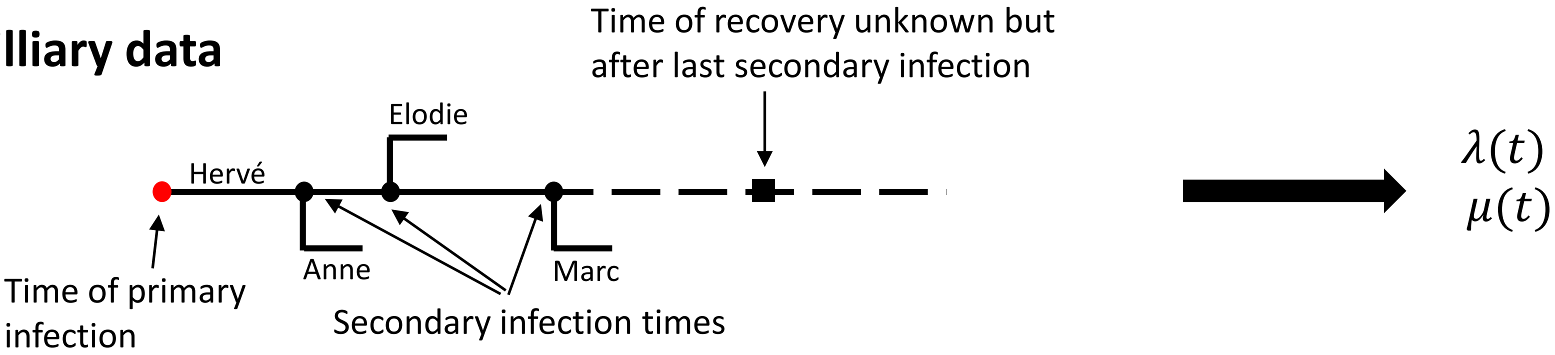
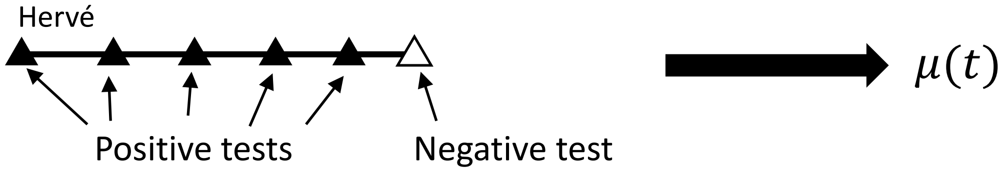
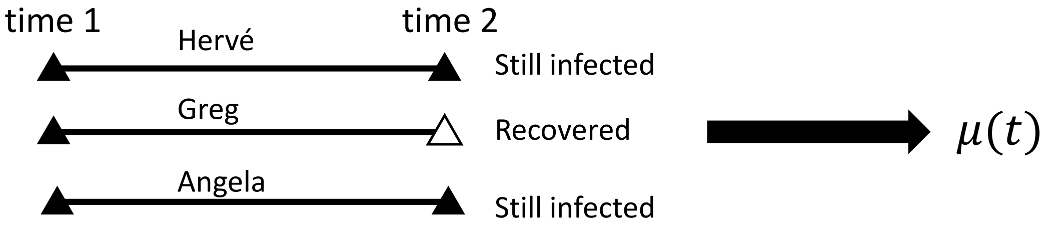
- Transmission chains



