

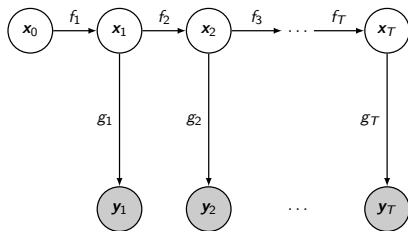
Bayesian Parameter Estimation of State-Space Models with Intractable Likelihood

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State-Space Model (SSM)

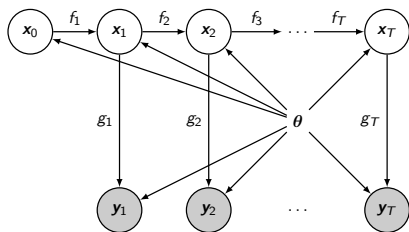


$$x_t = \sin x_{t-1} + \epsilon_t, \quad \epsilon_t \sim \mathcal{N}(0, \sigma_x^2)$$

$$y_t = 0.5x_t + \eta_t, \quad \eta_t \sim \mathcal{N}(0, \sigma_y^2)$$

- Interest in $p(\mathbf{x}_{0:T} \mid \mathbf{y}_{1:T})$.
- Solvable via filtering.

State-Space Model (SSM)



$$\mathbf{x}_t = \mathbf{A} \mathbf{x}_{t-1} + \boldsymbol{\epsilon}_t, \quad \boldsymbol{\epsilon}_t \sim \mathcal{N}(\mathbf{0}, \boldsymbol{\Sigma}_x^2)$$

$$\mathbf{y}_t = \mathbf{C} \mathbf{x}_t + \boldsymbol{\eta}_t, \quad \boldsymbol{\eta}_t \sim \mathcal{N}(\mathbf{0}, \boldsymbol{\Sigma}_y^2)$$

$$\boldsymbol{\theta} = (\mathbf{C}, \boldsymbol{\Sigma}_x^2, \boldsymbol{\Sigma}_y^2)^\top$$

- Interest in $p(\boldsymbol{\theta}, \mathbf{x}_{0:T} \mid \mathbf{y}_{1:T}) = p(\mathbf{x}_{0:T} \mid \boldsymbol{\theta}, \mathbf{y}_{1:T})p(\boldsymbol{\theta} \mid \mathbf{y}_{1:T})$.
- $p(\boldsymbol{\theta} \mid \mathbf{y}_{1:T}) \propto p(\mathbf{y}_{1:T} \mid \boldsymbol{\theta})\pi(\boldsymbol{\theta})$.
- $p(\mathbf{y}_{1:T} \mid \boldsymbol{\theta}) = \int p(\mathbf{x}_{0:T}, \mathbf{y}_{1:T} \mid \boldsymbol{\theta}) \, d\mathbf{x}_{0:T}$ intractable in general.

Particle filter

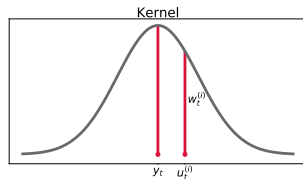
- Use weighted particles $\left\{ \left(\mathbf{x}_t^{(i)}, w_t^{(i)} \right) : i = 1, \dots, N \right\}$ to approximate the filtering distribution $p(\mathbf{x}_t \mid \mathbf{y}_{1:t}, \boldsymbol{\theta})$.
- Simulate the particles $\mathbf{x}_t^{(i)} \sim f_t(\mathbf{x}_t \mid \mathbf{x}_{t-1}^{(i)})$ and weight them according to $w_t^{(i)} = g_t(\mathbf{y}_t \mid \mathbf{x}_t^{(i)}, \boldsymbol{\theta})$.
- An unbiased likelihood estimator is

$$\hat{p}(\mathbf{y}_{1:T} \mid \boldsymbol{\theta}) = \prod_{t=1}^T \frac{1}{N} \sum_{i=1}^N w_t^{(i)}.$$

- Problem: the observation model $g_t(\mathbf{x}_t \mid \mathbf{y}_t, \boldsymbol{\theta})$ must be known and probabilistic.

Approximate Bayesian Computation (ABC)

- Still approximating the likelihood, different weight calculation.
- Simulate pseudo-observations \mathbf{u}_t from $g_t(\mathbf{y}_t \mid \mathbf{x}_t, \theta)$.
- Determine $w_t^{(i)}$ based on the distance of \mathbf{u}_t to the true \mathbf{y}_t measured by a kernel function.
- A flexible and robust approach no longer requiring a probabilistic observation model.



