Minimizing multi-pathogen risk and costs through control measures

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ArtiSaneFood: Biopreservation and Risk Modelling Approaches
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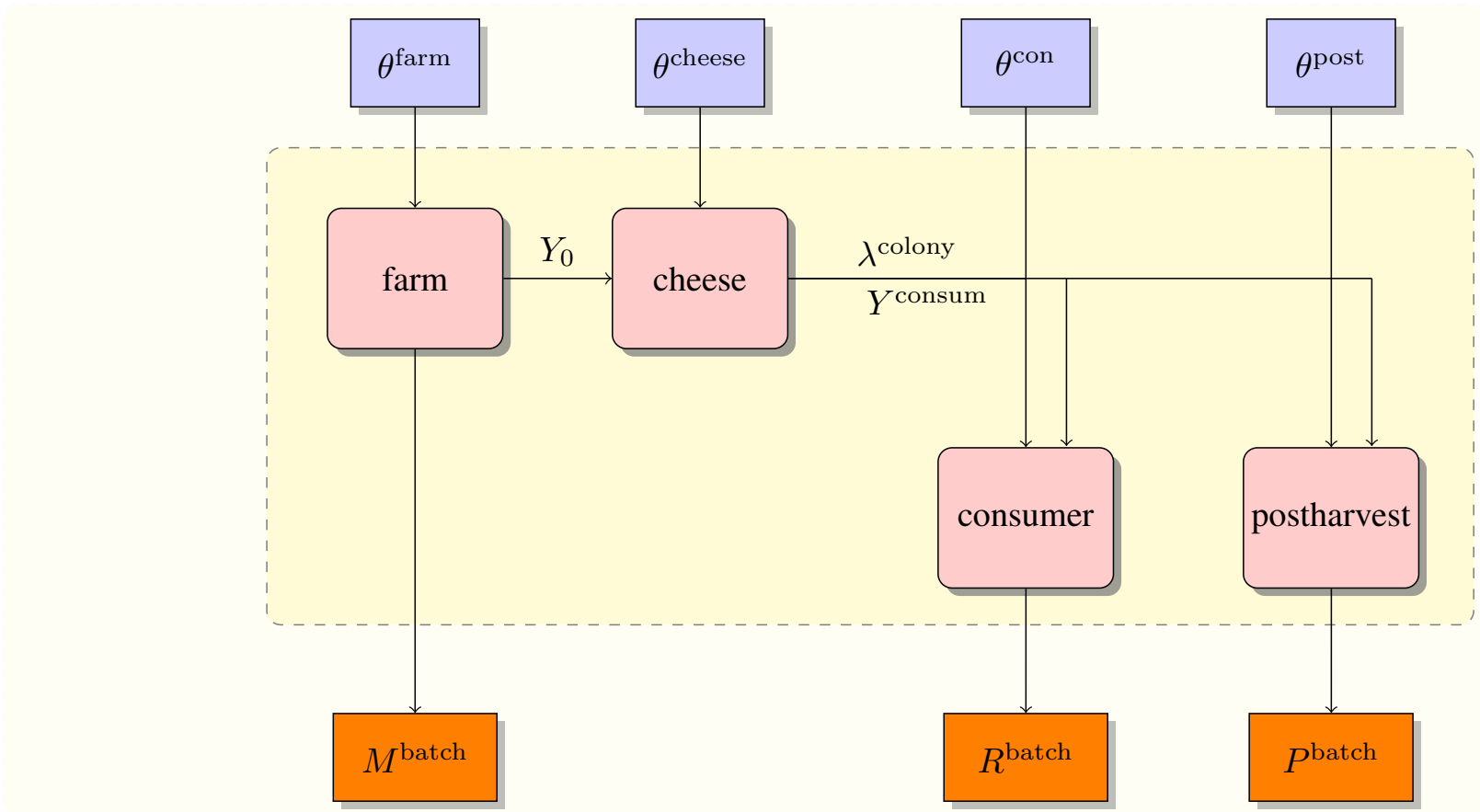
Motivation & application

- Aim : Control risk of illness from pathogens in raw milk cheese
  - STEC → Haemolytic Uremic Syndrome (HUS)

