

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 $\uparrow \downarrow$ trade-off

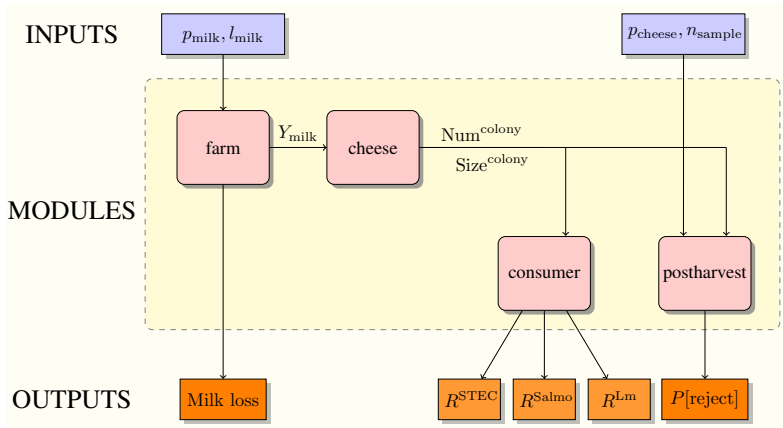
Cost of intervention

1. Quantitative Risk Assessment *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 Assessment – Raw milk cheese



Multipathogen QRA model



Farm module : Milk collection

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

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

- **Simulate concentration in milk**

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

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

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

- **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 $\mu_x^{\max}(t)$

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

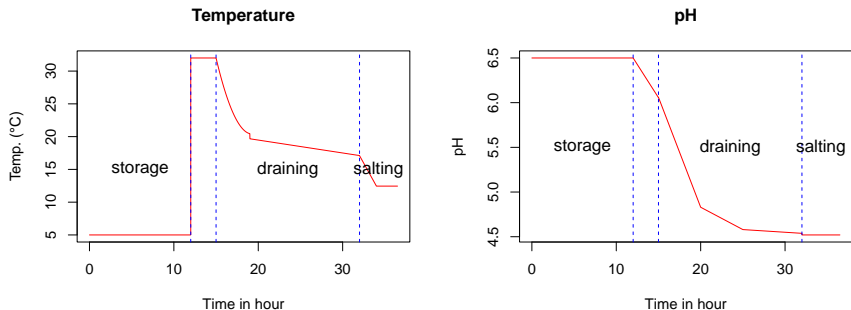


Figure 1: **Physico-chemical** params. for $\mu_x^{\max}(t)$, $x \in \{\text{STEC, Salmo., List.}\}$

Cheese module: Bacteria evolution

- Growth ↗ phase

$$\frac{dy}{dt} = \mu_x^{\max}(t) \cdot y(t) \cdot \left(1 - \frac{y(t)}{y^{\max}}\right)$$

Milk storage → Molding → Colony formation → Draining → Salting

- Decline ↘ phase

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

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

Listeria : No decline + Second growth phase

Ripening → Cheese storage → Consumption

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

Cheese module: Pre-molding steps

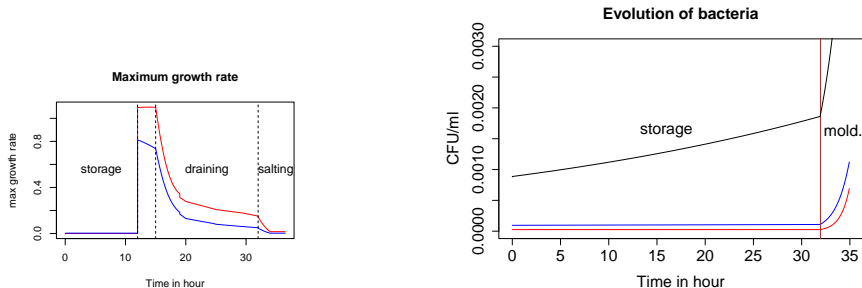


Figure 2: Growth rate $\mu_x^{\max}(t)$ and evolution for **STEC**, **Salmonella** & **Listeria**

→ **Number of colonies**: $N_x^{\text{colony}} \sim \text{Poisson}(Y_x^{\text{molding}} \cdot c)$

