Approximate Bayesian Computation

Sarah Filippi

Imperial College London

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SUMMARY OF MY RESEARCH

Computational statistics for biomedical problems

Stochastic models for biomedical problems

Understand

- causes of disease,
- mechanisms of their development,
- new treatment

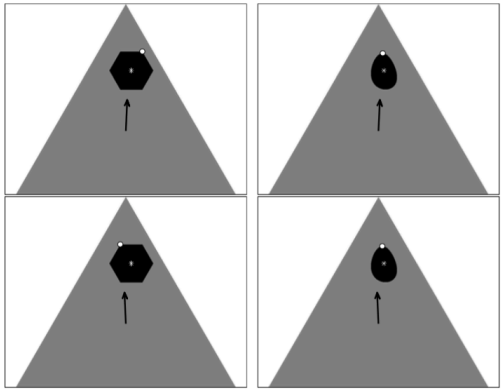
from (potentially large) datasets in 'omics and clinical studies.

Statistical machine learning methodological development

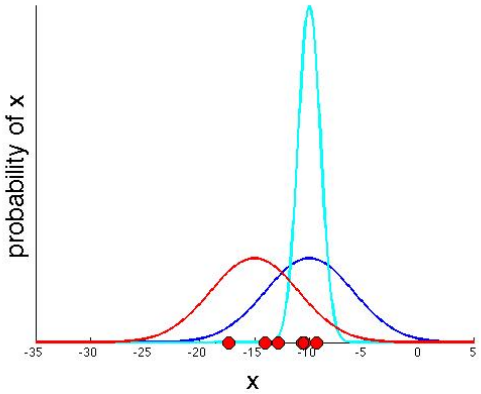
Develop methods that are

- scalable,
- robust
- flexible,
- take into account uncertainty in data-generating process.

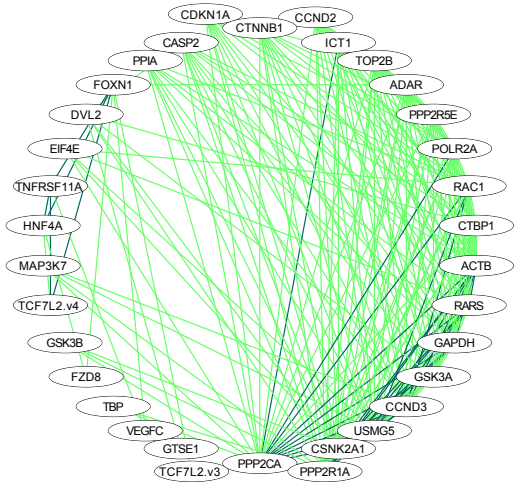
SOME OF MY RESEARCH INTERESTS



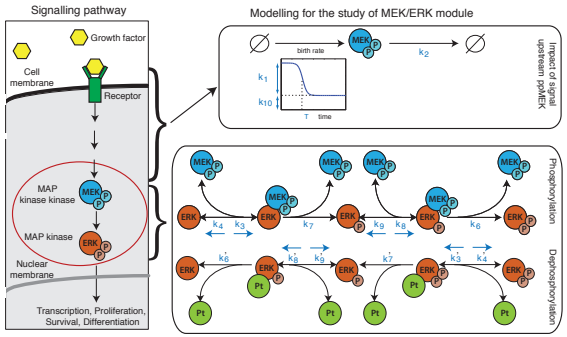
Decision process under uncertainty



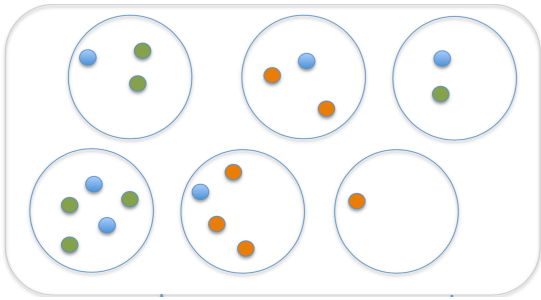
Bayesian (non-parametric) inference procedure



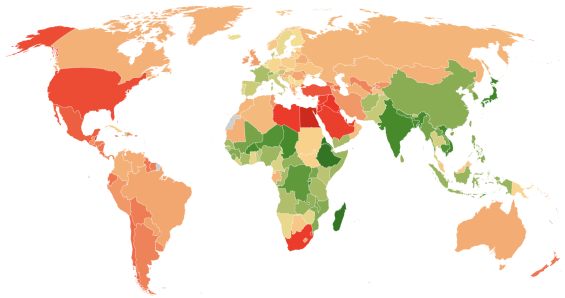
Measures of association and causal inference



Systems biology for biomedicine

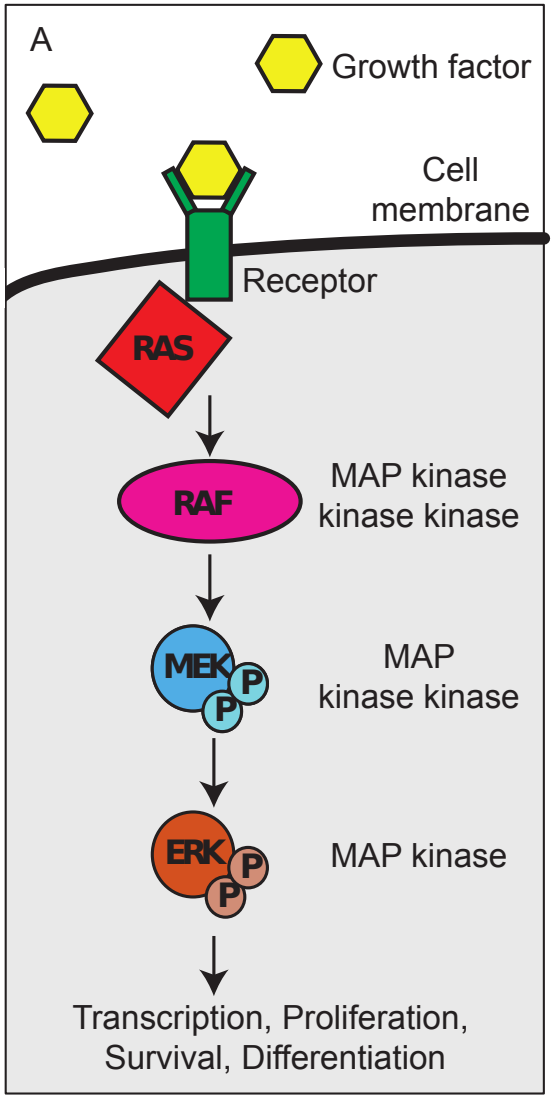


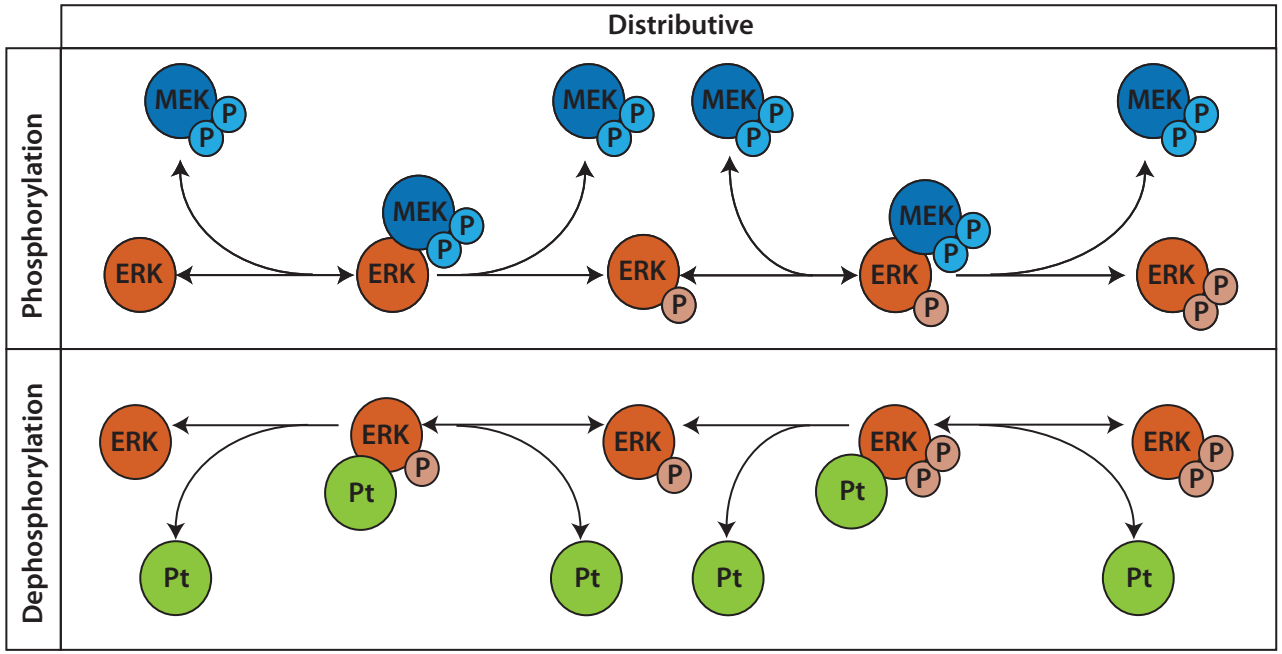
Single-cell genomics and proteomics

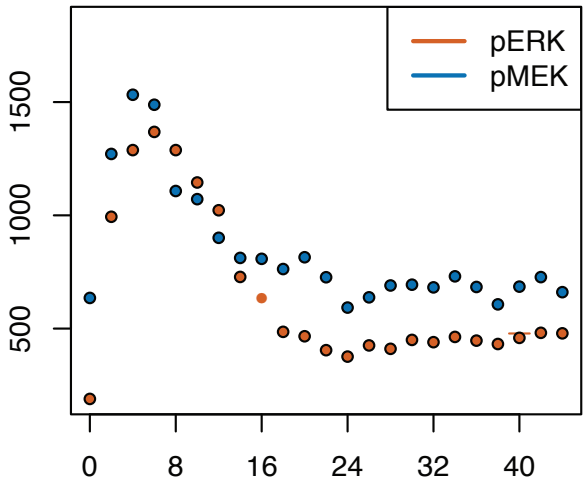


Global health

PARAMETER INFERENCE IN A SIGNALLING PATHWAY







Model via differential equations

Species	9
Parameters	16
Initial conditions	2

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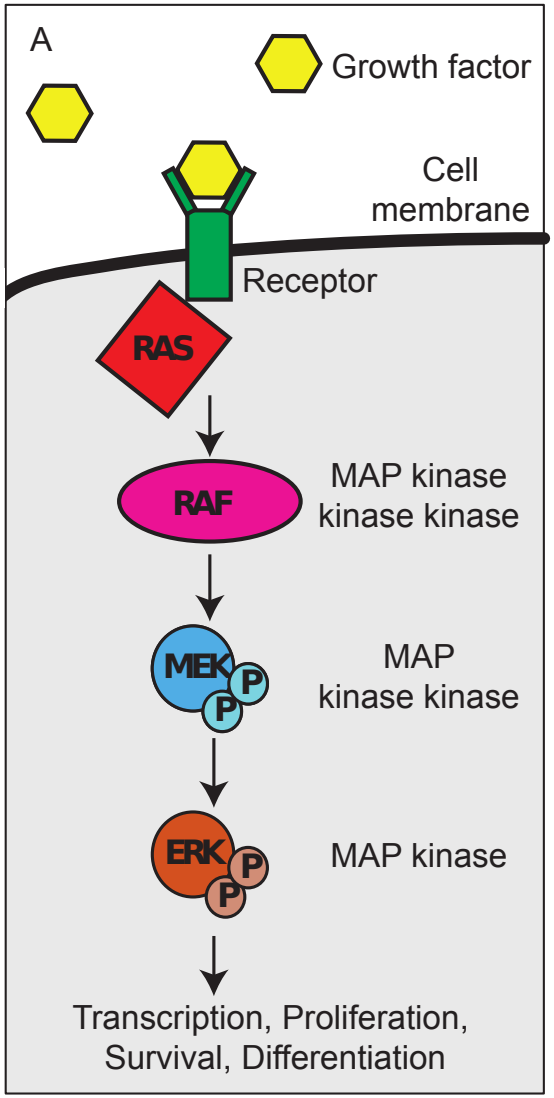

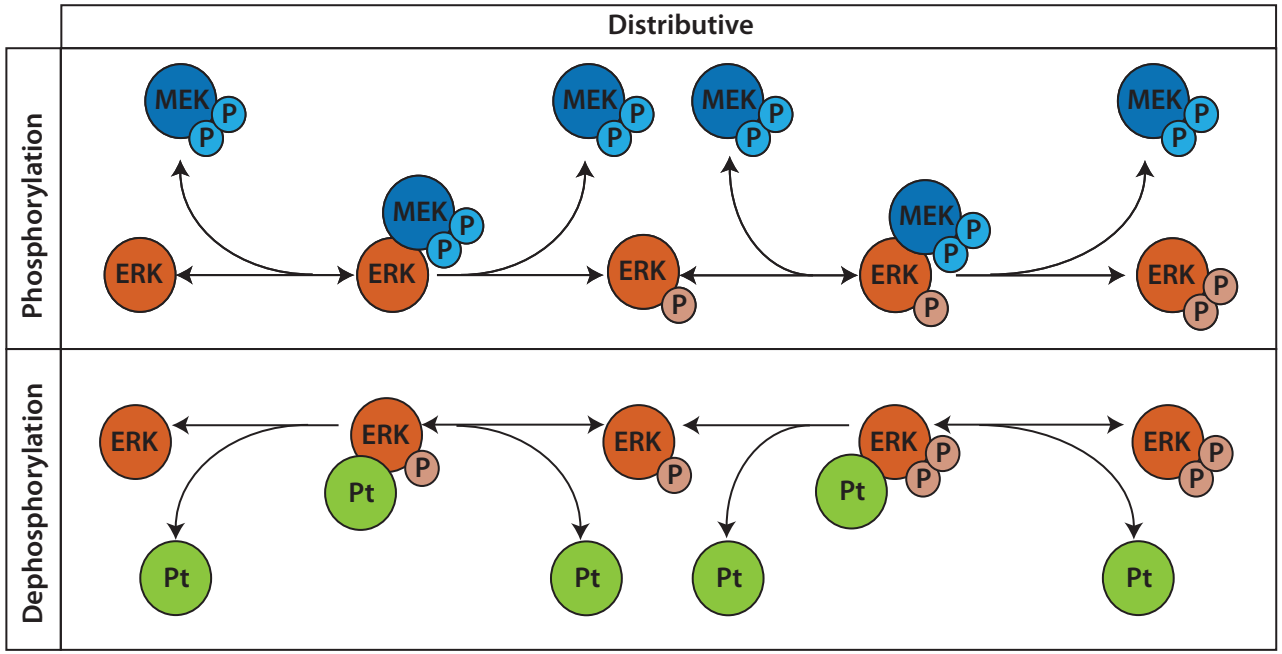

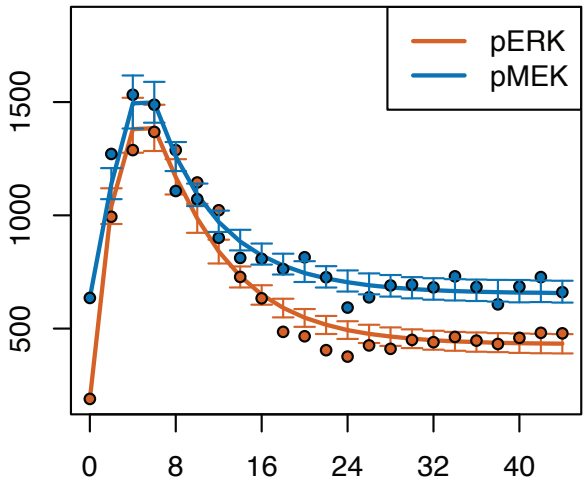

Model via differential equations

Species	9
Parameters	16
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What is Approximate Bayesian Computation?

- Approximate Bayesian Computation (ABC) is a statistical framework for bayesian parameter inference and model selection.
- It only requires to be able to simulate data from a model.
- It is also referred to likelihood-free inference.

NOTATIONS

We have:

- an observed dataset, denoted by x^*
- a parametric model, either deterministic or stochastic.

Model = data-generating process:
given a value of parameter $\theta \in \mathbb{R}^d$, the output of the system is

$$X \sim f(\cdot|\theta)$$

The likelihood function: $\theta \mapsto f(x^*|\theta)$

Aim:

- parameter inference: determine how likely it is for each value of θ to explain the data
- model selection: rank candidate models in terms of their ability to explain the data

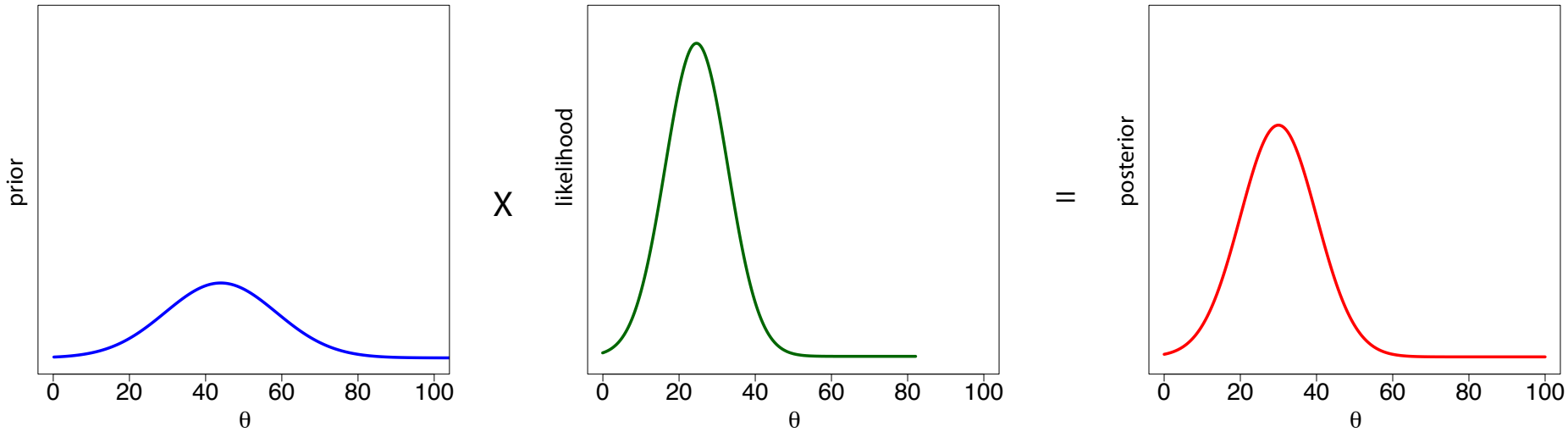
BAYESIAN METHODS

In the Bayesian framework, we combine

- the information brought by the data x^*, via the likelihood $f(x^*|\theta)$
- some a priori information, specified in a prior distribution $\pi(\theta)$

These informations are summarized in the posterior distribution, which is derived using the Bayes formula:

$$\pi(\theta|x^*) = \frac{f(x^*|\theta)\pi(\theta)}{\int f(x^*|\theta')\pi(\theta')d\theta'}$$



SAMPLE FROM THE POSTERIOR DISTRIBUTION

- In general, no closed-form solution of the posterior distribution
- Use computer simulation and Monte-Carlo techniques to sample from the posterior distribution
- Typical likelihood-based approaches:
  - Importance sampling
  - Markov Chain Monte-Carlo (MCMC)
  - Population Monte-Carlo
  - Sequential Monte-Carlo (SMC) sampler
  - ...

What if we can not compute the likelihood?

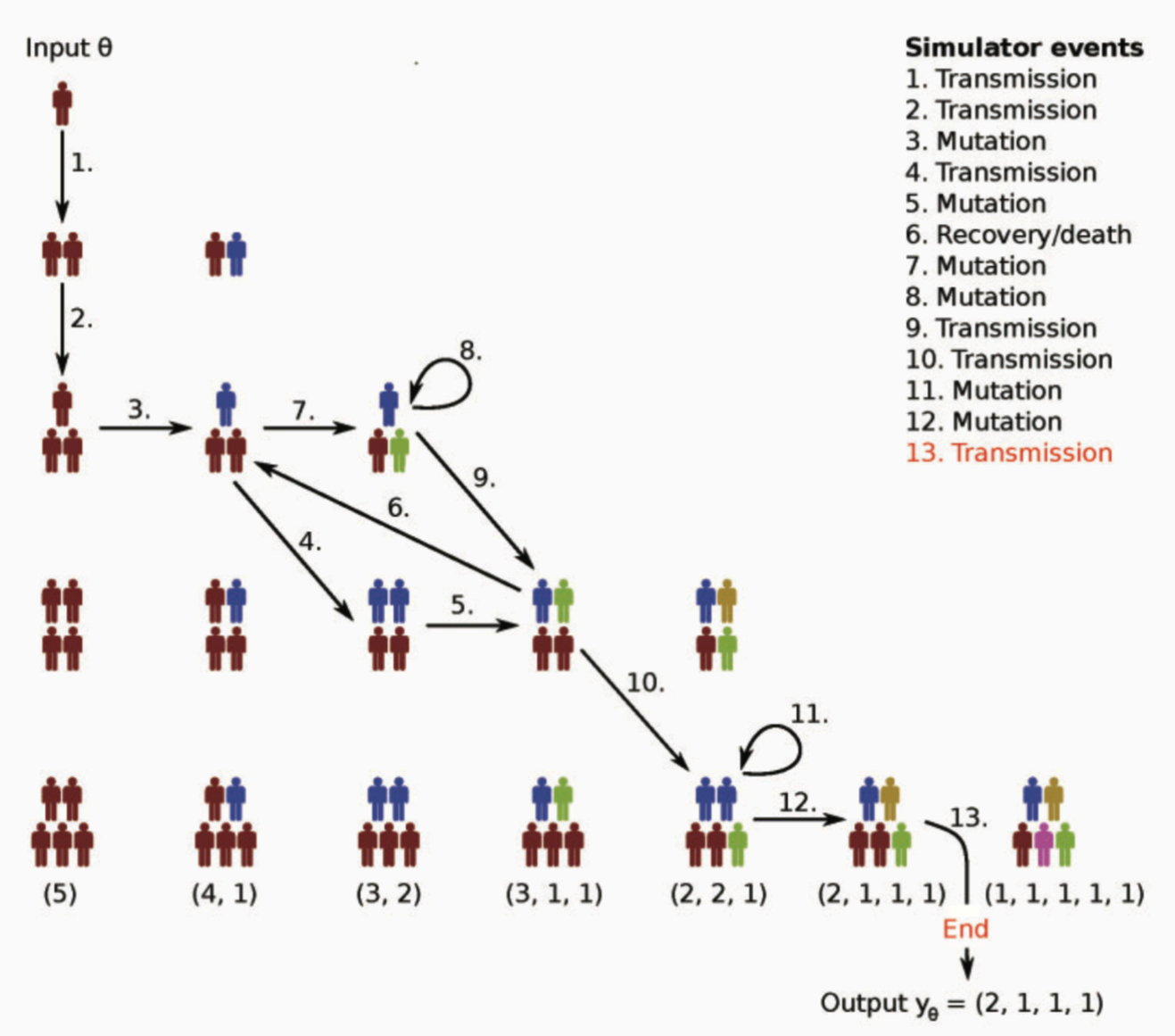
In many applications of interest: either impossible or computationally too expensive to evaluate the likelihood.

Domains of application include

- population genetics and evolutionary biology
- ecology
- infectious disease epidemiology
- astrophysic
- (biological) processes described by stochastic differential equations
- ...

Use so called likelihood-free method such as Approximate Bayesian Computation (ABC).

EXAMPLE: THE SPREAD OF TUBERCULOSIS



[Tanaka et al, 2006; Figure credit:Lintusaari et al, 2017]

WHY IS ABC SO POPULAR?

ABC methods are popular in many areas, particularly in biological disciplines,

Approximate Bayesian Computation is the main tool for parameter inference for a complex simulator for which we can not calculate the likelihood function.

