RECON

Building the next generation of statistical tools for outbreak response using R

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5th January 2017

Imperial College London
MRC Centre for Outbreak Analysis and Modelling

Outline

1. Lessons learnt from the Ebola outbreak response
2. The R Epidemics Consortium
3. RECON projects: from basic needs to active research
4. Methodological dialogue during outbreak response

Ebola response

Lessons learnt from the Ebola response

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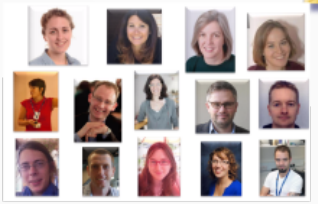

Imperial College Ebola team

Lessons learnt from the Ebola response

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Lessons learnt from the Ebola response

Most statistical/modelling tools for situation awareness missing.

What tools do we need?

Some examples:

- **data cleaning:** dictionaries, entry matching
- **graphics:** case incidence in space and time, contact tracing
- **parameter estimation:** key delays, transmissibility
- **estimate / test CFR:** gender, health care workers, treaments effects
- **predictions:** case incidence, mortality, evaluate interventions
- **report:** (semi-)automated situation reports

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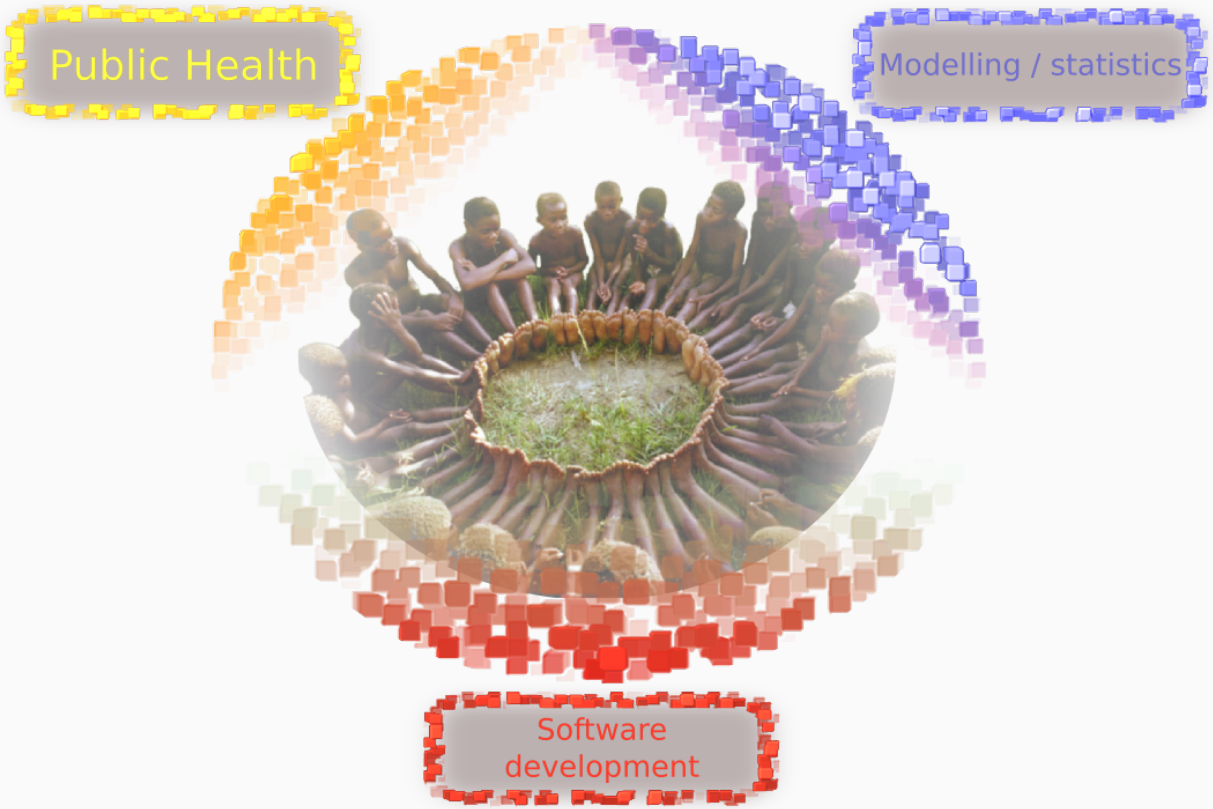
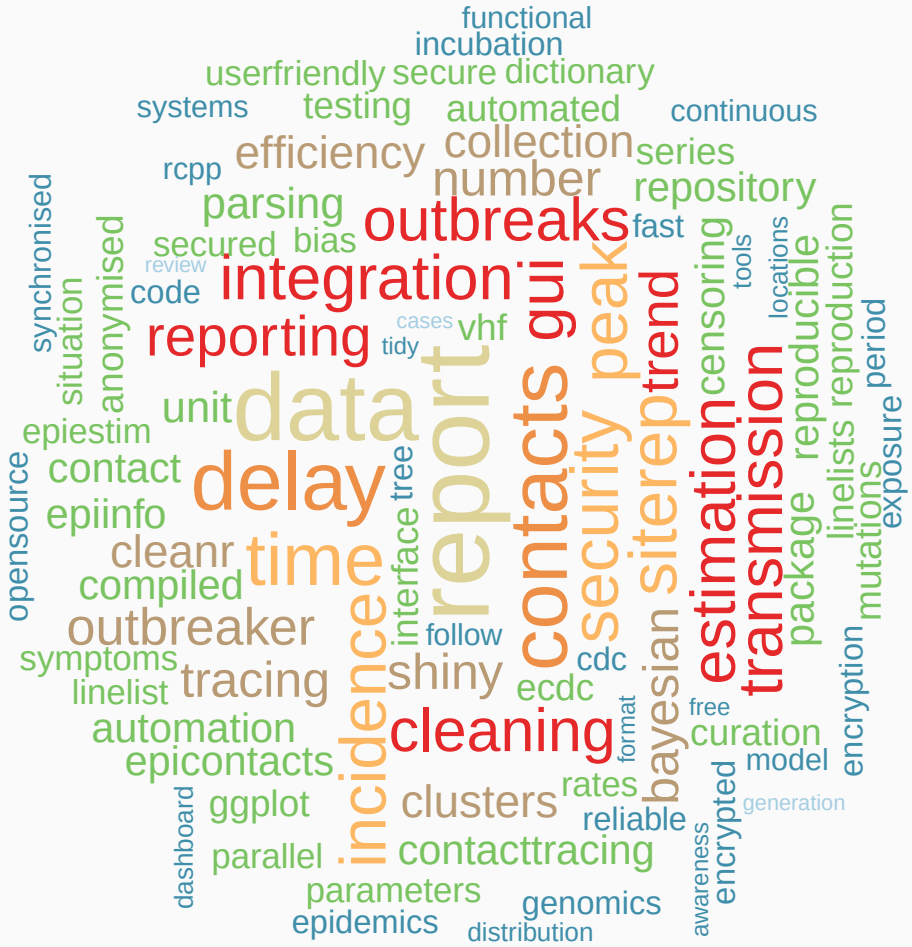


The R Epidemics Consortium

Hackout 3: a R hackathon for emergency outbreak response

Last summer at the *rOpenSci* headquarters (Berkeley)

Hackout 3: from ideas to projects to...



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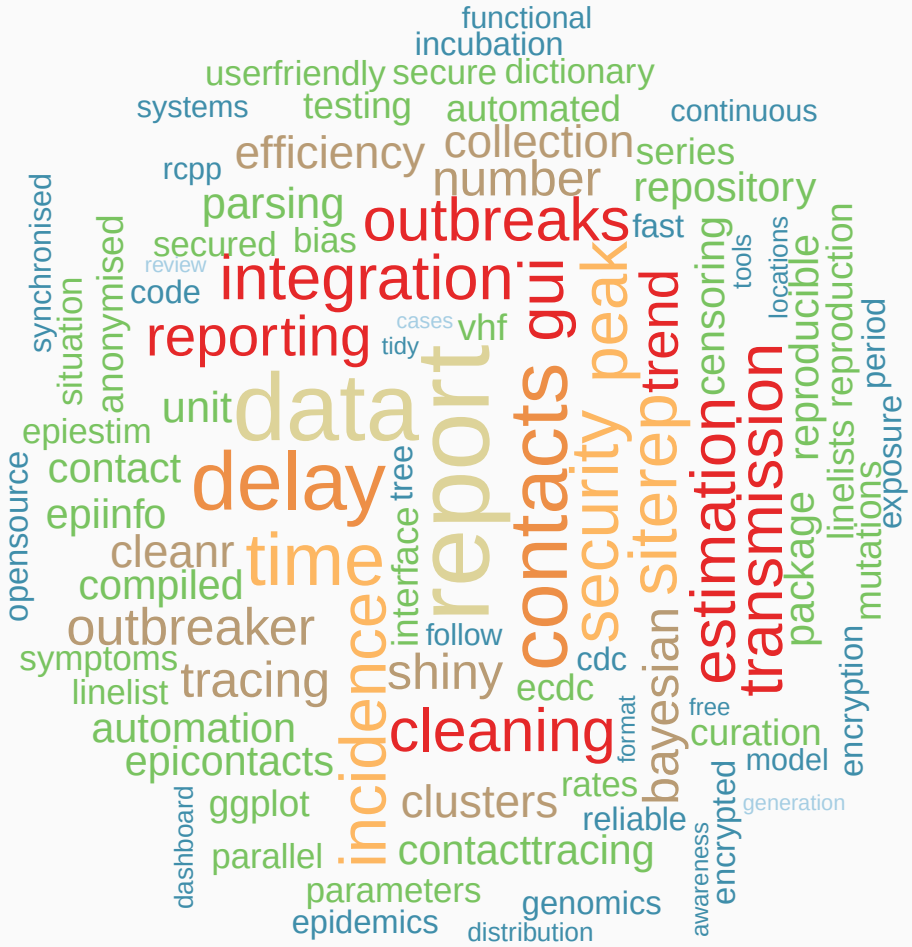
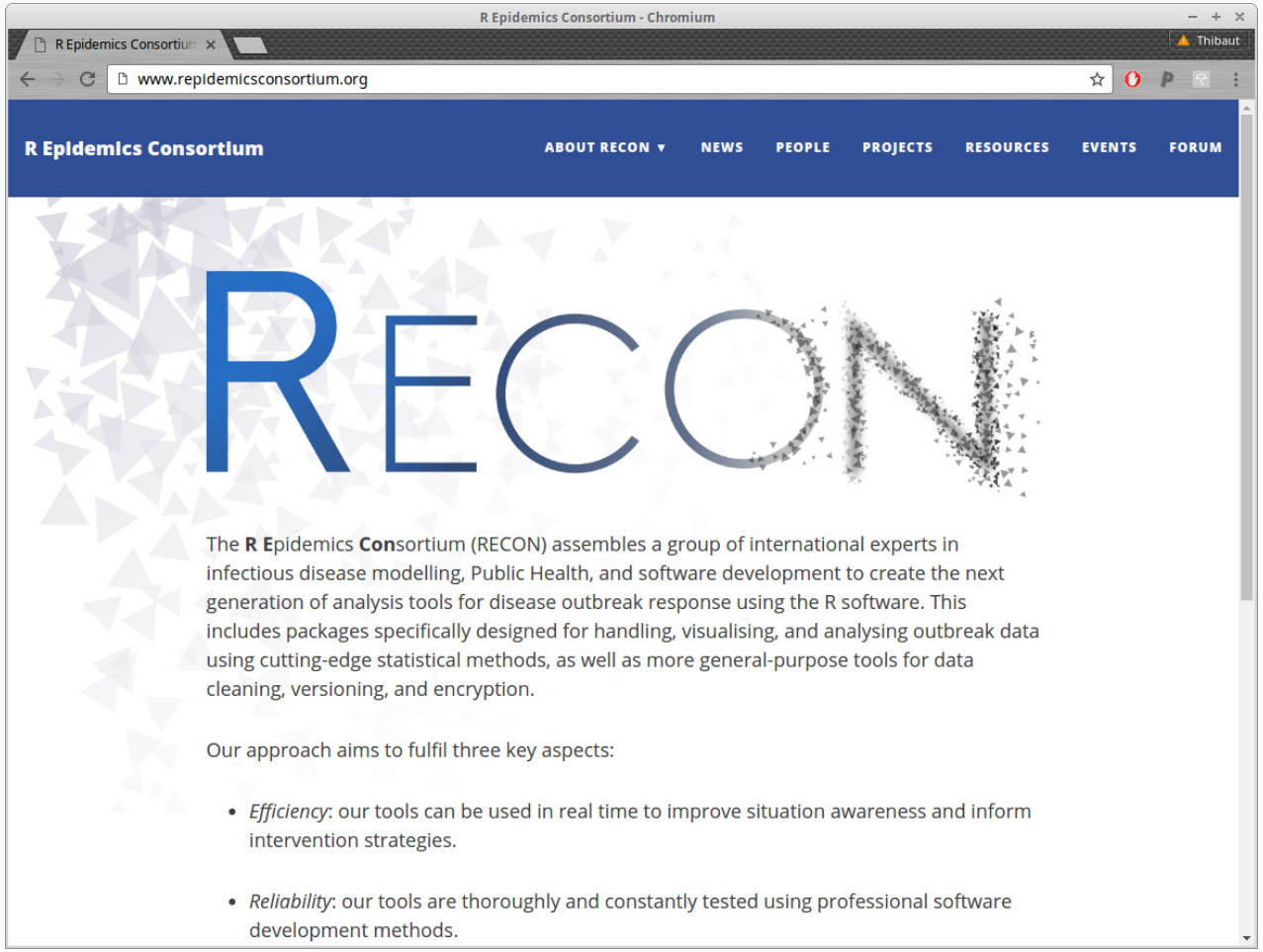


How do we keep momentum once the event is over?