- Duration of infection



- Incidence of recovery

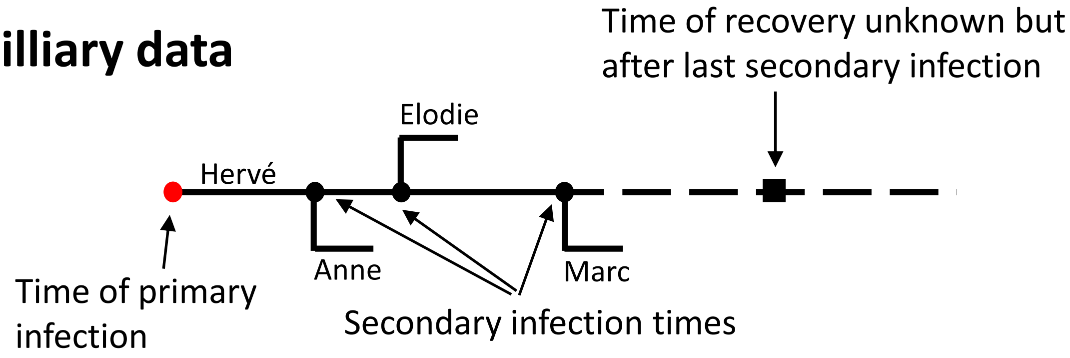


PHYLODYNAMICS – A NEW METHOD

4) Test of the method

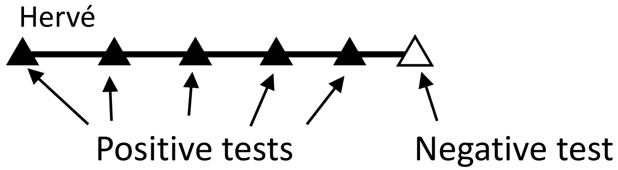
a) With various types of auxilliary data