Other advantages:

- Simple to implement
- Intuitive
- Parallelizable

OUTLINE

Basic components of ABC

Approximate Bayesian Computation is a statistical framework for bayesian parameter and model selection that only requires:

- Observed data, x^*
- A simulator, typically stochastic, to simulate new data $z \sim f(\cdot|\theta)$
- A distance to compare simulated data and observed data
- A threshold for determining what is similar enough
- Computational ressources

An exact rejection algorithm

Given an observation x^*, keep jointly simulating

- parameter θ from the prior distribution : $\theta \sim \pi(\theta)$
- auxiliary variables z from the simulator: $z \sim f(z|\theta)$

until the auxiliary variable z is equal to the observed value $z = x^*$.

[Tavaré et al, 1997]

The outcome $\theta^{(1)}, \ldots \theta^{(N)}$ resulting from this algorithm is an i.i.d. sample from the posterior distribution since

$$f(\theta^{(i)}) \propto \int \pi(\theta^{(i)}) f(z|\theta^{(i)}) \mathbb{1}\{y = z\} dz = \pi(\theta^{(i)}) f(x^*|\theta^{(i)}) \propto \pi(\theta^{(i)}|x^*)$$

AN APPROXIMATE METHOD

When x^* is a continuous random variable, equality $z = x^*$ is replaced with a tolerance condition

$$d(x^*, z) \leq \epsilon$$

where d is a distance.

The output is not anymore distributed from the posterior distribution but from $\pi(\theta | d(x^*, z) \leq \epsilon)$.

[Pritchard et al, 1999]

ABC ALGORITHM

1: **Input:** observation x^*, number of particles N, threshold ϵ
2: **for** $i = 1, \ldots, N$ **do**
3: **repeat**
4: generate θ from the prior distribution $\pi(\cdot)$
5: generate z from the simulator $f(\cdot|\theta)$
6: **until** $d(z, x^*) \leq \epsilon$
7: set $\theta^{(i)} = \theta$
8: **end for**

OUTPUT OF THE ALGORITHM

The ABC rejection algorithm samples from the marginal in z of the joint distribution

$$\pi_\epsilon(\theta, z|x^*) = \frac{\pi(\theta)f(z|\theta)\mathbb{1}_{A_{\epsilon,x^*}}(z)}{\int \pi(\theta)f(z|\theta)\mathbb{1}_{A_{\epsilon,x^*}}(z)d\theta dz}$$

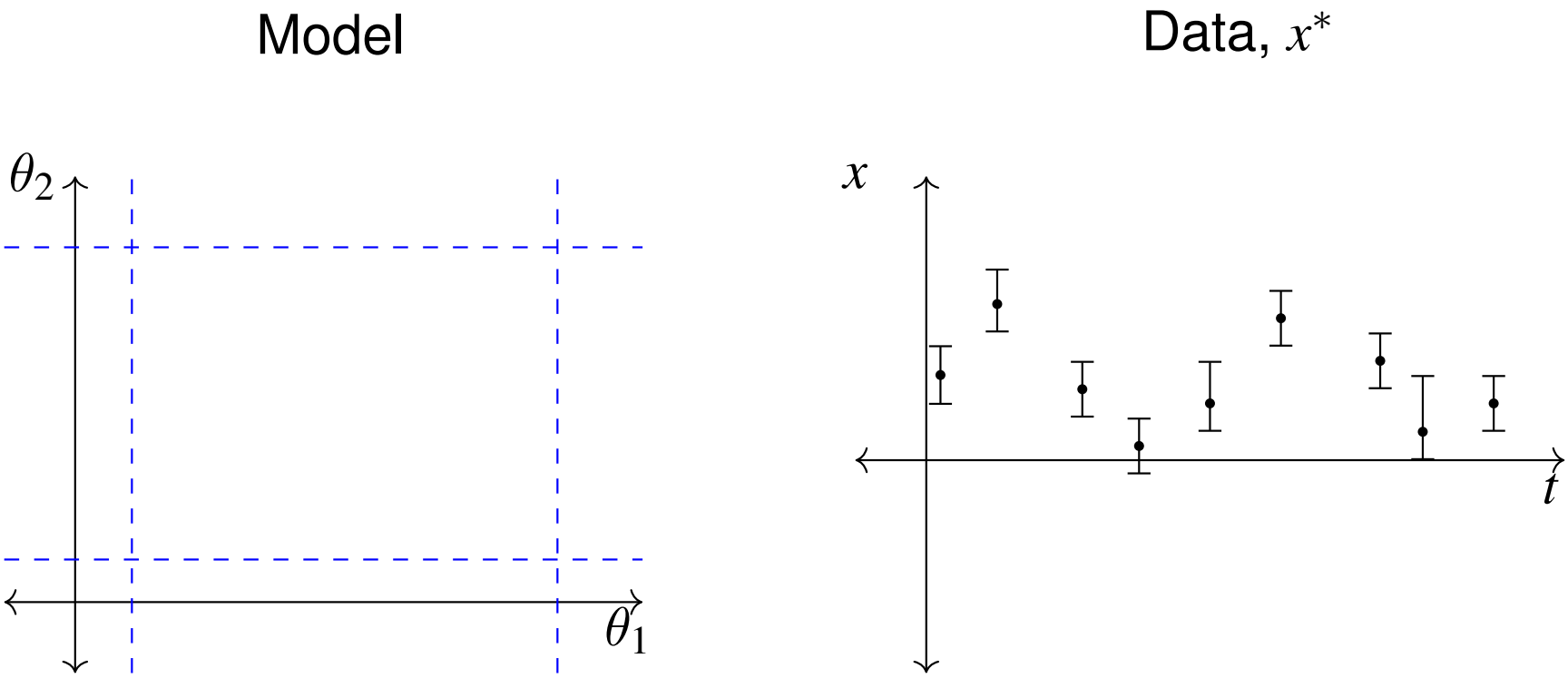
where $A_{\epsilon,x^*} = \{z \mid d(z, x^*) \leq \epsilon\}$.

The basic idea behind ABC is that using a small enough tolerance threshold ϵ coupled with a representative enough summary statistic η produce a good enough approximation of the posterior distribution, i.e.

$$\pi_\epsilon(\theta|x^*) = \int \pi_\epsilon(\theta, z|x^*)dz \approx \pi(\theta|x^*)$$

[Marin et al, 2012]

ILLUSTRATION OF THE ABC REJECTION ALGORITHM



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Toni & Stumpf, Bioinformatics (2010)

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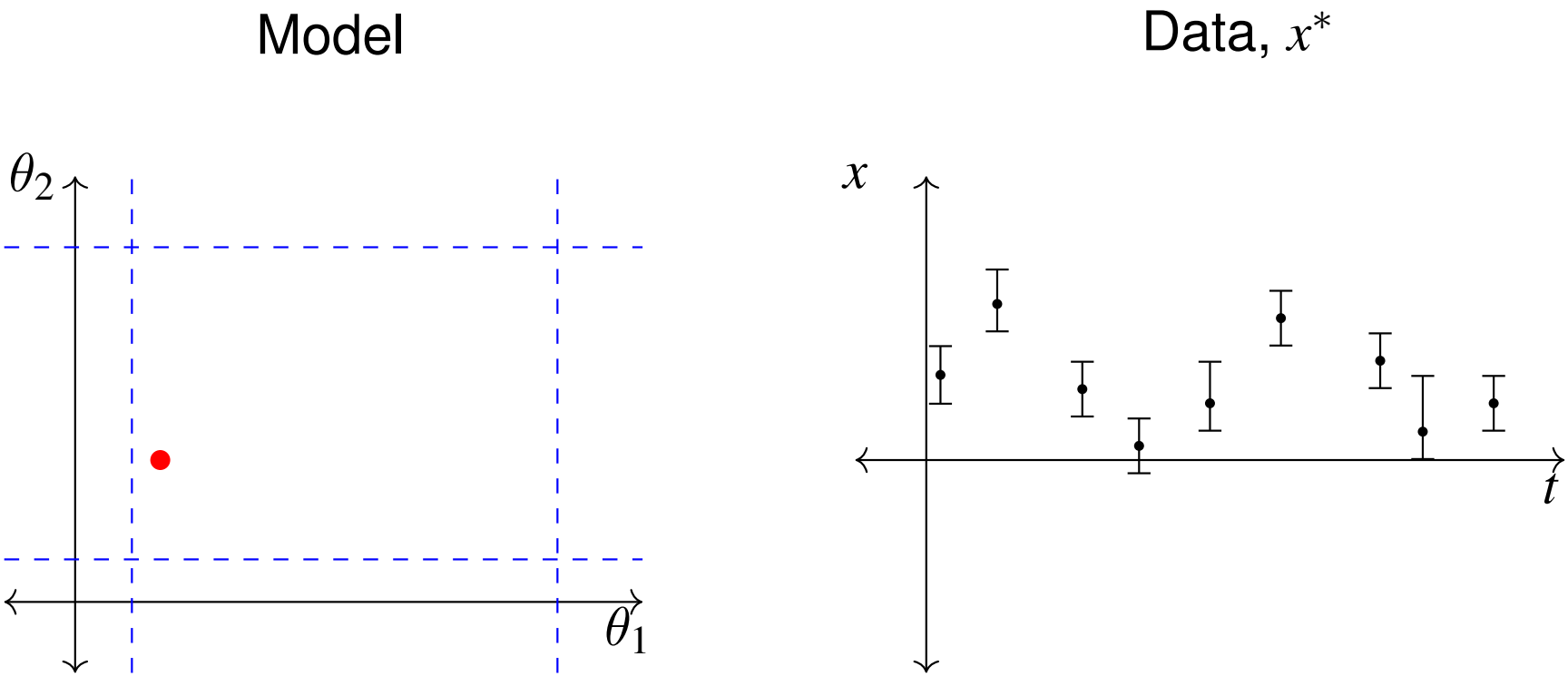

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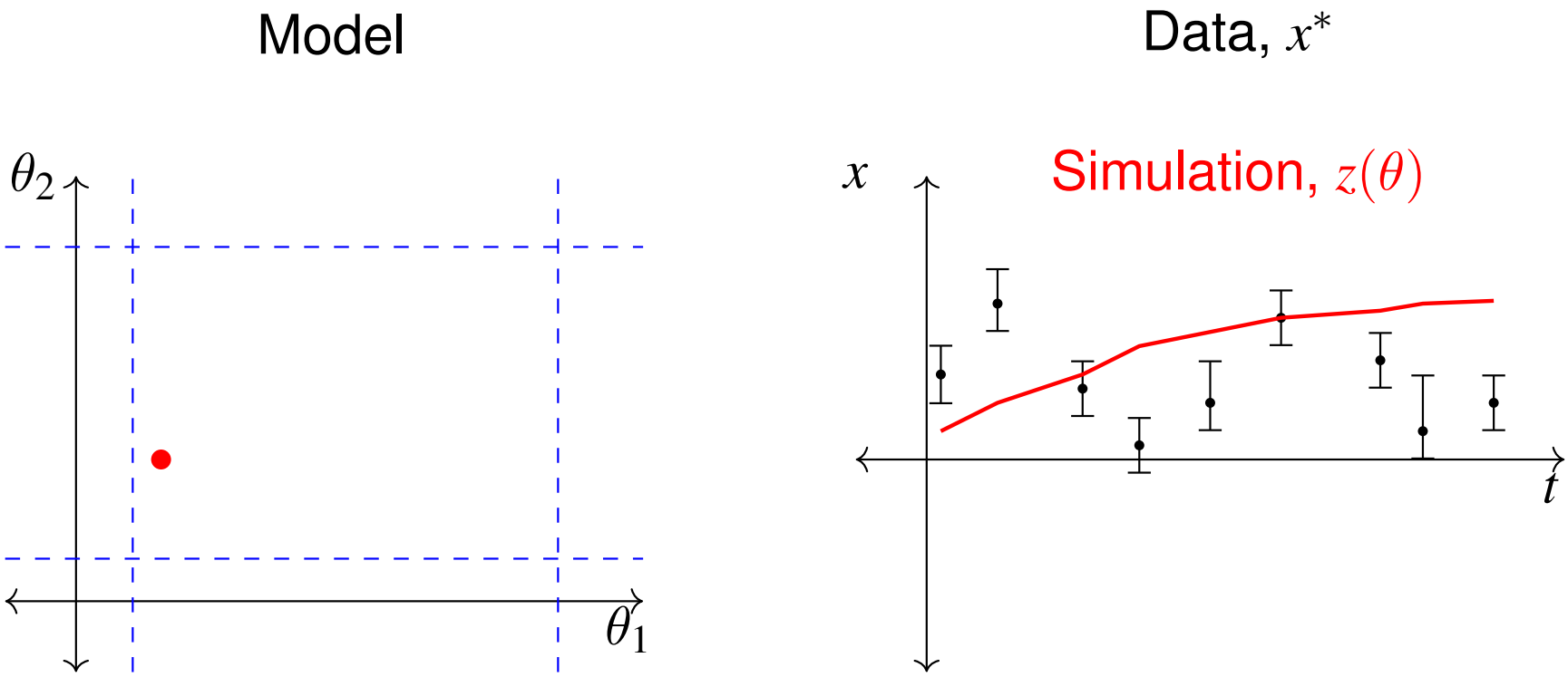

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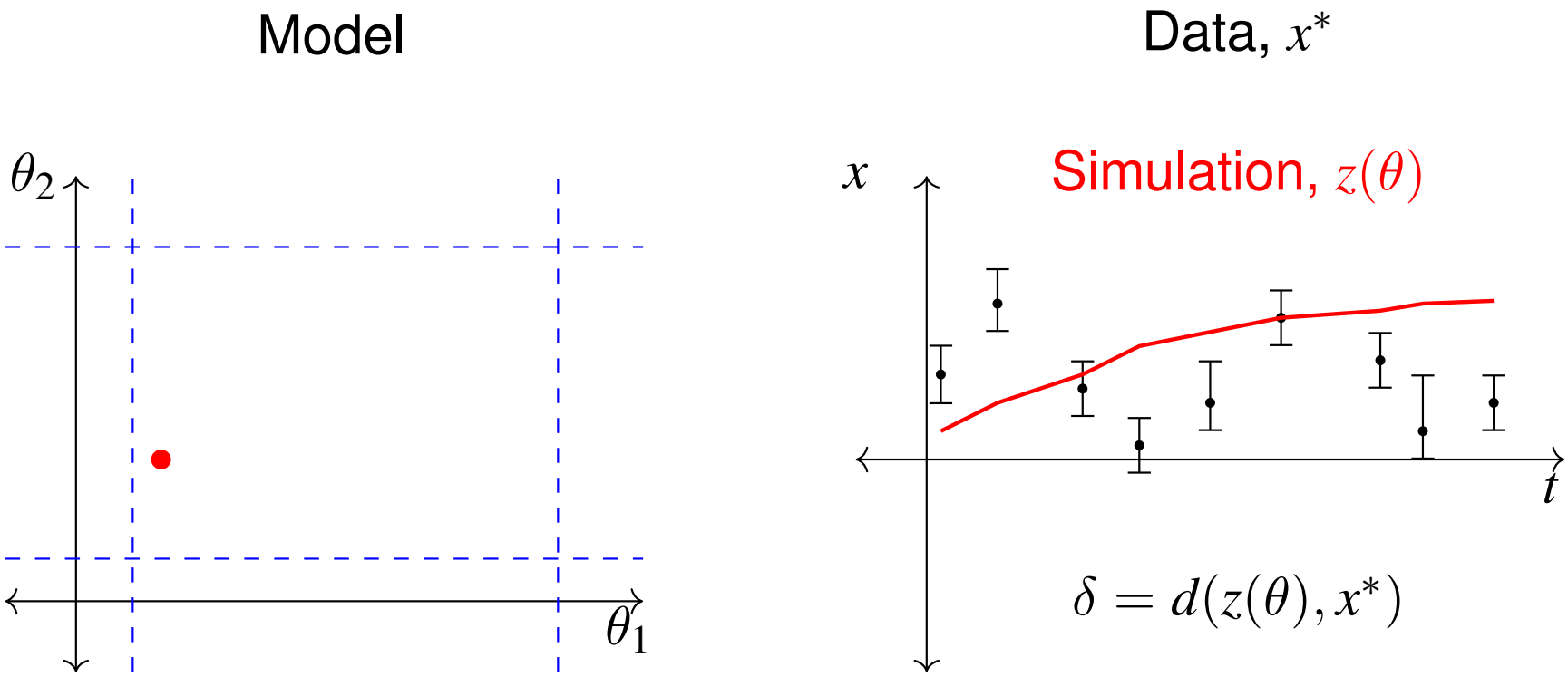

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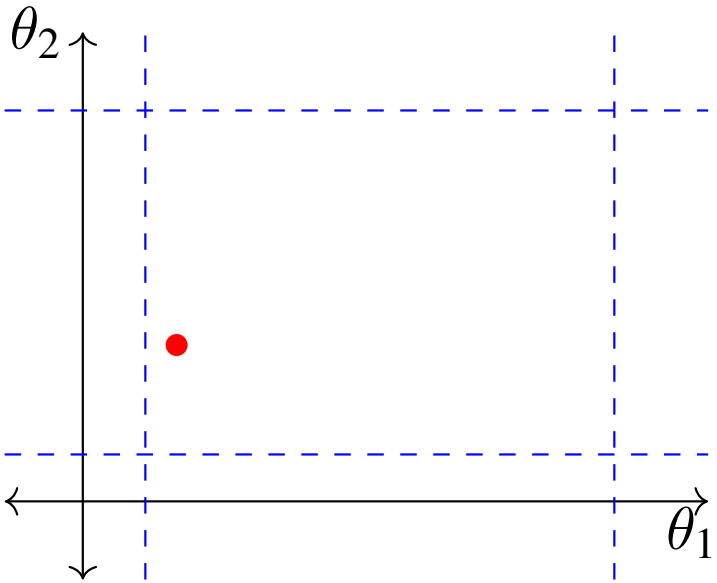
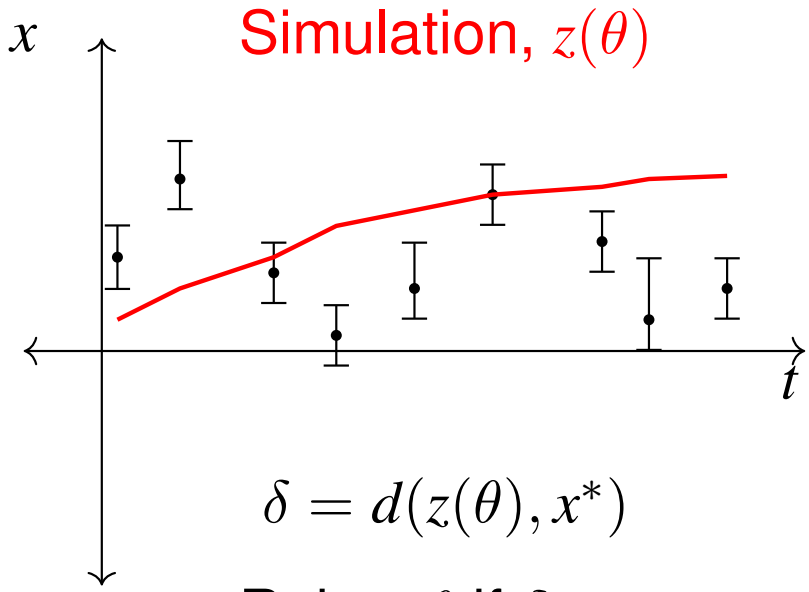
Illustration of the ABC rejection algorithm

Model



Data, x^*



Simulation, $z(\theta)$

$$\delta = d(z(\theta), x^*)$$

Reject θ if $\delta > \epsilon$
Accept θ if $\delta \leq \epsilon$

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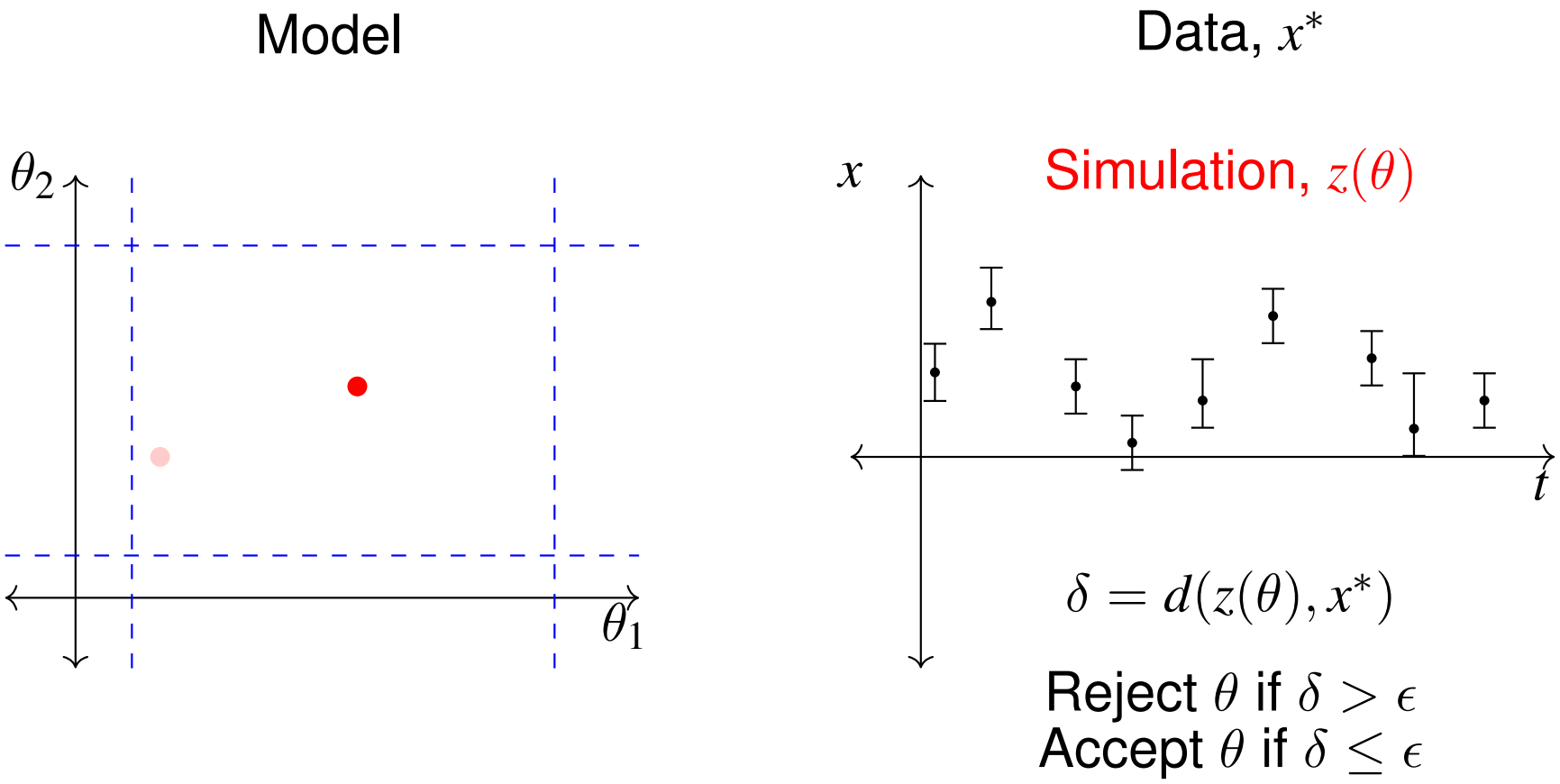