RECON: the R Epidemics Consortium

A taskforce to build a new generation of outbreak response tools in .



www.repidemicsconsortium.org

In a nutshell

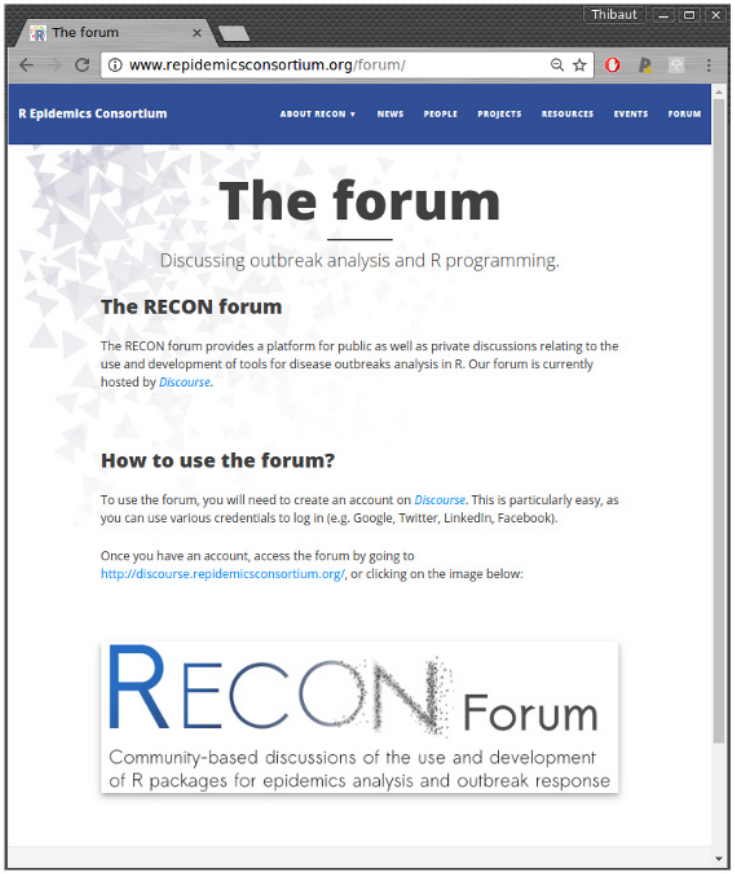
RECON

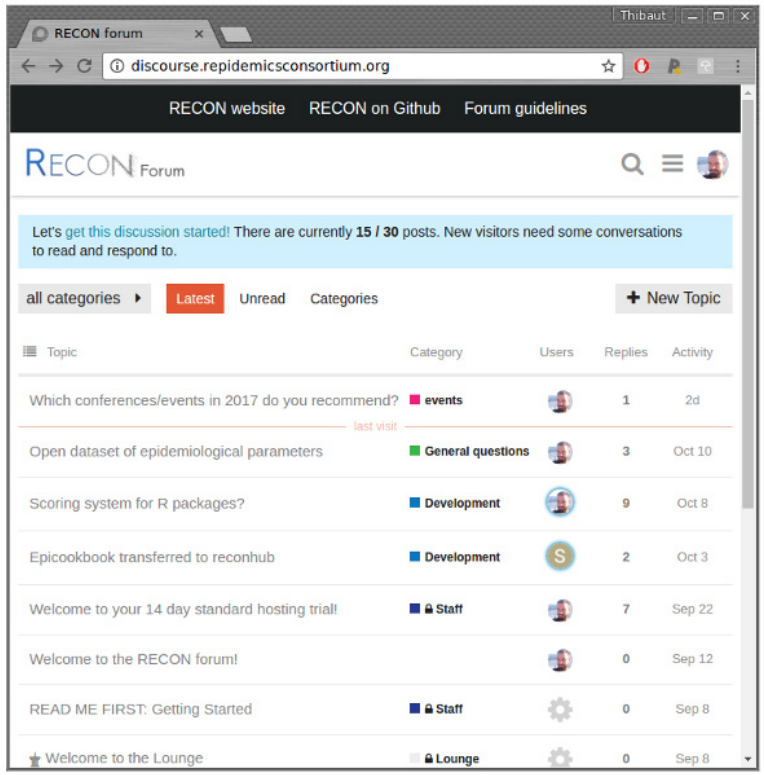
www.repidemicsconsortium.org

- started 6th September 2016
- 48 people (42 members, 6 board)
- 10 countries, $>$ 20 institutions
- $\sim$ 10 new packages coming
- public forum, blog, online resources

The RECON forum

A platform for discussing epidemics analysis in R .





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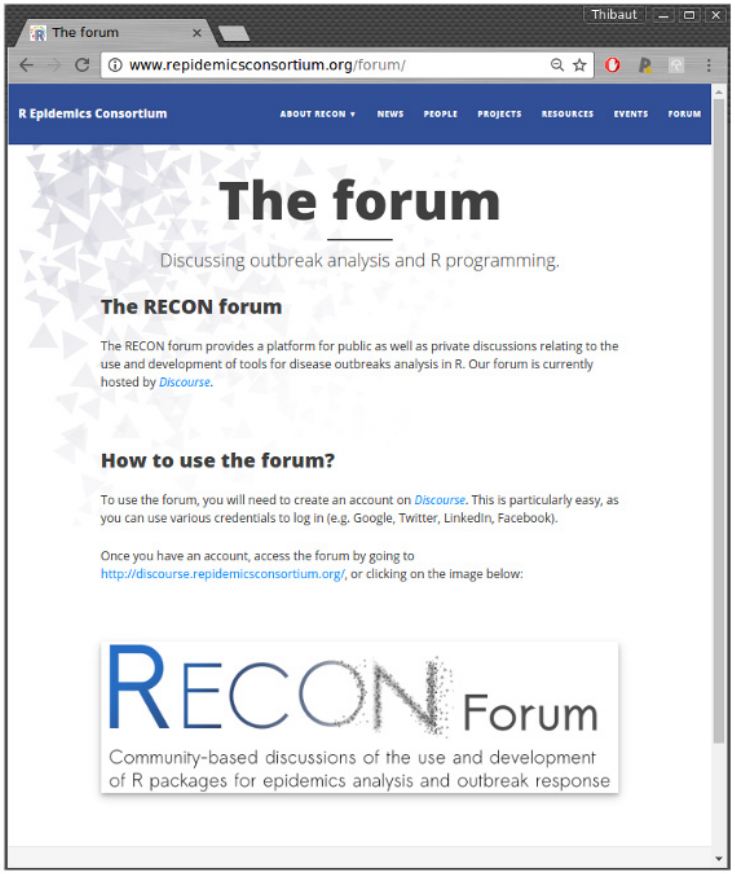

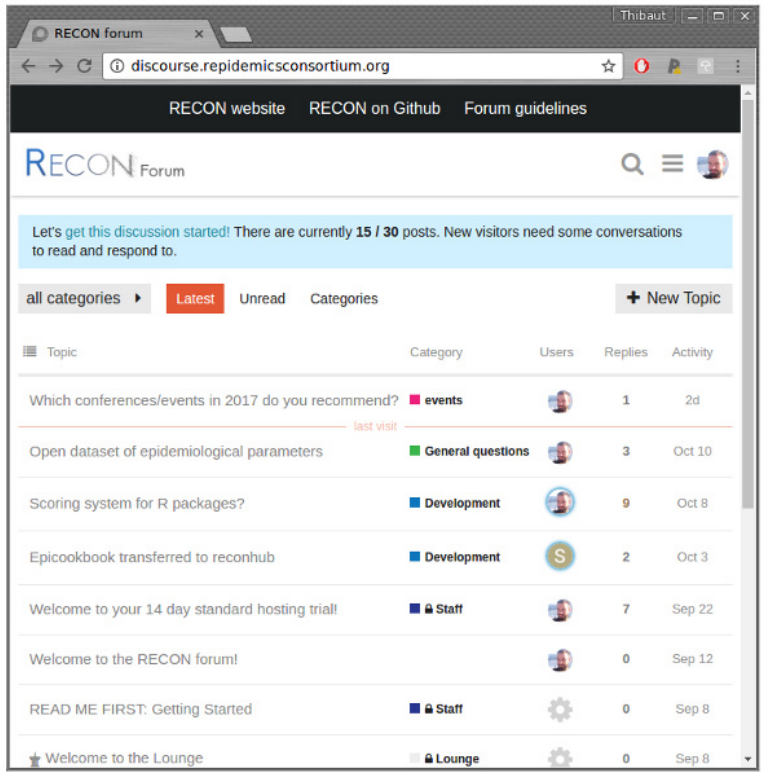

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Join us!

RECON package: what do we aim for?

- **efficiency**: useful for improving situation awareness in real time; cutting-edge, computer-efficient statistical methods

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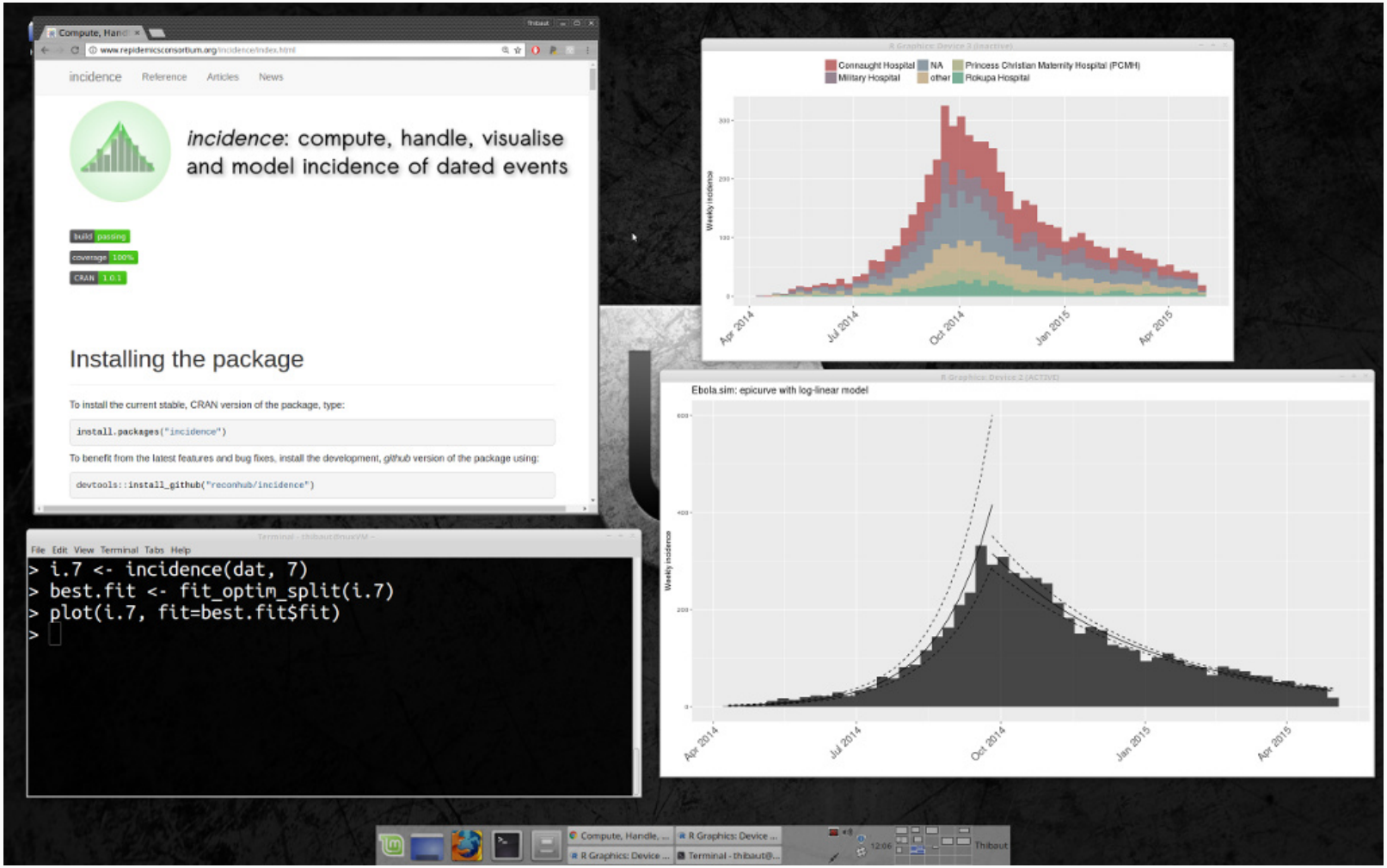
- **efficiency**: useful for improving situation awareness in real time; cutting-edge, computer-efficient statistical methods
- **reliability**: outputs can be trusted; continuous integration, extensive unit testing, code review, good practices
- **accessibility**: widely available, easy learning curve; extensive documentation, tutorials, websites, forum

