Minimizing the risk of foodborne illness and analytical costs using a QMRA model for raw milk cheeses.

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Motivation

- Aim : Control bacteria contamination in raw milk cheese
    1. Pathogenic *E. coli* (MPS-STEC) → Haemolytic Uremic Syndrome
    2. *Salmonella* → Salmonellosis
    3. *Listeria monocytogenes* → Listeriosis
- Control measures:

Farm milk testing

Test *E. coli* in farm milk

→ test frequency p_{milk}

→ threshold limit l_{milk}

Chesse batch testing

Test for cheese contamination

→ test frequency p_{cheese}

→ sample units n_{sample}

Optimal choice of parameters?

- Parameters: $\{p_{\text{milk}},\ l_{\text{milk}},\ p_{\text{cheese}},\ n_{\text{sample}}\}$
- Minimize both objectives:

Risk of illness

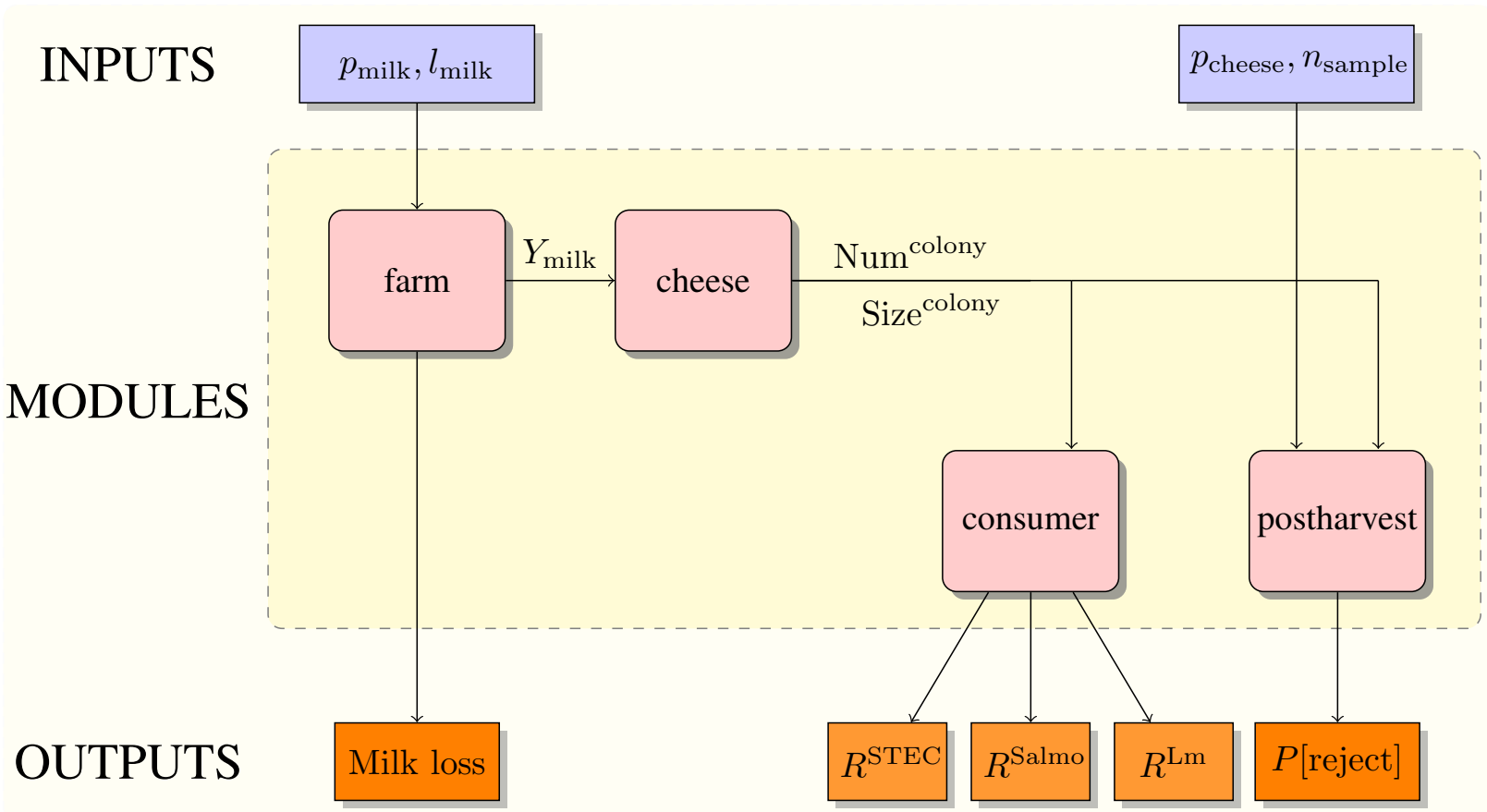
conflicting ↑ ↓ trade-off

Cost of intervention

1. Quantitative Risk Assesement *Perrin et al. (2014)*, *Basak et al. (in prep.)*
   - QRA model estimating risk and cost
2. Optimization algorithm *Barracosa et al. (2021)*, *Basak et al. (2022)*
   - Find best trade-off among the objectives & optimize parameters

Quantitative Risk Assessement – Raw milk cheese

Multipathogen QRA model



Farm module : Milk collection

- Milk testing: Rejecting farms with high *E. coli* contamination

$$Y_{\text{milk}}^{\text{Ecoli}} > l_{\text{milk}} \quad \text{CFU}$$

- Simulate concentration in milk
  - Indirect approach : limit of detection for $\text{x} \in \{\text{STEC},\ \text{Salmonella}\}$

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

$$Y_{\text{feces}}^{\text{Salmo}},\ Y_{\text{milk}}^{\text{Ecoli}},\ Y_{\text{feces}}^{\text{Ecoli}} \sim \text{Lognormal},\ Y_{\text{feces}}^{\text{STEC}} \sim \text{Weibull}$$

  - Direct approach : $Y_{\text{milk}}^{\text{Lm}} \sim \text{Lognormal}$

- Parameters: *Perrin et al. (2014)*, *Bonifait et al. (2021)* & *ACTALIA*

Cheese module: Maximum growth rate $\mu_{\mathrm{x}}^{\max}(t)$

- $\mu_{\mathrm{x}}^{\max}(t)$ is defined by a secondary cardinal model *(Augustin et al., 2005)*