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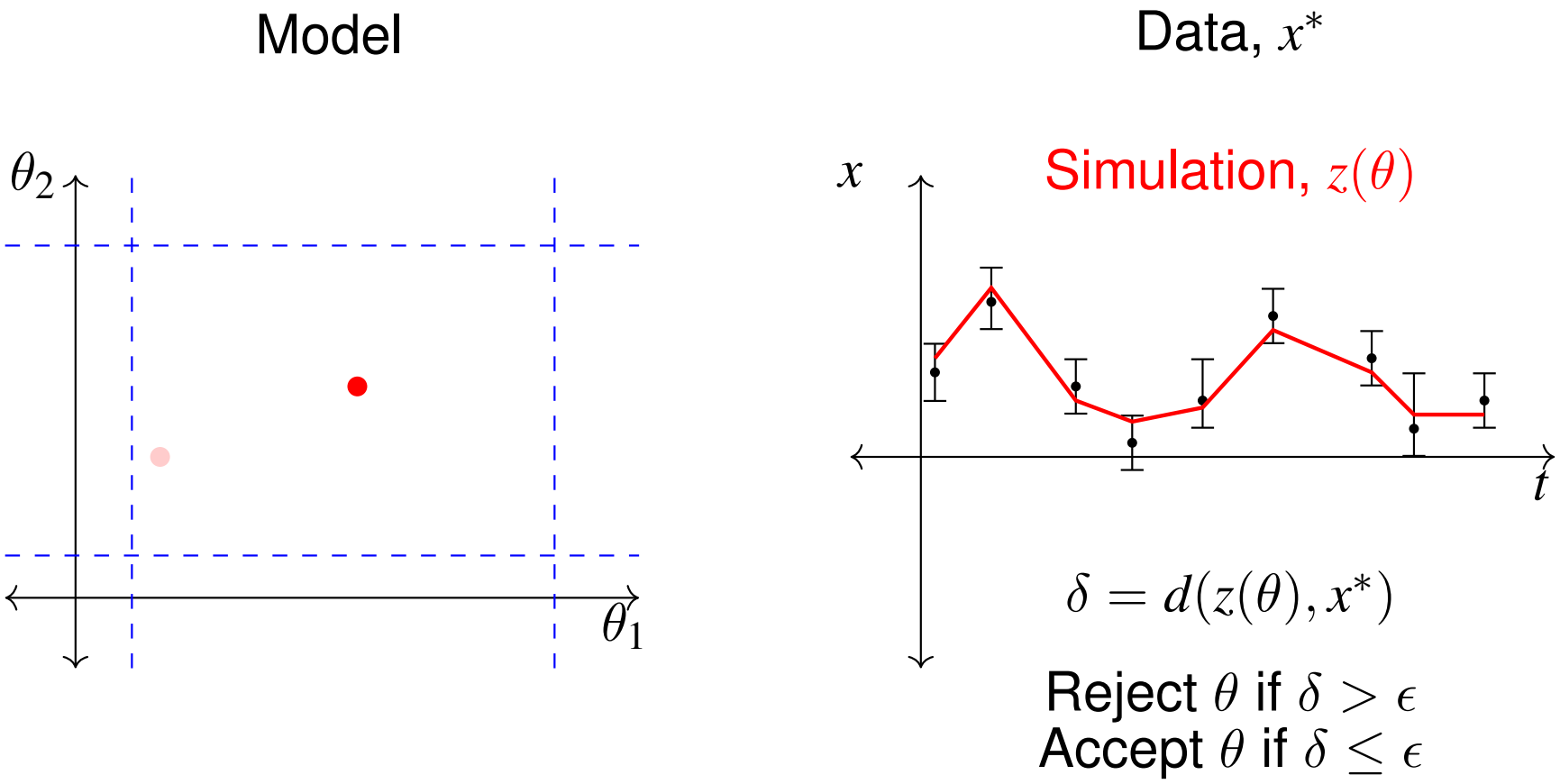

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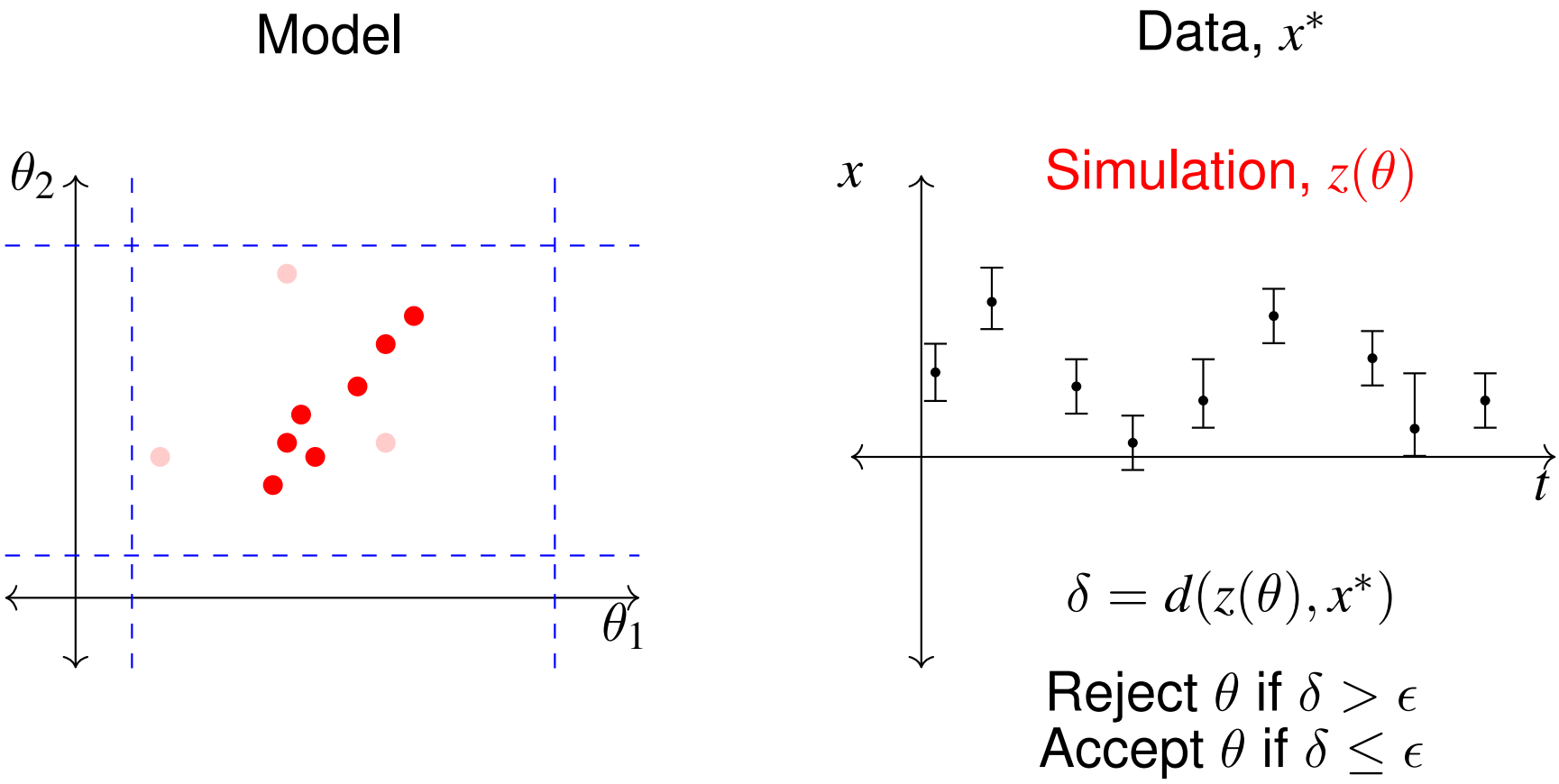

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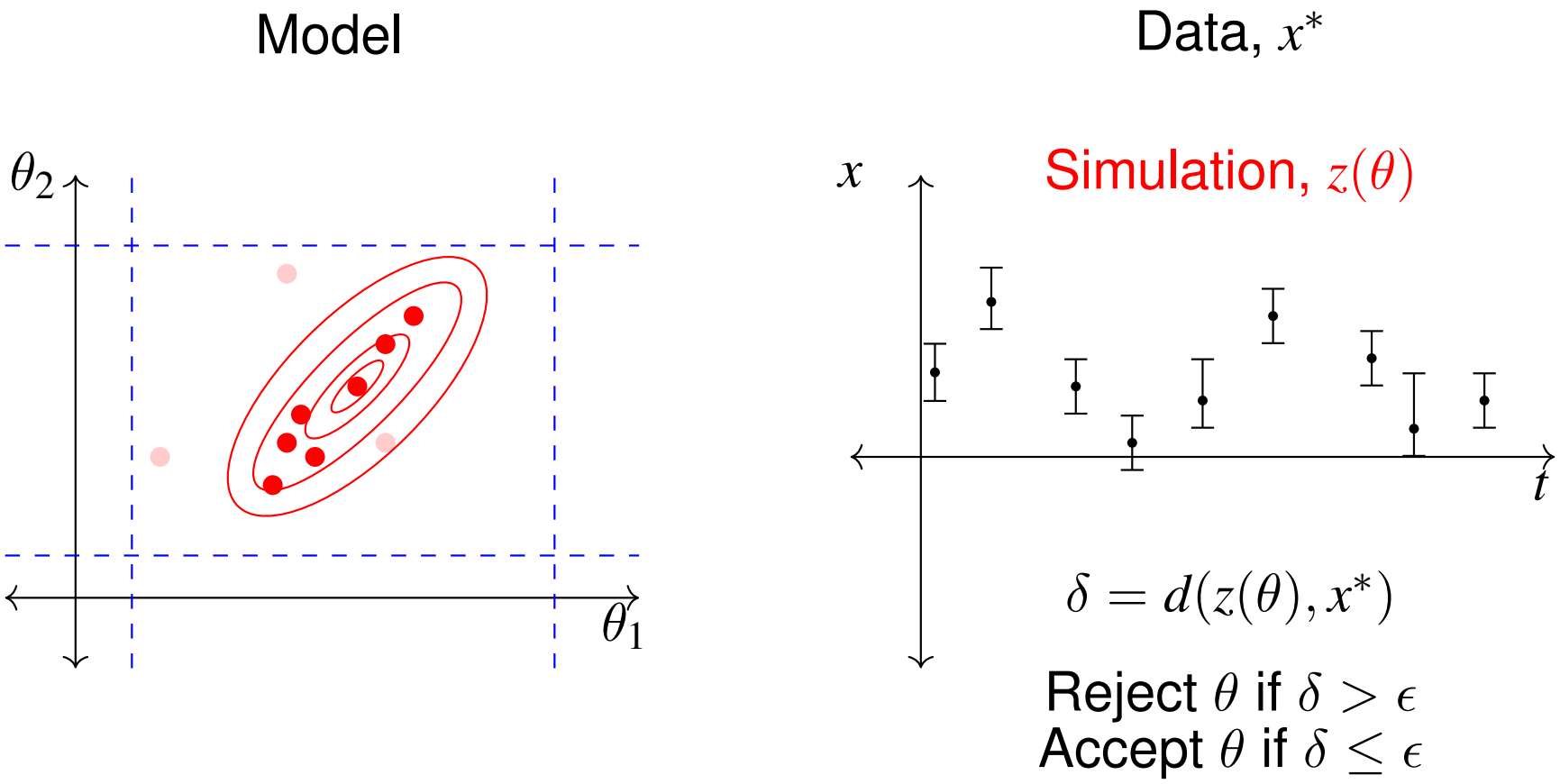

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EXAMPLE: THE MA PROCESS

The MA(q) process is a stochastic process $(y_k)_{k\in\mathbb{N}^*}$ defined by

$$y_k = u_k + \sum_{i=1}^{q} \theta_i u_{k-i}$$

where $(u_k)_{k\in\mathbb{Z}}$ is an i.i.d. sequence of standard Gaussians $\mathcal{N}(0,1)$.

Simple prior: uniform over the inverse roots in

$$Q(x) = 1 - \sum_{i=1}^{q} \theta_i x^i$$

under the identifiability condition.
For $q = 2$, this leads to a uniform prior over a triangle.

[Marin et al, 2012]

EXAMPLE: THE MA PROCESS

Why using ABC ?

- The likelihood associated with $(y_k)_{1\leq k\leq n}$ is complex because of the need to integrate out $u_{-q+1}, \ldots u_{-1}, u_0$.
- MCMC algorithm feasible mainly for small values of n

Running one iteration of ABC for this problem simply requires:

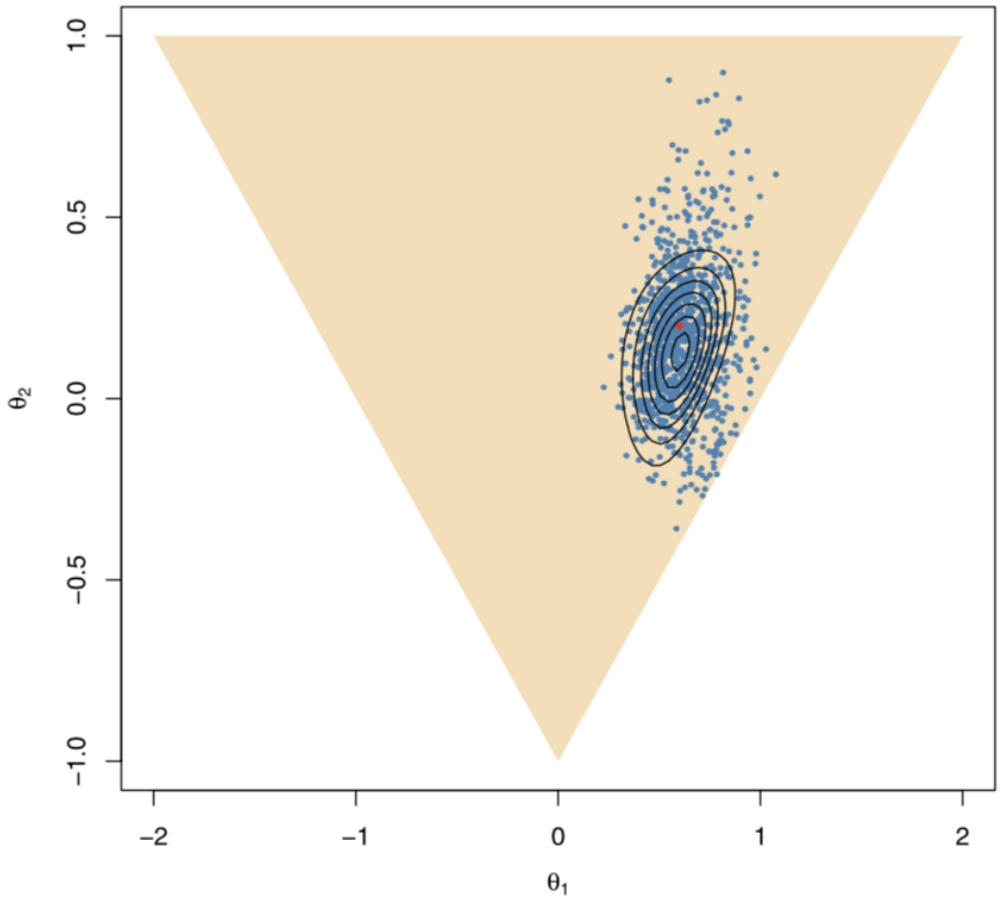
1. Simulating the MA(q) coefficients θ uniformly over the acceptable range,
2. generating an i.i.d sequence $(u_k)_{-q\leq k\leq n}$,
3. producing a simulated series $(y_k)_{1\leq k\leq n}$.

Two distances:

- raw distance: $d^2((z_k)_{1\leq k\leq n}, (x_k^*)_{1\leq k\leq n}) = \sum_{k=1}^n (y_k - x_k^*)^2$
- quadratic distance between q autocovariances $\tau_j = \sum_{k=j+1}^n y_k y_{k-j}$

[Marin et al, 2012]

EXAMPLE: THE MA PROCESS



Model: MA(2) with $n = 100$ and $\theta = (0.6, 0.2)$; autocovariance distance;
ϵ chosen so that 0.1% of $N = 10^6$ simulated data are accepted

[Figure credit:Marin et al, 2012]

CHOICE OF THE THRESHOLD

- ϵ should be close to 0 to obtain samples from a distribution close to the posterior distribution

$$\lim_{\epsilon \to 0} \pi_\epsilon(\theta|x^*) = \pi(\theta|x^*)$$

- choice of ϵ is mostly a matter of computational costs:
  - small ϵ are associated with high computational costs
  - Practice of ABC: select ϵ as a small percentile of the simulated distance $d(\eta(z), \eta(x^*))$ [Beaumont et al, 2009]

$$\epsilon_N = q_\alpha(d_1, \ldots, d_N)$$

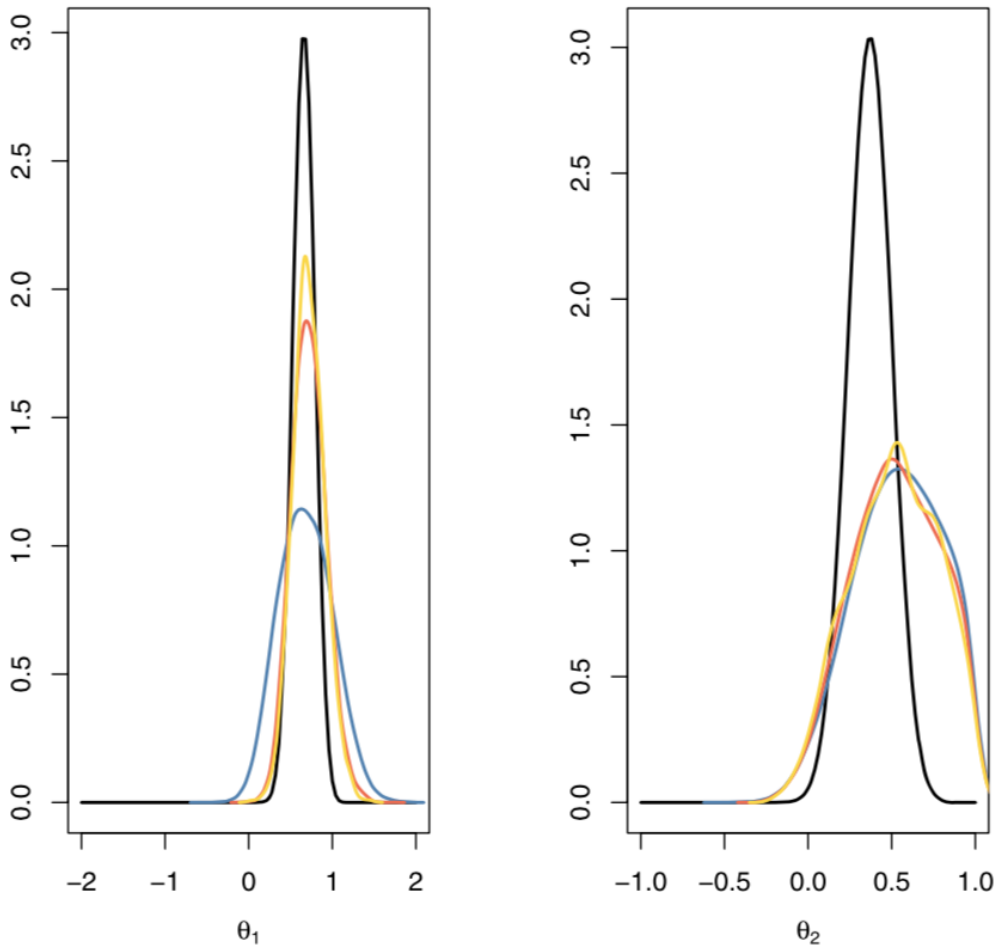
  - other possible approach: including ϵ in the inferential framework [Ratmann et al, 2009]

ABC ALGORITHM WITH QUANTILE DISTANCE

1: **Input:** observation x^*, number of particles N, parameter α
2: **for** $i = 1, \ldots, N$ **do**
3: generate $\theta^{(i)}$ from the prior distribution $\pi(\cdot)$
4: generate $z^{(i)}$ from the simulator $f(\cdot|\theta)$
5: **end for**
6: compute $\epsilon = \alpha$-th quantile of $\{d(\eta(z^{(i)}), \eta(x^*))\}_i$
7: **Return:** $\{\theta^{(i)}$ s.t. $d(\eta(z^{(i)}), \eta(x^*)) \leq \epsilon\}$

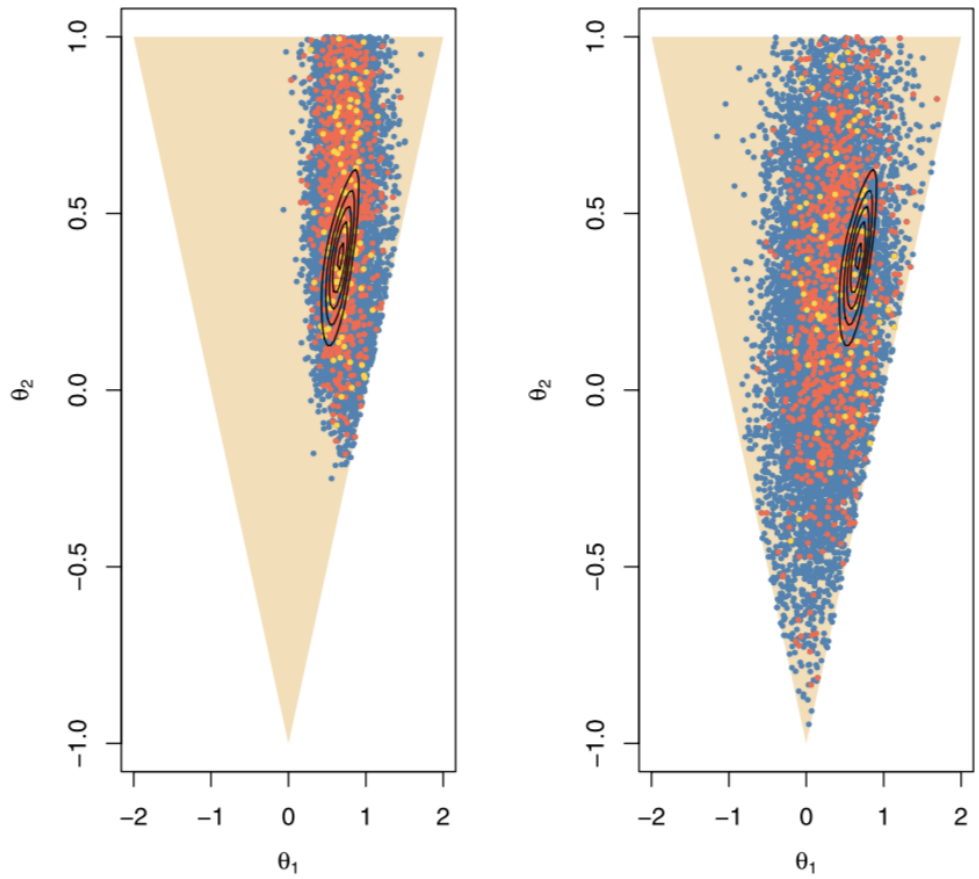
The retuned sample consists of $\alpha \times N$ particles.

EXAMPLE: THE MA PROCESS – THRESHOLD CHOICE



Evolution of the distribution of ABC samples using different quantiles for $\epsilon = 10\%$ (blue), 1% (red) or 0.1% (yellow) compared to the true marginal density (black).

EXAMPLE: THE MA PROCESS – DISTANCE CHOICE



Distance: autocavriance (left), raw distance (right); ϵ chosen based on different quantile (1%, 0.1% and 0.01%).

[Figure credit: Marin et al, 2012]

ABC FOR HIGH DIMENSIONAL DATA

ABC algorithm

1: **Input:** observation x^*, number of particles N, threshold ϵ
2: **for** $i = 1, \ldots, N$ **do**
3: **repeat**
4: generate θ from the prior distribution $\pi(\cdot)$
5: generate z from the simulator $f(\cdot|\theta)$
6: **until** $d(z, x^*) \leq \epsilon$
7: set $\theta^{(i)} = \theta$
8: **end for**

- Curse of dimensionality: If the data are high dimensional, we might never observe simulations close to the observed data.
- Solution: Reduce the dimension using summary statistics.

ABC WITH SUMMARY STATISTICS

- Curse of dimensionality: If the data are high dimensional, we might never observe simulations close to the observed data.
- Solution: Reduce the dimension using summary statistics.
- Algorithm equivalent to the previous one i.f.f. sufficient statistic.

