Poster #594

Phylodynamics of HCV acute infection in men having sex with men

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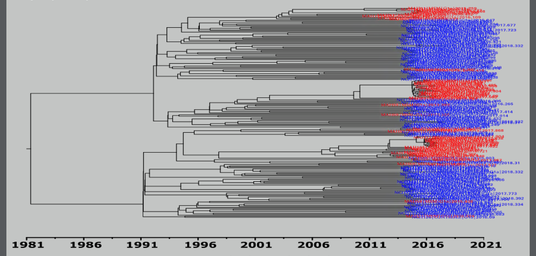
Background

- Opioid substitution and syringes exchange programs have drastically reduced hepatitis C virus (HCV) spread in France.
- HCV sexual transmission in men who have sex with men (MSM) has recently arose as a significant phenomenon.
- Epidemiological data such as prevalence and incidence rates can quantify an epidemic at its chronic stage but are less meaningful in the early stages of the epidemics or if the transmission of the pathogen only occurs in a subgroup of individuals.
- Phylodynamic inferences use both pathogen phylogenies based on genetic sequences and epidemiological data to describe infectious diseases transmission dynamic.
- **We estimate R_0 and infectious period duration of acute HCV in two types of hosts using ABC-regression phylodynamics.**

Data

We witness two ongoing epidemics in two host types:

- **Classical hosts**
  Injection drug users
  HIV+
  Detection during chronic infection
- **New hosts being detected**
  MSM
  HIV- and HIV+
  Detection during acute infection
- 213 sequences (NS5B gene, 322bp) and sampling dates
- HCV is a rapidly-evolving RNA virus, which facilitates phylodynamic inference.



Time-scaled viral phylogeny

Model & methods

Epidemiological model

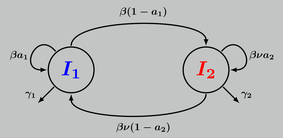
We assumed a Birth-Death model with two host types.

Host compartments

- I_1 : "Classical" injection drug users
- I_2 : New MSM hosts

Parameters

- β : transmission rate
- a_i : assortativity
- $1/\gamma_i$: infectious period
- ν : number of times I_2 transmit more than I_1



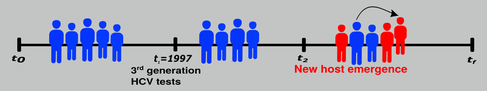
$$\dot{I}_1 = a_1\beta I_1 + (1-a_2)\nu\beta I_2 - \gamma_1 I_1$$
$$\dot{I}_2 = a_2\beta\nu I_2 + (1-a_1)\beta I_1 - \gamma_2 I_2$$

Priors & simulations

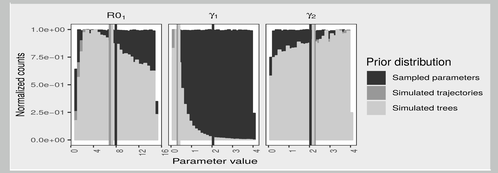
- We consider 3 time intervals: before new HCV detection tests ($t_1 = 1997$), before second epidemics onset (t_2 estimated).
- The priors of the parameters follow a uniform distribution.

	γ_1	γ_2	ν	R_0^1	a_i
t_0 to t_1	$U(0.1, 4)$	0	0	$U(0.9, 15)$	$U(0, 1)$
t_1 to t_2	-	0	0	$U(0.1, 3)$	-
t_2 to t_f	-	$U(0.1, 4)$	$U(1, 10)$	-	-

$$\beta_{t1} = R^1_{0,t1}\gamma_1$$
$$\beta_{t2} = R^1_{0,t2}\gamma_1$$
$$R^2_{0,t3} = \frac{\beta_{t2}\nu}{\gamma_2}$$



- We generated 61.000 simulated transmission trees from 2.10^6 sets of parameters, using a simulator we implemented in R using Rcpp.



- The feasibility of the simulations reduces the prior distribution.

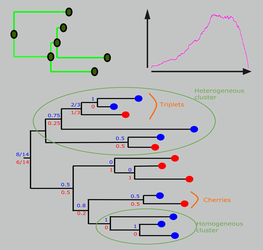
Summary statistics

Trees are complex objects, therefore, to describe them and compare them, we use summary statistics:

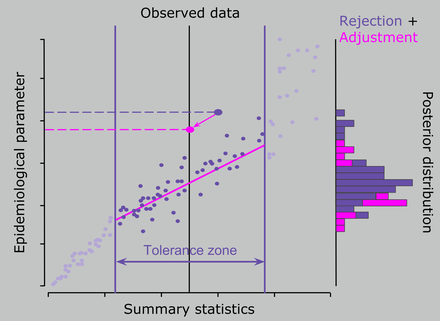
- Branch lengths
- LTT (lineage through-time) plot
- Topology

New summary statistics

- Cherries, triplets
- Branch lengths on homogeneous and heterogeneous clusters
- LLT 'label' plot



Regression ABC



- Define a tolerance parameter which represents a percentile of the simulations that are close to the target.
- Reject the simulations that are outside the tolerance zone.
- Adjust the posterior distribution by a regression model (Elastic Net) used to project the non-rejected simulated values to the target.

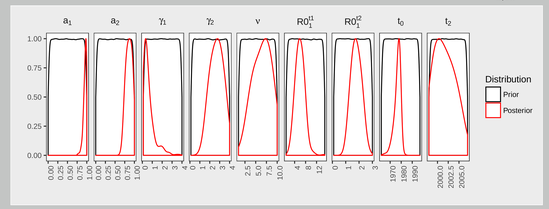
For further details about the summary statistics and regression ABC phylodynamics, see *Saulnier, Gascuel & Alizon (2017, PLoS Comput Biol 13(3): e1005416).*

Results & conclusions

Posterior distributions

Estimations

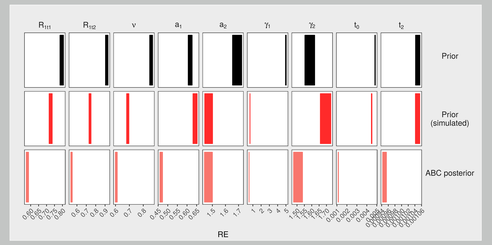
- a_1 = 0.96
- a_2 = 0.86
- ν = 6.5
- $1/\gamma_1$ = 1.7 yrs
- $1/\gamma_2$ = 0.4 yrs
- t_0 = 1976
- t_1 = 2001
- $R^1_{0,t1}$ = 5.94
- $R^1_{0,t2}$ = 1.80
- $R^2_{0,t3}$ = 2.35



- **New MSM hosts transmit more than classical IDU hosts.**
- **The R_0 for the "classical" (chronic HCV infections) and the "new" (acute HCV in MSM) epidemics are respectively 1.80 and 2.35.**
- **The new epidemic is characterized by a shorter infectious period duration (3 months) than the classical epidemic (18 months).**
- **The origin of the "classical" and the "news" epidemics are respectively estimated to be in 1976 and 2001.**

Cross validation

- 100 replicates : 1 test data × 60.000 training data
- Inference error measurement using relative error (RE)



Given the phylogeny structure, our ABC-regression method has the power to infer most parameters.