Sequential Bayesian Experimental Design for Prediction in Physical Experiments Informed by Computer Models

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19 June 2026

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mODa 14
Model-Oriented Data Analysis and Optimum Design

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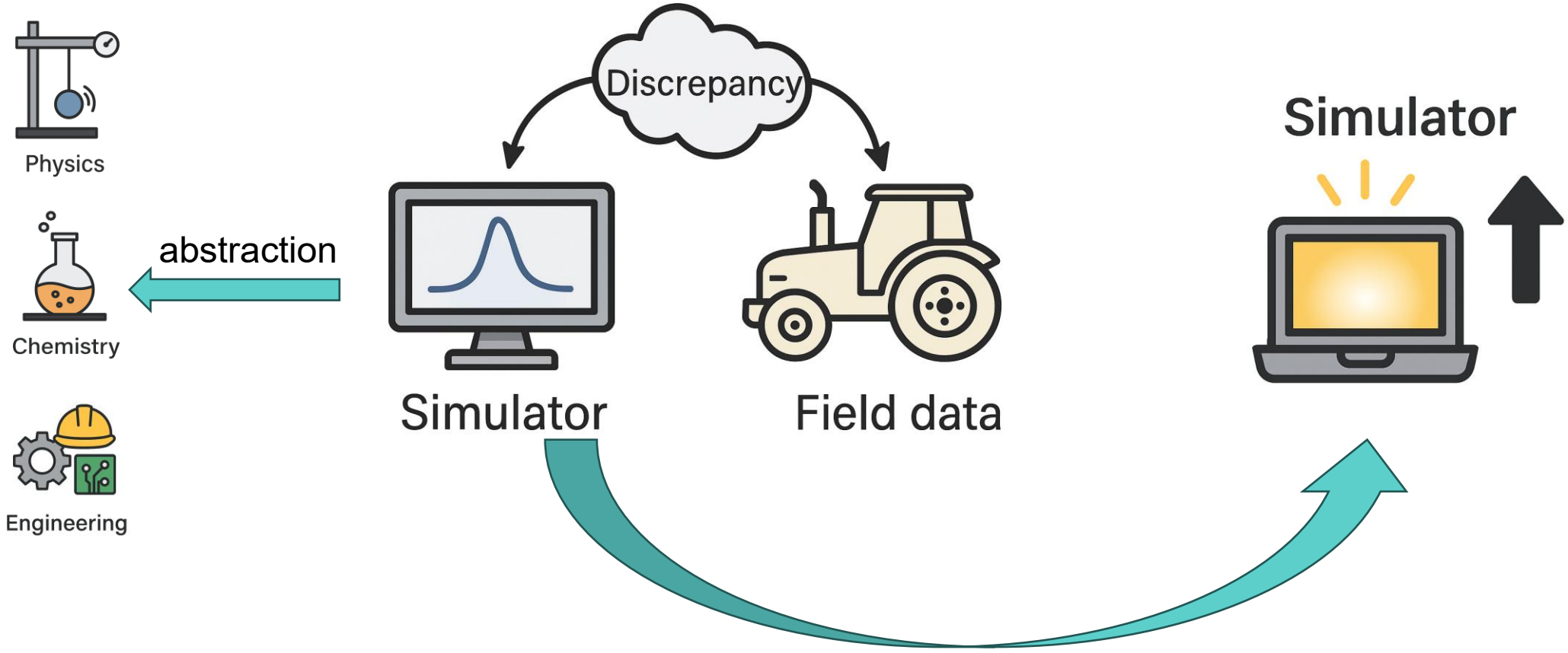
CONTENT

Background of Kennedy & O'Hagan (KOH) Model



Jointly modeling the simulator data and physical experimental data

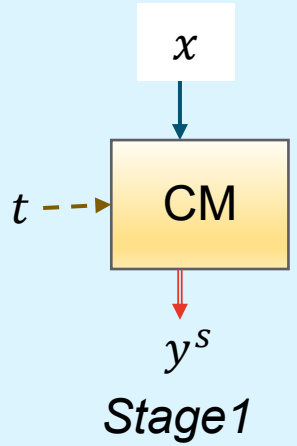
Kennedy & O'Hagan (KOH) Model

Computer Model ------ CM

Two types of input:

- *Experimenter-controlled input (known) --------* x
- *Calibration parameter input: capture unknown features of the system -------* t