1: **Input:** observation x^*, number of particles N, threshold ϵ
2: **for** $i = 1, \ldots, N$ **do**
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5: generate z from the simulator $f(\cdot|\theta)$
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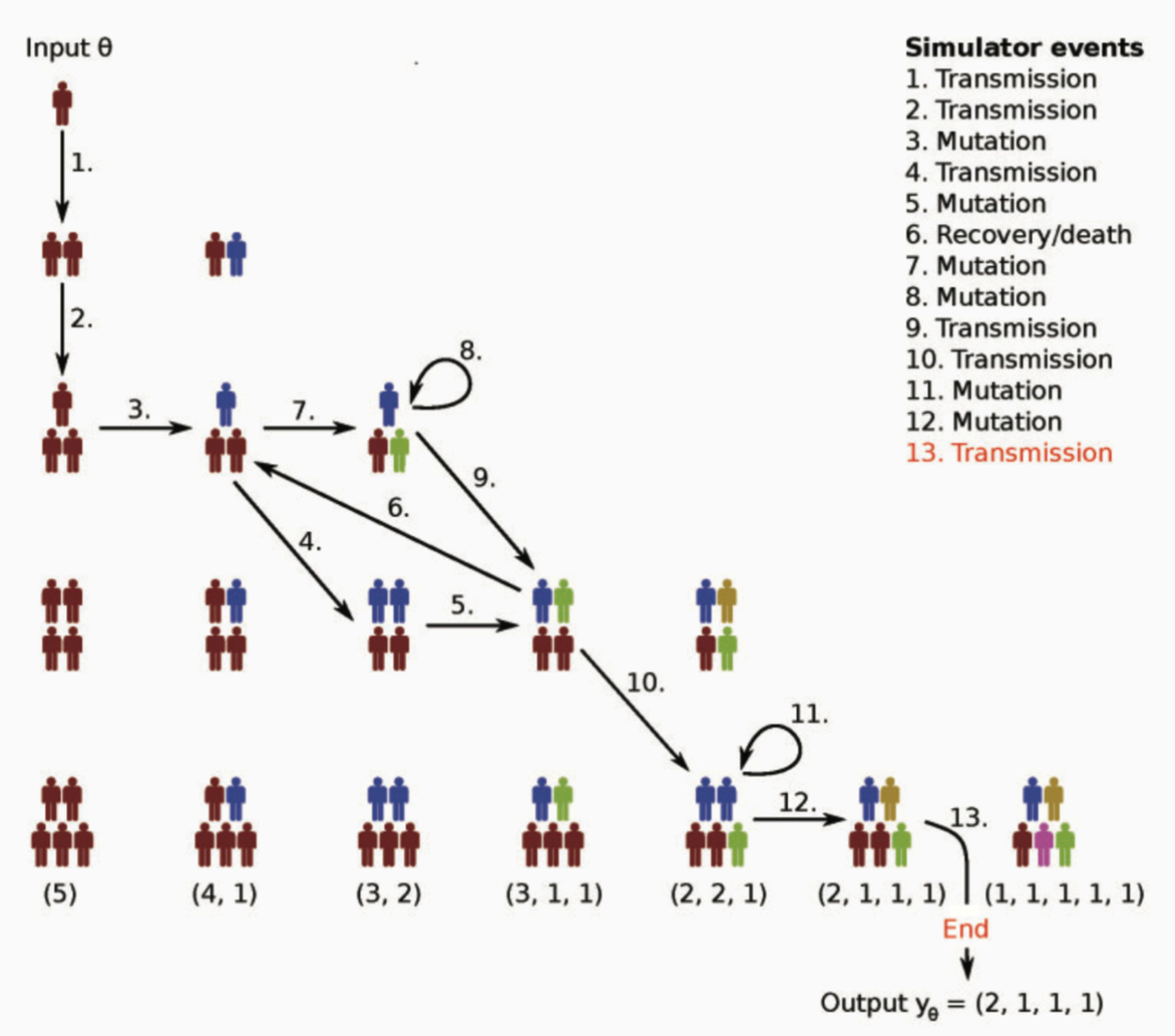
EXAMPLE: THE SPREAD OF TUBERCULOSIS



[Tanaka et al, 2006; Figure credit: Lintusaari et al, 2017]

EXAMPLE: THE SPREAD OF TUBERCULOSIS

Parameters of the model:

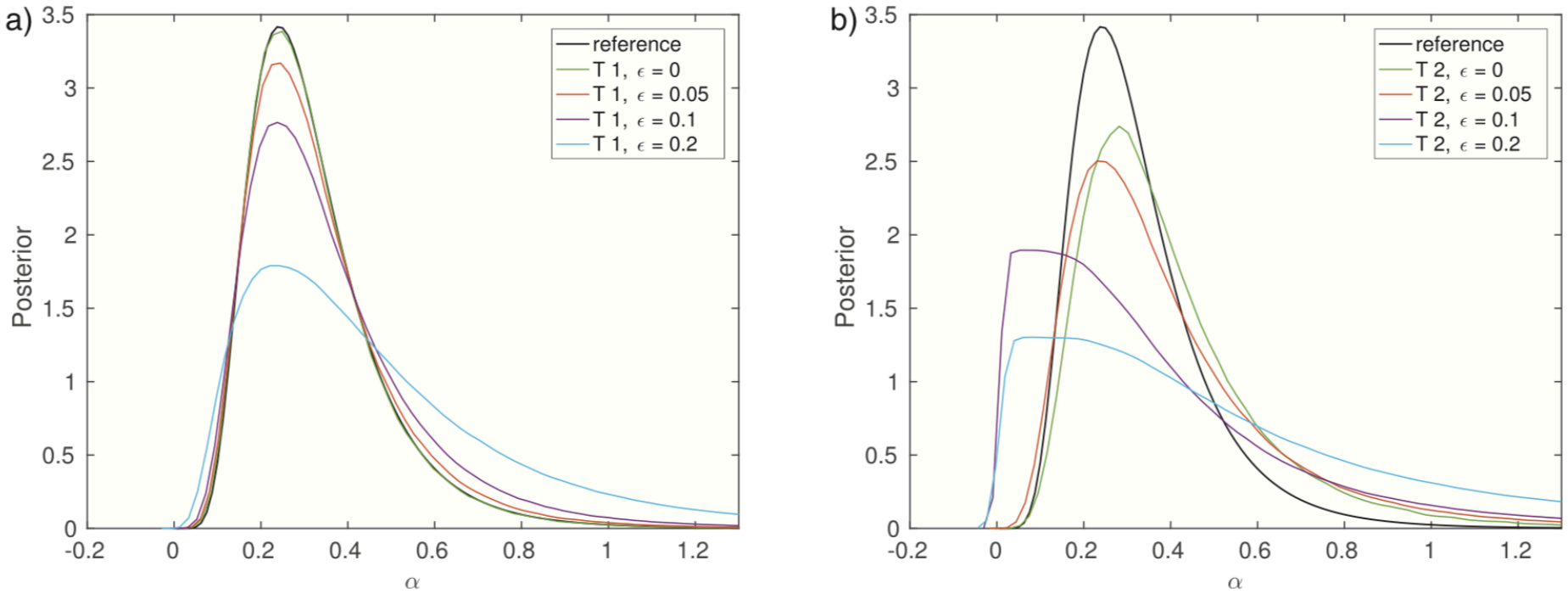
- transmission rate, α
- probability that a host stops being infectious, δ
- mutation rate, τ

Observations: Number of people infected with different pathogens in a subsample n of the population size m.
Example: $x^* = (6, 4, 2, 2, 1, 1, 1)$

Why ABC?
Intractable likelihood is population size m large or death rate, $\delta > 0$.

EXAMPLE: THE SPREAD OF TUBERCULOSIS

Inference of the transmission rate, α, for $x^* = (6, 3, 2, 2, 1, 1, 1, 1, 1, 1, 1)$ i.e. $n = 20$
Two summary statistics: $T_1(z) =$ nb of clusters$/samplesize$ and
$T_2(z) =$ genetic diversity $= 1 - \sum_i \frac{n_i}{n}$

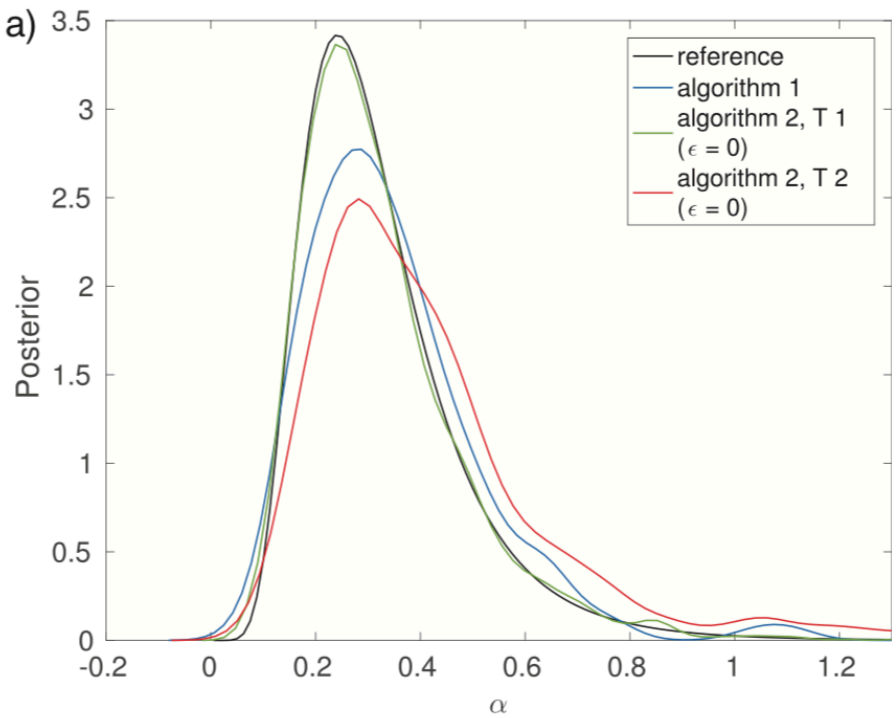


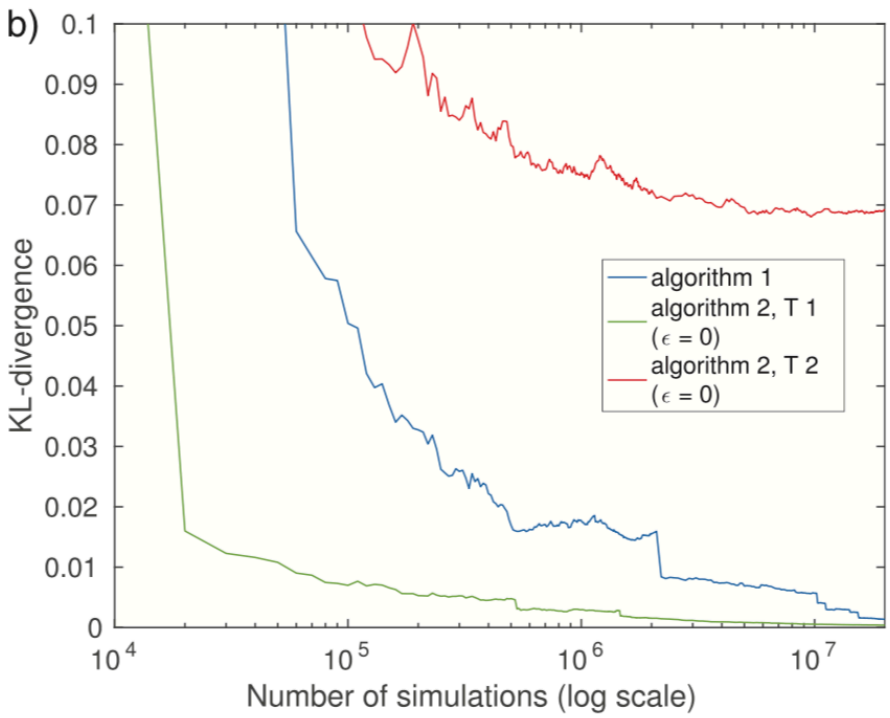
Posterior distribution obtained using the ABC rejection algorithm with 20 million simulated datasets.

[Figure credit: Lintusaari et al, 2017]

EXAMPLE: THE SPREAD OF TUBERCULOSIS

Comparison of the efficiency of (1) exact rejection and (2) ABC rejection samplers





Left: Computational budget of 100.000 iterations
Right: Accuracy versus computational cost.
Smaller KL divergence means more accurate inference of the posterior distribution.

[Figure credit: Lintusaari et al, 2017]

Error in ABC

ABC contains two levels of approximation:

1. the use of a threshold: $\pi(\theta|\eta(x^*)) \approx \pi_\epsilon(\theta|\eta(x^*))$
2. the use of a summary statistic: $\pi(\theta|x^*) \approx \pi(\theta|\eta(x^*))$.
   If $\eta : \mathcal{X} \to \mathbb{R}^k$ is a sufficient statistics: $\pi(\theta|x^*) = \pi(\theta|\eta(x^*))$.

In general, trade-off:

- If k is small, $\pi(\theta|\eta(x^*)) \approx \pi_\epsilon(\theta|\eta(x^*))$ but $\pi(\theta|x^*) \neq \pi(\theta|\eta(x^*))$
- If k is large, $\pi(\theta|x^*) \approx \pi(\theta|\eta(x^*))$ but $\pi(\theta|\eta(x^*)) \neq \pi_\epsilon(\theta|\eta(x^*))$

Ideal situation: k small and $\eta(\cdot)$ informative like a sufficient statistic.

Summary statistics in ABC

- Summary statistics are particularly useful if the observed data sets contain many exchangeable elements
- E.g. data is a n-sample from a model
- Distance metrics, such as Euclidian, on the raw data are inefficient as they do not take into account exchangeability [Sousa et al, 2009]

How can we choose good low dimensional summary statistics?

Summary statistics in ABC

Suppose we are given a candidate set $\mathcal{S} = \{s_1, \ldots s_p\}$ of summary statistics from which to choose.

Two main approaches:

- Identify best subset selection
  [Joyce & Marjoram, 2008; Nunes & Balding, 2010]
- Find an optimal projection of $\mathcal{S}$ onto a lower dimension
  [Wegmann et al, 2009; Fearnhead and Prangle, 2012]

Warning: Automated methods are a poor replacement for expert knowledge.

POST-PROCESSING OF ABC OUTPUT

Abc algorithm

1: **Input:** observation x^*, number of particles N, threshold ϵ
2: **for** $i = 1, \ldots, N$ **do**
3: **repeat**
4: generate θ from the prior distribution $\pi(\cdot)$
5: generate z from the simulator $f(\cdot|\theta)$
6: **until** $d(\eta(z), \eta(x^*)) \leq \epsilon$
7: set $\theta^{(i)} = \theta$
8: **end for**

Could we use all the simulated data instead of throwing away a lot of them?

POST-PROCESSING OF ABC OUTPUT

ABC algorithm provides a sample $(\theta^{(i)}, z^{(i)})_i \sim \pi_\epsilon(\theta, z|\eta(x^*))$.

Two post-processing ideas:

1. weighting the $\theta^{(i)}$ according to $d(\eta(z^{(i)}), x^*)$
2. adjust the value of $\theta^{(i)}$ using local regression to weaken the effect of the discrepancy between $\eta(z^{(i)})$ and $\eta(x^*)$.

Regression adjustments

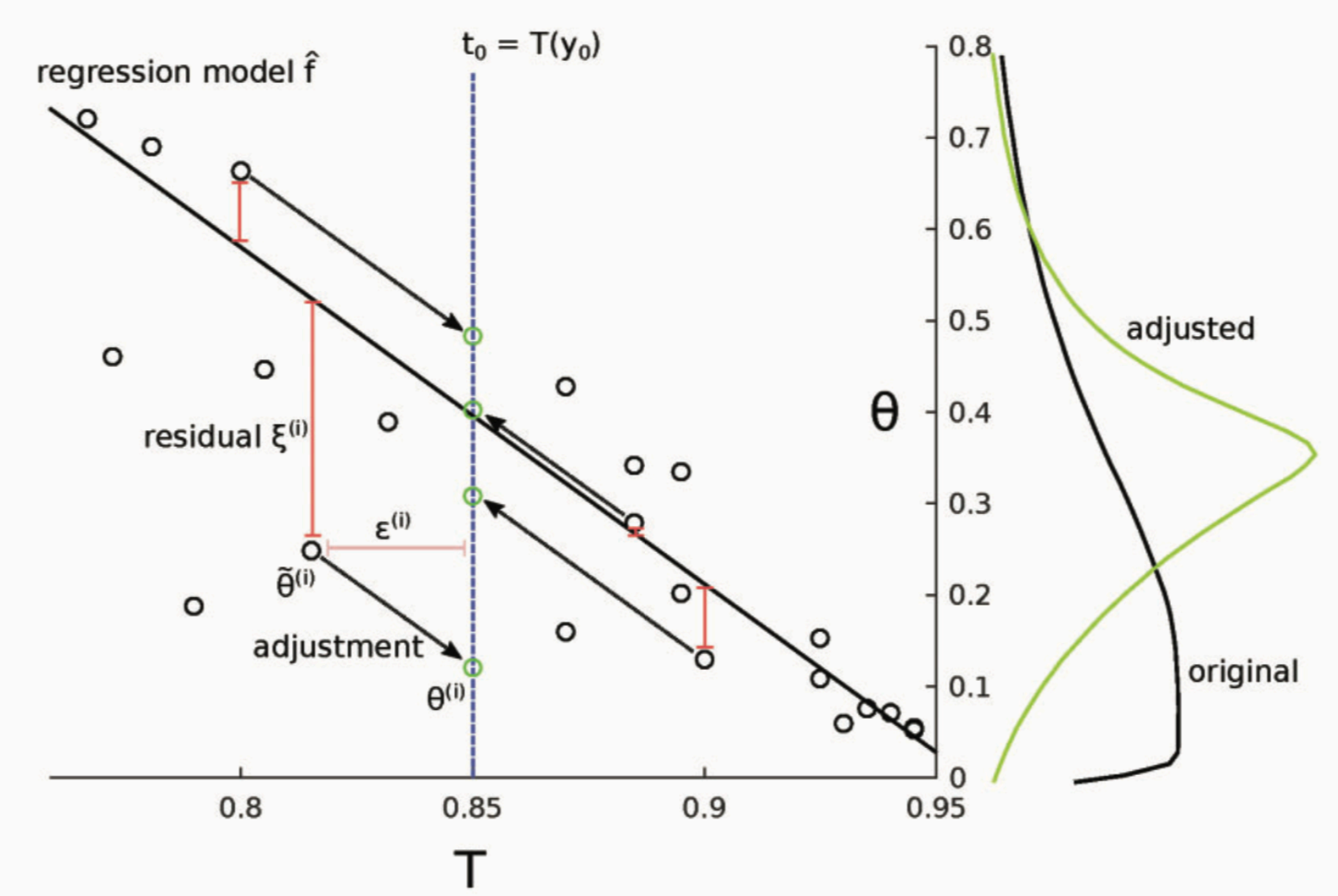
Regression adjustments have been shown to often give improved convergence of $\pi_\epsilon(\theta, z|\eta(x^*))$ to the ideal target $\pi(\theta|\eta(x^*))$.

1. Instead of throwing away θ values such that $d(\eta(z), \eta(x^*)) \geq \epsilon$, adjust each sample $\theta^{(i)}$ as

$$\tilde{\theta}^{(i)} = \theta^{(i)} - [\hat{E}(\theta|\eta(z^{(i)})) - \hat{E}(\theta|\eta(x^*))]$$

2. Use regression to estimate $\hat{E}(\theta|\eta(z))$

ILLUSTRATION



[Figure credit: Lintusaari et al, 2017]

POST-PROCESSING OF ABC OUTPUT

Local linear regression [Beaumont et al, 2002]:

$$\tilde{\theta}^{(i)} = \theta^{(i)} - (\eta(z) - \eta(x^*))^T \hat{\beta}$$

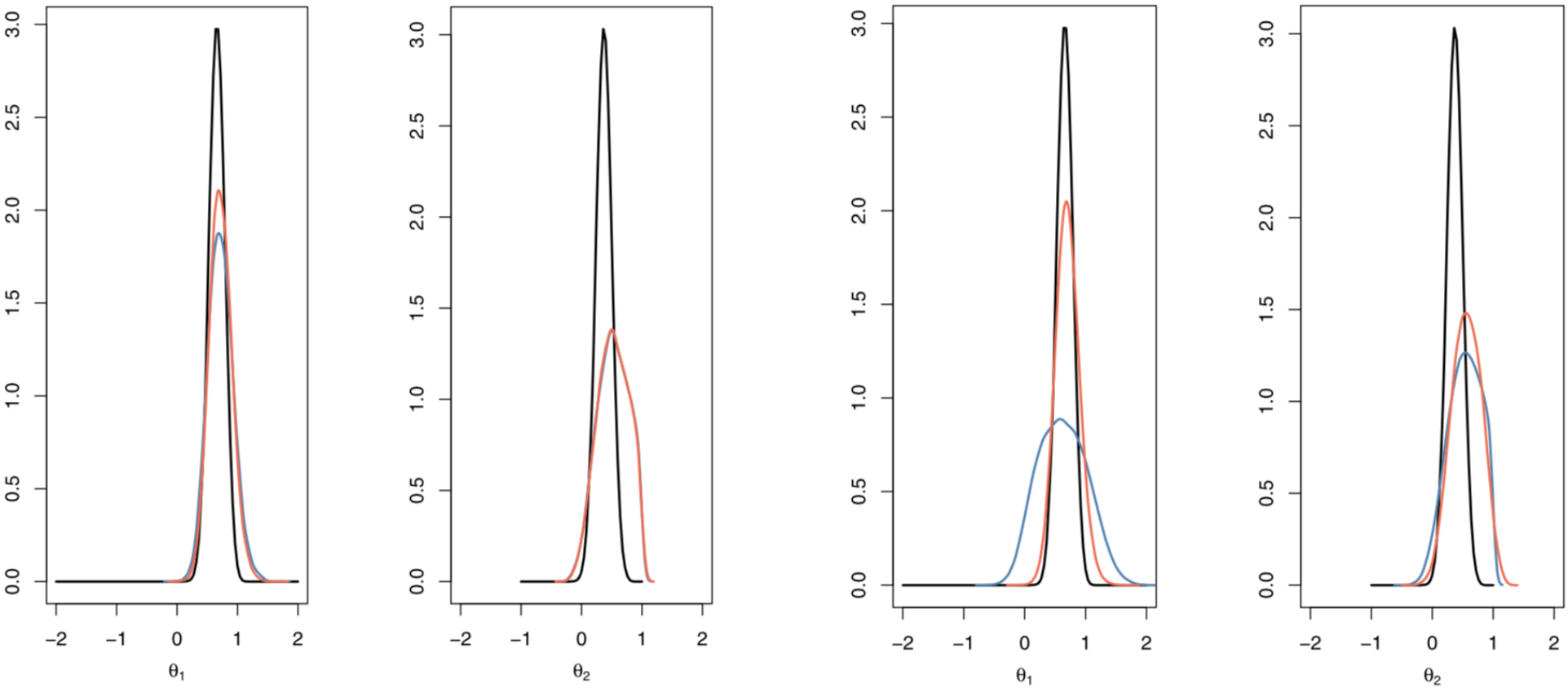
where $\hat{\beta}$ is obtained by a weighted least square regression on $(\eta(z(\theta)) - \eta(x^*))$, using weights of the form $K_\delta(d(\eta(z), \eta(x^*))$ for a non-parametric kernel K_δ with bandwidth δ.

Non-linear regression approaches include

- one-layer neural network [Blum & Francois, 2010]
- kernel-ridge regression [Nakagome et al, 2013]

Possible limitations: Regression-adjustment can yield values of $\tilde{\theta}$ that are outside of the range of the prior. [Leuenberger & Wegmann, 2010; Fen et al, 2013]

EXAMPLE: THE MA PROCESS



$\epsilon = 0.1\%$ quantile

$\epsilon = 20\%$ quantile

Blue: ABC posterior; Red: Beaumont correction

[Figure credit: Marin et al, 2012]

Theoretical results on ABC

POSTERIOR CONSISTENCY

As more data accumulates, we would like the posterior to stabilise around some true value.