RECON projects: from basic needs to active research

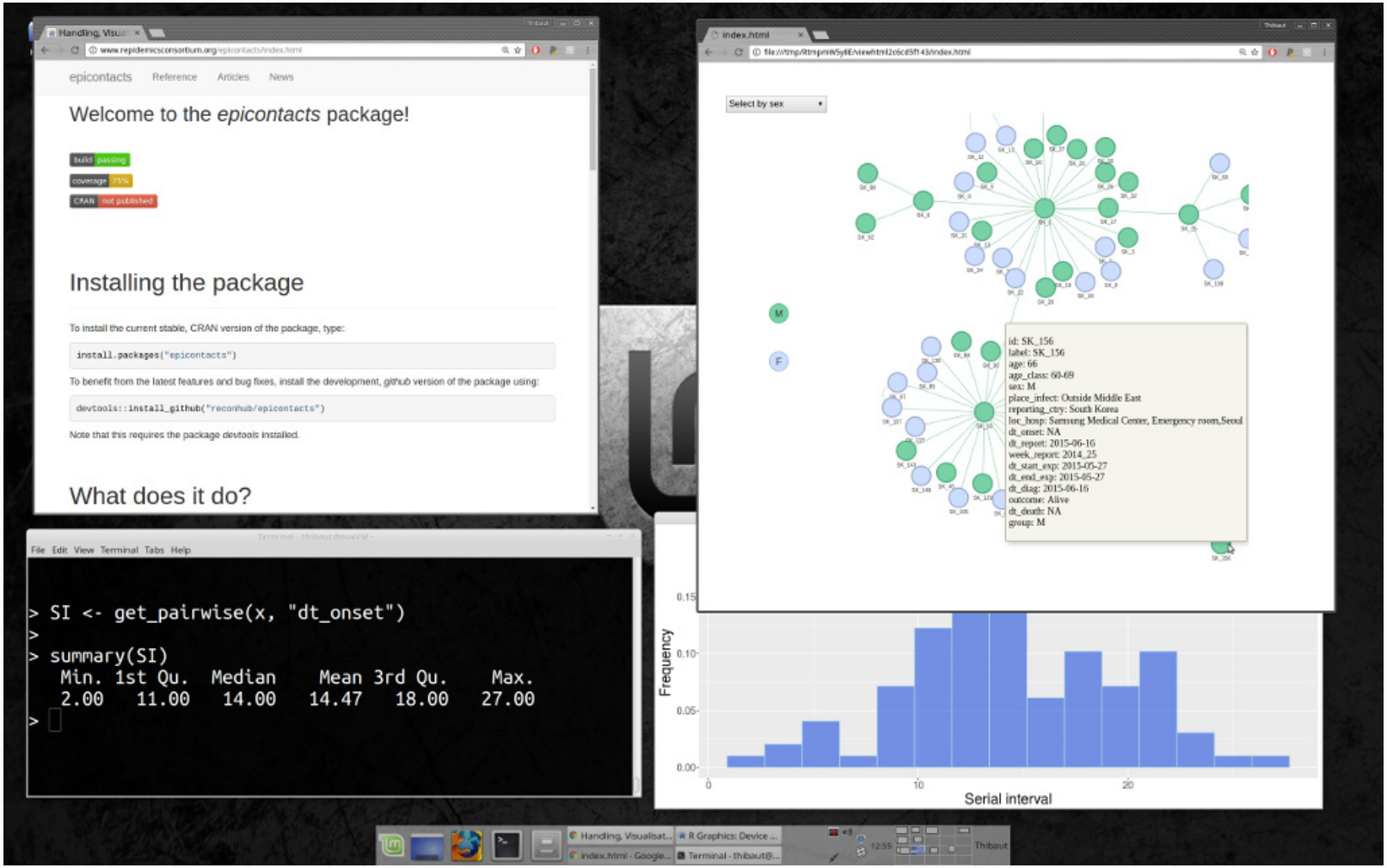
incidence: computation, handling, visualisation and modelling of epicurves



www.repidemicsconsortium.org/incidence

[released]

epicontacts: handling, visualisation and analysis of epidemiological contacts



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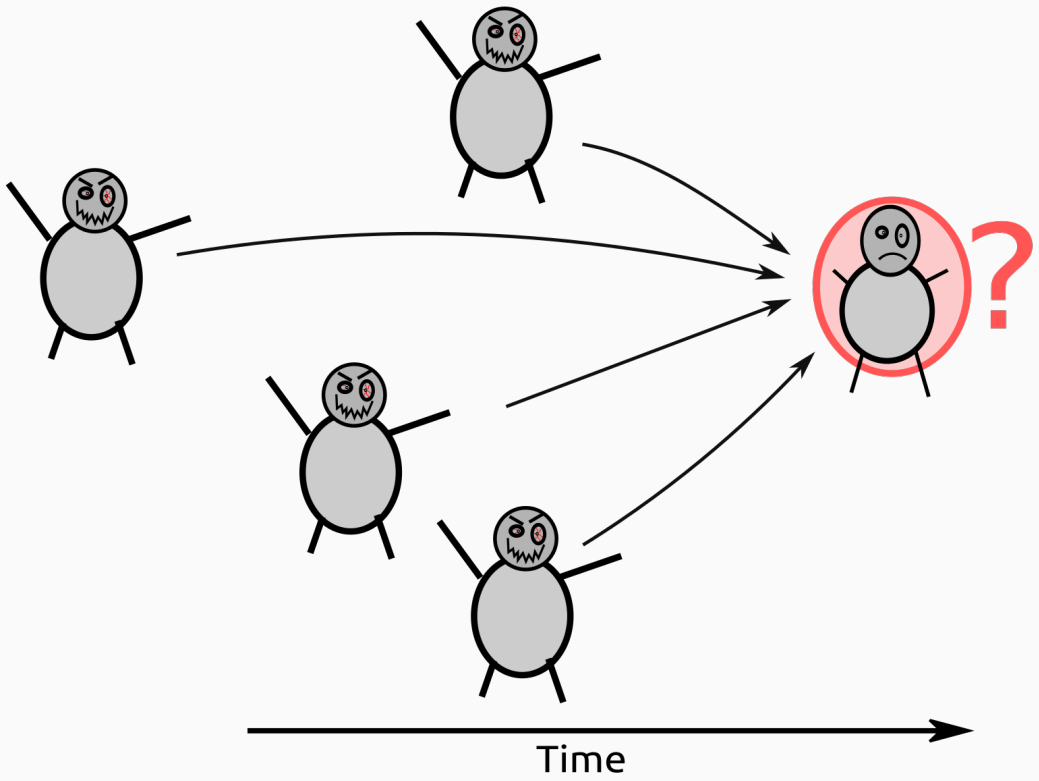
[release February 2017]

outbreaker: infering who infects whom from epi/genetic data (1/2)

Use timing of symptoms and pathogen genomes to infer infectors

(Jombart *et al*, PLoS Comp Biol, 2014)



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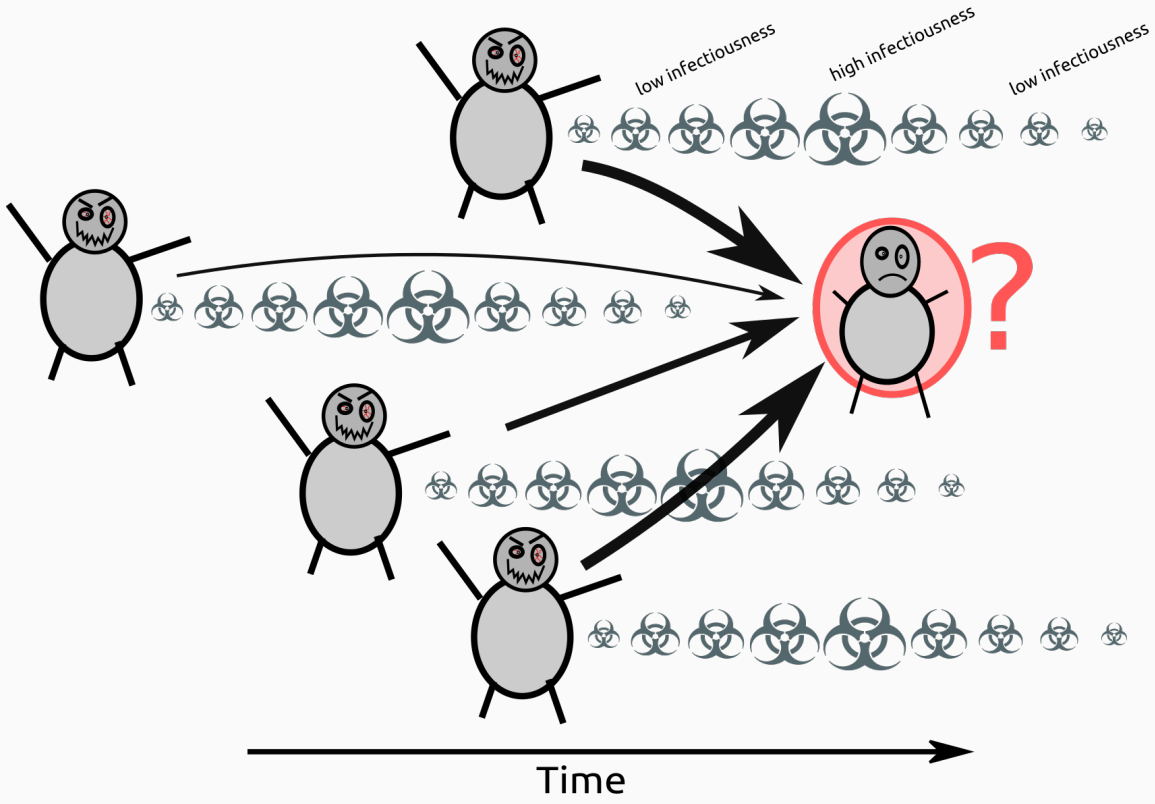

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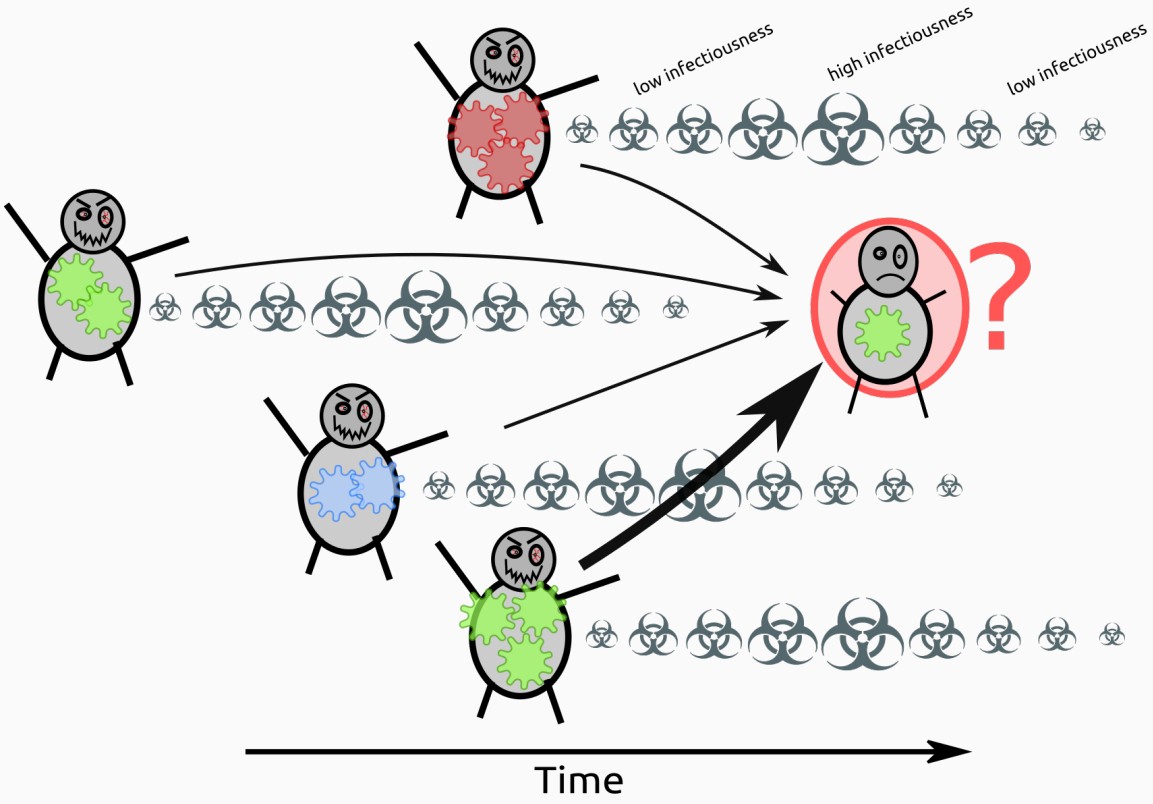

outbreaker: infering who infects whom from epi/genetic data (2/2)