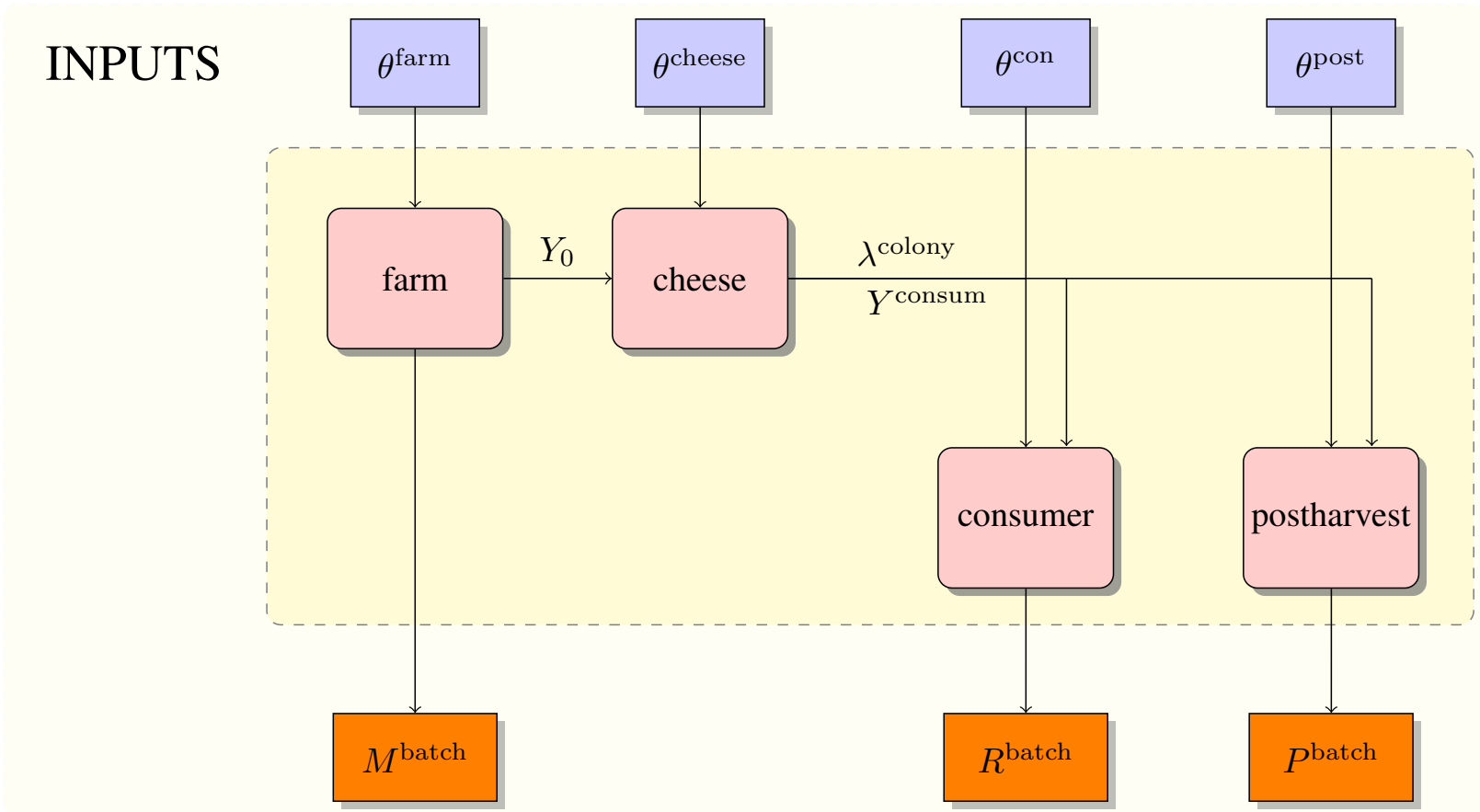
    STEC & MPS STEC
  - Salmonella → Salmonellosis

    High & Low Virulent Salmonella
- Quantitaive Risk Assesement (QRA)
  - Based on *Perrin et al. (2014)* and *Basak et al. (in prep.)*
- Optimization : Find intervention parameters that minimize the objectives
  - Relative risk of illness & intervention cost (€)