Cheese module: Evolution of colonies

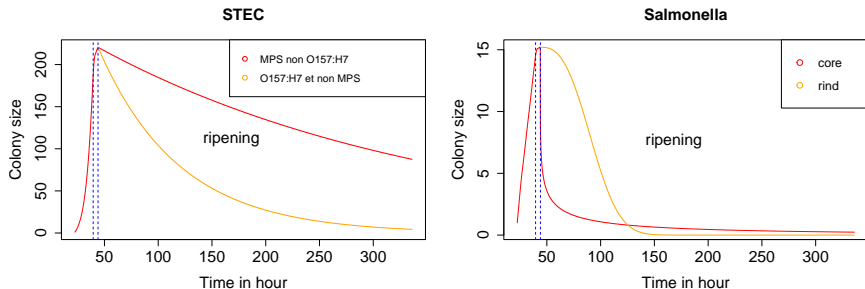


Figure 3: Evolution of colonies of different strains of STEC and Salmonella

→ Size of colonies: Y_x^{colony} based on Y_x^{consume}

Consumer module

- Dose in cheese serving: $\Gamma_x = \sum_{s \in \text{strains}} N_{x,s}^{\text{colony}} \cdot Y_{x,s}^{\text{colony}}$

- Dose-response model:

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

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

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

- Batch risk:

$$R_x^{\text{batch}} = \sum_{\text{age}=1}^{15} g(\text{age}) \cdot \mathbb{E}_{\Gamma_x} [P_x^{\text{illness}}]$$

→ Effect of Salmonella is independent of consumer age

Quantities of interest (QoI)

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

$$R_x^{\text{illness}} = \frac{\mathbb{E}[R_x^{\text{batch}} \cdot (1 - P_X^{\text{batch}} \cdot p^{\text{cheese}})]}{\mathbb{E}[1 - P^{\text{batch}} \cdot p^{\text{cheese}}]}$$

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

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

Multiobjective optimization of QRA simulator

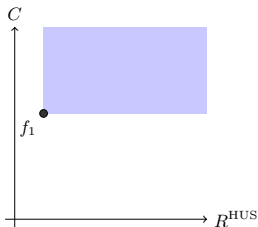


Multi-objective optimization $\rightarrow f = (R^{\text{HUS}}, C)$

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

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

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

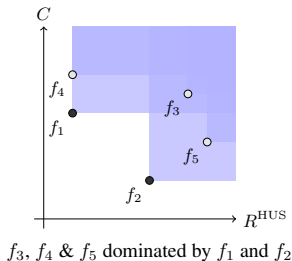


Dominated area by f_1 in objective space

Pareto optimal solutions

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

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

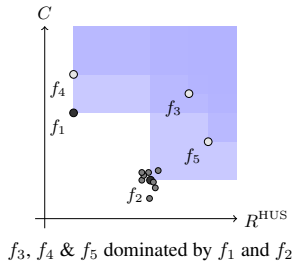


- **Goal:** Estimate the **Pareto set** $\mathcal{P} = \{x_1, x_2\}$ and **Pareto front** $\mathcal{F} = \{f_1, f_2\}$

Multi-objective **stochastic** optimization

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

QRA simulator produces **noisy** outputs



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 $\hat{\mathcal{P}}$ and $\hat{\mathcal{F}}$ 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 $j = 1, 2, \dots, q$ -th objective

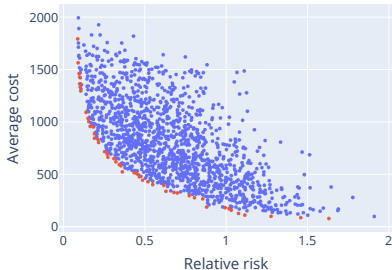
→ $\sigma_{j,n}^2(x)$ is the GP posterior variance at $x \in \mathbb{X}$

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

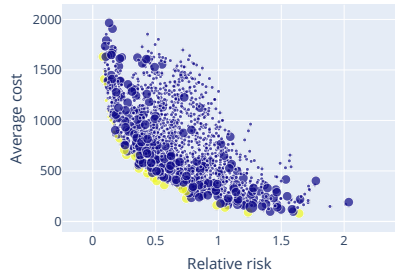
PALS w/ quantiles (Basak et al., 2022)

- Input points: $(p_{\text{milk}}^i, l_{\text{milk}}^i, p_{\text{cheese}}^i, n_{\text{sample}}^i)_{i=1,2,\dots,1500}$

Monte Carlo: True Pareto front



PALS: Estimated Pareto front



(a) Samples ALL 1500 points \times 5000 (b) Samples only 300 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 parameters in a **limited budget**
- **Perspectives**: Optimization on DALY metrics

Thank you for your attention!



COPIL ArtiSaneFood 2022, Caen, Normandie

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