General approach

- Bayesian framework
- augmented data for ancestries, infection dates, unobserved cases
- MCMC (Metropolis-Hasting) to sample from posterior
- identification of imported cases (outliers)

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Likelihood

- $p(\text{transmission tree}) = \prod_i p(\text{branch}_i)$
- $p(\text{branch}) = p(\text{infection date}) \times p(\text{collection date}) \times$
  $p(\text{unobserved cases}) \times p(\text{genetic variation})$

outbreaker: detail of epidemiological likelihood

Likelihood for case i with ancestor α_i:

$$
\begin{aligned}
&p(\text{collection date}) \times p(\text{infection date}) \times p(\text{unobserved cases}) \\
&= p(t_i|T_i^{inf}) \times p(T_i^{inf}|\alpha_i, T_{\alpha_i}^{inf}, \kappa_i) \times p(\kappa_i|\pi) \\
&= f(t_i - T_i^{inf}) \times w^{(\kappa_i)}(T_i^{inf} - T_{\alpha_i}^{inf}) \times f_{\mathcal{G}}(1|\kappa_i - 1, \pi)
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with:

- t_i: collection date of i
- T_i^{inf}: date of infection of i
- κ_i: number of generations between i and α_i
- π: proportion of the outbreak sampled
- f: distribution of colonisation duration (assumed known)
- w: distribution of generation time ($w^{(\kappa_i)}$: κ_i convolutions of w; w assumed known)
- $f_{\mathcal{G}}$: geometric distribution

outbreaker: detail of genetic likelihood

Likelihood for case i with ancestor α_i:

$$\mu^{d(s_i, s_{\alpha_i})}(1-\mu)^{(\kappa_i \times l(s_i, s_{\alpha_i})) - d(s_i, s_{\alpha_i})}$$

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with:

- s_i: sequence of i
- μ: mutation rate
- $d(s_i, s_{\alpha_i})$: number of mutations between case i and α_i
- κ_i: number of generations between i and α_i
- $l(s_i, s_{\alpha_i})$: number of comparable sites between s_i and s_{α_i}

The R package *outbreaker*

Original implementation aimed at computer efficiency:

- C implementation embedded within R package
- multi-platform: linux, MacOS X, Windows, Solaris, ...
- supports parallelization
- post-processing of MCMC, simulations, graphics
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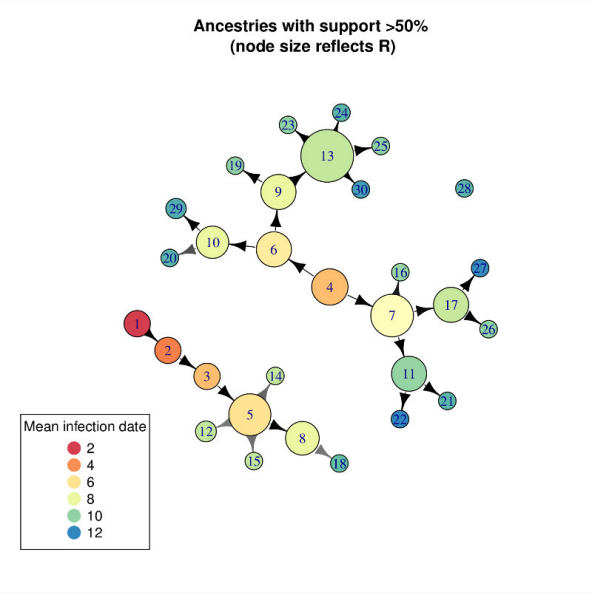
New methods emerged since.

Methods differ by their treatment of genetic data



[*outbreaker*]

Quick and dirty

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- less accurate but computer efficient
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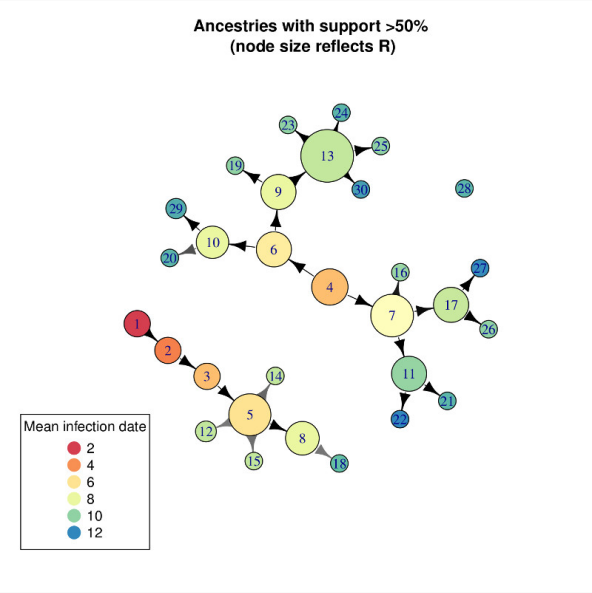

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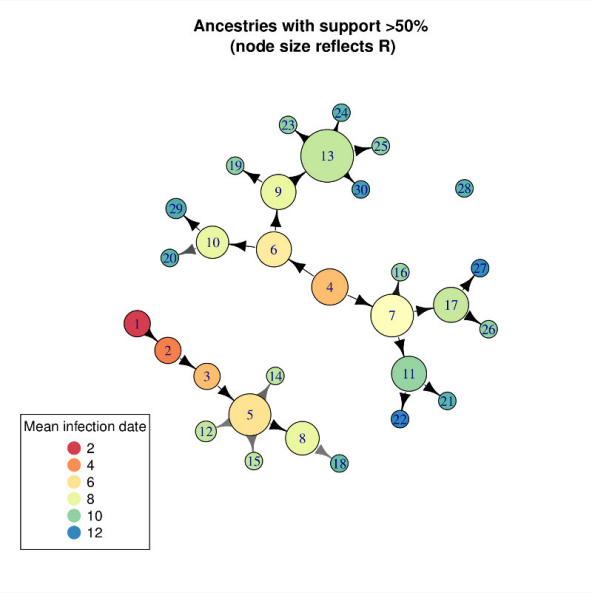

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Focus on genome sequences *vs* integrate various types of data.

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Can we find a general formulation for the different models?

What do these models look like?

- a, b, c: different types of data
- θ: parameters / augmented data

Different types of data often assumed to be *conditionally independent*:

$$p(a, b, c|\theta) = p(a|\theta)p(b|\theta)p(c|\theta)$$

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Components can be treated as plugins.

outbreaker2: a general cauldron for cooking methods

Use-your-own: data type, likelihood, prior, MCMC.

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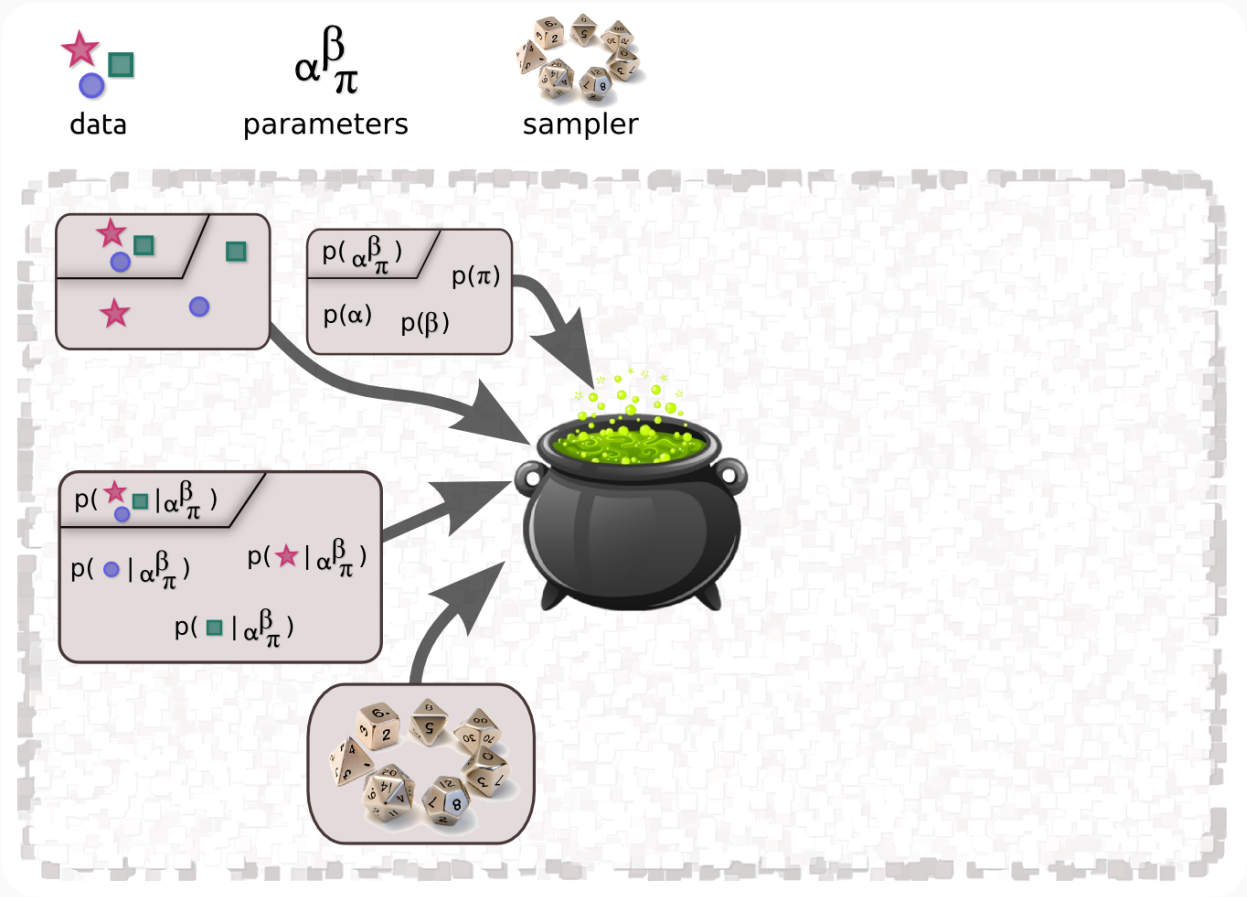

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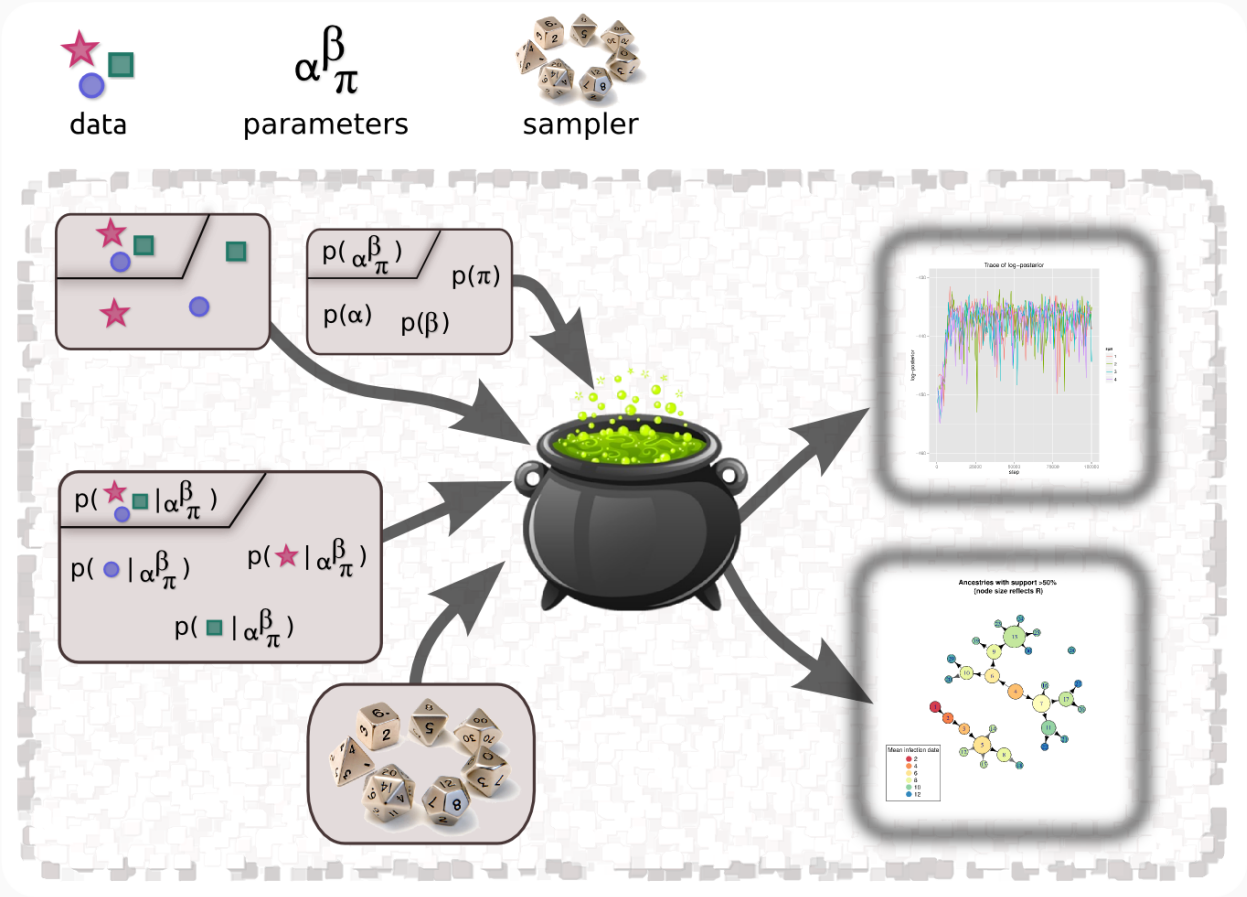