- Transmission chains



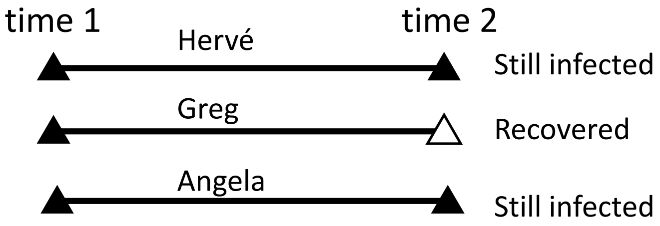
→ $\lambda(t)$ $\mu(t)$

- Duration of infection



→ $\mu(t)$

- Incidence of recovery



→ $\mu(t)$

- Incidence of new cases

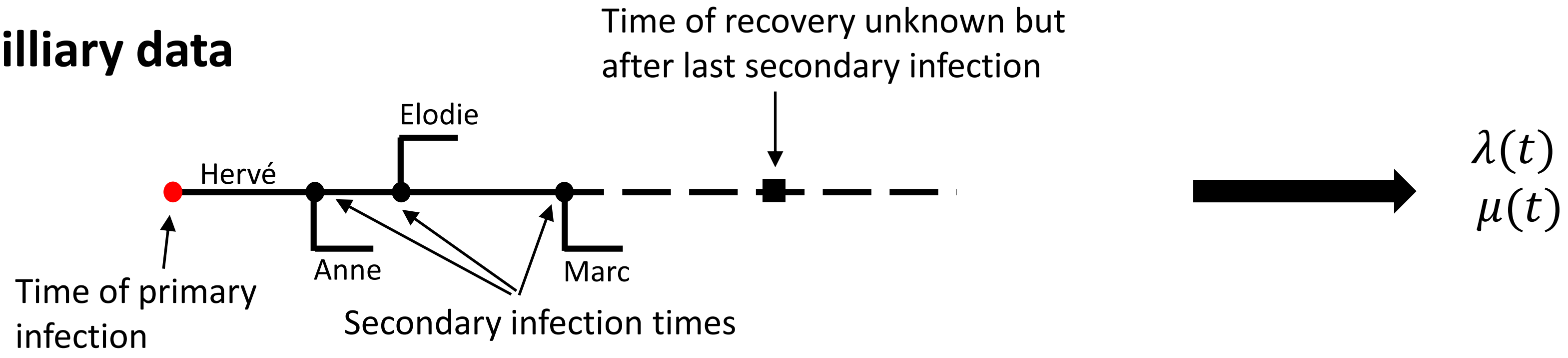
→ $\lambda(t) \times N(t)$

PHYLODYNAMICS – A NEW METHOD

4) Test of the method

a) With various types of auxilliary data

- Transmission chains



Time of recovery unknown but after last secondary infection

Elodie

Hervé

Anne

Marc

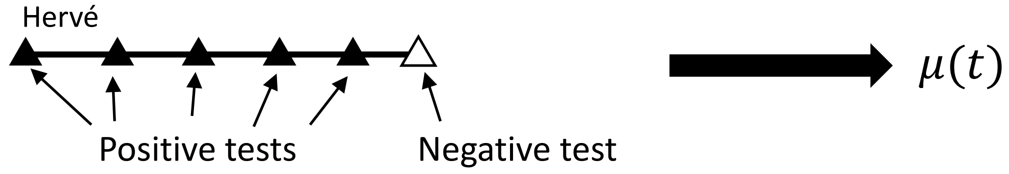
Time of primary infection

Secondary infection times

$\lambda(t)$

$\mu(t)$

- Duration of infection