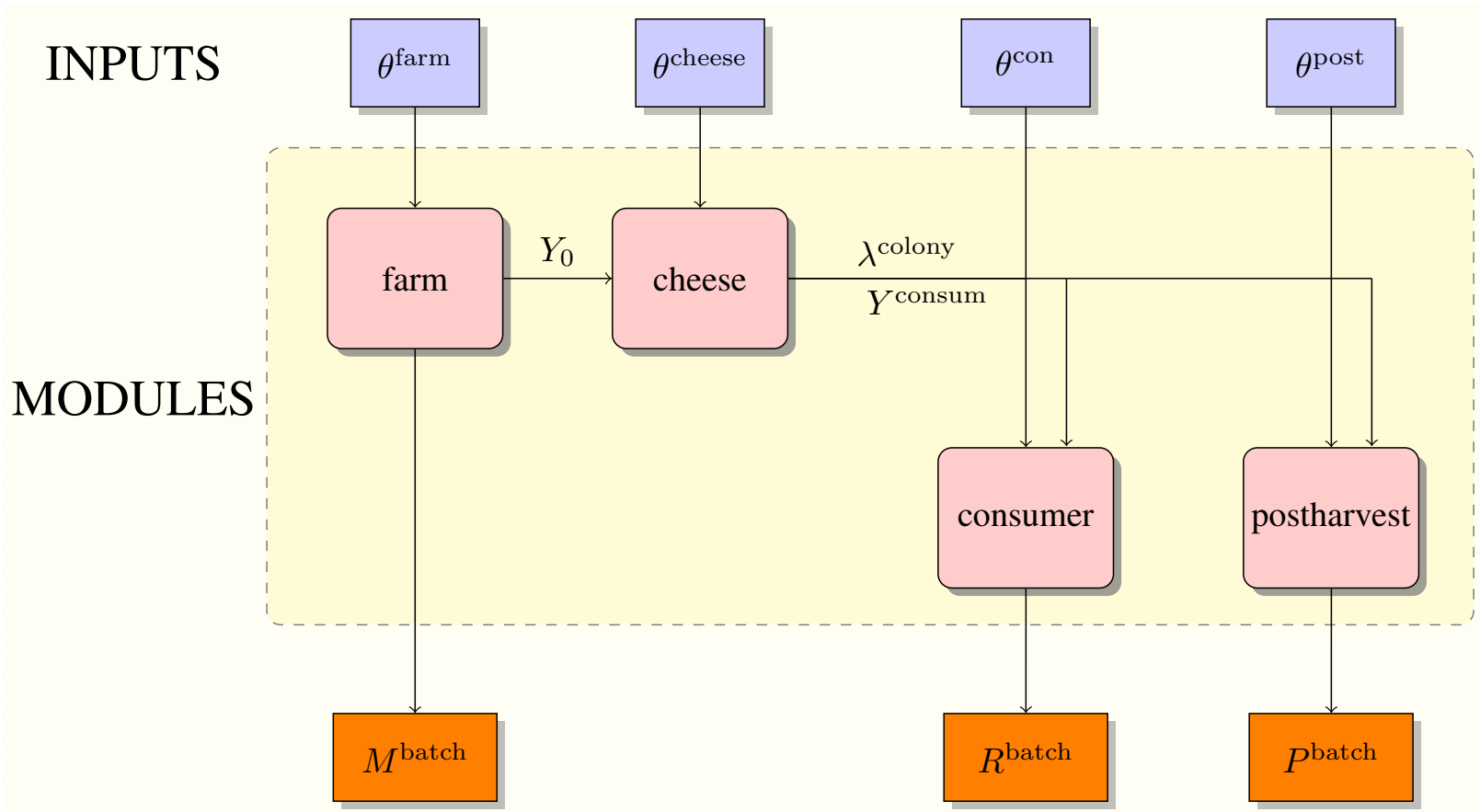
QRA model – Raw milk cheese



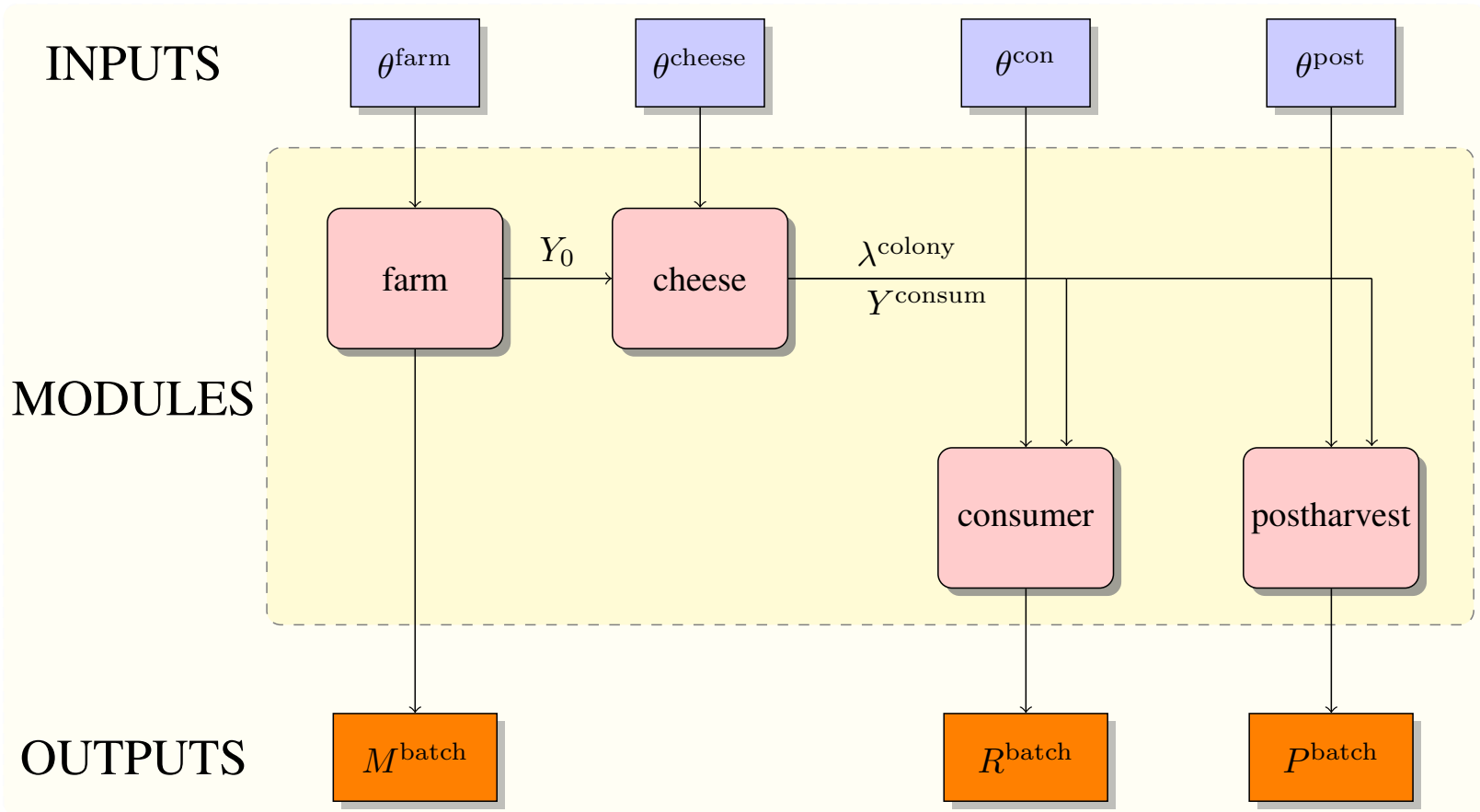
QRA model – Raw milk cheese



QRA model – Raw milk cheese



QRA model – Raw milk cheese



Farm module : Milk collection

- Milk sorting: Reject farm if E.coli conc. $(Y_{\text{milk}}^{\text{Ecoli}}) >$ threshold

  $Y_{\text{milk}}^{\text{Ecoli}} \sim$ Lognormal with parameters based on *CNIEL + ACTALIA* data

- Concentrations are computed indirectly due to limit of detection

$$Y_{\text{milk}}^{\text{X}} = Y_{\text{milk}}^{\text{Ecoli}} \cdot (Y_{\text{feces}}^{\text{X}} / Y_{\text{feces}}^{\text{Ecoli}})$$

  - $\text{X} \in \{\text{STEC}, \text{Salmonella}\}$
  - $Y_{\text{feces}}^{\text{Salmo}} \sim$ Lognormal, $Y_{\text{feces}}^{\text{STEC}} \sim$ Weibull, $Y_{\text{feces}}^{\text{Ecoli}} \sim$ Lognormal

- Prevalence rates and distribution parameters:
  - *(Perrin et al., 2014)* & *(Bonifait et al., 2021)*