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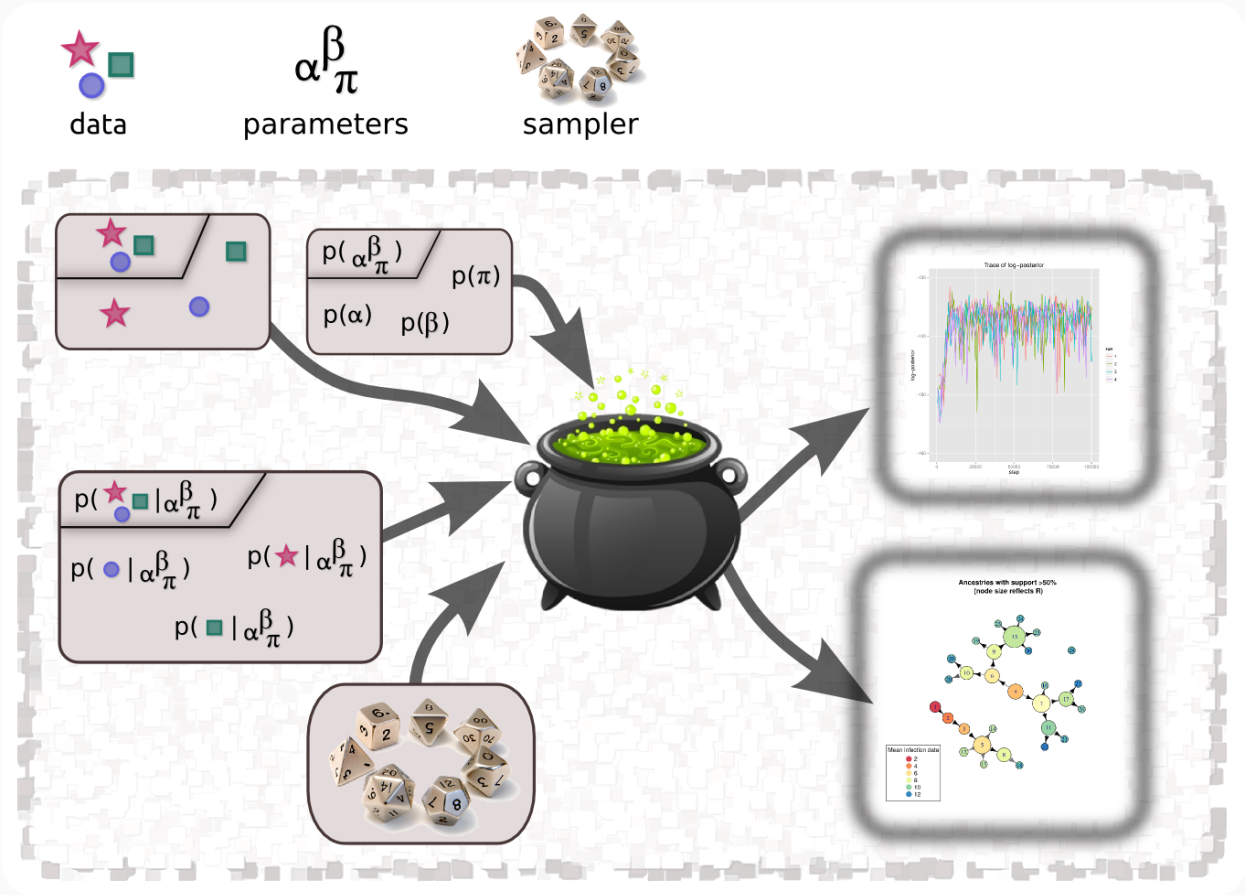
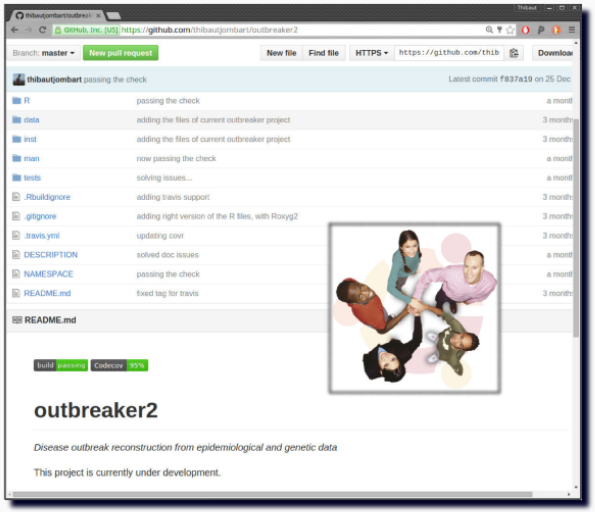
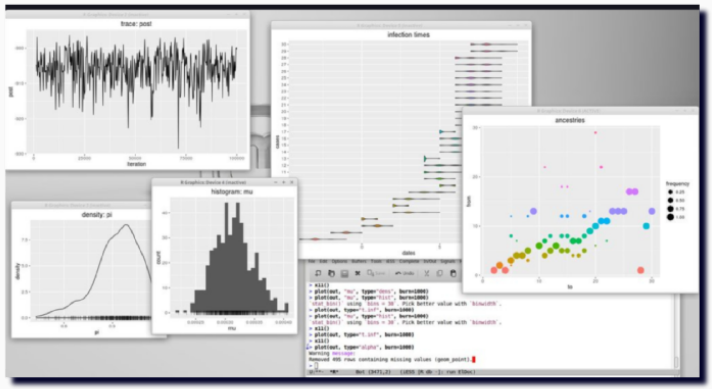


Modularity is key to generalising approaches

outbreaker2: a general tool for outbreak reconstruction





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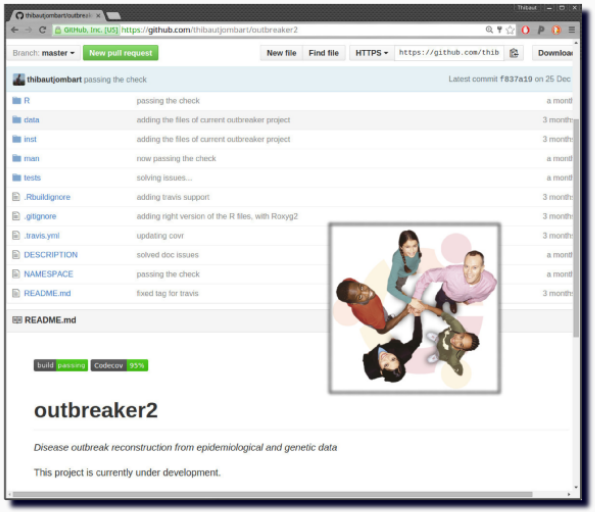

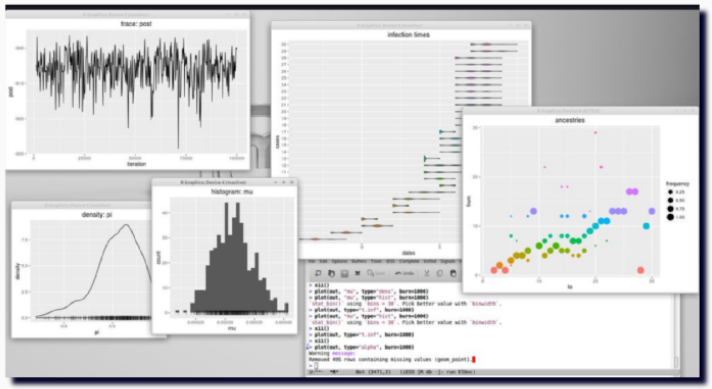

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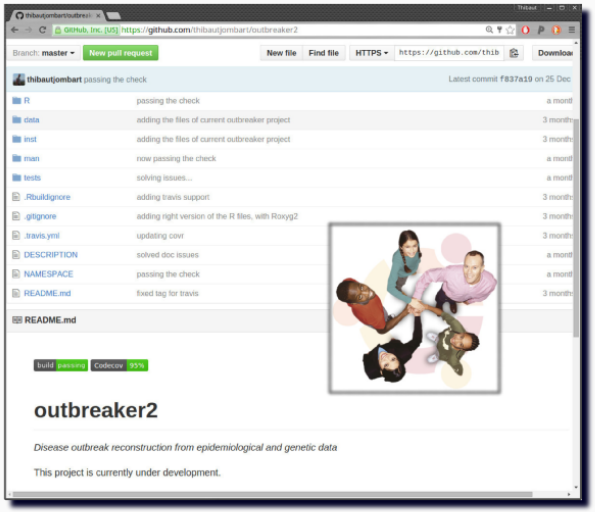

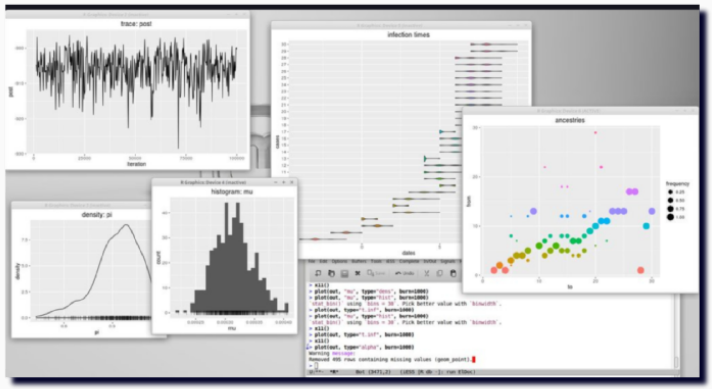

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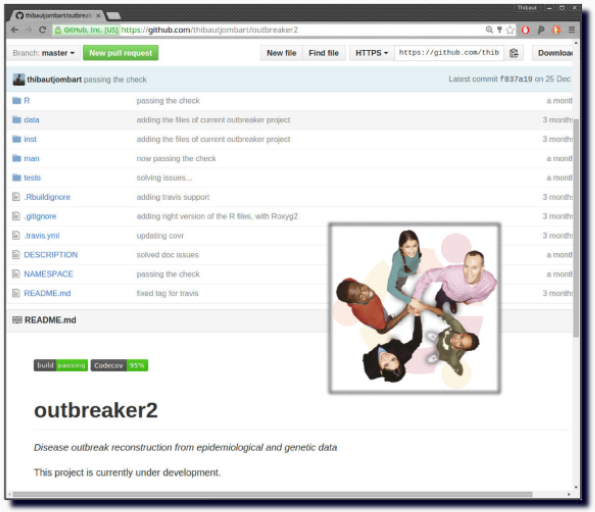

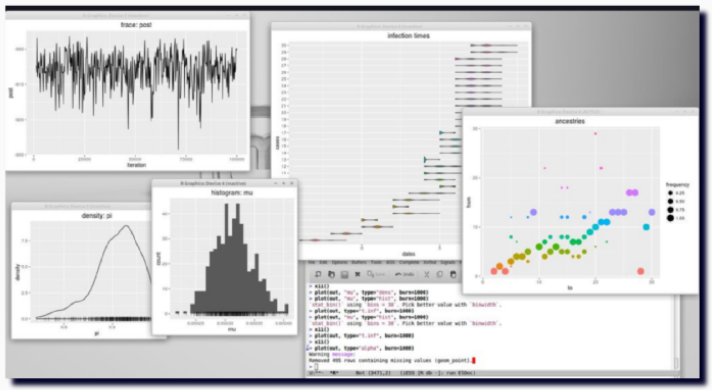

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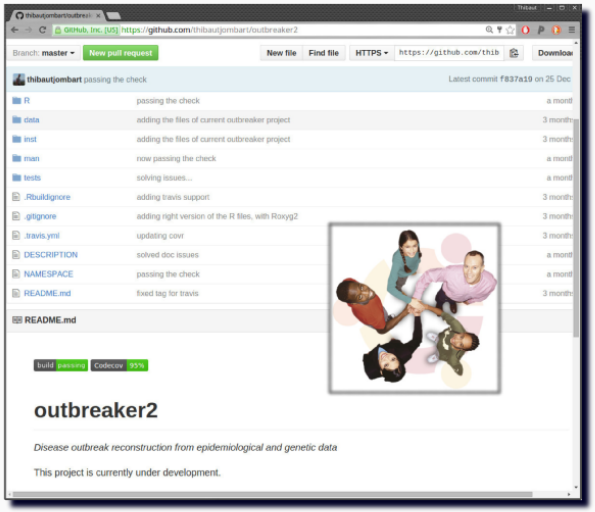