Output: y^s



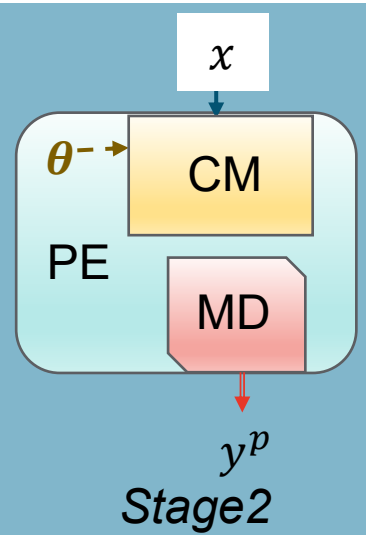
Physical Experiments ------ PE

Model Discrepancy ------ MD

Input: *Experimenter-controlled input (known) --------* x

Parameter: *Calibration parameter* θ

Output: y^p



Kennedy & O'Hagan (KOH) Model

Two-stage model (Kennedy and O'Hagan (2001))

$$y^p(x_i) = y^c(x_i, \theta) + \delta(x_i) + \epsilon_i, \qquad i = 1, \dots, n$$

$$y^s(x_j, t_j) = y^c(x_j, t_j), \qquad j = 1, \dots, m$$

$$y^c(\cdot,\cdot) \sim GP\left(m_c(\cdot,\cdot), K_{\phi_1}(\cdot,\cdot)\right)$$

$$\delta(\cdot) \sim GP\left(m_\delta(\cdot), K_{\phi_2}(\cdot,\cdot)\right)$$

θ: *design calibrated parameter*

design input $x = (x_1, \dots, x_r)$

calibration parameter input $t = (t_1, \dots, t_h)$

$y^s(x_j, t_j)$ *denotes the output from the simulator model*

$y^c(x_i, \theta)$ *denotes the simulator output at input* x *given calibration parameter* θ

$y^p(x_i)$ *denotes the observation from the physical experiment*

$\delta(x_i)$ *captures the model discrepancy*

$\epsilon_i \sim N(0, \lambda^2)$

Uncertainty Quantification

Problem:

- Field data are scarce → Small training data
- Point prediction is not reliable
- Safety margin / risk assessment
- …

Fully Bayesian GP (MCMC)

↓

Bayesian Design

Design Target

Improving **future predictions** by selecting the optimal points to carry out experiments

Candidate points: $\mathbf{D}^{cand} = \{d_1, \ldots, d_J\}$

Future prediction points: $\mathbf{D}^{pred} = \{d_1^{pred}, \ldots, d_K^{pred}\}$

Parameters: $\psi = (\theta, \phi)$ → Hyperparameter

Calibration parameter

Carry out the experiment

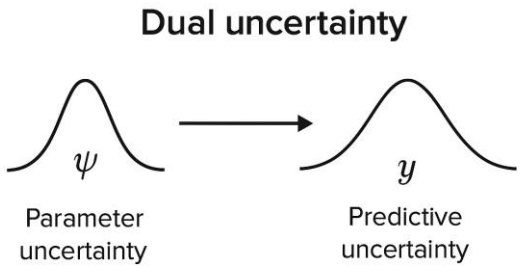
Initial field data : $\mathbf{D}$ → $y^p(\mathbf{D}^{cand})$ → KOH Model → $y^p(\mathbf{D}^{pred})$

Optimally predict the future observations

$$y^p(\mathbf{D}^{pred}) \mid y^p(\mathbf{D}), y^p(\mathbf{D}^{cand}), \psi \sim \mathcal{N}(\mu, \Sigma)$$

Bayesian Design Criteria

Driven by predictive uncertainty reduction:



Mutual information gain maximization:

$$U(d_t) = I\big(y^p(\mathbf{D}^{pred});\, y^p(d_t) \mid y^p(d_{1:t-1}), d_t\big)$$

$$= \int p\big(y^p(\mathbf{D}^{pred}), y^p(d_t) \mid y^p(d_{1:t-1}), d_t\big)\, \log\left(\frac{p\big(y^p(\mathbf{D}^{pred}), y^p(d_t) \mid y^p(d_{1:t-1}), d_t\big)}{p\big(y^p(d_t) \mid d_t, y^p(d_{1:t-1})\big)\, p\big(y^p(\mathbf{D}^{pred}) \mid y^p(d_{1:t-1})\big)} \right) \mathrm{d}\big(y^p(\mathbf{D}^{pred}), y^p(d_t)\big)$$

where

$$p\big(y^p(d_t) \mid d_t,\, y^p(d_{1:t-1})\big) = \int p\big(y^p(d_t) \mid d_t,\, y^p(d_{1:t-1}),\, \boldsymbol{\psi}\big)\, p\big(\boldsymbol{\psi} \mid y^p(d_{1:t-1})\big)\, \mathrm{d}\boldsymbol{\psi},$$

$$p\big(y^p(\mathbf{D}^{pred}) \mid y^p(d_{1:t-1})\big) = \int p\big(y^p(\mathbf{D}^{pred}) \mid y^p(d_{1:t-1}),\, \boldsymbol{\psi}\big)\, p\big(\boldsymbol{\psi} \mid y^p(d_{1:t-1})\big)\, \mathrm{d}\boldsymbol{\psi},$$

$$p\big(y^p(\mathbf{D}^{pred}), y^p(d_t) \mid y^p(d_{1:t-1}), d_t\big) = \int p\big(y^p(\mathbf{D}^{pred}), y^p(d_t) \mid y^p(d_{1:t-1}), d_t,\, \boldsymbol{\psi}\big)\, p\big(\boldsymbol{\psi} \mid y^p(d_{1:t-1})\big)\, \mathrm{d}\boldsymbol{\psi}$$