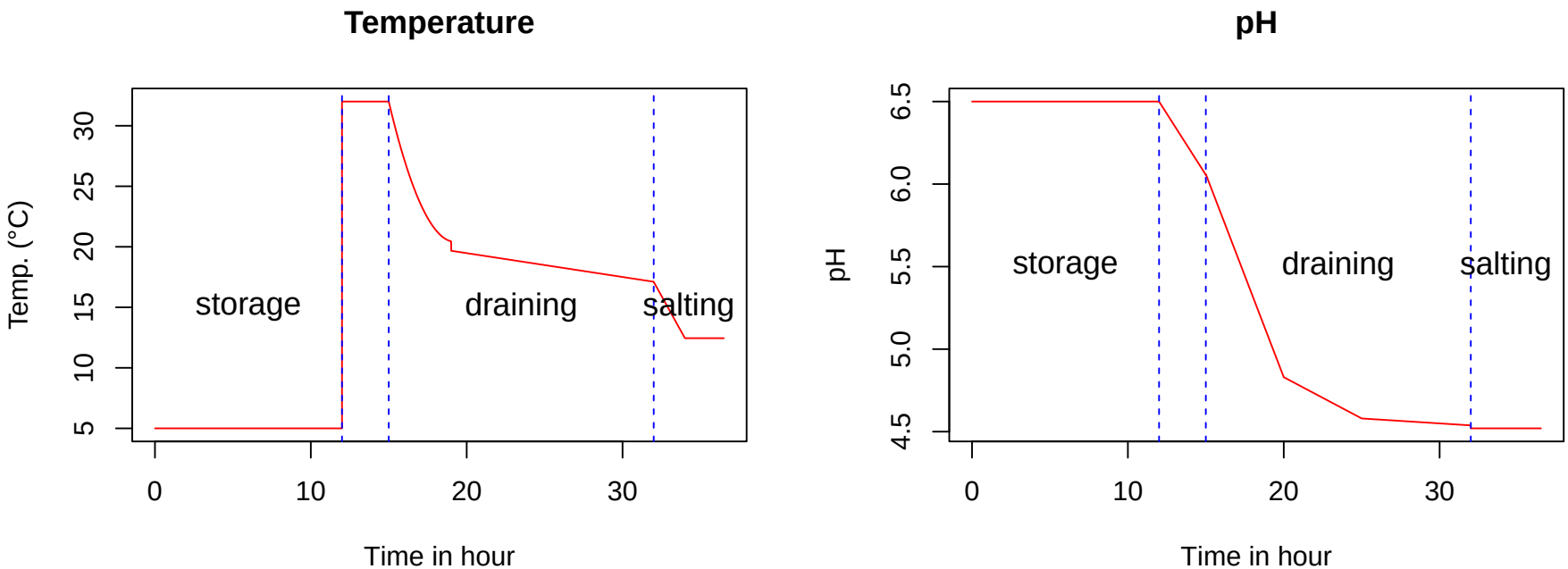


Figure 1: Physico-chemical params. for $\mu_{\mathrm{x}}^{\max}(t)$, $\mathrm{x} \in \{\mathrm{STEC},\ \mathrm{Salmo.},\ \mathrm{List.}\}$