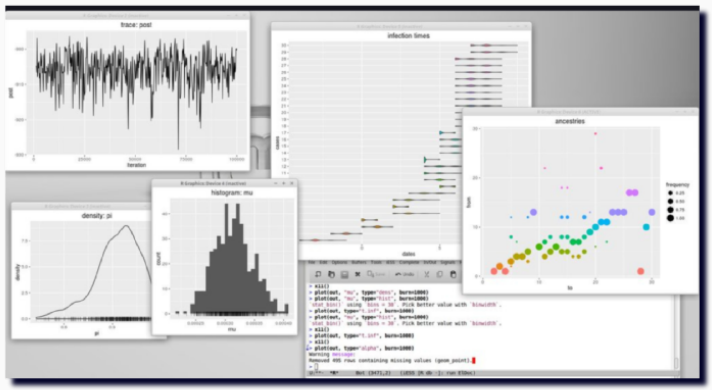

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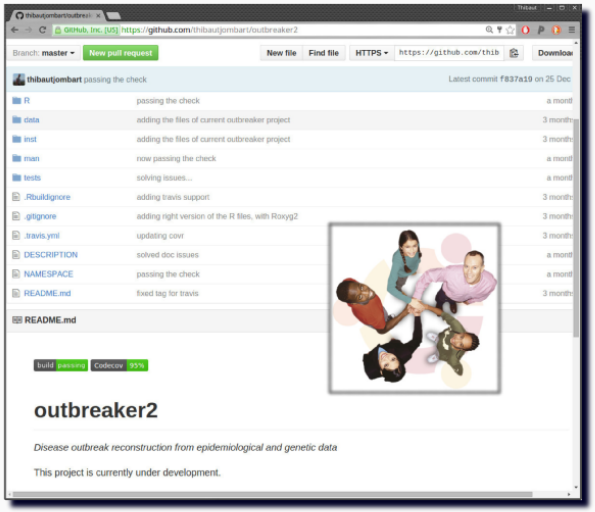

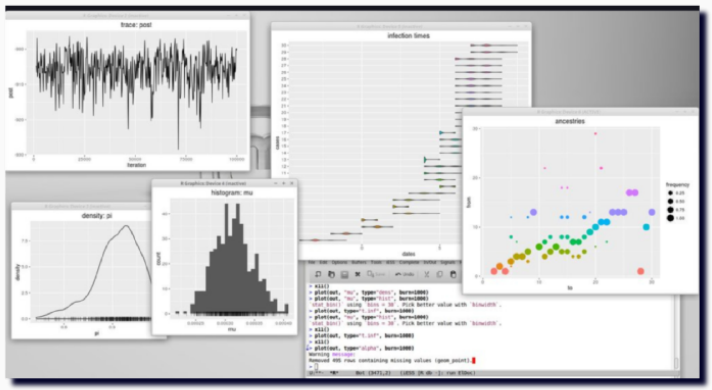

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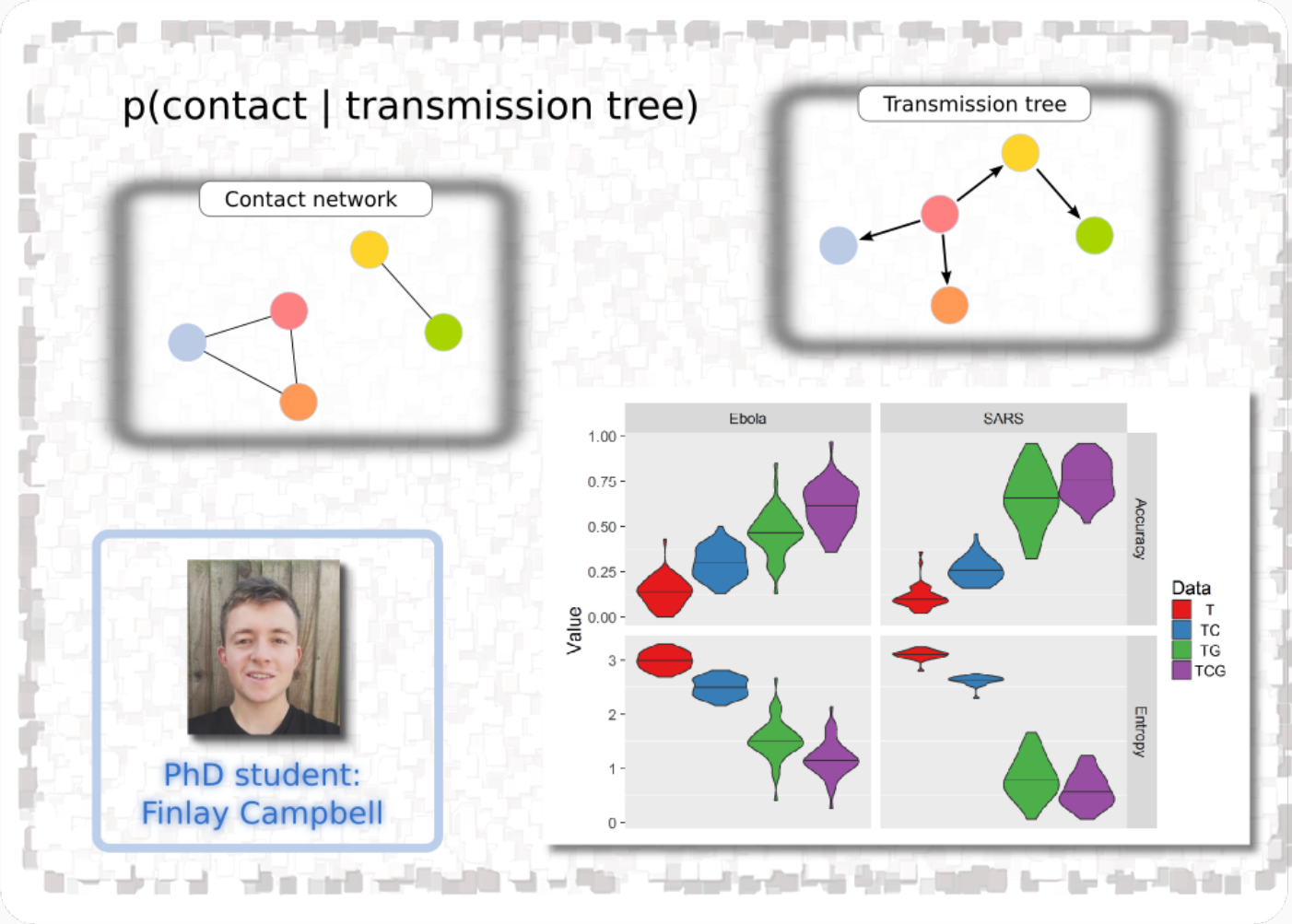
- **prettier**: plot methods using *ggplot2*, interactive networks visualisation
- should facilitate new contributions

outbreaker2 developments: contact data

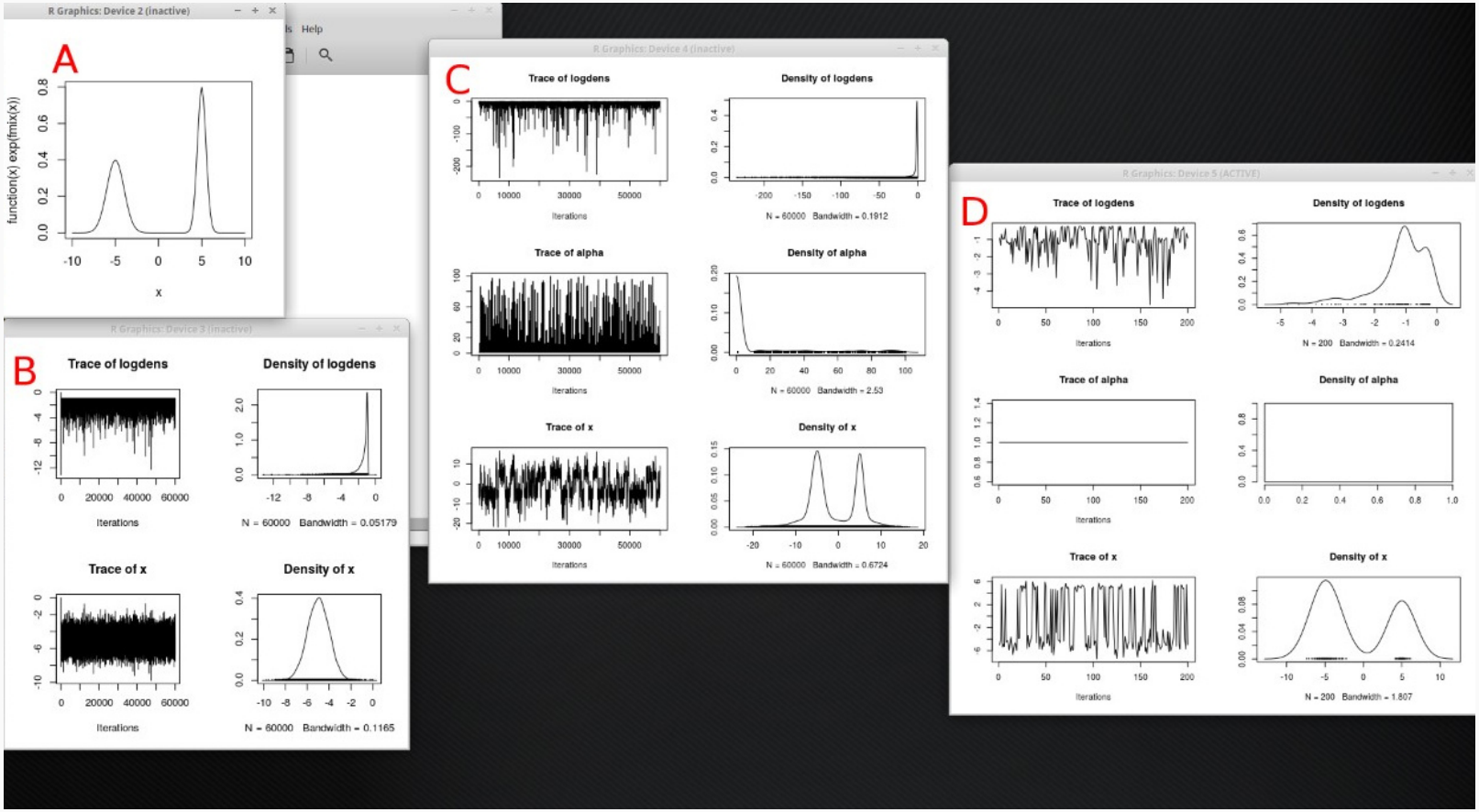
Integration of contact data for improving tree reconstruction.