Bayesian consistency:

- Assuming the dataset $x^*(n)$ of size n isgenerated from the model with parameter value θ_0
- A posterior density $\pi(\theta|x^*(n))$ is Bayesian consistent if for any $\delta > 0$

$$\Pi\big(\|\theta - \theta_0\| > \delta \mid x^*(n)\big) \xrightarrow[n\to\infty]{P} 0$$

Posterior consistency and ABC

Bayesian consistency of posterior densities obtained from ABC

- requires $n \to \infty$ and $\epsilon \to 0$
- depends on the choice of $\eta(\cdot) : \mathcal{X} \to \mathbb{R}^d$ with $d \geq p$

Bayesian consistency for ABC

Assuming

- the dataset $x^*(n)$ of size n is generated from the model with parameter value $\theta_0 \in \Theta \subset \mathbb{R}^p$
- concentration of $\eta(\cdot)$

thenthe ABC posterior density $\pi_\epsilon(\theta|\eta(x^*(n)))$ is Bayesian consistent, i.e. for any $\delta > 0$

$$\Pi_\epsilon\left(\|\theta - \theta_0\| > \delta \mid x^*(n)\right) \xrightarrow[n\to\infty \text{ and } \epsilon\to 0]{P} 0$$

[Frazier et al, 2015]

Bayesian consistency for ABC

Assuming

- the dataset $x^*(n)$ of size n is generated from the model with parameter value $\theta_0 \in \Theta \subset \mathbb{R}^p$
- concentration of $\eta(\cdot)$

thenthe ABC posterior density $\pi_\epsilon(\theta|\eta(x^*(n)))$ is Bayesian consistent, i.e. for any $\delta > 0$

$$\Pi_\epsilon\big(\|\theta - \theta_0\| > \delta \mid x^*(n)\big) \xrightarrow[n\to\infty \text{ and } \epsilon\to 0]{P} 0$$

Concentration of $\eta(\cdot)$:

Consider a deterministic function $\theta \mapsto b(\theta)$ such that

- $\eta(x^*(n)) \xrightarrow[n\to\infty]{} b(\theta_0)$
- and for all θ, $\eta(z(\theta, n)) \xrightarrow[n\to\infty]{} b(\theta)$

[Frazier et al, 2015]

ABC POSTERIOR SHAPE

- Posterior consistency guaranties that when the number of data increases and the threshold tends to 0, the ABC posterior stabilises around the true value.
- It does not indicate precisely how this mass accumulate.

This depends on the rate of convergence σ_n of the summary statistics $\eta(z(\theta, n))$ towards $b(\theta)$:

- if $\lim_{n\to\infty} \sigma_n/\epsilon_n = 0$, the posterior distribution converges towards a uniform distribution
- if $\sigma_n \gg \epsilon_n$, the posterior distribution converges towards a Normal distribution

[Frazier et al, 2018]

PRACTICAL CONSEQUENCE

No need to choose ϵ_n arbitrarily small: just need $\sigma_n \gg \epsilon_n$.
No gain in being more precise!

Model misspecification

"All models are wrong but some are useful."

George Box

ABC under model misspecification:

- Different versions of ABC can yield substantially different results.
- Under regularity conditions, the accept/reject ABC approach concentrates posterior mass on an appropriately defined pseudo-true parameter value.
- Posterior obtained from regression-adjustments are potentially more misleading than the use of a standard rejection.

[van der Vart et al, 2015; Frazier et al, 2017; Beaumont, 2019]

SUMMARY OF THE FIRST PART

WHEN TO USE ABC?

To perform parameter inference for a complex model for which the likelihood can not be calculated.

ABC ALGORITHM

1: **Input:** observation x^*, number of particles N, threshold ϵ
2: **for** $i = 1, \ldots, N$ **do**
3: **repeat**
4: generate $\theta \sim \pi(\cdot)$
5: generate $z \sim f(\cdot|\theta)$
6: **until** $d(\eta(z), \eta(x^*)) \leq \epsilon$
7: set $\theta^{(i)} = \theta$
8: **end for**

What we covered:

- Choice of statistic $\eta(\cdot)$
- Post-processing
- Posterior consistency

OUTLINE

More efficient variants of ABC include:

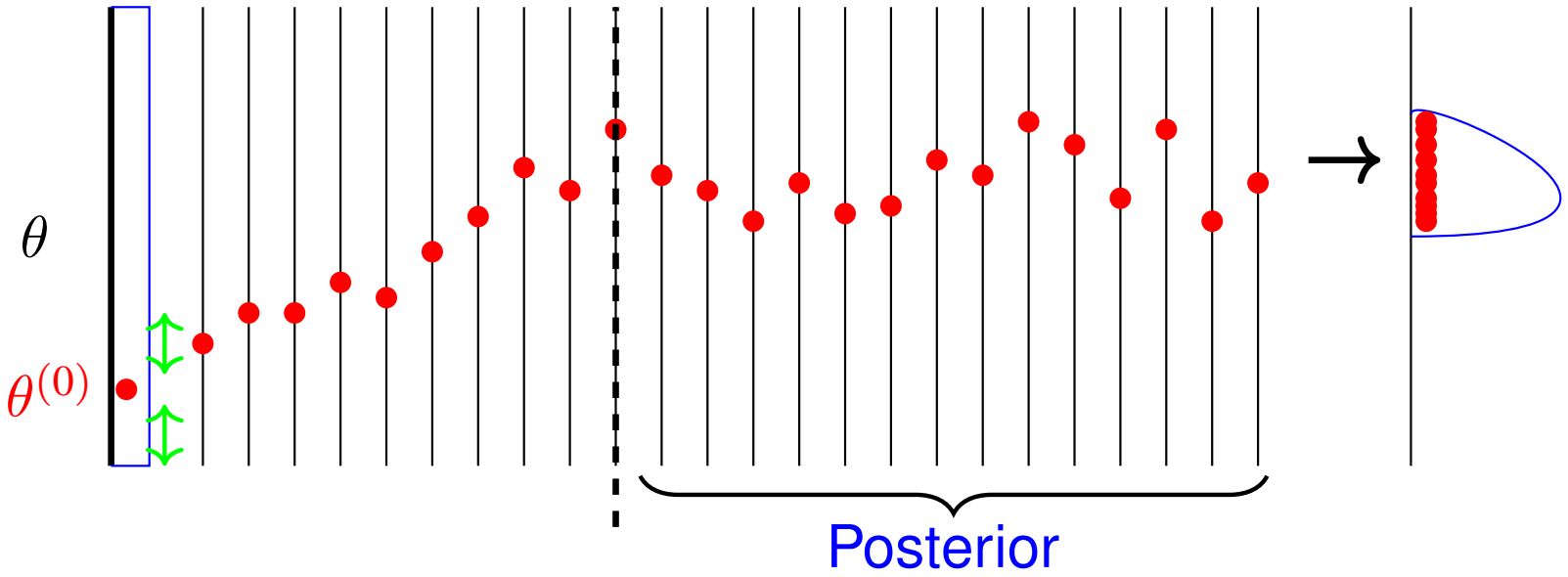
- Markov chain Monte Carlo ABC schemes
  [Marjoram and Molitor, 2003; Ratmann et al., 2007]
- ABC implementing some variant of sequential importance sampling (SIS) or sequential Monte Carlo (SMC)
  [Sisson et al., 2007; Beaumont et al., 2009; Toni et al., 2009; Del Moral et al., 2011]

THE METROPOLIS-HASTING ALGORITHM

- start from an arbitrary point $\theta^{(0)}$
- for $t = 1, \cdots$
  - generate $\tilde{\theta} \sim q(\tilde{\theta}|\theta^{(t)})$
  - take

$$\theta^{(t+1)} = \begin{cases} \tilde{\theta} & \text{with probability } p = \min\left(1, \frac{f(x^*|\tilde{\theta})\pi(\tilde{\theta})q(\theta^{(t)}|\tilde{\theta})}{f(x^*|\theta^{(t)})\pi(\theta^{(t)})q(\tilde{\theta}|\theta^{(t)})}\right) \\ \theta^{(t)} & \text{with probability } 1-p \end{cases}$$

Target = stationnary distribution = $\pi(\theta|x^*) \propto f(x^*|\theta)\pi(\theta)$



ABC-MCMC METHOD

- MCMC approaches require to be able to evaluate the likelihood
The acceptance ratio is

$$p = \min\left(1, \frac{f(x^*|\tilde{\theta})\pi(\tilde{\theta})q(\theta^{(t)}|\tilde{\theta})}{f(x^*|\theta^{(t)})\pi(\theta^{(t)})q(\tilde{\theta}|\theta^{(t)})}\right)$$

- How can we construct a Markov-Chain Monte Carlo algorithm in the context of ABC?
- Idea: produce an MCMC algorithm which targets $\pi_\epsilon(\theta, z|x^*)$ as its stationary distribution [Marjoram et al, 2003]

ABC-MCMC METHOD

1: Use ABC rejection algorithm to get a realization $(\theta^{(0)}, z^{(0)})$ from the trarget $\pi_\epsilon(\theta, z|x^*)$
2: **for** $t = 1, \ldots, N$ **do**
3: generate θ from a Markov kernel $q(\cdot|\theta^{(t-1)})$
4: generate z from the simulator $f(\cdot|\theta)$
5: generate u from $\mathcal{U}(0,1)$
6: **if** $u \leq \frac{\pi(\theta)q(\theta^{(t-1)}|\theta)}{\pi(\theta^{(t-1)})q(\theta|\theta^{(t-1)})}$ and $d(\eta(z), \eta(x^*)) \leq \epsilon$ **then**
7: set $(\theta^{(t)}, z^{(t)}) = (\theta, z)$
8: **else**set $(\theta^{(t)}, z^{(t)}) = (\theta^{(t-1)}, z^{(t-1)})$
9: **end if**
10: **end for**

ABC-MCMC – Why does it work?

- Target distribution: $\pi_\epsilon(\theta, z|x^*) = \pi(\theta)\, f(z|\theta)\, \mathbb{1}_{A_{\epsilon,x^*}}(z)$
- Markov kernel from $(\theta^{(t-1)}, z^{(t-1)})$ to (θ, z): $q(\theta|\theta^{(t-1)}) f(z|z^{(t-1)})$

The acceptance ratio is therefore

$$\frac{\pi_\epsilon(\theta, z|x^*)}{\pi_\epsilon(\theta^{(t-1)}, z^{(t-1)}|x^*)} \times \frac{q(\theta^{(t-1)}|\theta)\, f(z^{(t-1)}|\theta^{(t-1)})}{q(\theta|\theta^{(t-1)})\, f(z|\theta)}$$

$$= \frac{\pi(\theta)\, f(z|\theta)\, \mathbb{1}_{A_{\epsilon,x^*}}(z)}{\pi(\theta^{(t-1)})\, f(z^{(t-1)}|\theta^{(t-1)})\, \mathbb{1}_{A_{\epsilon,x^*}}(z^{(t-1)})} \times \frac{q(\theta^{(t-1)}|\theta)\, f(z^{(t-1)}|\theta^{(t-1)})}{q(\theta|\theta^{(t-1)})\, f(z|\theta)}$$

$$= \frac{\pi(\theta)\, q(\theta^{(t-1)}|\theta)}{\pi(\theta^{(t-1)})\, q(\theta|\theta^{(t-1)})} \mathbb{1}_{A_{\epsilon,x^*}}(z)$$

and does not involve calculating the likelihood.

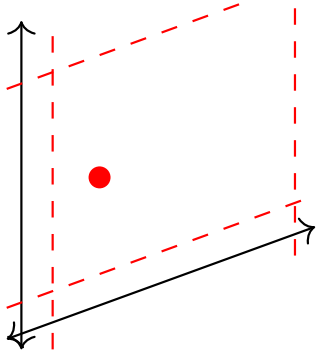
SEQUENTIAL ABC

- Sequential approaches to ABC proposed by [Beaumont et al., 2009; Toni et al., 2009]
- Aim: computational efficiency
- Instead of directly producing a sample from $\pi_\epsilon(\theta|\eta(x^*))$ for a small threshold ϵ
- Produce samples from $\pi_{\epsilon_t}(\theta|\eta(x^*))$ for a decreasing sequence of thresholds $(\epsilon_t)_t$

SEQUENTIAL ABC – A SCHEMATIC REPRESENTATION

Population 1

Prior, $\pi(\theta)$

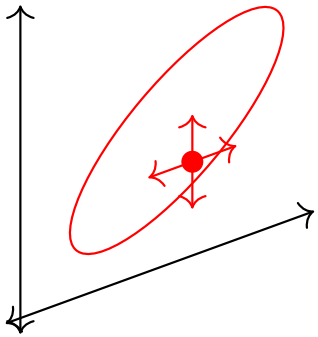


Define set of intermediate distributions, $\pi_t, t = 1, ..., T$

$$\epsilon_1 > \epsilon_2 > ..... > \epsilon_T$$

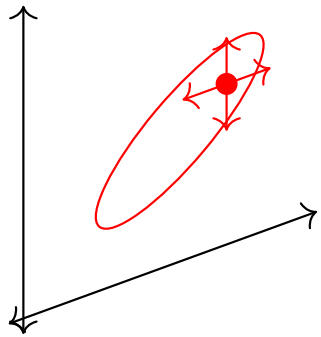
Population $t-1$

$\pi_{t-1}(\theta|d(x^*, x(\theta)) < \epsilon_{t-1})$



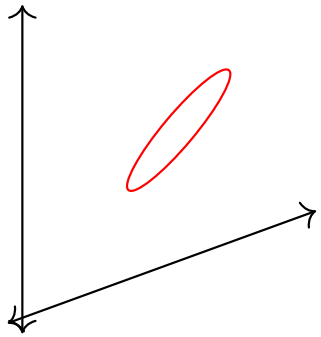
Population t

$\pi_t(\theta|d(x^*, x(\theta)) < \epsilon_t)$



Population T

$\pi_T(\theta|d(x^*, x(\theta)) < \epsilon_T)$



Acknowledgement to Prof. Michael Stumpf (Theoretical System Biology group, Imperial College London) for the slides.
Toni et al. , J.Roy.Soc. Interface (2009); Toni & Stumpf, Bioinformatics (2010).

POPULATION MONTE-CARLO

The sequential ABC algorithms are related to the population Monte-Carlo algorithm [Cappé *et al*, 2004] and invoke importance sampling arguments:

- if a sample $(\theta^{(1,t)}, \ldots \theta^{(N,t)})$ is produced by simulating each $\theta^{(i,t)} \sim q_{it}$ independently of one another conditional on the past samples
- and if each point $\theta^{(i,t)}$ is associated to an important weight

$$\omega^{(i,t)} \propto \frac{p(\theta^{(i,t)})}{q_{it}}$$

then $\frac{1}{N}\sum_{i=1}^{N} \omega^{(i,t)} h(\theta^{(i,t)})$ is an unbiased estimator of $\int h(\theta)\, p(\theta) d\theta$.

The population Monte-Carlo algorithm produces a weighted sample $(\theta^{(i,t)}, \omega^{(i,t)})_{i=1}^{N}$ from the target distribution $p(\theta)$.

POPULATION MONTE-CARLO FOR ABC

- In ABC, the weight should not involve calculating the likelihood
- To do so, same trick as in ABC-MCMC: consider the join target

$$\pi_\epsilon(\theta, z|x^*) = \pi(\theta)\, f(z|\theta)\, \mathbb{1}_{A_{\epsilon,x^*}}(z)$$

- At each iteration t, the sequential ABC algorithm produces a weighted sample $(\theta^{(i,t)}, z^{(i,t)}, \omega^{(i,t)})_{i=1}^N$ from the target distribution.

SEQUENTIAL ABC – THE APPROACH (1)

At iteration t, for every $1 \leq i \leq N$, $(\theta^{(i,t)}, z^{(i,t)})$ is sampled as follows:

- θ is sampled from the previous population $\{\theta^{(i,t-1)}, \omega^{(i,t-1)}\}_{1 \leq i \leq N}$,
- then it is perturbed using a perturbation kernel $\tilde{\theta} \sim K_t(.|\theta)$
- a simulated data z is generated from the simulator $f(\cdot|\tilde{\theta})$
- and $(\theta^{(i,t)}, z^{(i,t)}) = (\tilde{\theta}, z)$ if $d(\eta(z), \eta(x^*)) \leq \epsilon_t$

therefore the proposal distribution is

$$q_t(\theta^{(i,t)}, z^{(i,t)}) = \sum_{j=1}^{n} \omega^{(j,t-1)} K_t(\theta^{(i,t)}|\theta^{(j,t-1)}) f(z^{(i,t)} \; \mathbb{1}_{A_{\epsilon_t, x^*}}(z^{(i,t)})$$

SEQUENTIAL ABC – THE APPROACH (2)

At iteration t, for every $1 \leq i \leq N$, $(\theta^{(i,t)}, z^{(i,t)})$ is sampled from

$$q_t(\theta^{(i,t)}, z^{(i,t)}) = \sum_{j=1}^{n} \omega^{(j,t-1)} K_t(\theta^{(i,t)} | \theta^{(j,t-1)}) f(z^{(i,t)} \; \mathbb{1}_{A_{\epsilon_t, x^*}}(z^{(i,t)}) \; .$$

The associated importance weight is

$$\begin{aligned}
\omega(i,t) &\propto \frac{\text{Target}(\theta^{(i,t)}, z^{(i,t)})}{\text{Proposal}(\theta^{(i,t)}, z^{(i,t)})} \\
&= \frac{\pi(\theta^{(i,t)}) \, f(z^{(i,t)} | \theta^{(i,t)}) \; \mathbb{1}_{A_{\epsilon_t, x^*}}(z^{(i,t)})}{\sum_{j=1}^{n} \omega^{(j,t-1)} K_t(\theta^{(i,t)} | \theta^{(j,t-1)}) f(z^{(i,t)} \; \mathbb{1}_{A_{\epsilon_t, x^*}}(z^{(i,t)})} \\
&= \frac{\pi(\theta^{(i,t)})}{\sum_{j=1}^{n} \omega^{(j,t-1)} K_t(\theta^{(i,t)} | \theta^{(j,t-1)})}
\end{aligned}$$

and does not involve calculating the likelihood !

SEQUENTIAL ABC – THE ALGORITHM

for all t **do**
  $i \leftarrow 1$
  repeat
    if t=1 **then**
      sample $\tilde{\theta}$ from $\pi(\theta)$
    else
      sample θ from the previous population $\{\theta^{(i,t-1)}, \omega^{(i,t-1)}\}_{1 \leq i \leq N}$
      perturb $\tilde{\theta}$ from $K_t(\cdot|\theta)$ so that $\pi(\tilde{\theta}) > 0$
    end if
    sample z from $f(\cdot|\tilde{\theta})$
    if $d(\eta(z), \eta(x^*)) \leq \epsilon_t$ **then**
      $\theta^{(i,t)} \leftarrow \tilde{\theta}$; $i \leftarrow i+1$
    end if
  until $i = N+1$
  calculate the weights: $\omega^{(i,t)} \propto \frac{\pi(\theta^{(i,t)})}{\sum_{j=1}^{n} \omega^{(j,t-1)} K_t(\theta^{(i,t)}|\theta^{(j,t-1)})}$; $\omega^{(i,1)} = 1/N$
end for

[Toni *et al*, 2009; Beaumont *et al*, 2009]

SEQUENTIAL ABC – THE ALGORITHM

Impact on computational efficiency:

- perturbation kernels $\{K_t\}_t$
- threshold schedule $\{\epsilon_t\}_t$

for all t **do**
  $i \leftarrow 1$
  repeat
    if t=1 **then**
      sample $\tilde{\theta}$ from $\pi(\theta)$
    else
      sample θ from the previous population $\{\theta^{(i,t-1)}, \omega^{(i,t-1)}\}_{1 \leq i \leq N}$
      perturb $\tilde{\theta}$ from $K_t(\cdot|\theta)$ so that $\pi(\tilde{\theta}) > 0$
    end if
    sample z from $f(\cdot|\tilde{\theta})$
    if $d(\eta(z), \eta(x^*)) \leq \epsilon_t$ **then**
      $\theta^{(i,t)} \leftarrow \tilde{\theta}$; $i \leftarrow i+1$
    end if
  until $i = N+1$
  calculate the weights: $\omega^{(i,t)} \propto \frac{\pi(\theta^{(i,t)})}{\sum_{j=1}^{n} \omega^{(j,t-1)} K_t(\theta^{(i,t)}|\theta^{(j,t-1)})}$; $\omega^{(i,1)} = 1/N$
end for

Toni *et al*, 2009; Beaumont *et al*, 2009

CHOICE OF THE PERTURBATION KERNEL

Use adaptive perturbation kernel

- Local perturbation kernel:
  - hardly moves particles
  - high acceptance rate if successive values of ϵ close enough
- Widely spread kernel:
  - exploration of the parameter space
  - low acceptance rate

Balance between exploring the parameter space and ensuring a high acceptance rate

[Filippi et al, 2013]

PROPERTIES OF OPTIMAL KERNEL

1. **From sequential importance sampling theory:**

   similarity between two joint distributions of $(\theta^{(t-1)}, \theta^{(t)})$ where $\theta^{(t-1)} \sim \pi_{\epsilon_{t-1}}$ and
   - $\theta^{(t)}$ either constructed by perturbing $\theta^{(t-1)}$ using kernel K and accepting according to threshold ϵ_t
   - or$\theta^{(t)} \sim \pi_{\epsilon_t}$

2. **Computational efficiency:** high acceptance rate

3. **Theoretical requirements for convergence:**
   - kernel with larger support than the target distribution
     $\Rightarrow$ guarantee asymptotic unbiasedness of the empirical mean
   - vanish slowly enough in the tails of the target
     $\Rightarrow$ guarantee finite variance of the estimator

[Filippi et al, 2013]

DERIVATION OF OPTIMAL KERNEL

Criteria 1: Resemblance between the two distributions

$$q_{\epsilon_{t-1},\epsilon_t}(\theta^{(t-1)},\theta^{(t)}) = \frac{\pi_{\epsilon_{t-1}}(\theta^{(t-1)}|x^*)K_t(\theta^{(t)}|\theta^{(t-1)})\int f(z|\theta^{(t)})\ \mathbb{1}_{A_{\epsilon_t,x^*}}(z)dz}{\alpha(K_t,\epsilon_{t-1},\epsilon_t,x)}$$

and

$$q^*_{\epsilon_{t-1},\epsilon_t}(\theta^{(t-1)},\theta^{(t)}) = \pi_{\epsilon_{t-1}}(\theta^{(t-1)}|x)\pi_{\epsilon_t}(\theta^{(t)}|x)$$

in terms of the KL divergence [Douc *et al*, 2007; Cappé *et al*, 2008; Beaumont *et al*, 2009)]

$$KL(q_{\epsilon_{t-1},\epsilon_t}; q^*_{\epsilon_{t-1},\epsilon_t}) = -Q(K_t,\epsilon_{t-1},\epsilon_t,x) + \log\alpha(K_t,\epsilon_{t-1},\epsilon_t,x) + C(\epsilon_{t-1},\epsilon_t,x)$$

where

$$Q(K_t,\epsilon_{t-1},\epsilon_t,x) = \iint \pi_{\epsilon_{t-1}}(\theta^{(t-1)}|x)\pi_{\epsilon_t}(\theta^{(t)}|x)\log K_t(\theta^{(t)}|\theta^{(t-1)})d\theta^{(t-1)}d\theta^{(t)}$$

[Filippi et al, 2013]

DERIVATION OF OPTIMAL KERNEL

Criteria 1: mimise the KL divergence:

$$KL(q_{\epsilon_{t-1},\epsilon_t}; q^*_{\epsilon_{t-1},\epsilon_t}) = -Q(K_t, \epsilon_{t-1}, \epsilon_t, x) + \log \alpha(K_t, \epsilon_{t-1}, \epsilon_t, x) + C(\epsilon_{t-1}, \epsilon_t, x)$$

[Filippi et al, 2013]

Derivation of optimal kernel

Criteria 1: mimise the KL divergence:

$$KL(q_{\epsilon_{t-1},\epsilon_t}; q^*_{\epsilon_{t-1},\epsilon_t}) = -Q(K_t, \epsilon_{t-1}, \epsilon_t, x) + \log \alpha(K_t, \epsilon_{t-1}, \epsilon_t, x) + C(\epsilon_{t-1}, \epsilon_t, x)$$

Criteria 2: maximise the acceptance rate $\alpha(K_t, \epsilon_{t-1}, \epsilon_t, x)$

Method

Select the kernel K_t which maximises $Q(K_t, \epsilon_{t-1}, \epsilon_t, x)$ which is equivalent to maximise $-KL(q_{\epsilon_{t-1},\epsilon_t}; q^*_{\epsilon_{t-1},\epsilon_t}) + \log \alpha(K_t, \epsilon_{t-1}, \epsilon_t, x)$.