Cheese module: Bacteria evolution

- 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

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

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

$$\text{Listeria} : \text{No decline} + \text{Second growth phase}$$

Ripening → Cheese storage → Consumption

- Parameters: *Perrin et al. (2014)*, *ACTALIA* challenge tests data

Cheese module: Pre-molding steps

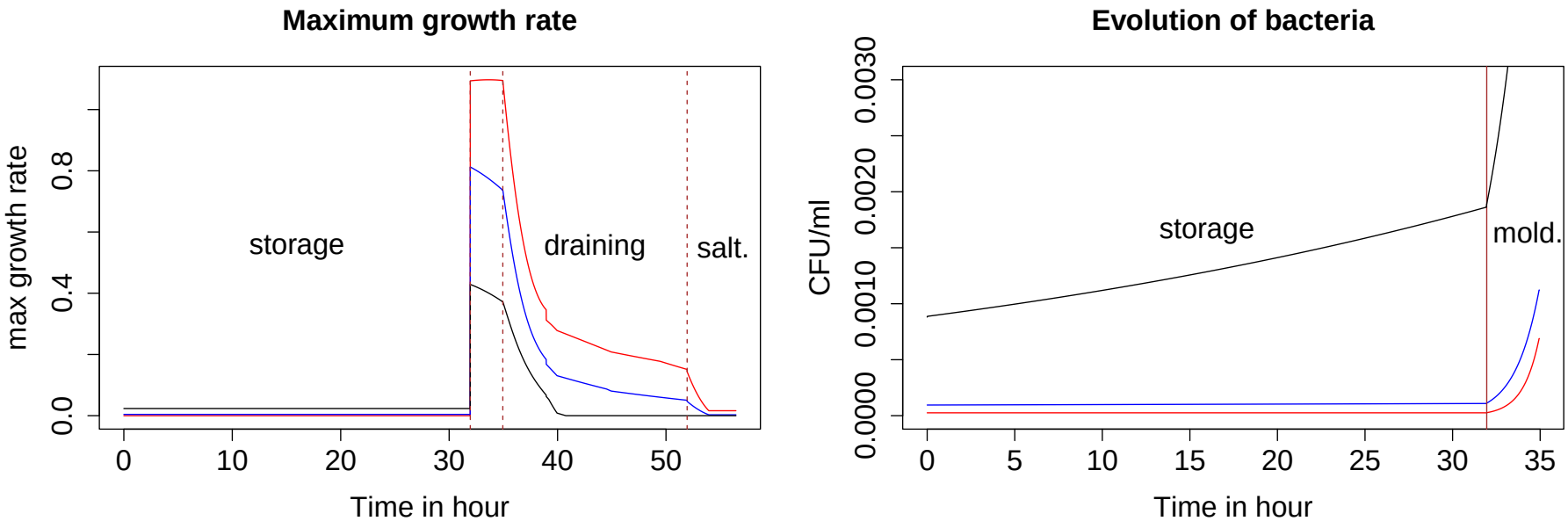


Figure 2: Growth rate $\mu_{\mathrm{x}}^{\max}(t)$ and evolution for STEC, Salmonella & Listeria

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

Cheese module: Evolution of colonies

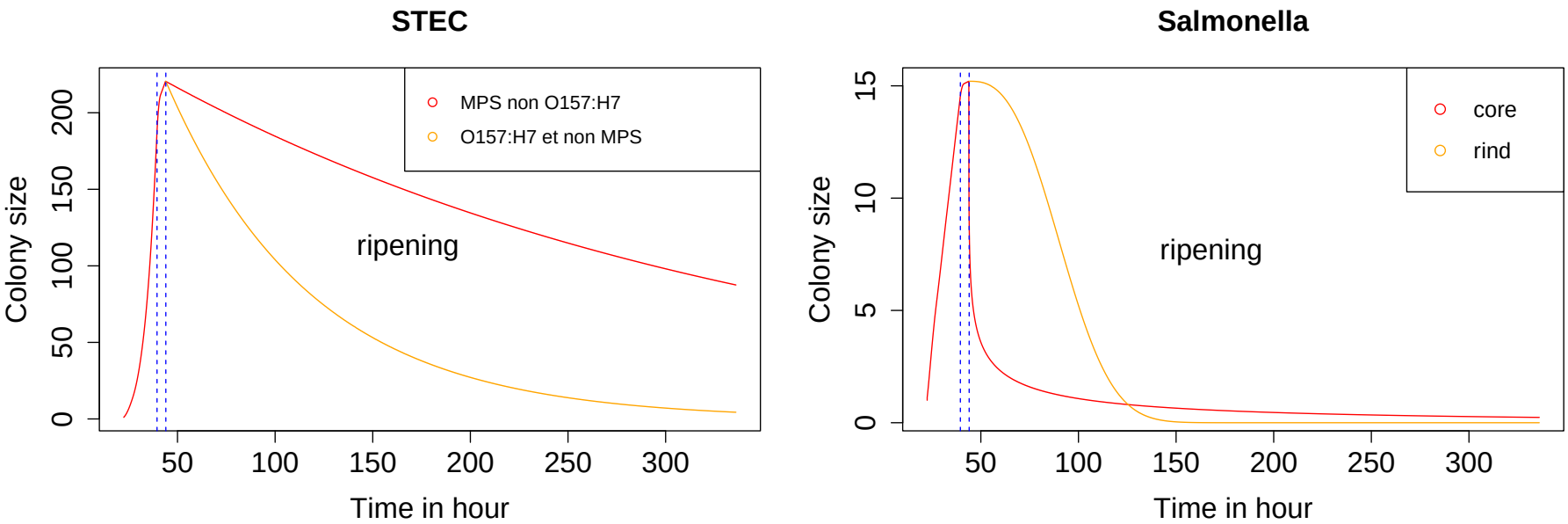


Figure 3: Evolution of colonies of different strains of STEC and Salmonella

$\rightarrow$ Size of colonies: $Y_{\mathrm{x}}^{\mathrm{colony}}$ based on $Y_{\mathrm{x}}^{\mathrm{consume}}$