[collaboration with Neil Ferguson & Anne Cori]

outbreaker2 developments: eMCMC

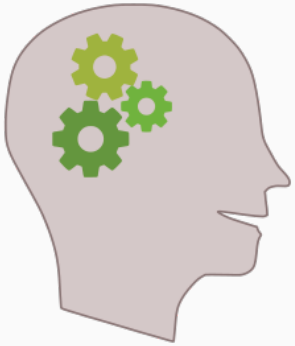
Eruptive MCMC: a new MCMC to sample from multi-modal densities



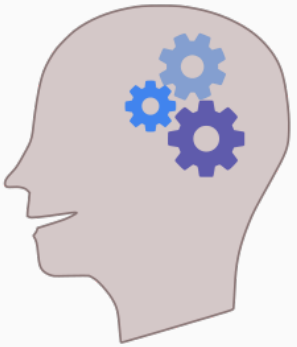
[collaboration with Jukka Corander]

Methodological dialogue

Methodological development relies on an interdisciplinary dialogue



Epidemiologist



Methodologist

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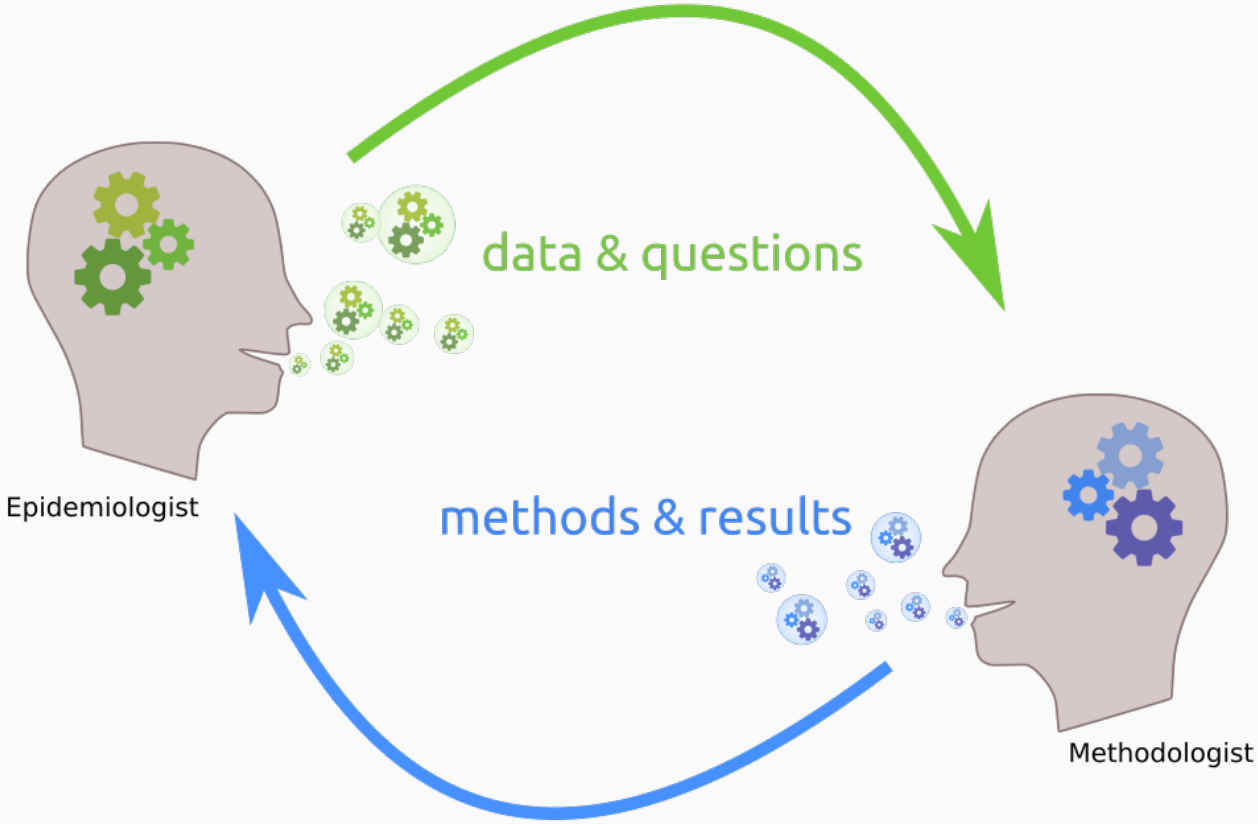

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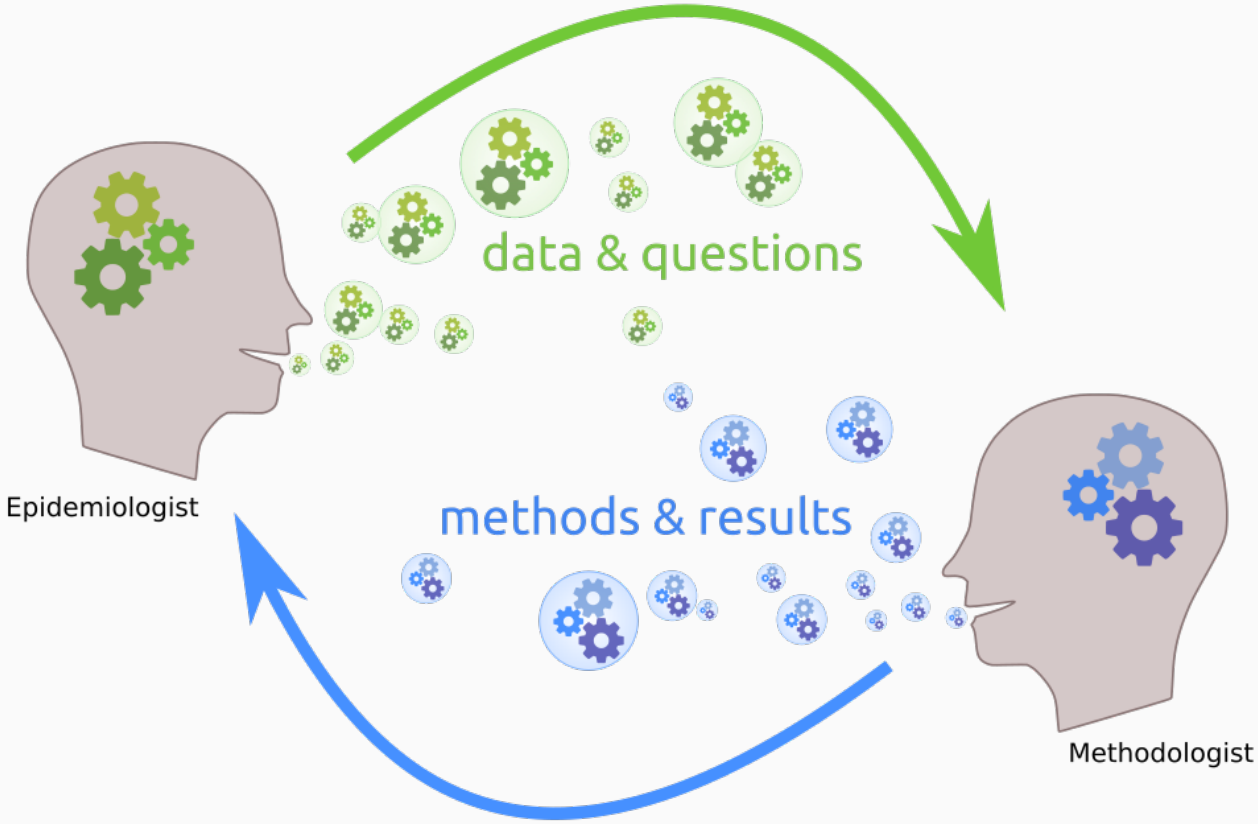

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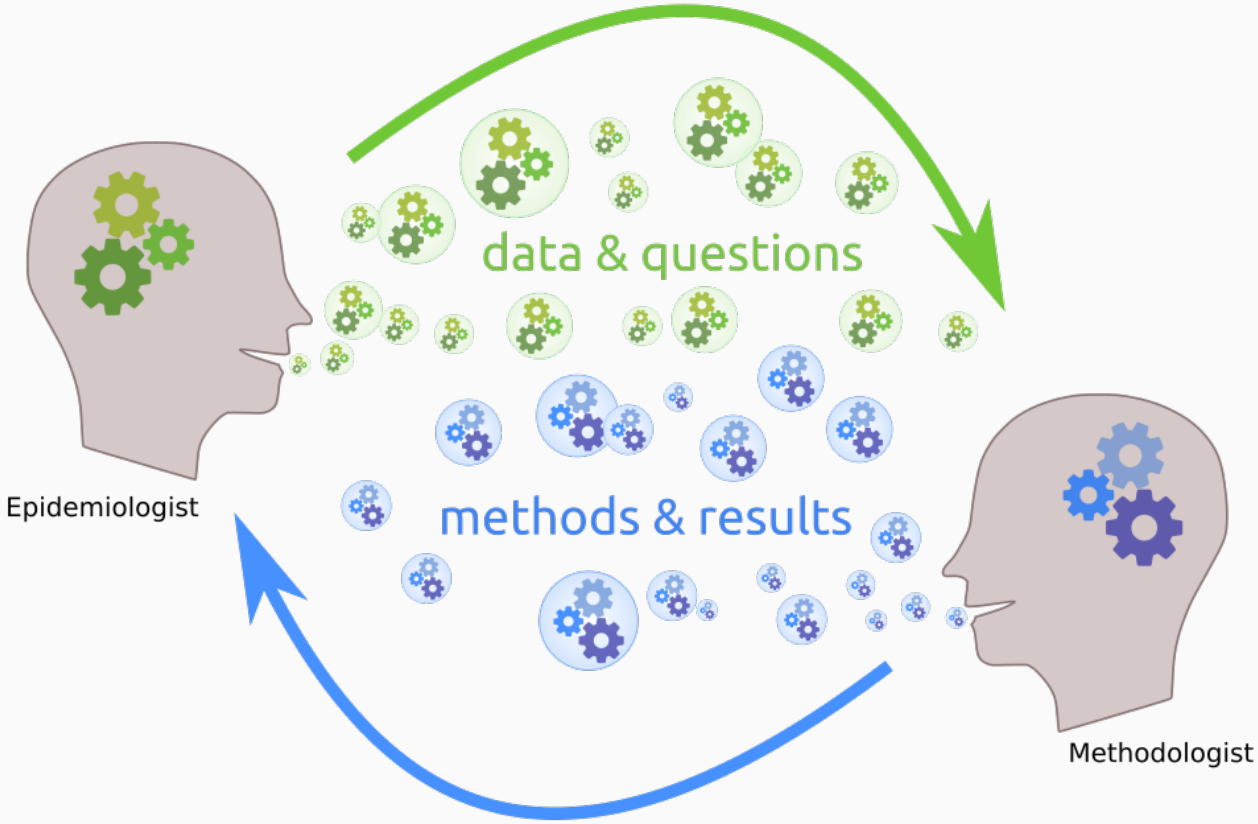

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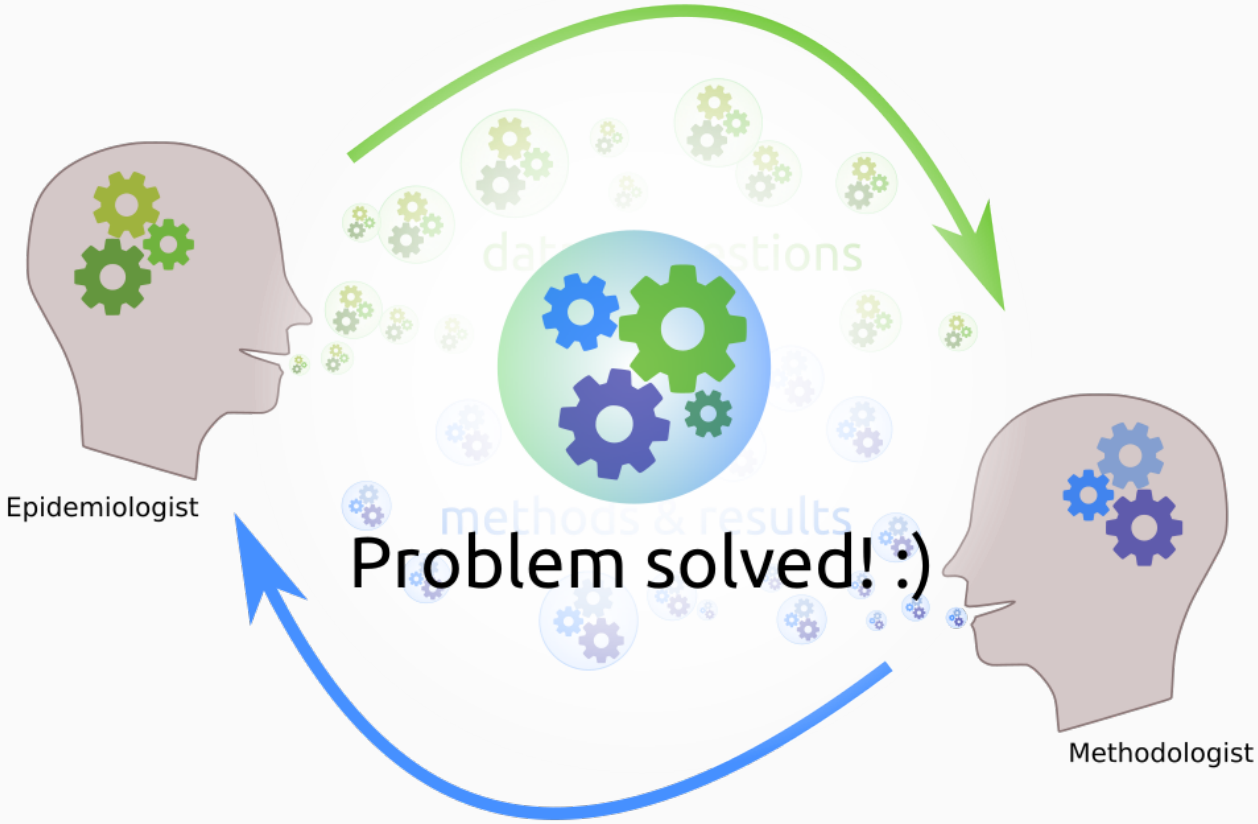