Lotka-Volterra model

- A simplified system of interacting prey (\mathcal{X}_1) and predator (\mathcal{X}_2) species described by

$$\mathcal{R}_1 : \quad \mathcal{X}_1 \rightarrow 2\mathcal{X}_1,$$

$$\mathcal{R}_2 : \quad \mathcal{X}_1 + \mathcal{X}_2 \rightarrow 2\mathcal{X}_2,$$

$$\mathcal{R}_3 : \quad \mathcal{X}_2 \rightarrow \emptyset.$$

- Assume $\mathbf{y}_t = \mathbf{x}_t = (x_{1,t}, x_{2,t})^\top$, Gaussian observation model and the unknown parameters to be $\boldsymbol{\theta} = (\mathbf{c}_1, \mathbf{c}_2, \mathbf{c}_3)^\top$.
- Denoting the number of species j present at the beginning of \mathcal{R}_i by p_{ij} ,

$$\mathbf{c}_i \prod_{j=1}^2 \binom{x_{j,t}}{p_{ij}}$$

is the mean time to the next occurrence of \mathcal{R}_i at time t .

Lotka-Volterra model

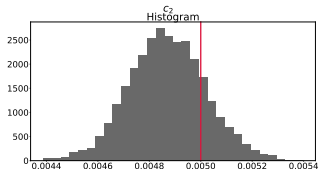


Figure: Well-specified PF.

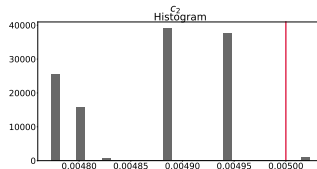


Figure: Misspecified PF.

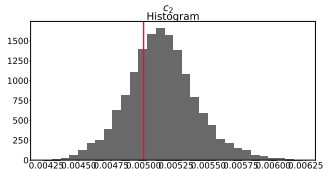


Figure: Well-specified ABC.

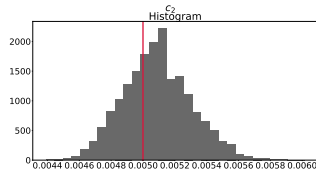
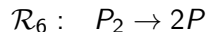
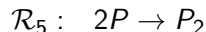
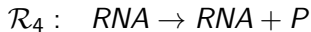
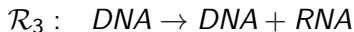
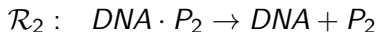
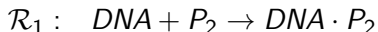


Figure: Misspecified ABC.

Prokaryotic autoregulation model



- Unknown parameters $\theta = (c_1, c_2, c_3, c_4, c_7, c_8)^\top$, Gaussian observation model.
- $\mathbf{x}_t = (\text{RNA}_t, P_t, (P_2)_t, \text{DNA}_t)^\top$.
- $\mathbf{y}_t = P_t + 2(P_2)_t$.

Prokaryotic autoregulation model

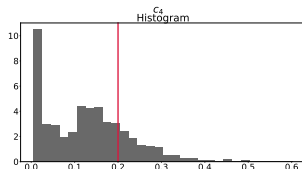


Figure: Well-specified PF.

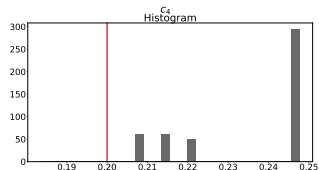


Figure: Misspecified PF.

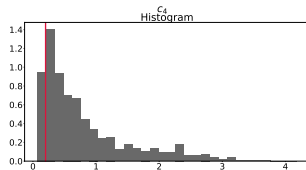


Figure: Well-specified ABC.

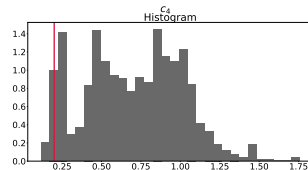


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Prokaryotic autoregulation model

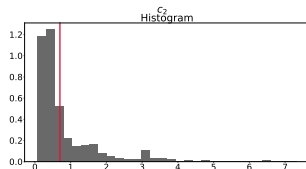


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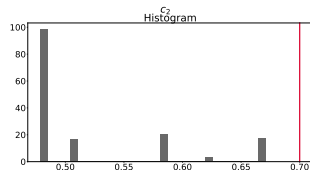


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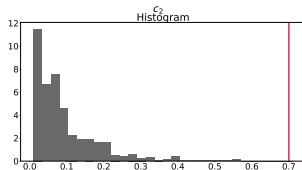


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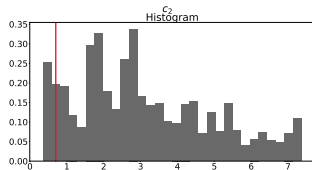


Figure: Misspecified ABC.

Summary

- Static parameters complicate inference.
- Intractable likelihood can be approximated through the particle filter, assuming a known observation density $g_t(\mathbf{y}_t \mid \mathbf{x}_t, \boldsymbol{\theta})$.
- When only a deterministic observation process is available, ABC methods can be used instead.
- Robust to outliers and model misspecification.
- Flexibility in kernel choice.