Consumer module

- Dose in cheese serving: $\Gamma_{\mathrm{x}} = \sum_{s \in \mathrm{strains}} N_{\mathrm{x,s}}^{\mathrm{colony}} \cdot Y_{\mathrm{x,s}}^{\mathrm{colony}}$
- Dose-response model:

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

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

$P_{\mathrm{Listeria}}^{\mathrm{illness}} \rightarrow$ EFSA model *(Ricci et al., 2018)* + JEMRA *(Cadavez et al.)*

- 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

Quantities of interest (QoI)

- Outputs corresponding to one simulated batch
  - Consumer module → Risk of illness $\underline{R_{\mathrm{x}}^{\mathrm{batch}}}$
  - Cheese testing → Prob. of batch rejection $\underline{P^{\mathrm{batch}}}$
  - Milk testing → Milk loss (in liters) $\underline{M^{\mathrm{batch}}}$
- Several batches are simulated to estimate the QoIs

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

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

→ c_i's denote cost values *(COPIL ArtiSaneFood, Caen, Normandie, 2022)*

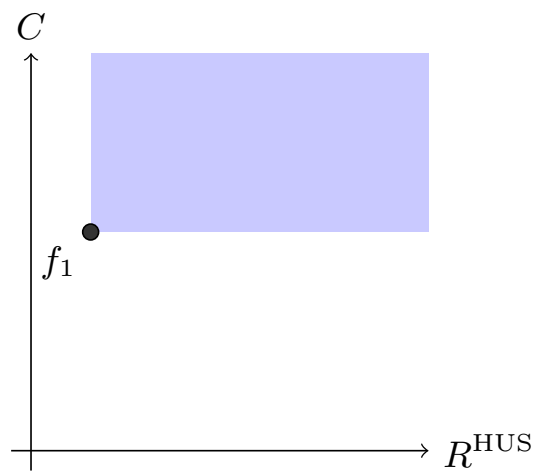
Multiobjective optimization of QRA simulator

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

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

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

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

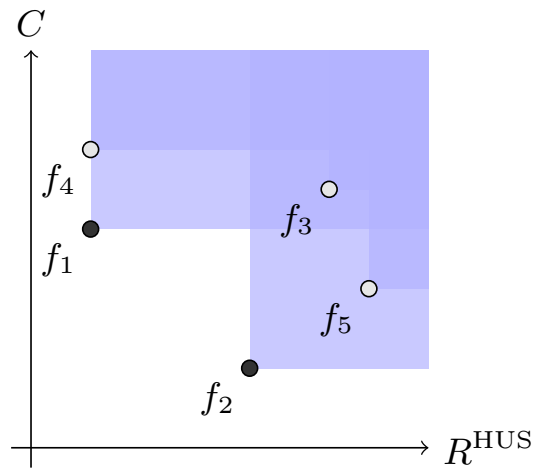


Dominated area by f_1 in objective space

Pareto optimal solutions

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

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



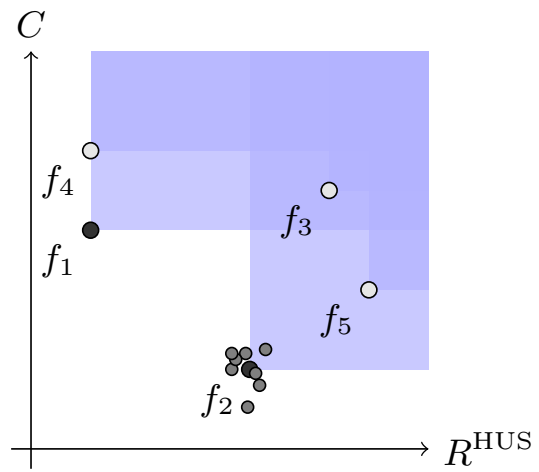
f_3, f_4 & f_5 dominated by f_1 and f_2

- 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 $i = 1, \ldots, 5$

QRA simulator produces noisy outputs



f_3, f_4 & f_5 dominated by f_1 and f_2

Naive approach Use Monte Carlo simulations → computationally expensive

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

Choice of acquisition function

- PALS *(Barracosa et al., 2021)* + extension *(Basak et al., 2022)*
- Weighted Mean Squared Error → measure of uncertainty
- The new sample X_{n+1} corresponds to highest uncertain region of $\mathbb{X}$