Outbreak response context creates distance and delays

Affected countries

data collection

Outbreak response context creates distance and delays

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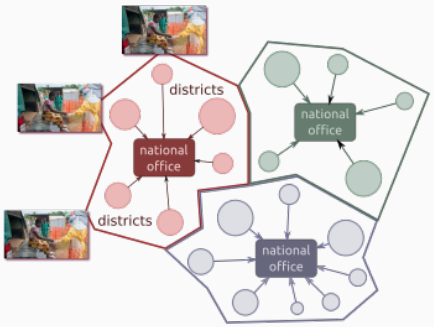

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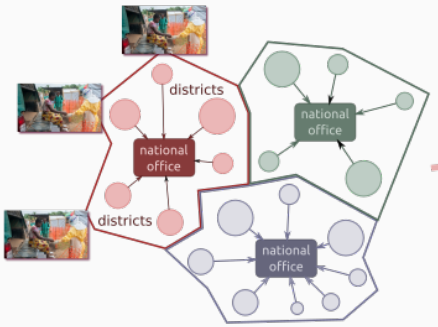
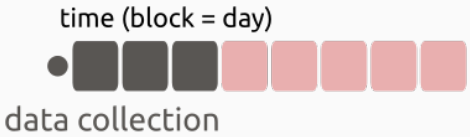


Affected countries

Public Health agencies



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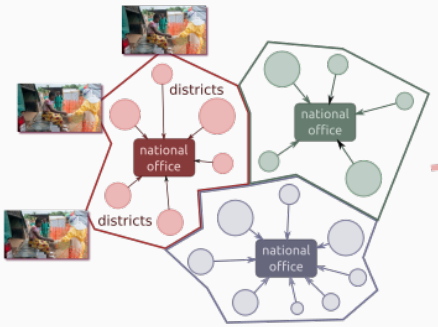


Affected countries

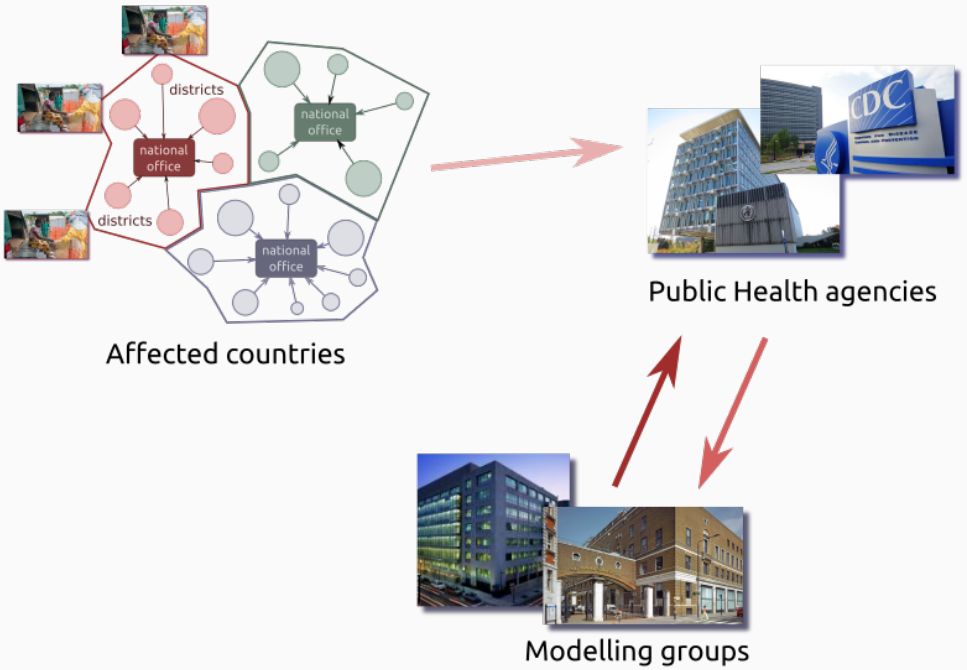
Public Health agencies

Modelling groups

time (block = day)

data collection

Outbreak response context creates distance and delays



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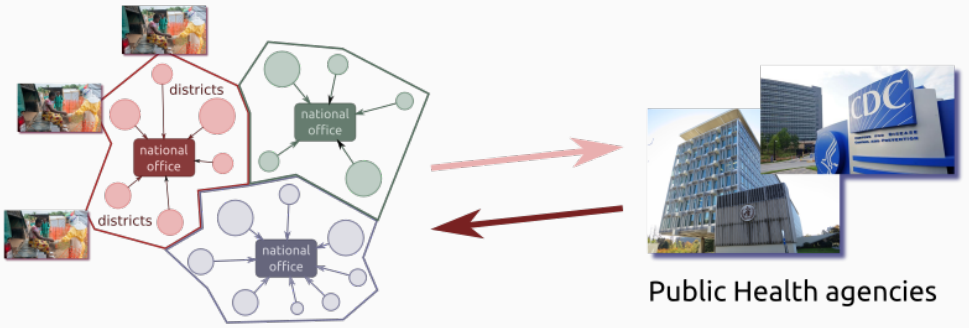

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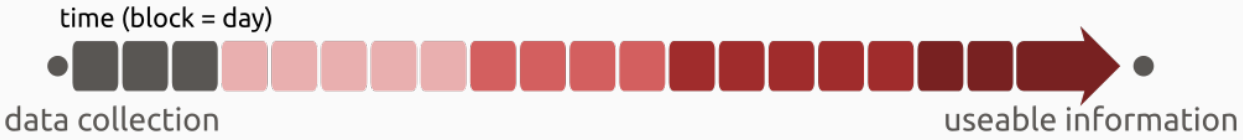

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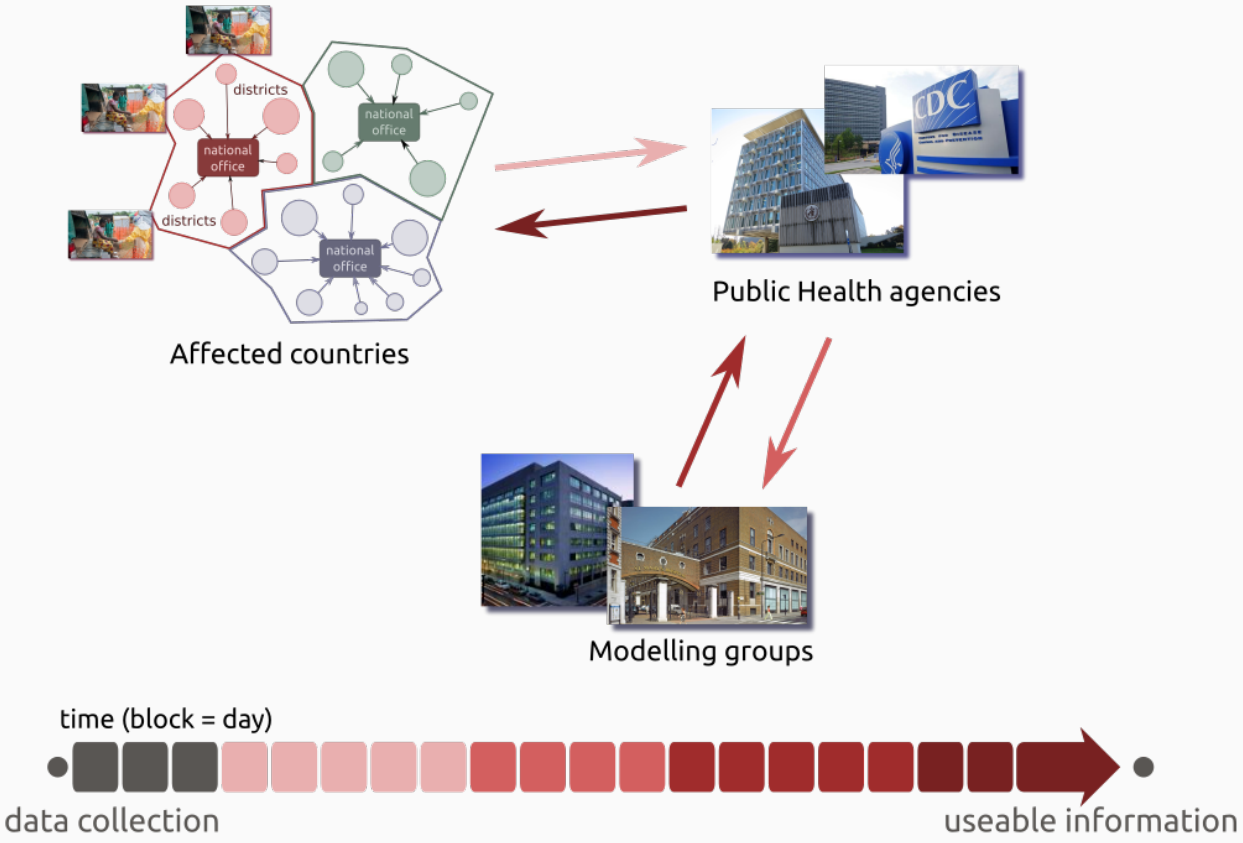
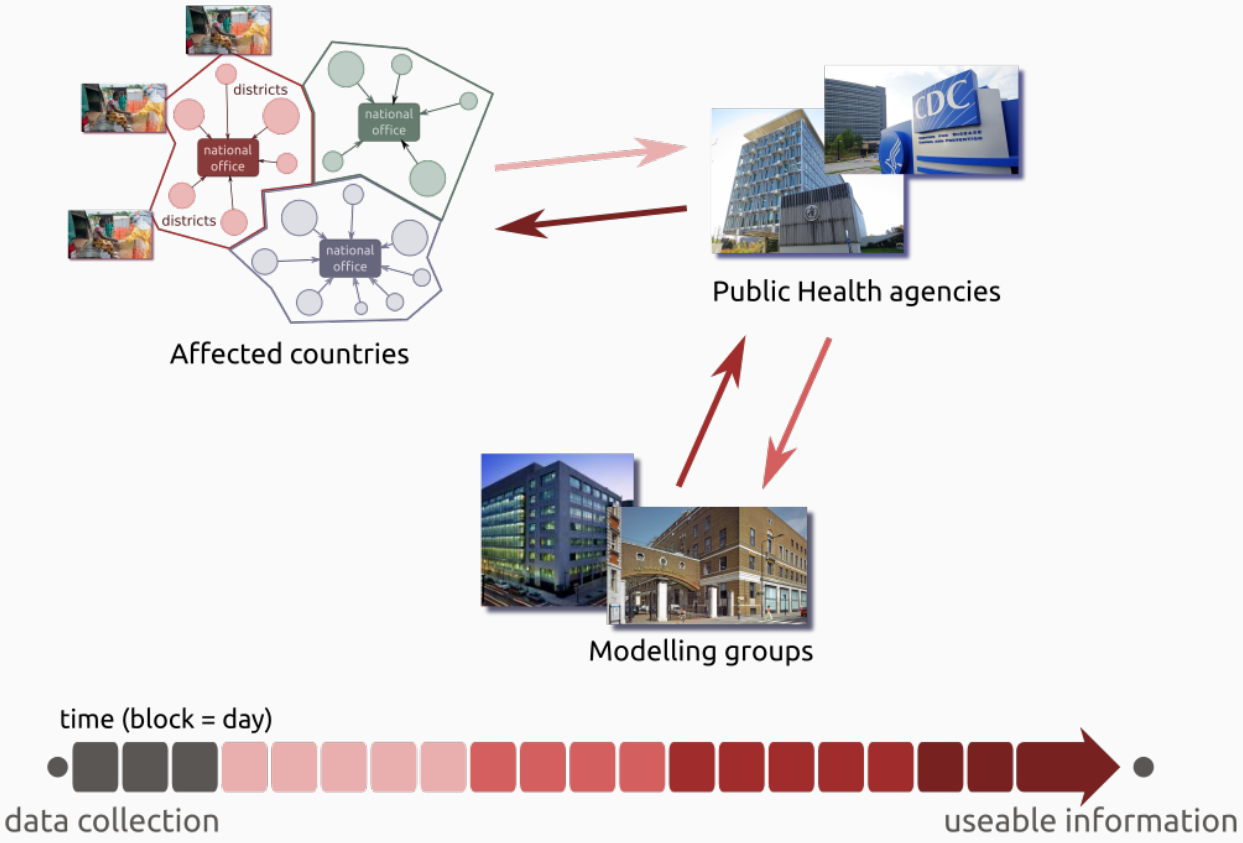


- efficient tools can shorten delays

Outbreak response context creates distance and delays



- efficient tools can shorten delays
- potential of embedding methodologists in outbreak response teams

Summary

- outbreak response creates its own methodological field

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- RECON is a joint effort for addressing these challenges through free, open-source statistical software development
- **We are recruiting!**
  Check 'news' on `www.repidemicsconsortium.org`

Thanks to...

- **Vincent Daubin**
- **Imperial College:** Neil Ferguson, Rich Fitzjohn, Anne Cori, Finlay Campbell, Evgenia Markvardt, James Hayward
- **UC Berkeley:** Karthik Ram
- **Groups:** WHO Ebola Response Team, Hackout 1/2/3, RECON members, GOARN
- **funding:** HPRU-NIHR, MRC

More on:

www.repidemicsconsortium.org

Questions?