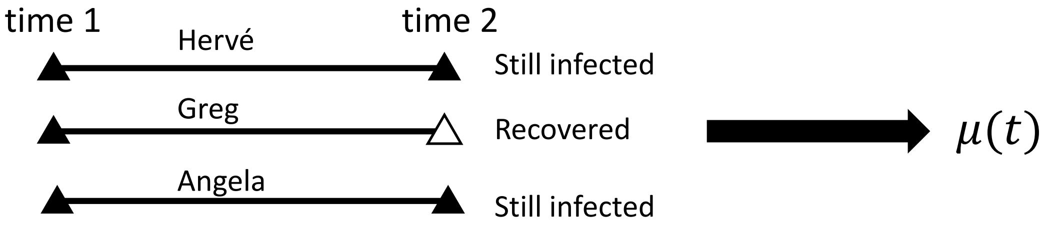
Hervé

Positive tests

Negative test

$\mu(t)$

- Incidence of recovery



time 1

time 2

Hervé

Still infected

Greg

Recovered

Angela

Still infected

$\mu(t)$

- Incidence of new cases

time 1

237 new cases

time 2

$\lambda(t) \times N(t)$

- Prevalence

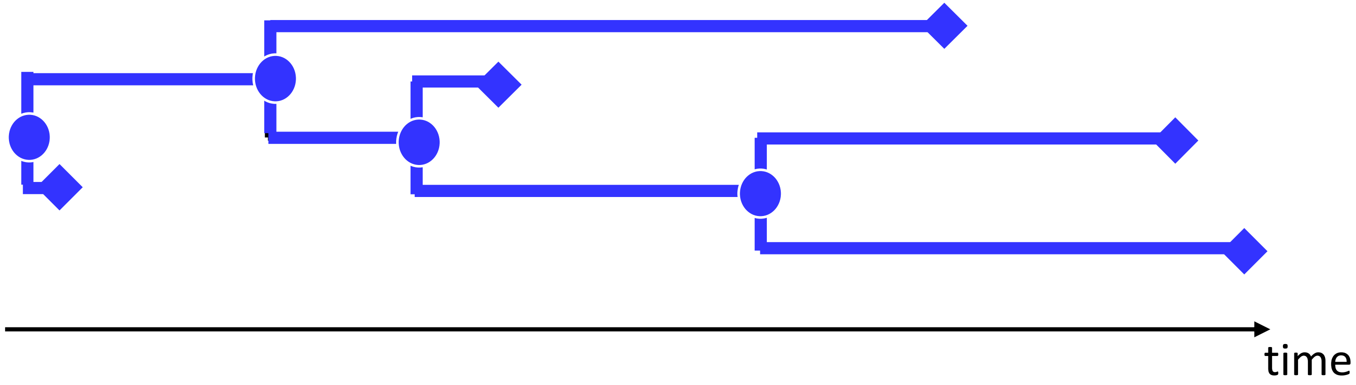
time t

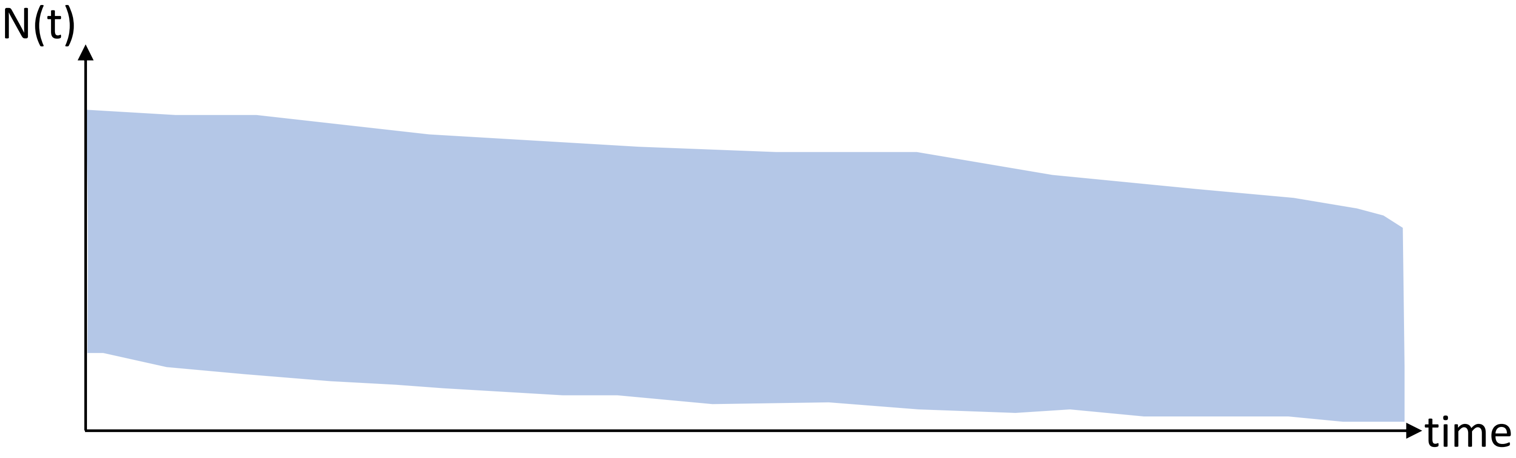
$N(t)/K$

PHYLODYNAMICS – A NEW METHOD

4) Test of the method

a) With various types of auxilliary data





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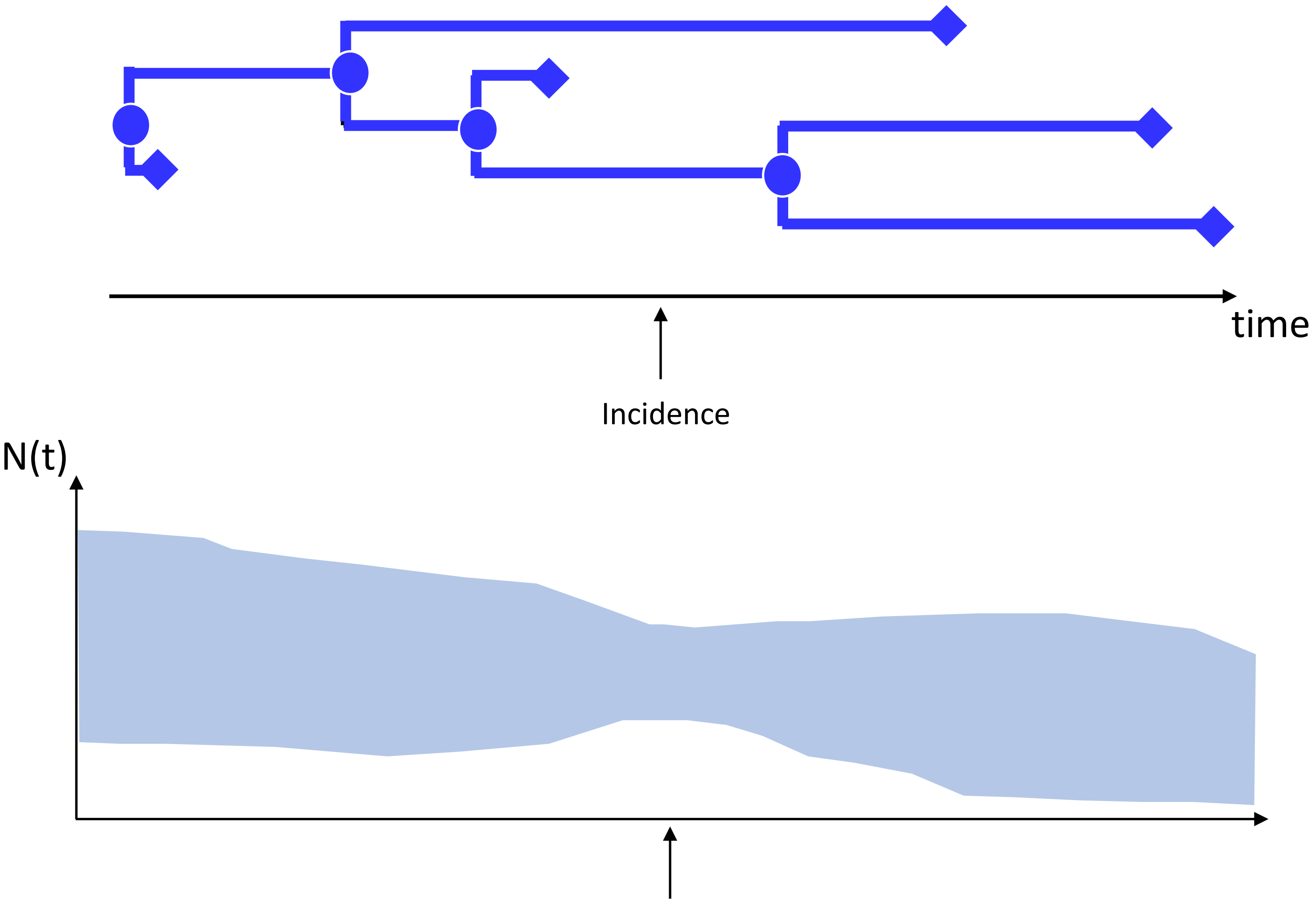