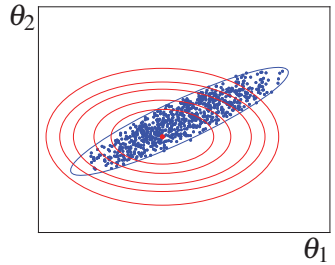
Remark:

$$Q(K_t, \epsilon_{t-1}, \epsilon_t, x) = \iint \pi_{\epsilon_{t-1}}(\theta^{(t-1)}|x)\pi_{\epsilon_t}(\theta^{(t)}|x) \log K_t(\theta^{(t)}|\theta^{(t-1)}) d\theta^{(t-1)} d\theta^{(t)}$$

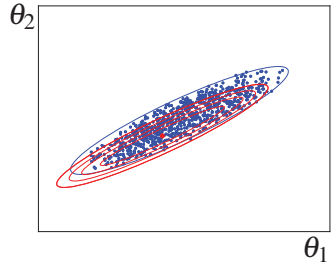
can be maximized easily for some families of kernels. [Filippi et al, 2013]

GAUSSIAN RANDOM WALK KERNELS

- **Component-wise kernel:**
  diagonal covariance matrix $\Sigma^{(t)}$ Beaumont *et al*, 2009
- **Multi-variate normal kernel:**



$$\Sigma^{(t)} \approx \sum_{i=1}^{N} \sum_{k=1}^{N_0} \omega^{(i,t-1)} \tilde{\omega}^{(k)} \left(\tilde{\theta}^{(k)} - \theta^{(i,t-1)}\right)\left(\tilde{\theta}^{(k)} - \theta^{(i,t-1)}\right)^T$$



where $\left\{\tilde{\theta}^{(k)}\right\}_{1 \leq k \leq N_0} = \left\{\theta^{(i,t-1)} \text{ s.t. } z^{(i,t-1)}) \in \mathbb{1}_{A_{\epsilon_t, x^*}}\right\}$

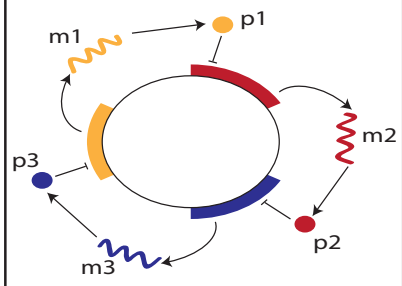
- **Local multi-variate normal kernels:**
  use a different kernel for each particle $\theta^{(t-1)}$.
  - Nearest neighbours: $\Sigma^{(t)}_{\theta^{(t-1)},M}$ based on the M nearest neighbours
  - Optimal local covariance matrix:

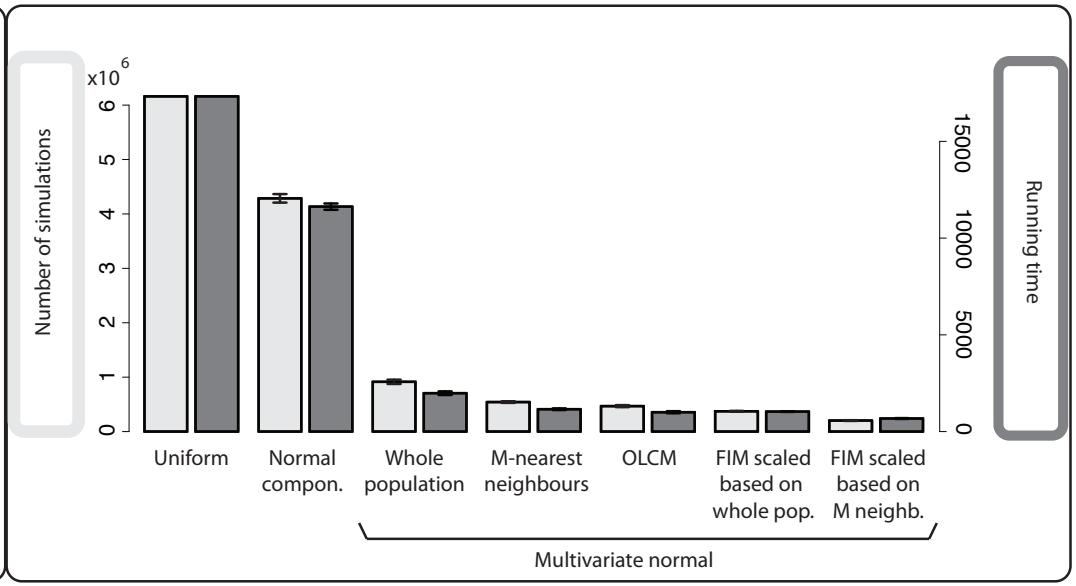
$$\Sigma^{(t)}_{\theta^{(t-1)}} \approx \sum_{k=1}^{N_0} \tilde{\omega}^{(k)} \left(\tilde{\theta}^{(k)} - \theta^{(t-1)}\right)\left(\tilde{\theta}^{(k)} - \theta^{(t-1)}\right)^T$$

[Filippi et al, 2013]

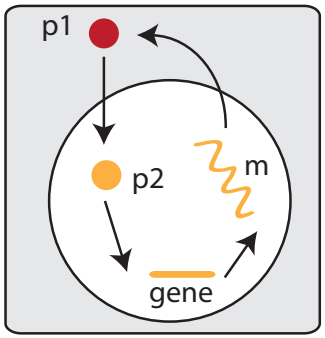
COMPUTATIONAL EFFICIENCY AND KERNEL

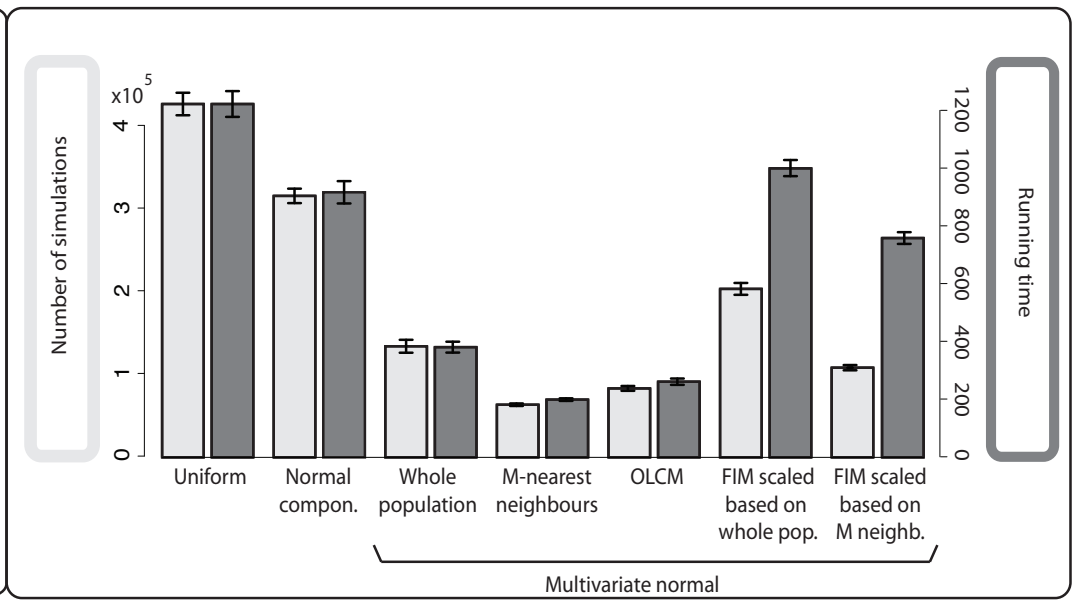
The Repressilator system





The Hes1 transcriptional regulation model





COMPUTATIONAL COST OF PERTURBATION KERNEL

- simulating the data dominates
- computational cost of perturbation kernel implementation:

Component-wise normal	$O(dN^2)$
Multivariate normal based on the whole previous population	$O(d^2N^2)$
Multivariate normal based on the M nearest neighbours	$O((d+M)N^2 + d^2M^2N)$
Multivariate normal with OLCM	$O(d^2N^2)$
Multivariate normal based on the FIM (normalized with entire population)	$O(dCN + d^2N^2)$

$N =$ population size; $d =$ parameter dimension

RECOMMENDATION

Use of multivariate kernels with OLCM

- highest acceptance rate in our examples
- relatively easy to implement at acceptable computational cost

[Filippi et al, 2013]

CHOICE OF THE THRESHOLD SCHEDULE

- final value of ϵ close to 0
- minimise number of simulations:
  - minimise number of populations
  - maximise acceptance rate per pop.

1: **for** all t **do**
2: $i \leftarrow 1$
3: **repeat**
4: **if** t=1 **then**
5: sample $\tilde{\theta}$ from $\pi(\theta)$
6: **else**
7: sample θ from the previous population $\{\theta^{(i,t-1)}, \omega^{(i,t-1)}\}_{1 \leq i \leq N}$
8: perturb $\tilde{\theta}$ from $K_t(\cdot|\theta)$ so that $\pi(\tilde{\theta}) > 0$
9: **end if**
10: sample z from $f(\cdot|\tilde{\theta})$
11: **if** $d(\eta(z), \eta(x^*)) \leq \epsilon_t$ **then**
12: $\theta^{(i,t)} \leftarrow \tilde{\theta}$; $i \leftarrow i+1$
13: **end if**
14: **until** $i = N+1$
15: calculate the weights: $\omega^{(i,t)} \propto \frac{\pi(\theta^{(i,t)})}{\sum_{j=1}^{n} \omega^{(j,t-1)} K_t(\theta^{(i,t)}|\theta^{(j,t-1)})}$; $\omega^{(i,1)} = 1/N$
16: **end for**

CHOICE OF THE THRESHOLD SCHEDULE

PREVIOUS APPROACHES

- Trial and error
- Adaptive method based on quantile

  Beaumont *et al*, 2009; Del Moral *et al*, 2008; Drovandi *et al*, 2011

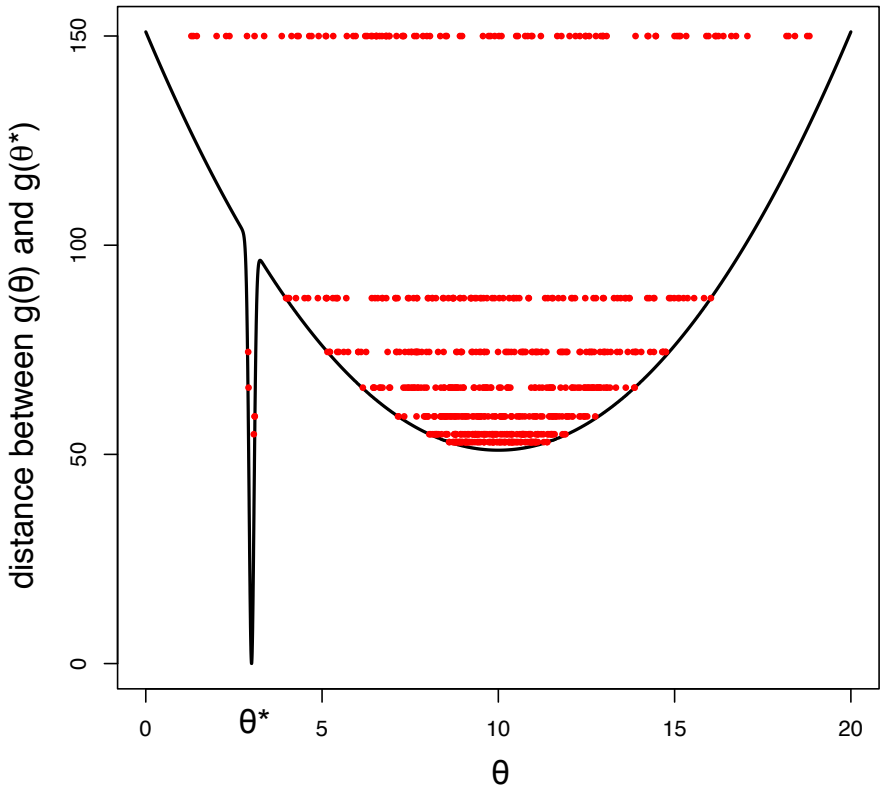
- ...

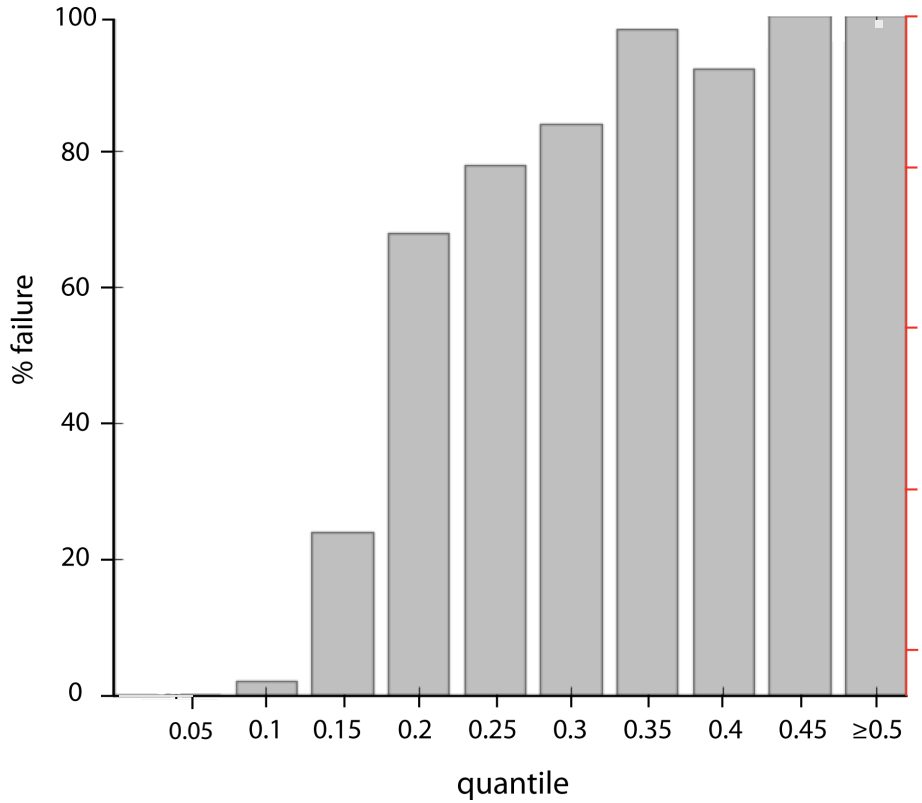
The quantile based approach:

$\epsilon_t = \alpha$ - quantile of the distances $\{d(\eta(x^{(i,t-1)}), \eta(x^*))\}_{1 \leq i \leq N}$

Which value of α should we chose?

DRAWBACK OF THE QUANTILE APPROACH





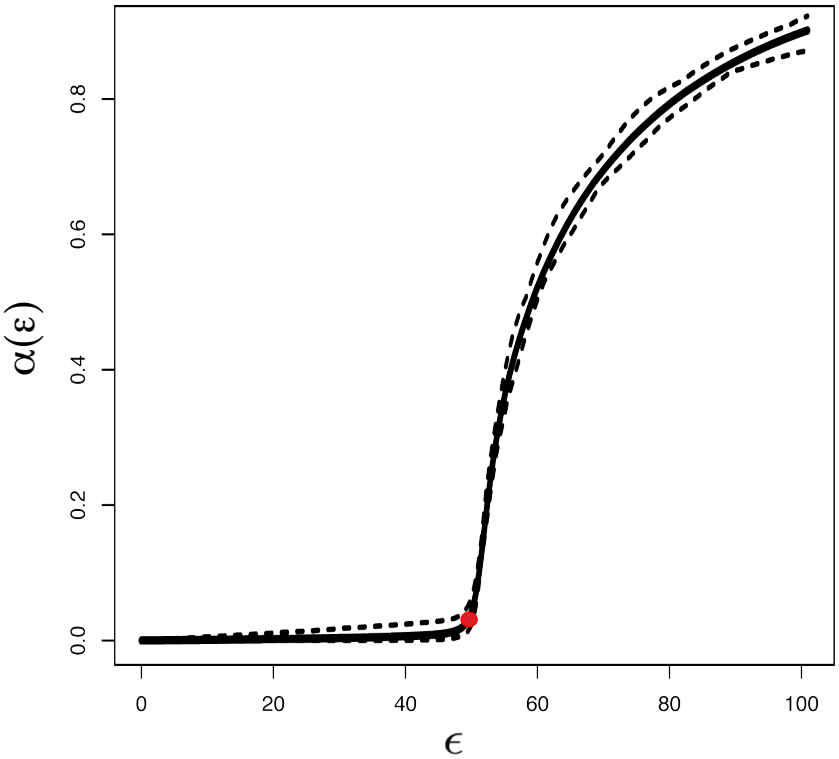
- For large α, the algorithm 'fails'.
- The optimal (or safe) choice of α depends on the data, the model and the prior range.

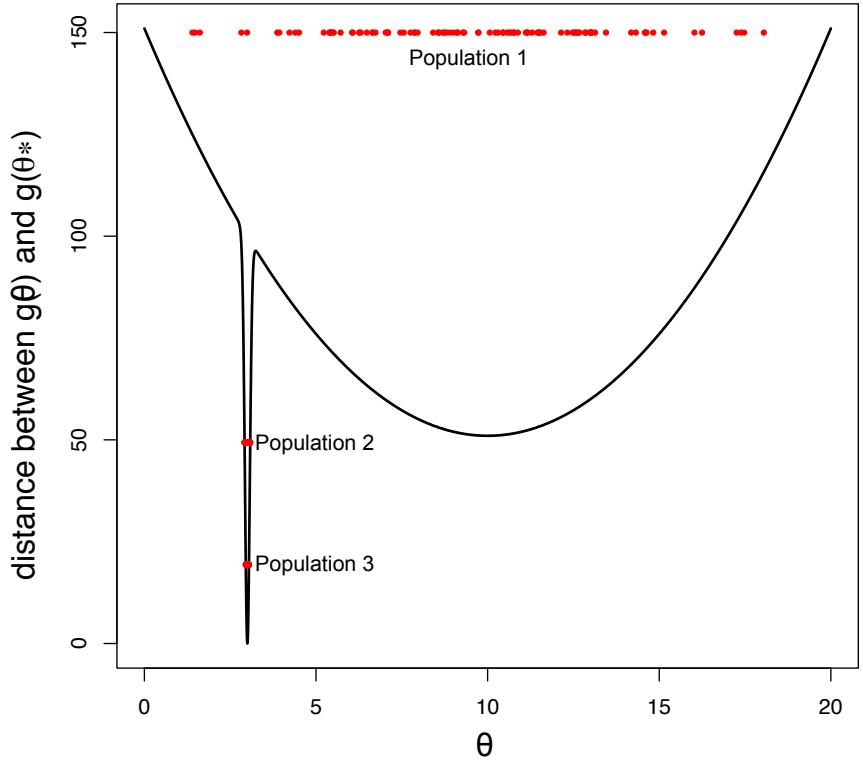
[Silk et al. 2013]

THE THRESHOLD-ACCEPTANCE RATE CURVE

Idea:

- estimate the threshold-acceptance rate curve
- avoid area with excessively high acceptance rate



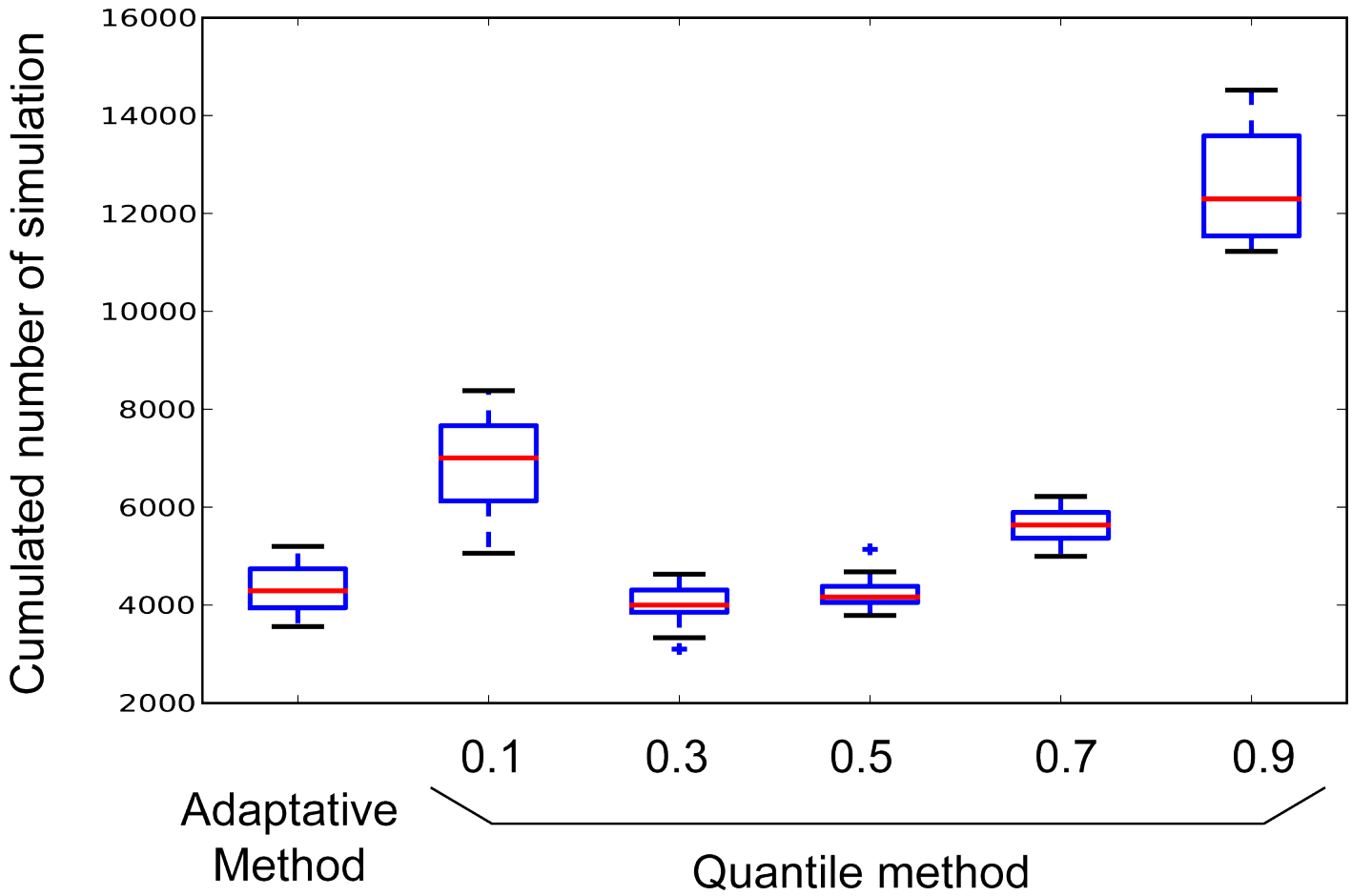


Possible solution: use Unscented Transform to estimate the threshold-acceptance rate curve.