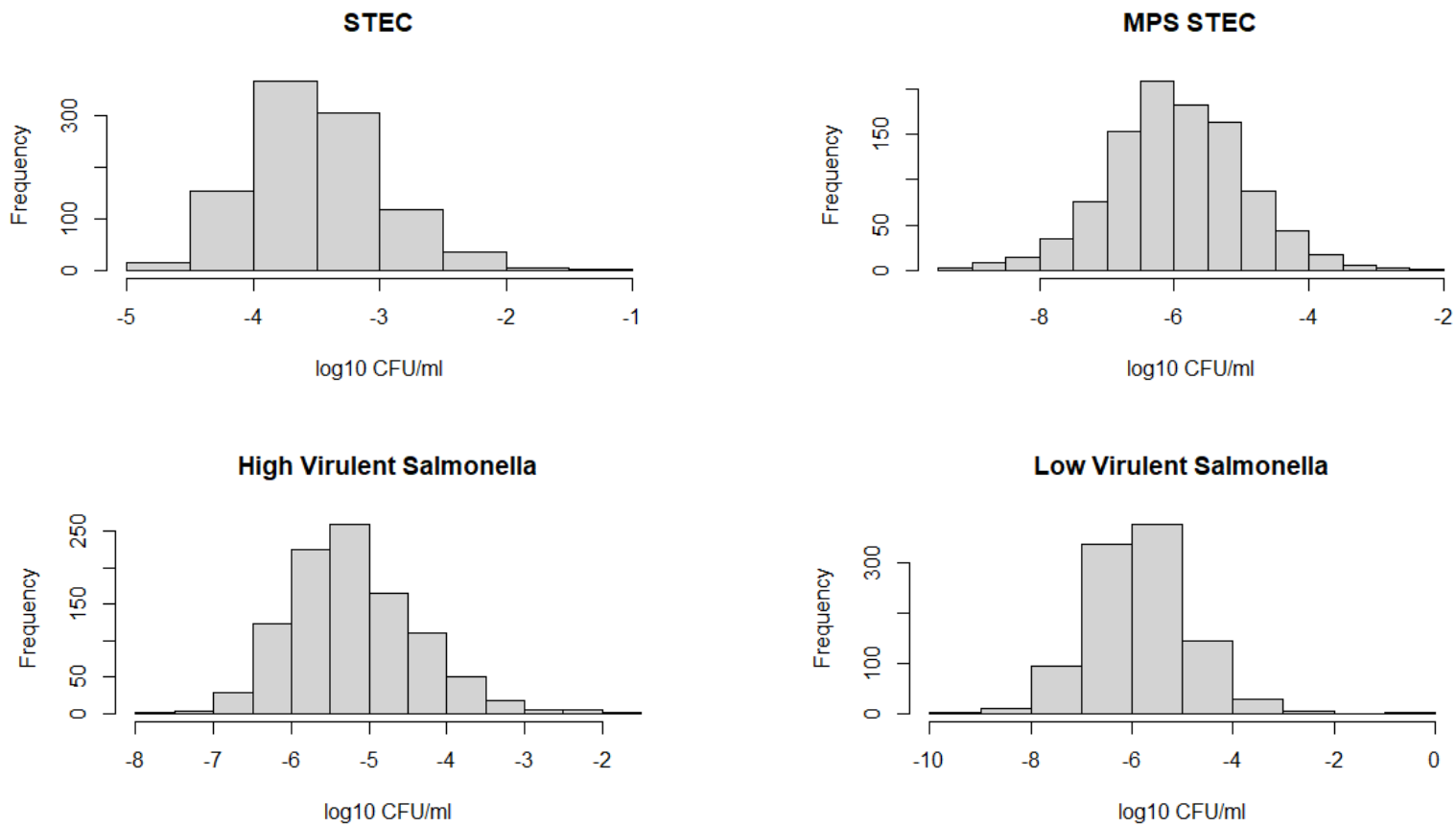


Figure 1: Simulated concentration of bacterias in milk in production

Farm module outputs

Cheese module

- Growth ↗ phase

$$\frac{dy}{dt} = \mu_{\mathrm{X}}^{\max}(t) \cdot y(t) \cdot (1 - \frac{y(t)}{y^{\max}})$$

Milk storage → Molding → *Colony formation* → Draining → Salting

- Decline ↘ phase

$$\text{STEC} : Y_{\mathrm{STEC}}^{\mathrm{consume}} = Y_{\mathrm{STEC}}^{\mathrm{salting}} \cdot 10^{-\rho \cdot t}$$

$$\text{Salmonella} : Y_{\mathrm{Salmo}}^{\mathrm{consume}} = Y_{\mathrm{Salmo}}^{\mathrm{salting}} \cdot 10^{-(t/\delta)^{p}}$$

Ripening → Cheese storage → Consumption

→ Decline rates based on *ACTALIA* report

Cheese module : Pre-molding stages

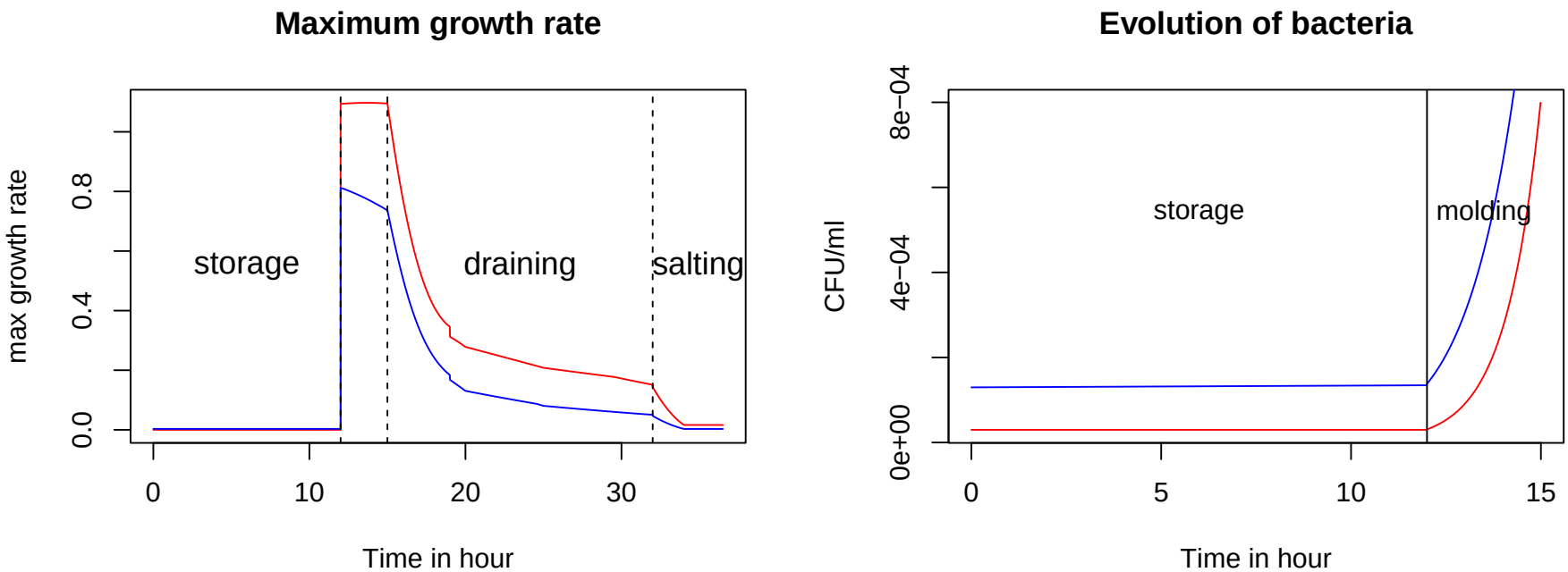


Figure 2: Growth rate $\mu^{\max}(t)$ and evolution $y(t)$ of STEC and Salmonella

$\rightarrow$ Number of colonies: $N_{\mathrm{X}}^{\mathrm{colony}} \sim \mathrm{Poisson}(Y_{\mathrm{X}}^{\mathrm{molding}} \cdot c)$