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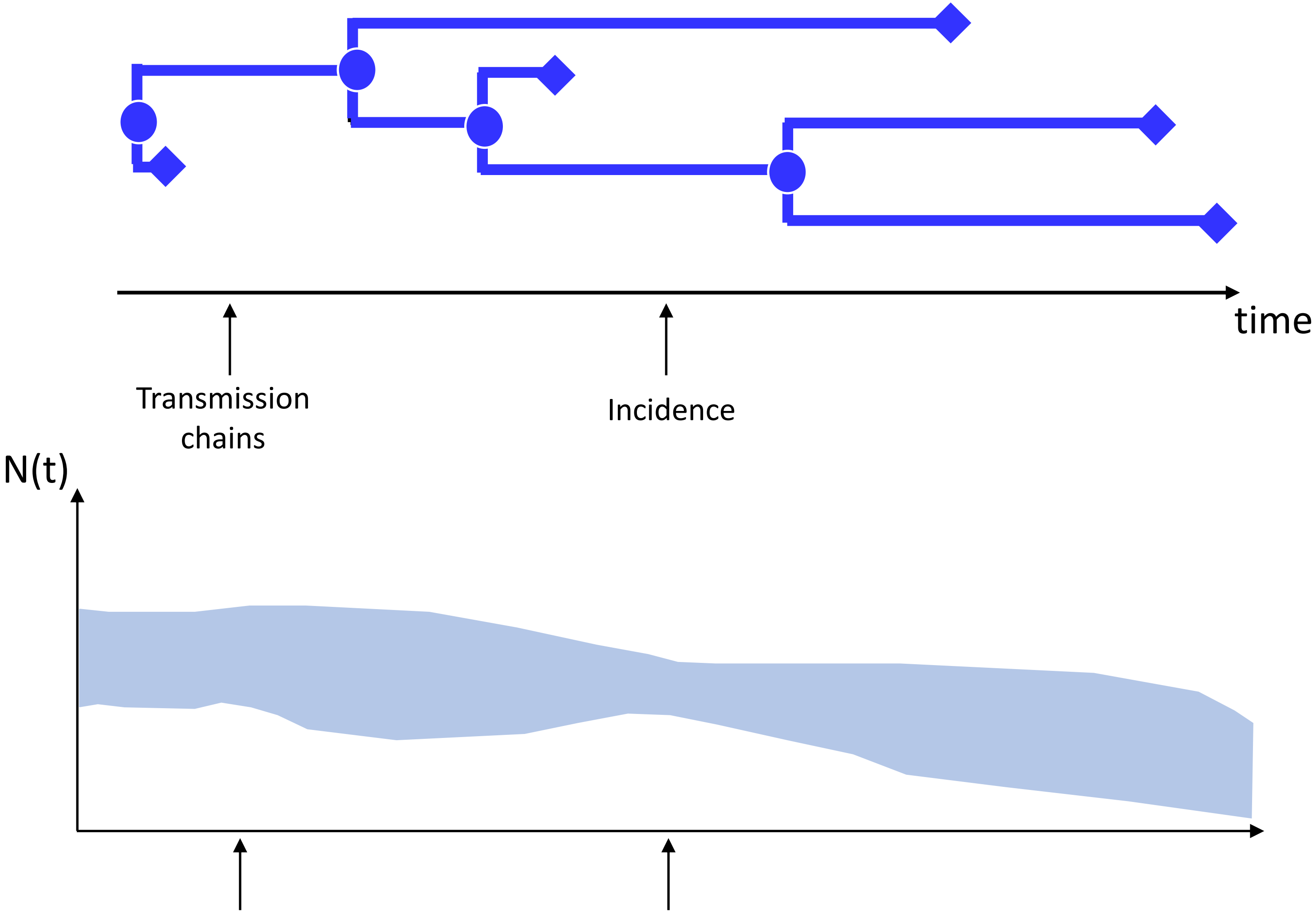