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

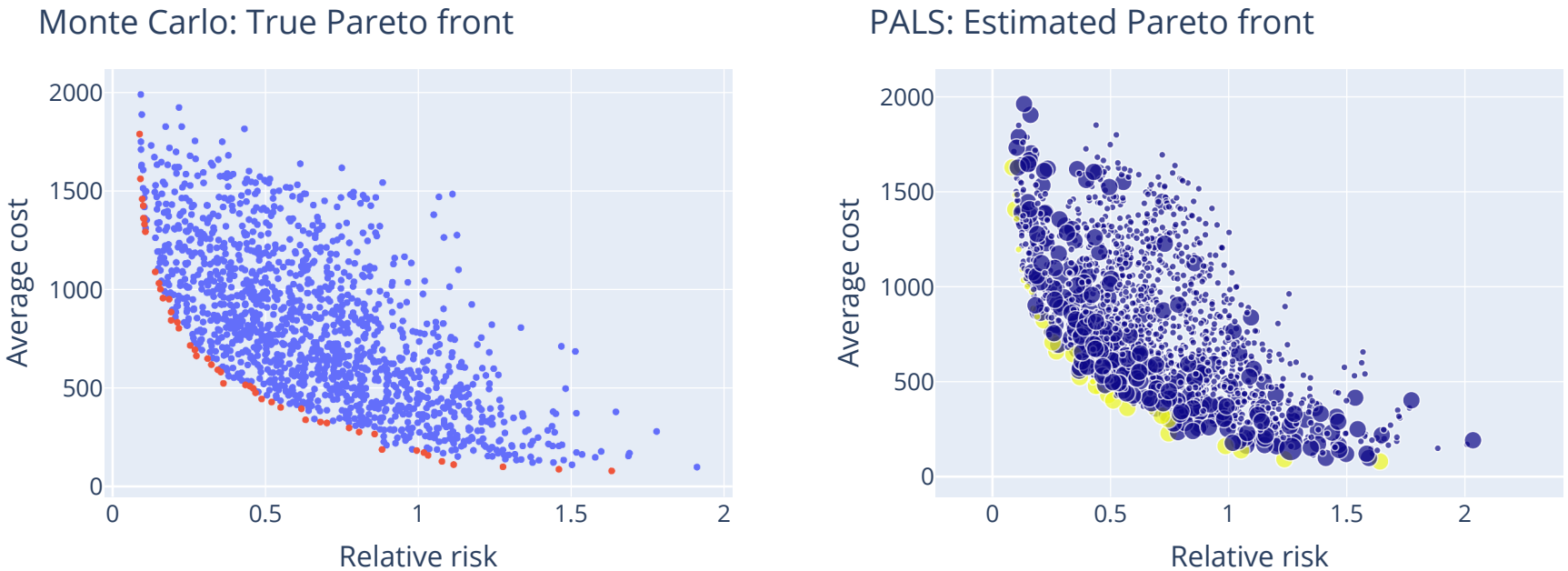
→ $R_{j,n}$ is a normalizing constant for $j = 1, 2, \ldots, q$ -th objective

→ $\sigma_{j,n}^2(x)$ is the GP posterior variance at $x \in \mathbb{X}$

- Non-zero weights are given to "potentially Pareto optimal" points

PALS w/ quantiles (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

Contributions of this work

- Multipathogen QRA model
  - STEC, Salmonella and Listeria monocytogenes
- Implementation of the model in R + FSKX
- Bayesian optimization algorithm
  - To optimize noisy and costly simulators
  - Multiple conflicting objectives
  - Finding Pareto optimal parmeters in a limited budget

$\rightarrow$ Perspectives: Optimization on DALY metrics

Thank you for your attention!

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