Cheese module : Evolution of colonies

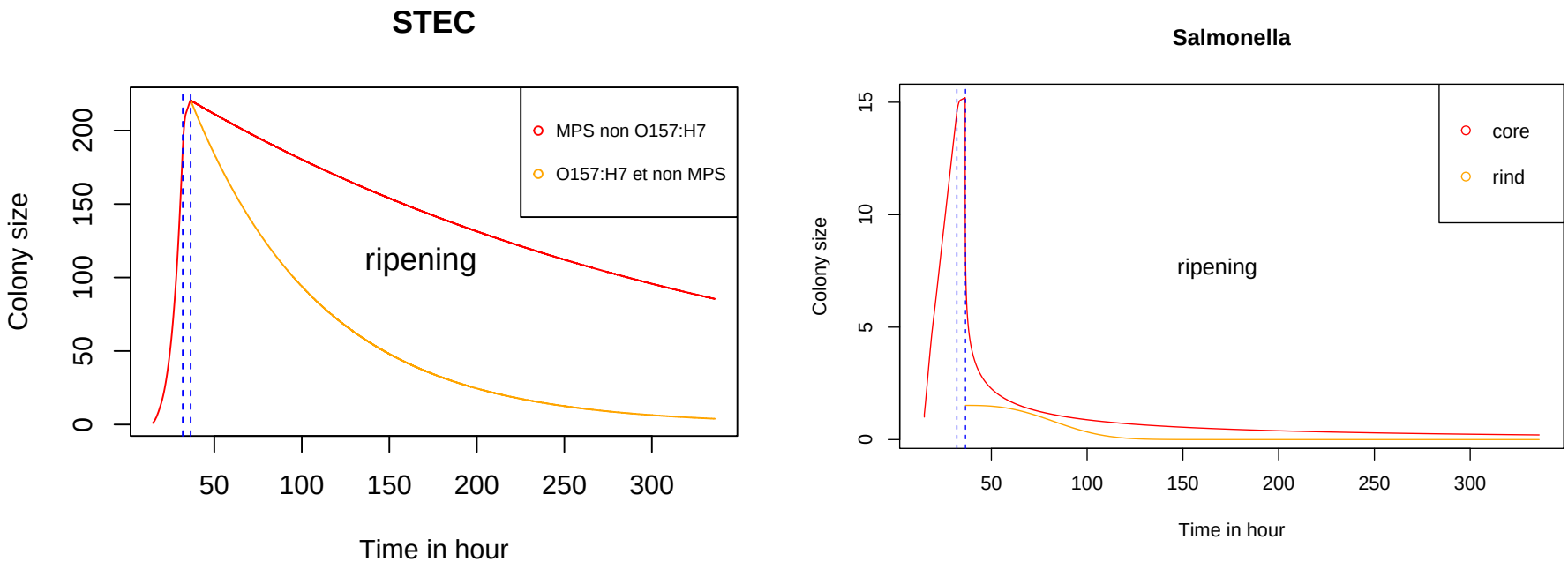


Figure 3: Evolution of colonies of different strains of STEC and Salmonella

$\rightarrow$ Size of colonies: $Y_{\mathrm{X}}^{\mathrm{colony}} \sim \mathrm{Lognormal}$ with median $Y_{\mathrm{X}}^{\mathrm{consume}}$

Consumer module

- Dose in cheese serving:

$$\Gamma_{\mathrm{X}} = \sum_{s \in \mathrm{strains}} N_s^{\mathrm{colony}} \cdot Y_s^{\mathrm{colony}}$$

- Dose-response model:

$$P_{\mathrm{STEC}}^{\mathrm{illness}} = 1 - (1 - r_{\mathrm{age}})^{\Gamma_{\mathrm{STEC}}} \textit{ (Perrin et al., 2014)}$$

$$P_{\mathrm{Salmo}}^{\mathrm{illness}} = 1 - (1 + \frac{\Gamma_{\mathrm{Salmo}}}{\beta})^{-\alpha} \textit{ (Strickland et al., 2023)}$$

- Batch risk:

$$R_{\mathrm{X}}^{\mathrm{batch}} = \sum_{\mathrm{age}=1}^{15} g(\mathrm{age}) \cdot \mathbb{E}_{\Gamma_{\mathrm{X}}}[P_{\mathrm{X}}^{\mathrm{illness}}]$$

$\rightarrow$ Effect of Salmonella is independent of consumer age

Intervention steps

- Milk testing: Farm module
  - Proportion of farm milk tested $\rightarrow p_{\text{milk}}$
  - Threshold of E.coli test $\rightarrow l_{\text{milk}}$

  $\rightarrow$ Computes M^{batch} milk rejected (in liters)
- Cheese testing: Postharvest module
  - Proportion of cheese batch tested $\rightarrow p_{\text{cheese}}$
  - Number of cheese samples tested $\rightarrow n_{\text{sample}}$

  $\rightarrow$ Computes $P_{\text{X}}^{\text{batch}}$ Probability of rejecting the batch

$$P_{\text{X}}^{\text{batch}} = 1 - (1 - P[\Gamma_{\text{X}} > 0])^{n_{\text{sample}}}$$

Quantities of interest (QoI)