[Silk et al, 2013]

COMPUTATIONAL EFFICIENCY

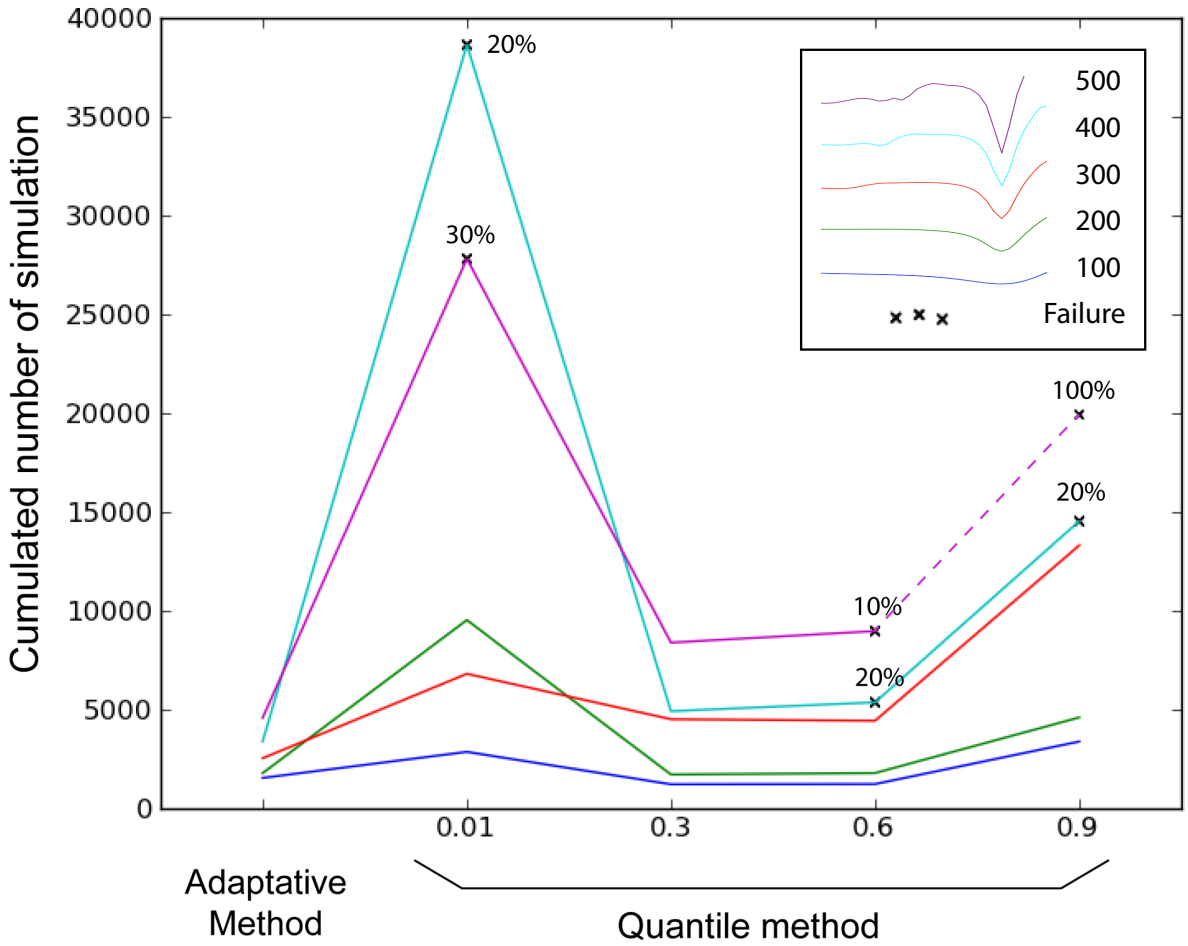
The Repressilator system:



[Silk et al, 2013]

COMPUTATIONAL EFFICIENCY

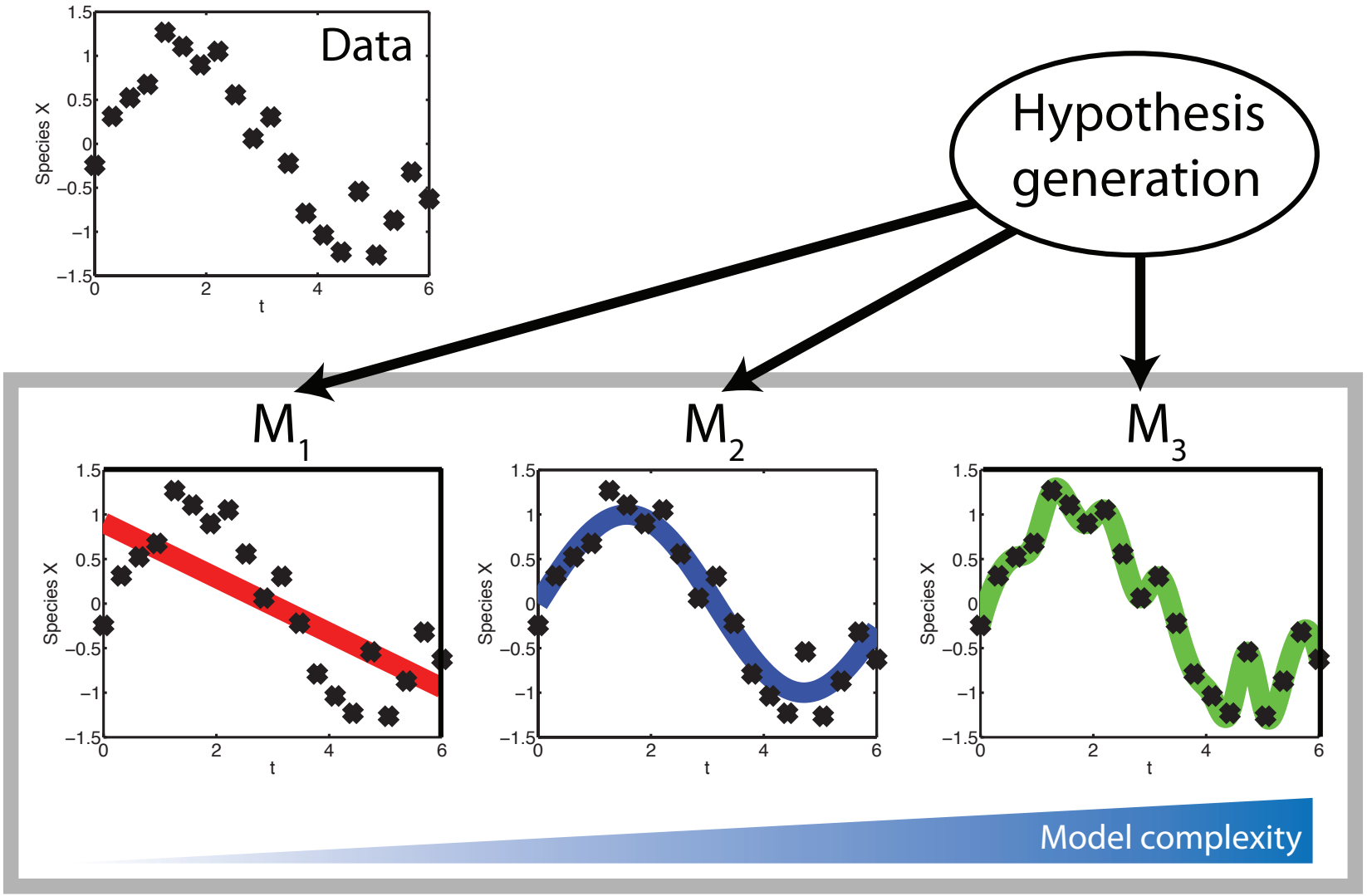
Chemical reaction system illustrating the ”local minimum problem”



[Silk et al, 2013]

OUTLINE

Model selection



[Kirk *et al*, 2013]

BAYESIAN APPROACH FOR MODEL SELECTION

- How likely is a model $\mathcal{M}$ given the observed data x^*?

$$\pi(\mathcal{M}|x^*) \propto f(x^*|\mathcal{M})\pi(\mathcal{M})$$

- Model evidence

$$\pi(x^*|\mathcal{M}) = \int f(x^*|\theta, \mathcal{M})\pi(\theta|\mathcal{M})d\theta$$

- Bayes factor to discriminate between two models $\mathcal{M}_1$ and $\mathcal{M}_2$:

$$B_{1,2} = \frac{\pi(\mathcal{M}_1|x^*)}{\pi(\mathcal{M}_2|x^*)} = \frac{\pi(x^*|\mathcal{M}_1)\pi(\mathcal{M}_1)}{\pi(x^*|\mathcal{M}_2)\pi(\mathcal{M}_2)}$$

Use Jeffrey's scale to interpret values of Bayes factor

COMPUTATION OF THE EVIDENCE

Model evidence:

$$\pi(x^*|\mathcal{M}) = \int f(x^*|\theta, \mathcal{M})\pi(\theta|\mathcal{M})d\theta$$

- Analytically (?)
- Using importance sampling methods
- Some parameter inference methods also allows us to compute model evidence
- Perform inference on the joint space (parameter and model) and then marginalisation

GENERIC ABC FOR MODEL CHOICE

1: **Input:** observation x^*, threshold ϵ, finite set of models
2: **for** $i = 1, \ldots, N$ **do**
3: **repeat**
4: generate m from the prior $\pi(\mathcal{M} = m)$
5: generate θ_m from the prior distribution $\pi_m(\cdot)$
6: generate z from the simulator $f_m(\cdot|\theta_m)$
7: **until** $d(\eta(z), \eta(x^*)) \leq \epsilon$
8: set $m^{(i)} = m$ and $\theta^{(i)} = \theta_m$
9: **end for**

Notation: Here we index by m the priors and likelihood functions to highlight the fact that they are different for each model.

ABC FOR MODEL SELECTION

	M_1	M_2	M_3	M_4
Model accepted	-	-	-	-

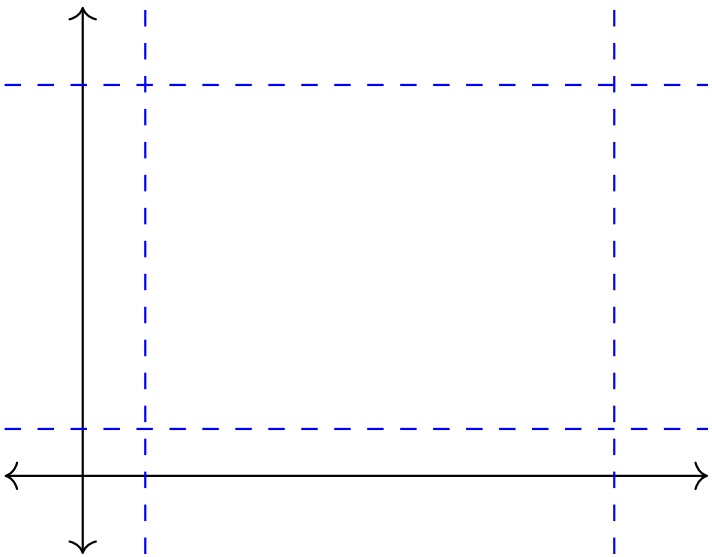
ABC FOR MODEL SELECTION

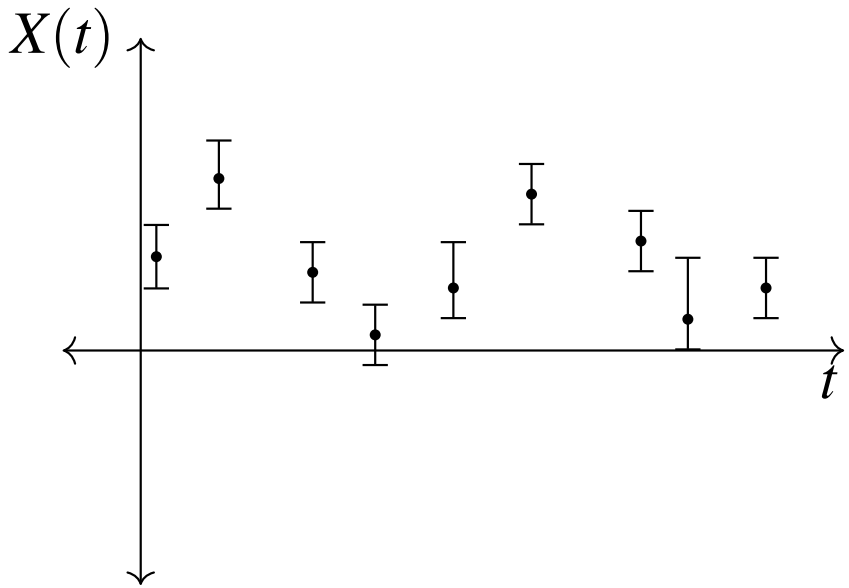
	M_1	M_2	M_3	M_4
Model accepted	-	-	-	-

ABC FOR MODEL SELECTION

	M_1	M_2	M_3	M_4
Model accepted	-	-	-	-

Model M_2

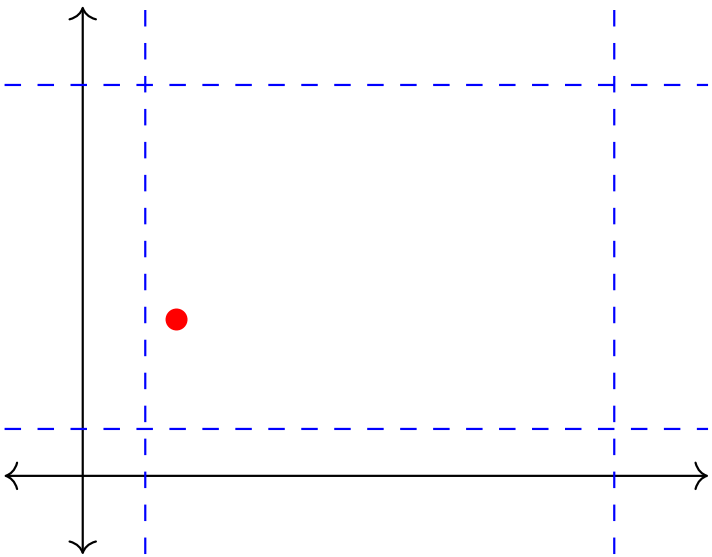


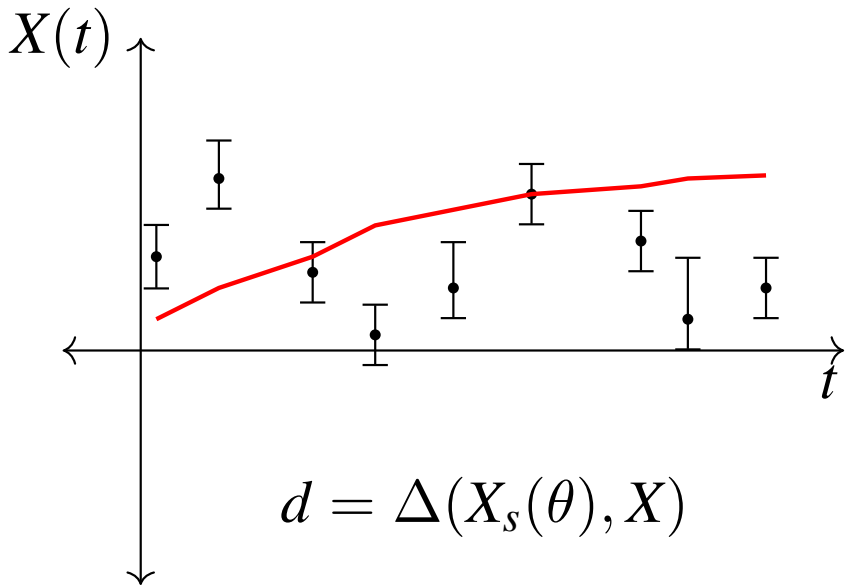


ABC FOR MODEL SELECTION

	M_1	M_2	M_3	M_4
Model accepted	-	-	-	-

Model M_2



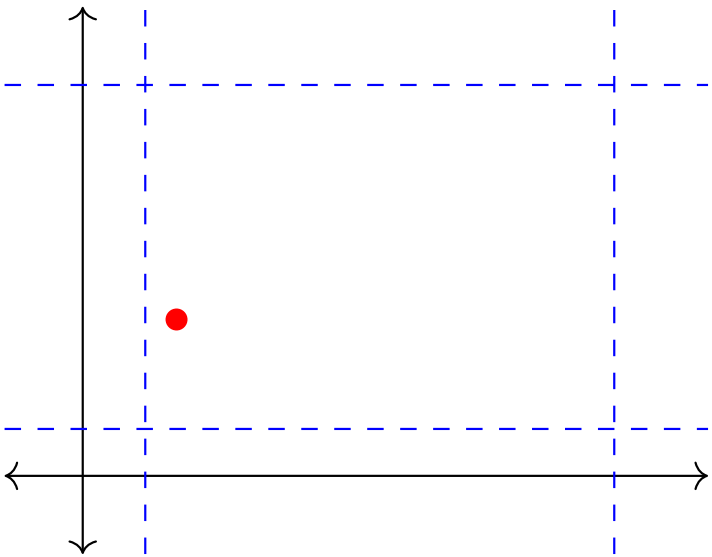


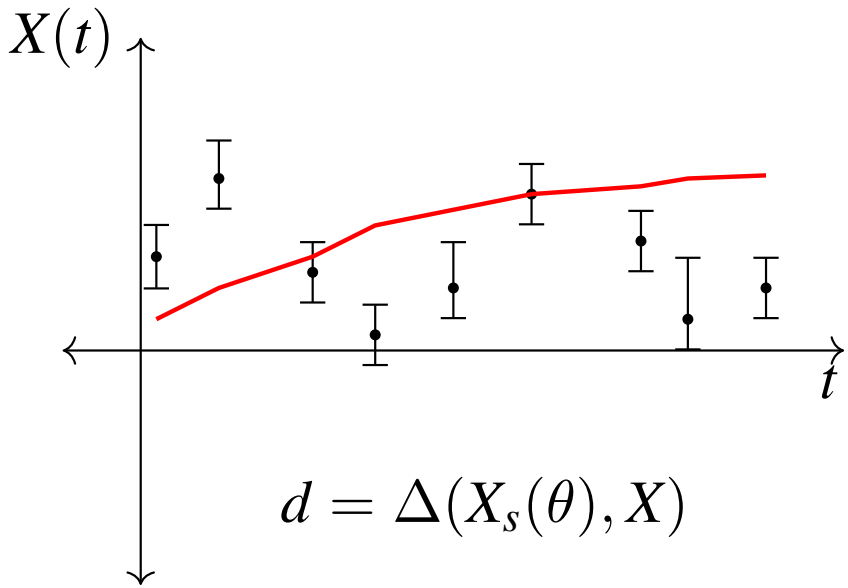
$$d = \Delta(X_s(\theta), X)$$

ABC FOR MODEL SELECTION

	M_1	M_2	M_3	M_4
Model accepted	-	0	-	-

Model M_2





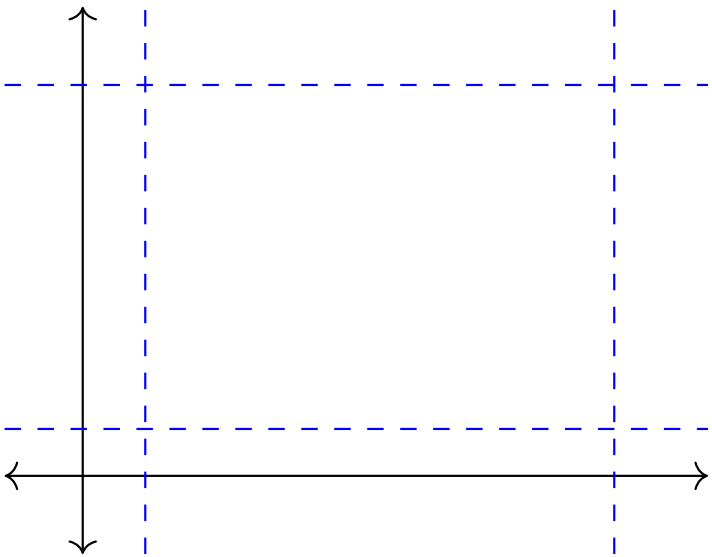
$$d = \Delta(X_s(\theta), X)$$

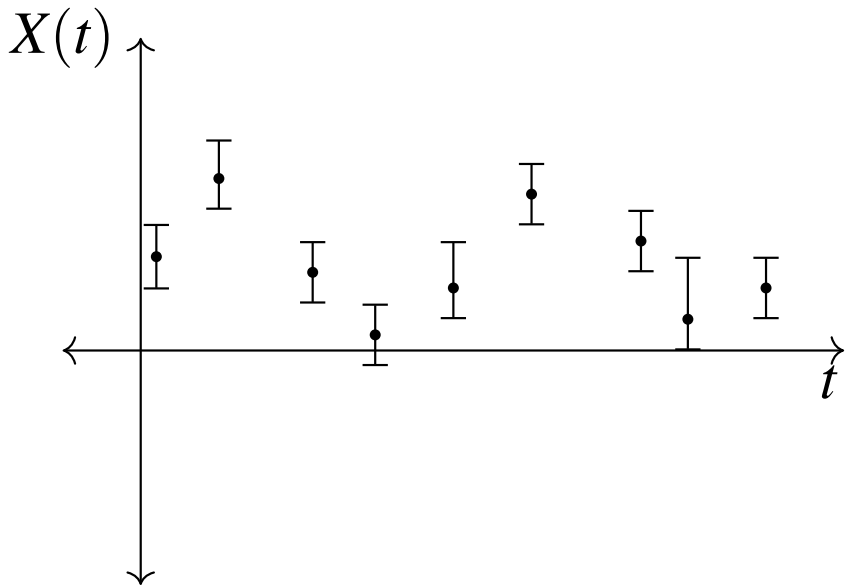
Reject (M, θ) if $d > \epsilon$
Accept (M, θ) if $d \leq \epsilon$

ABC FOR MODEL SELECTION

	M_1	M_2	M_3	M_4
Model accepted	-	0	-	-

Model ?