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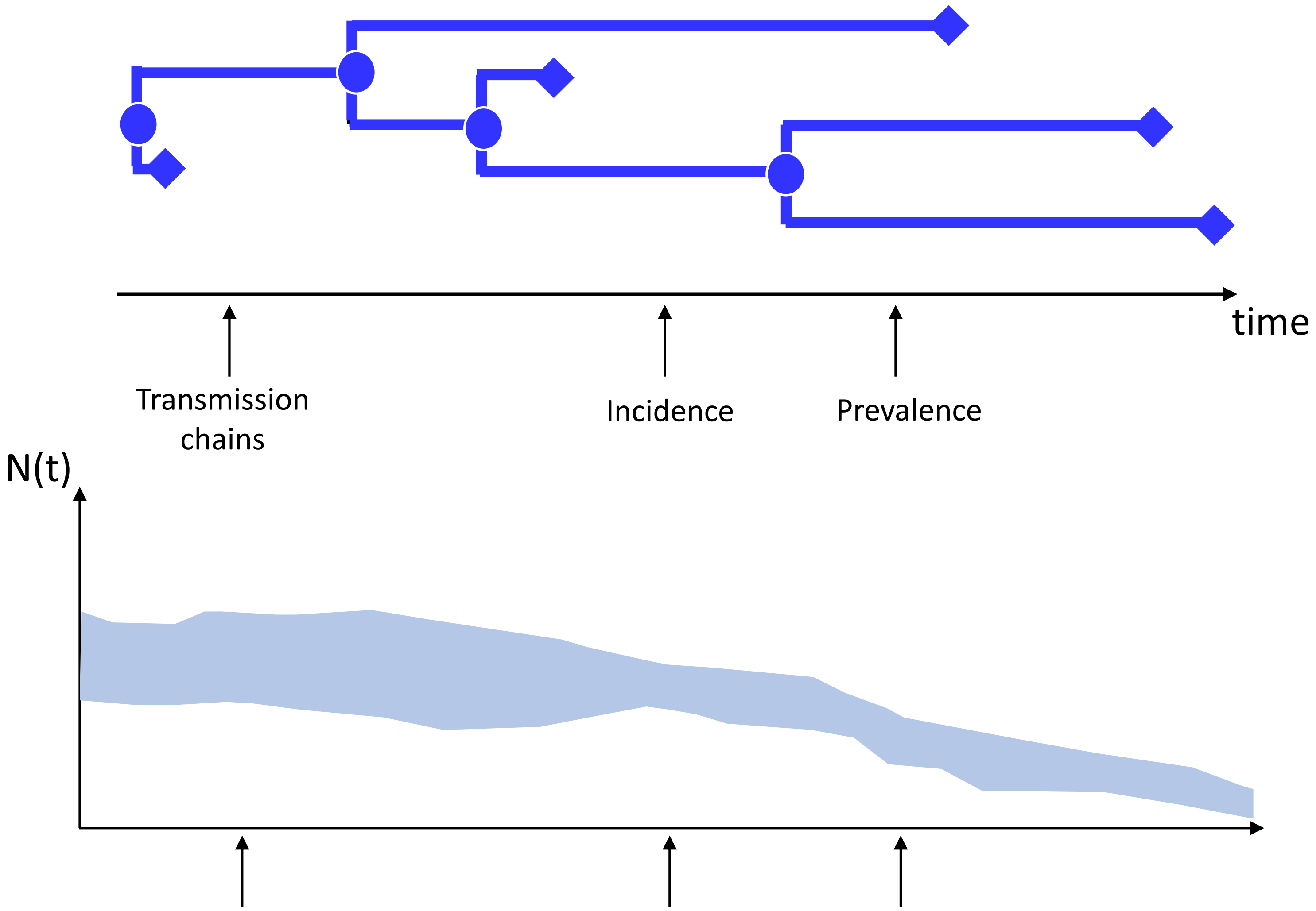

PHYLODYNAMICS – A NEW METHOD

4) Test of the method

b) With structured models

- Geographic structure
- Different types of individuals (multi-stage infections)
- Different variants

THANK YOU FOR YOUR ATTENTION