- QoIs are computed using $R_{\mathrm{X}}^{\mathrm{batch}}$, $P_{\mathrm{X}}^{\mathrm{batch}}$ and M^{batch}

$$R_{\mathrm{X}}^{\mathrm{illness}} = \frac{\mathbb{E}[R_{\mathrm{X}}^{\mathrm{batch}} \cdot (1 - P_{\mathrm{X}}^{\mathrm{batch}} \cdot p^{\mathrm{cheese}})]}{\mathbb{E}[1 - P_{\mathrm{X}}^{\mathrm{batch}} \cdot p^{\mathrm{cheese}}]}$$

$$C^{\mathrm{avg}} = (c_1 + c_2 \cdot \mathbb{E}[M^{\mathrm{batch}}]) + (c_3 + c_4 \cdot \mathbb{E}[P_{\mathrm{X}}^{\mathrm{batch}} \cdot p^{\mathrm{cheese}}])$$

- Several batches are simulated to estimate

  $\rightarrow$ c_i's denote cost values *(COPIL ArtiSaneFood, Caen, Normandie, 2022)*

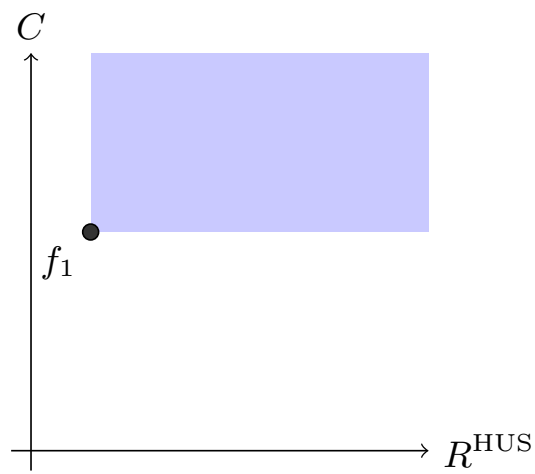
- DALY: Disability-adjusted life year
  - Batch risk for HUS and Salmonellosis are computed
  - Overall risk was assessed by combining the burden of disease metrics

Multi-objective optimization $\rightarrow f = (R^{\mathrm{HUS}}, C)$

- Consider an input: $x_1 = (p_{\mathrm{milk}},\, l_{\mathrm{milk}},\, p_{\mathrm{cheese}},\, n_{\mathrm{sample}})$

$$p_{\mathrm{milk}} = 30\%,\; l_{\mathrm{milk}} = 50\,\mathrm{CFU},\; p_{\mathrm{cheese}} = 50\%,\; n_{\mathrm{sample}} = 5\,\mathrm{units}$$

- Corresponding actual output: $f_1 = (R_1^{\mathrm{HUS}} = 2.2, C_1 = 1000\,\mathrm{EUR})$

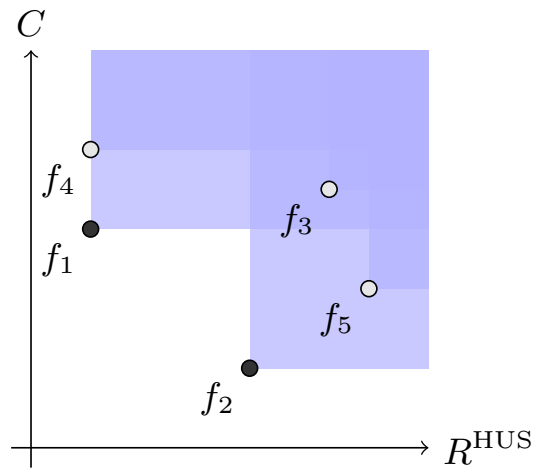


Dominated area by f_1 in objective space

Pareto optimal solutions

- Example: Inputs $\{x_i\}$ and outputs $\{f_i\}$, for $i = 1, \ldots, 5$

Minimizing two conflicting functions: $\min_x f(x)$



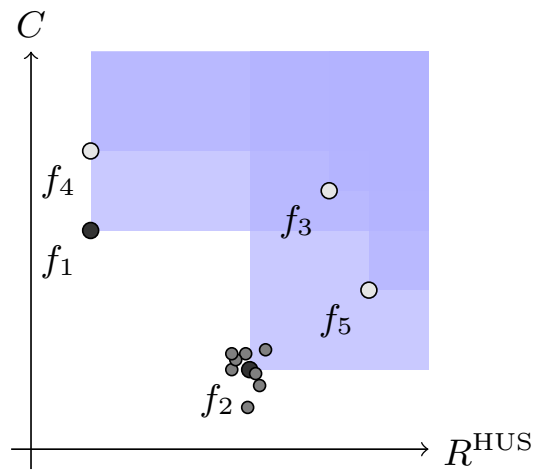
f_3, f_4 & f_5 dominated by f_1 and f_2

- Goal: Estimate the Pareto set $\mathcal{P} = \{x_1, x_2\}$ and Pareto front $\mathcal{F} = \{f_1, f_2\}$

Multi-objective stochastic optimization

- Simulator: Inputs $\{x_i\}$ and outputs $\{z_i = f_i + \text{noise}\}$, for $i = 1, \ldots, 5$