Prokaryotic autoregulation model

- The model assumes that the dimer of a protein P , denoted P_2 , represses the transcription of its coding gene by binding to a regulatory region in the gene.

| | | |
|-------------------|---------------------------------------|---------------------|
| $\mathcal{R}_1 :$ | $DNA + P_2 \rightarrow DNA \cdot P_2$ | Repression |
| $\mathcal{R}_2 :$ | $DNA \cdot P_2 \rightarrow DNA + P_2$ | (Reversible) |
| $\mathcal{R}_3 :$ | $DNA \rightarrow DNA + RNA$ | Transcription |
| $\mathcal{R}_4 :$ | $RNA \rightarrow RNA + P$ | Translation |
| $\mathcal{R}_5 :$ | $2P \rightarrow P_2$ | Dimerization |
| $\mathcal{R}_6 :$ | $P_2 \rightarrow 2P$ | (Reversible) |
| $\mathcal{R}_7 :$ | $RNA \rightarrow \emptyset$ | RNA degradation |
| $\mathcal{R}_8 :$ | $P \rightarrow \emptyset$ | Protein degradation |

Gillespie algorithm

All operations for $i = 1, \dots, v$, the number of reactions.

1. Set $t = 0$, initialize \mathbf{x}_t .

2. While $t \leq T$:

2.1 Calculate $h_i(\mathbf{x}_t, c_i) = c_i \prod_{j=1}^u \binom{x_{j,t}}{p_{ij}}$.

2.2 Sample $dt \sim \text{Exp}(\sum_{i=1}^v h_i(\mathbf{x}_t, c_i))$.

2.3 Sample i with probability $\propto h_i(\mathbf{x}_t, c_i)$.

2.4 Set \mathbf{x}_{t+dt} by updating \mathbf{x}_t according to \mathcal{R}_i .

2.5 $t = t + dt$.

3. Output \mathbf{x}_t , t .

ABC filter

All operations for $i = 1, \dots, N$.

1. Sample $\mathbf{x}_0^{(i)} \sim p(\mathbf{x}_0 \mid \boldsymbol{\theta})$, set $w_0^{(i)} = \frac{1}{N}$.
2. For $t = 1, \dots, T$:
 - 2.1 Sample $\mathbf{x}_t^{(i)} \sim f_t(\mathbf{x}_t \mid \mathbf{x}_t^{(i)}, \boldsymbol{\theta})$.
 - 2.2 Simulate $\mathbf{u}_t^{(i)}$ from $g_t(\cdot \mid \mathbf{x}_t^{(i)}, \boldsymbol{\theta})$.
 - 2.3 Identify $\mathbf{u}_t^{[\alpha]}$, the α th closest pseudo-observation to \mathbf{y}_t .
 - 2.4 Set the kernel scale $\epsilon_t = \frac{|\mathbf{u}_t^{[\alpha]} - \mathbf{y}_t|}{F^{-1}(\frac{1+p}{2})}$.
 - 2.5 Set the weights $w_t^{(i)} \propto \kappa(\frac{\mathbf{u}_t^{(i)} - \mathbf{y}_t}{\epsilon_t}) w_{t-1}^{(i)}$.
 - 2.6 Resample $\mathbf{x}_t^{(i)}$ and reset $w_t^{(i)}$.
3. Output $\{w_1^{(1)}, \dots, w_1^{(N)}, \dots, w_T^{(1)}, \dots, w_T^{(N)}\}$.

ABC Metropolis-Hastings

1. Initialize $\theta^{(0)}$, estimate $\hat{p}(\mathbf{y}_{1:T} \mid \theta^{(0)})$.
2. For $m = 1, \dots, M$:
 - 2.1 Propose $\theta' \sim q(\cdot \mid \theta^{(m-1)})$.
 - 2.2 Estimate $\hat{p}(\mathbf{y}_{1:T} \mid \theta')$.
 - 2.3 Calculate the acceptance ratio

$$\alpha = \min \left\{ 1, \frac{\hat{p}(\mathbf{y}_{1:T} \mid \theta') \pi(\theta')}{\hat{p}(\mathbf{y}_{1:T} \mid \theta^{(m-1)}) \pi(\theta^{(m-1)})} \frac{q(\theta^{(m-1)} \mid \theta')}{q(\theta' \mid \theta^{(m-1)})} \right\}$$

- 2.4 With probability α , set $\theta^{(m)} = \theta'$. Otherwise, set $\theta^{(m)} = \theta^{(m-1)}$.
3. Output $\{\theta^{(1)}, \dots, \theta^{(M)}\}$.