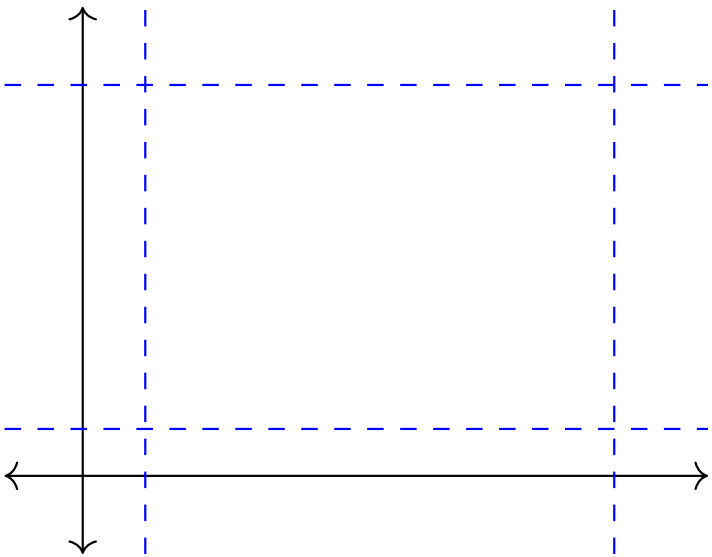


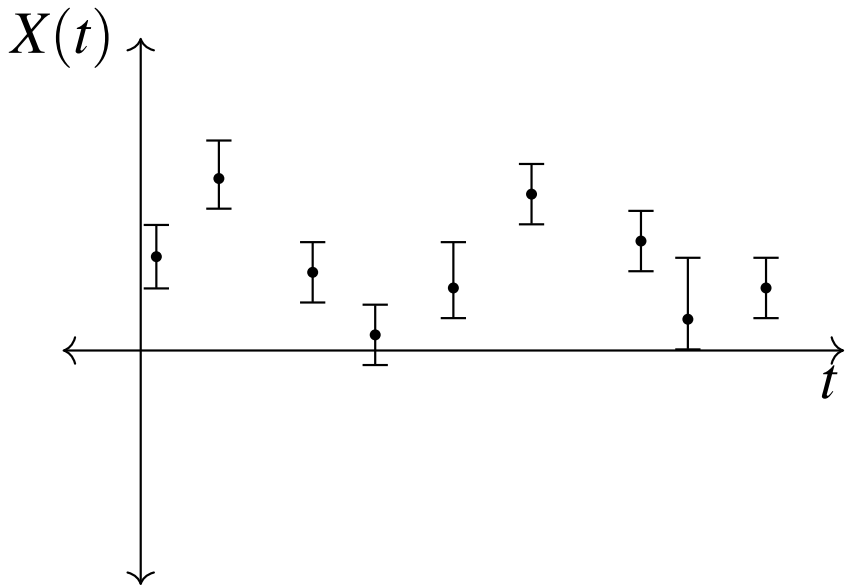


ABC FOR MODEL SELECTION

	M_1	M_2	M_3	M_4
Model accepted	-	0	-	-

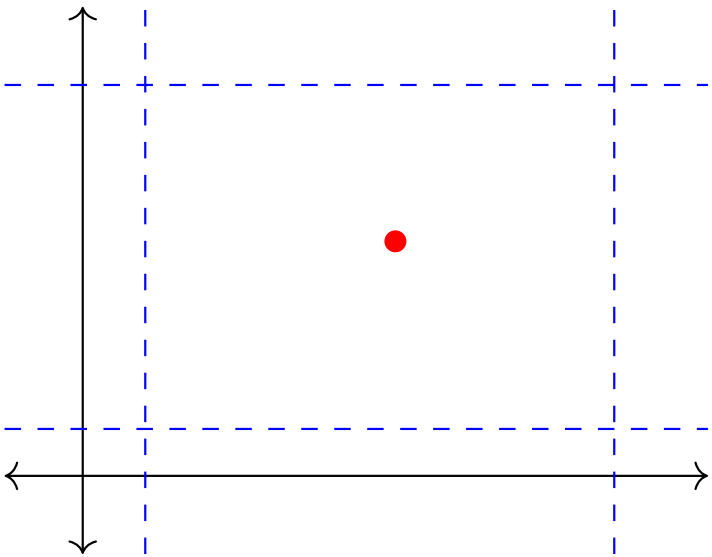
Model 3

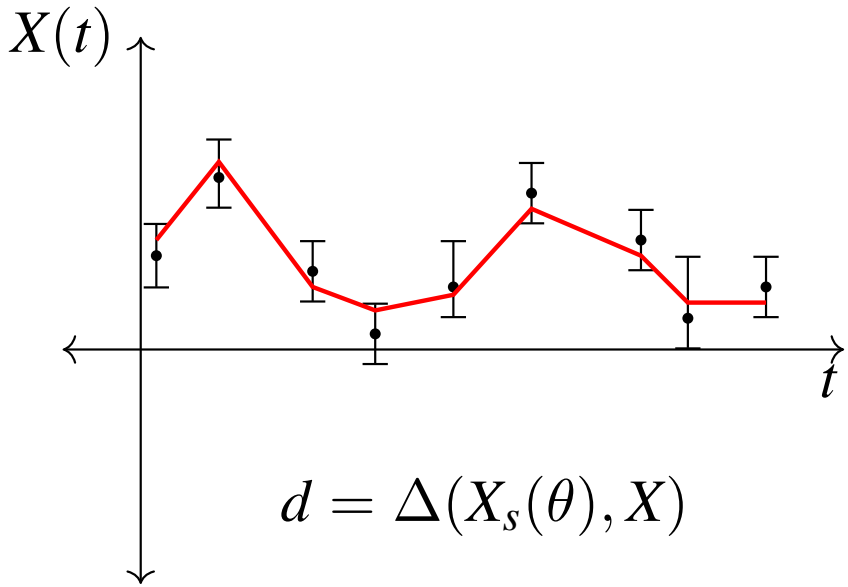




ABC FOR MODEL SELECTION

	M_1	M_2	M_3	M_4
Model accepted	-	0	1	-





$$d = \Delta(X_s(\theta), X)$$

Reject (M, θ) if $d > \epsilon$
Accept (M, θ) if $d \leq \epsilon$

At the end, we obtain

	M_1	M_2	M_3	M_4
Model accepted	3000	70	20	800

and we infer that the first model is the best to explain the data.

ABC FOR MODEL SELECTION

Posterior probability $\pi(\mathcal{M} = m|x^*)$ is approximated by the frequency of acceptances from model m

$$\frac{1}{N}\sum_{i=1}^{N} \mathbb{1}_{m^{(i)}=m} \ .$$

As with parameter inference,

- variants of the MCMC and SMC versions of ABC can be used for model selection
- regression-based variants of ABC can be used to estimate the posterior probability of each model using multinomial logistic regression [Beaumount, 2009] or logistic regression with neural network [Blum & Francois, 2010]

POTENTIAL ISSUES

- Should tolerance ϵ be the same for all models?
- Should summary statistics vary across models?
- Should the distance measure vary as well?

ABC approximation to a Bayes factor

Consider two models $\mathcal{M}_1$ and $\mathcal{M}_2$ and an observation x^*. To discriminate between the two models, we wish to compute the Bayes factor

$$B_{1,2} = \frac{\pi(x^*|\mathcal{M}_1)\pi(\mathcal{M}_1)}{\pi(x^*|\mathcal{M}_2)\pi(\mathcal{M}_2)} = \frac{\pi(\mathcal{M}_1)}{\pi(\mathcal{M}_2)} \frac{\int \pi(\theta_1) f_1(x^*|\theta_1) d\theta_1}{\int \pi(\theta_2) f_2(x^*|\theta_2) d\theta_2}$$

The ABC approximation to the Bayes factor resulting from the previous algorithm is

$$\hat{B}_{1,2} = \frac{\pi(\mathcal{M}_1)}{\pi(\mathcal{M}_2)} \frac{\sum_{t=1}^{T} \mathbb{1}_{m^{(t)}=1} \mathbb{1}_{d(\eta(z^{(t)}),\eta(x^*))\leq\epsilon}}{\sum_{t=1}^{T} \mathbb{1}_{m^{(t)}=2} \mathbb{1}_{d(\eta(z^{(t)}),\eta(x^*))\leq\epsilon}}$$

where the pair $(m^{(t)}, z^{(t)})$ is simulated from the joint prior and T is the number of simulations necessary for N acceptance.

[Robert et al, 2011]

ABC approximation to a Bayes factor

Taking the limit when T goes to infinity:

$$\hat{B}_{1,2} \to B^{\epsilon}_{1,2} = \frac{\pi(\mathcal{M}_1)}{\pi(\mathcal{M}_2)} \frac{\iint \pi(\theta_1) f_1(z|\theta_1) \mathbb{1}_{d(\eta(z),\eta(x^*))\leq\epsilon} dz d\theta_1}{\iint \pi(\theta_2) f_2(z|\theta_2) \mathbb{1}_{d(\eta(z),\eta(x^*))\leq\epsilon} dz d\theta_2}$$
$$= \frac{\pi(\mathcal{M}_1)}{\pi(\mathcal{M}_2)} \frac{\iint \pi(\theta_1) f_1^{\boldsymbol{\eta}}(\boldsymbol{\eta}|\theta_1) \mathbb{1}_{d(\boldsymbol{\eta},\eta(x^*))\leq\epsilon} d\boldsymbol{\eta} d\theta_1}{\iint \pi(\theta_2) f_2^{\boldsymbol{\eta}}(\boldsymbol{\eta}|\theta_2) \mathbb{1}_{d(\boldsymbol{\eta},\eta(x^*))\leq\epsilon} d\boldsymbol{\eta} d\theta_2}$$

where $f_1^{\boldsymbol{\eta}}(\boldsymbol{\eta}|\theta_1)$ and $f_2^{\boldsymbol{\eta}}(\boldsymbol{\eta}|\theta_2)$ are the density of $\eta(z)$ when $z \sim f_1(z|\theta_1)$ and $z \sim f_2(z|\theta_2)$.
When ϵ goes to 0,

$$B^{\epsilon}_{1,2} \to B^{\eta}_{1,2} = \frac{\pi(\mathcal{M}_1)}{\pi(\mathcal{M}_2)} \frac{\int \pi(\theta_1) f_1^{\boldsymbol{\eta}}(\eta(x^*)|\theta_1) d\theta_1}{\int \pi(\theta_2) f_2^{\boldsymbol{\eta}}(\eta(x^*)|\theta_2) d\theta_2}$$

which depends only on the distribution of $\boldsymbol{\eta}$ under both models.

[Robert et al, 2011]

SUFFICIENT STATISTICS AND MODEL SELECTION

- If a summary statistic $\eta(\cdot)$ is sufficient for a model then $\pi(\theta|\eta(x^*)) = \pi(\theta|x^*)$.
- Warning ! $\eta(\cdot)$ being sufficient for both $f_1(x^*|\theta_1)$ and $f_2(x^*|\theta_2)$ does not usually implies fhat $\eta(\cdot)$ is sufficient for model selection.
- Explanation: for such a statistic, there exist $g_1(\cdot)$ and $g_2(\cdot)$ such that

$$f_i(x^*|\theta_i) = g_i(x^*) f_i^{\boldsymbol{\eta}}(\eta(x^*)|\theta_i)$$

and

$$\begin{aligned} B_{1,2} &= \frac{\pi(\mathcal{M}_1)}{\pi(\mathcal{M}_2)} \frac{\int \pi(\theta_1) f_1(x^*|\theta_1) d\theta_1}{\int \pi(\theta_2) f_2(x^*|\theta_2) d\theta_2} \\ &= \frac{\pi(\mathcal{M}_1)}{\pi(\mathcal{M}_2)} \frac{g_1(x^*) \int \pi(\theta_1) f_1^{\boldsymbol{\eta}}(\eta(x^*)|\theta_1) d\theta_1}{g_2(x^*) \int \pi(\theta_2) f_2^{\boldsymbol{\eta}}(\eta(x^*)|\theta_2) d\theta_2} = \frac{g_1(x^*)}{g_2(x^*)} B_{1,2}^{\eta} \end{aligned}$$

[Robert et al, 2011]

How to select summary statistics?

- Previous result implies that ABC model selection will only give accurate estimate of $B_{1,2}$ if $g_1(x^*)/g_2(x^*) = 1$.
- This holds in the case where models $\mathcal{M}_1$ and $\mathcal{M}_2$ are nested submodels of a model $\mathcal{M}$ for which $\eta(\cdot)$ is sufficient.
  [Didelot et al, 2011]
- A necessary condition for an ABC model choice algorithm to converge to the true model: as the sample size increases, the mean of the posterior predictive distribution of the summary statistics converge to different values under different models.
  [Marin et al, 2014]

Example: Laplace vs Normal

Consider the two following models with equal prior:

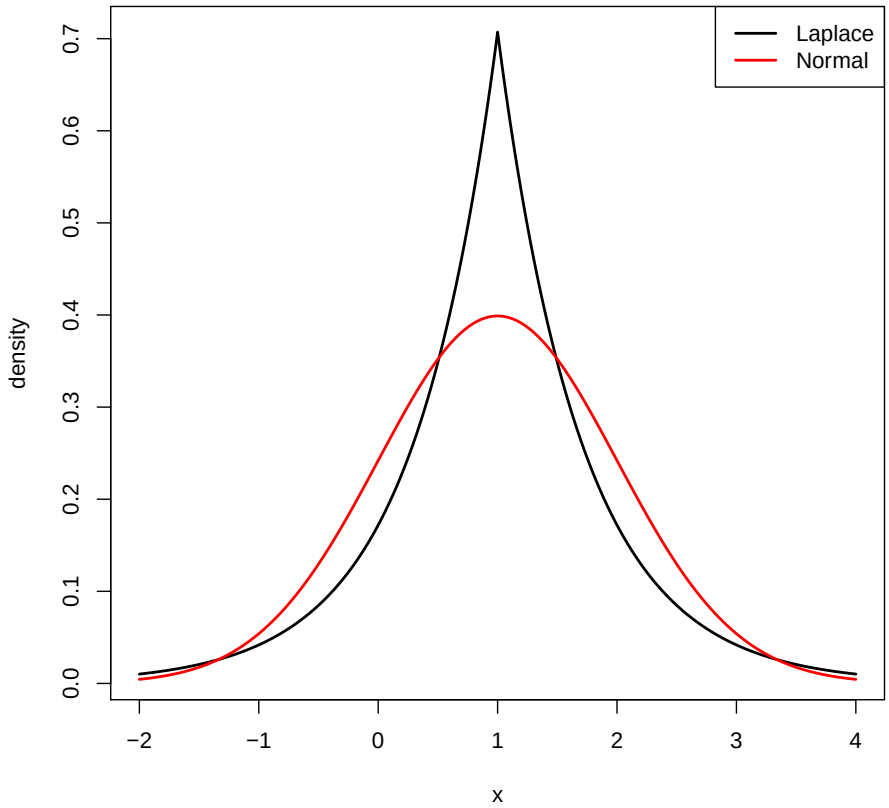
$$\mathcal{M}_1 : y \sim \mathcal{N}(\theta_1, 1) \qquad \text{and} \qquad \mathcal{M}_2 : y \sim \mathcal{L}(\theta_2, 1/\sqrt{2})$$

Prior distribution: $\mathcal{N}(0, 4)$

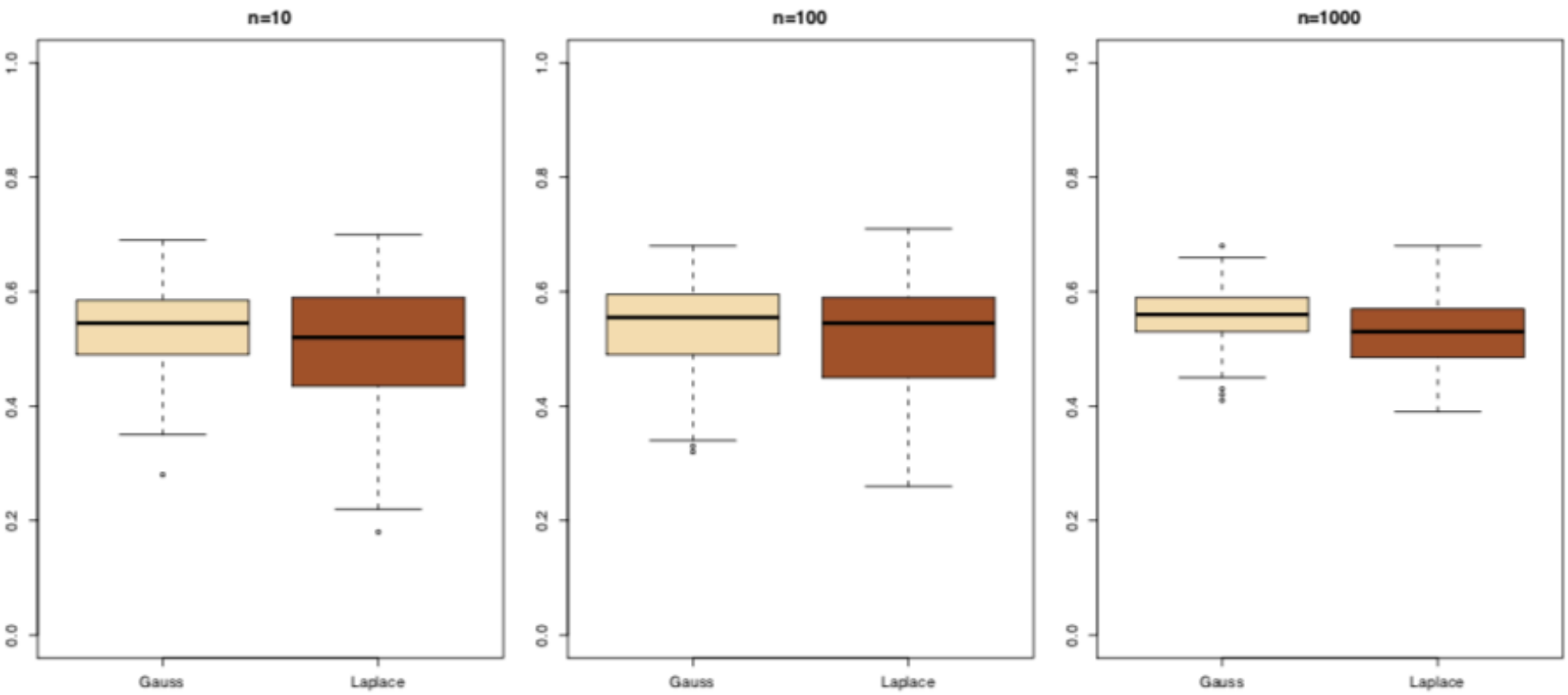
Summary statistics:

- sample mean
- sample median
- sample variance
- median absolute deviation
- sample fourth moment

sufficient statistics, ancillary statistics,
statistic for model selection



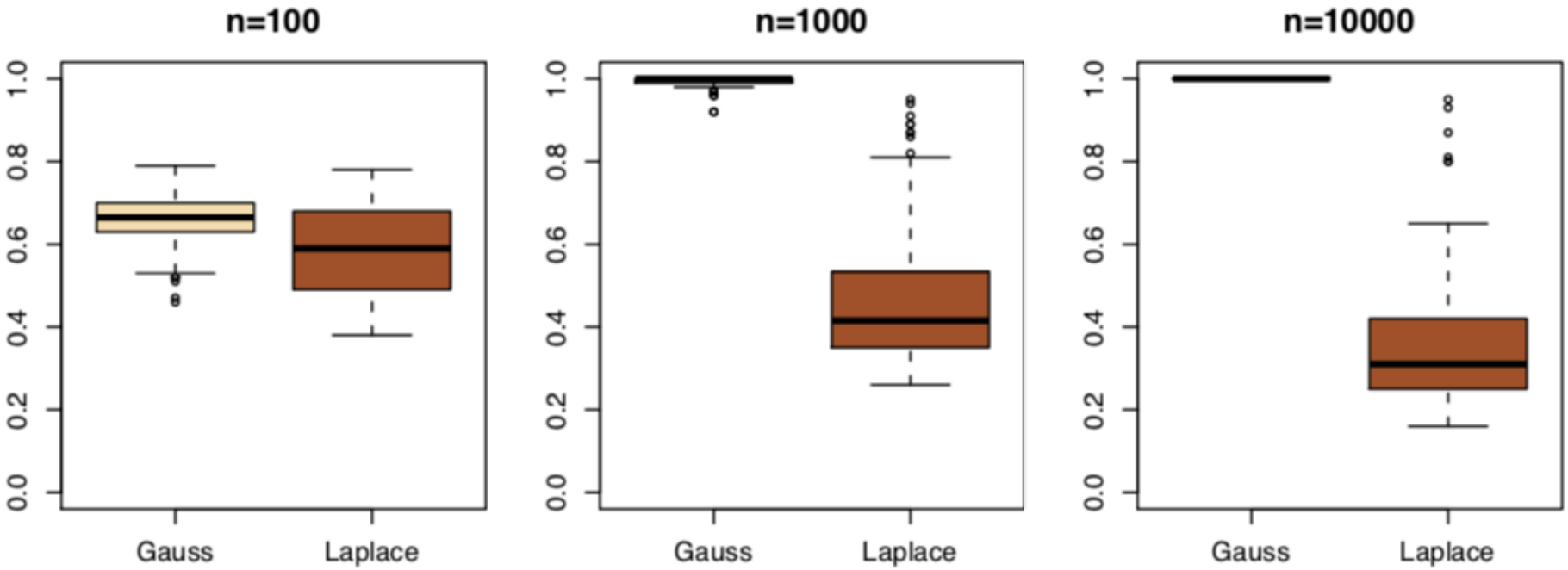
EXAMPLE: LAPLACE VS NORMAL



Data: sample of n observations either from a Gaussian or Laplace distribution with mean 0;
Summary statistics: sample mean, median and variance;
ABC : 5000 simulations for each model and ϵ=1% distance quantile.

[Marin et al, 2014]

EXAMPLE: LAPLACE VS NORMAL



Summary statistics: empirical fourth moment.
For Normal: $\theta^4 + 3 + 6\theta^2$ and for Laplace: $\theta^4 + 6 + 6\theta^2$

[Marin et al, 2014]

How to select summary statistics?

Theoretical result from [Marin et al, 2014] motivated approaches to discriminate models.

Recent approaches include:

- Simulating samples from posterior predictive distributions of the summary statistics and select statistics with different means under different models [Marin et al, 2014]
- Logistic regression to estimate posterior probability of of summary statistics from pilot simulations [Prangle et al, 2014]
- Linear discriminant analysis to maximize seprarability of the models [Estoup et al, 2012]
- Random forest [Pudlo et al, 2015]

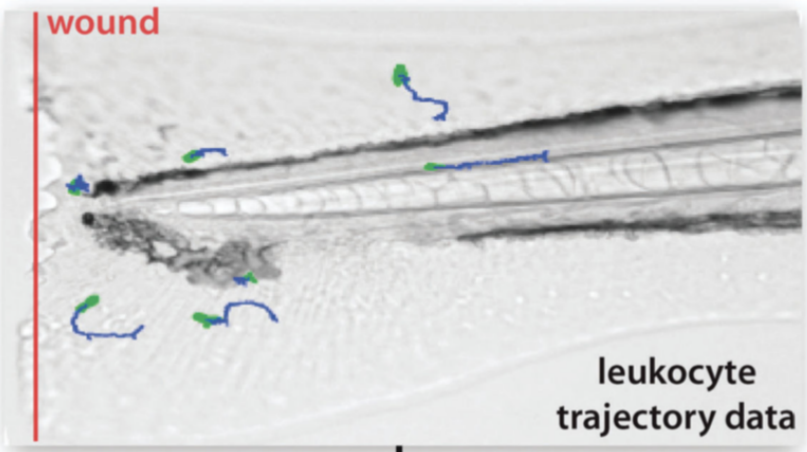
[Beaumont et al, 2019]

EXAMPLE: LEUKOCYTE MIGRATION

- Stimulus released from injury
- Observation: movements of the leukocytes
- Models to describe the leukocyte dynamics with 3 different stimulus gradient shapes

[Liepe et al, 2012]

EXAMPLE: LEUKOCYTE MIGRATION

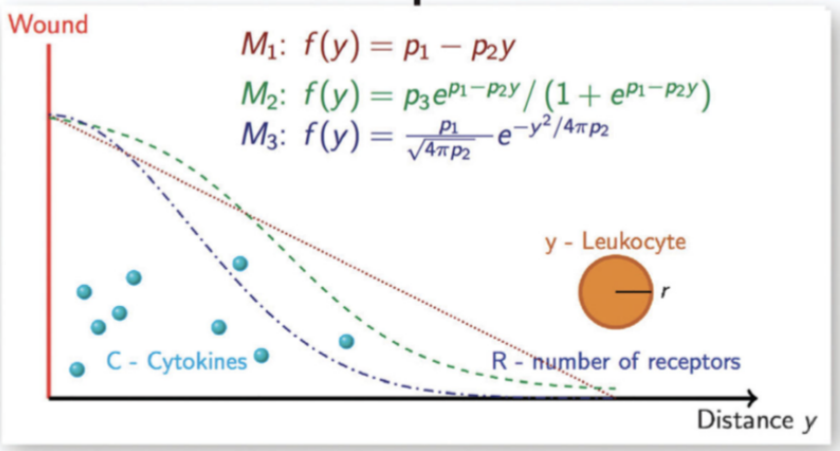


inference:
ABC SMC

selected model
(with inferred parameter)

information about stimulus gradient

information about migration process



[Liepe et al, 2012]

Take-home messages

Approximate Bayesian Computation

To be used for **parameter inference** and **model selection** when the likelihood can not be computed but it is possible to simulate from the model.

Simple approach

Only requires:

- a simulator
- a distance
- a threshold
- computational resources

Warning ! Be careful with choice of summary statistic.

Computational efficient approaches

- ABC-MCMC
- Sequential ABC – with an optimal choice of perturbation kernel

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