Minimizing two expensive & noisy functions: $\min_x f(x)$

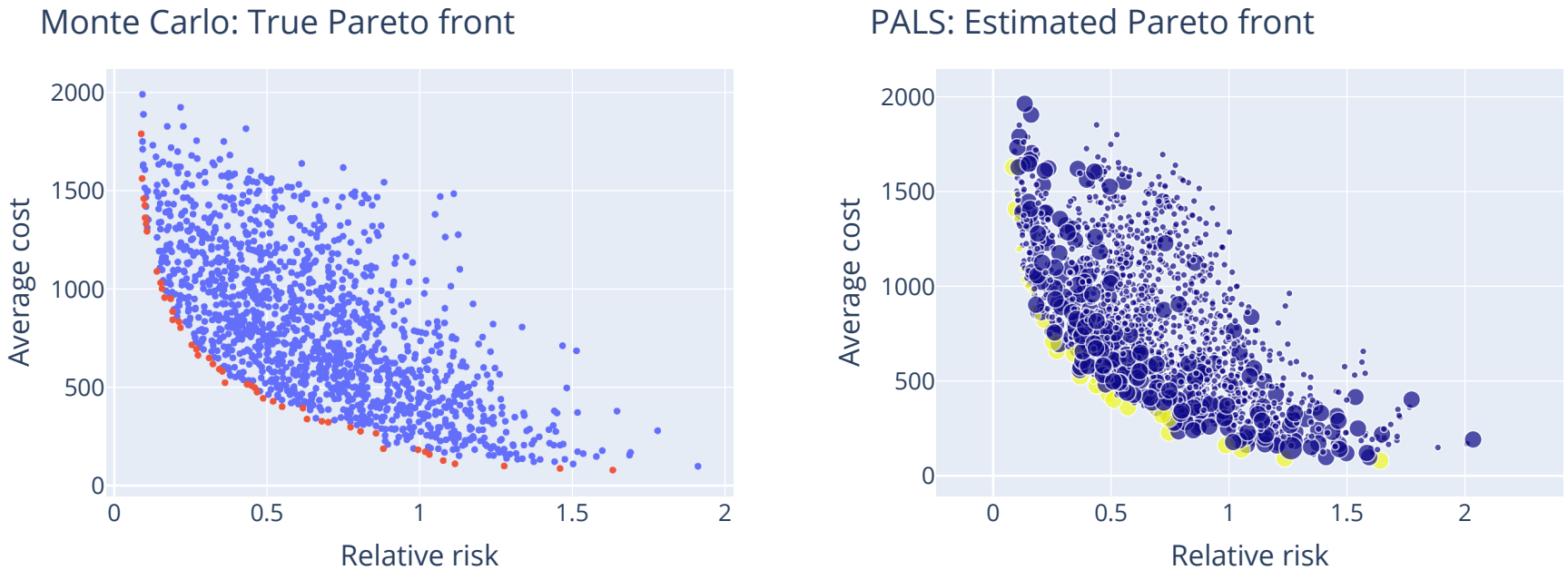


f_3, f_4 & f_5 dominated by f_1 and f_2

Naive approach Use Monte Carlo simulations → computationally expensive

PALS (Barracosa et al., 2021) and (Basak et al., 2022)

- Input points: $(p^i_{\text{milk}}, l^i_{\text{milk}}, p^i_{\text{cheese}}, n^i_{\text{sample}})_{i=1,2,\ldots,1500}$



(a) Samples ALL $\underline{1500 \text{ points}}$ $\times 5000$ (b) Samples only $\underline{300 \text{ points}}$ $\times 200$ (size)

- PALS has $\sim 4\%$ misclassification rate in estimating Pareto optimal points

Conclusions & Perspectives

- QRA model for STEC and Salmonella
- Bayesian Optimization for finding the optimal intervention parameters

→ Open sourcing (Github + FSKX) multipathogen QRA model

→ Optimization on DALY metrics

→ Propose a 3-pathogen model with Listeria

Thank you for your attention!

COPIL ArtiSaneFood 2022, Caen, Normandie

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A Bayesian Optimization (BO) framework

Expensive evaluations + Noisy observations

Algorithm 1 Using a Gaussian process regression (GPR) model ξ on f

Sample f at n_0 points ▷ initialization step
while budget > 0 **do**
  Update : GPR posterior ξ_n
  Compute : acquisition function $J_n(x)$
  Next point : $x_{n+1} = \arg\max_{x \in \mathbb{X}} J_n(x)$
  Sample : f at x_{n+1}
end while
Estimate $\widehat{\mathcal{P}}$ and $\widehat{\mathcal{F}}$ with GPR posterior mean ▷ Prediction step

Weighted Mean Square Error (W-MSE)

- PALS *(Barracosa et al., 2021)* + extension *(Basak et al., 2022)*
- MSE is used as a measure of uncertainty
- The new sample X_{n+1} corresponds to highest uncertain region of $\mathbb{X}$

$$X_{n+1} = \arg\max_{x \in \mathbb{X}} \left(w_n(x) \cdot \sum_{j=1}^{q} \frac{\sigma_{j,n}^2(x)}{R_{j,n}^2} \right)$$

- $R_{j,n}$ is a normalizing constant for $j = 1, 2, \ldots, q$ -th objective
- $\sigma_{j,n}^2(x)$ is the GP posterior variance at $x \in \mathbb{X}$
- Non-zero weights are given to "potentially Pareto optimal" points