Complexity–MI Hybrid Criterion

MI-only limitation:

1. May over-sample in high variance regions.

2. Miss critical structure (extrema, inflection)

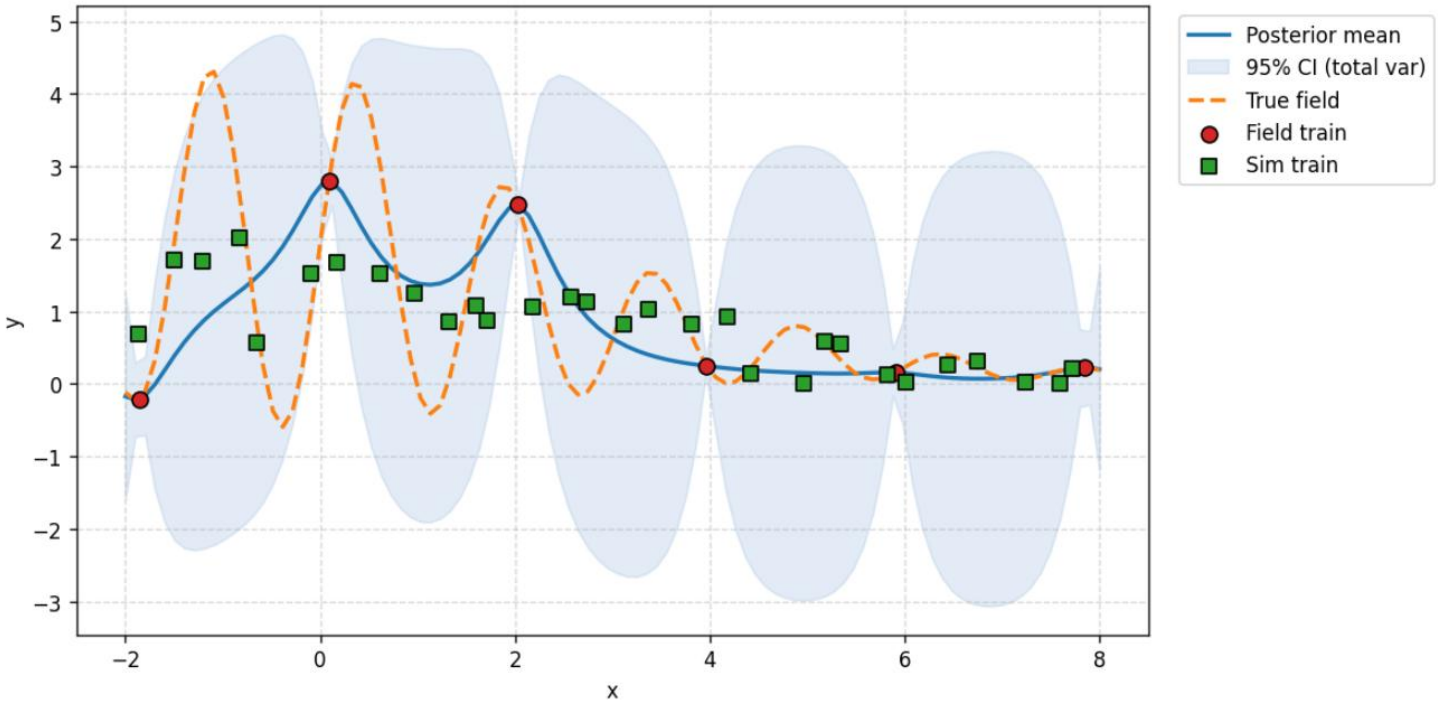
Compute complexity measure at each candidate point
- Based on $\|\nabla \mu(x)\|$
- Rate of slope change

↓

Standardize over candidates
- MI gain
- Complexity $\rightarrow \bar{C}(d)$

↓

Score
Choose design point with max Score



$$score_{mi+com}(d_t) = w_{\mathrm{MI}} \cdot \widehat{U}(d_t \mid d_{1:t-1}) + w_C \cdot C(d_t \mid d_{1:t-1})$$

Accelerating Mutual Information Computation via Gaussian Mixture Reduction

Direct double loop Monte Carlo is expensive

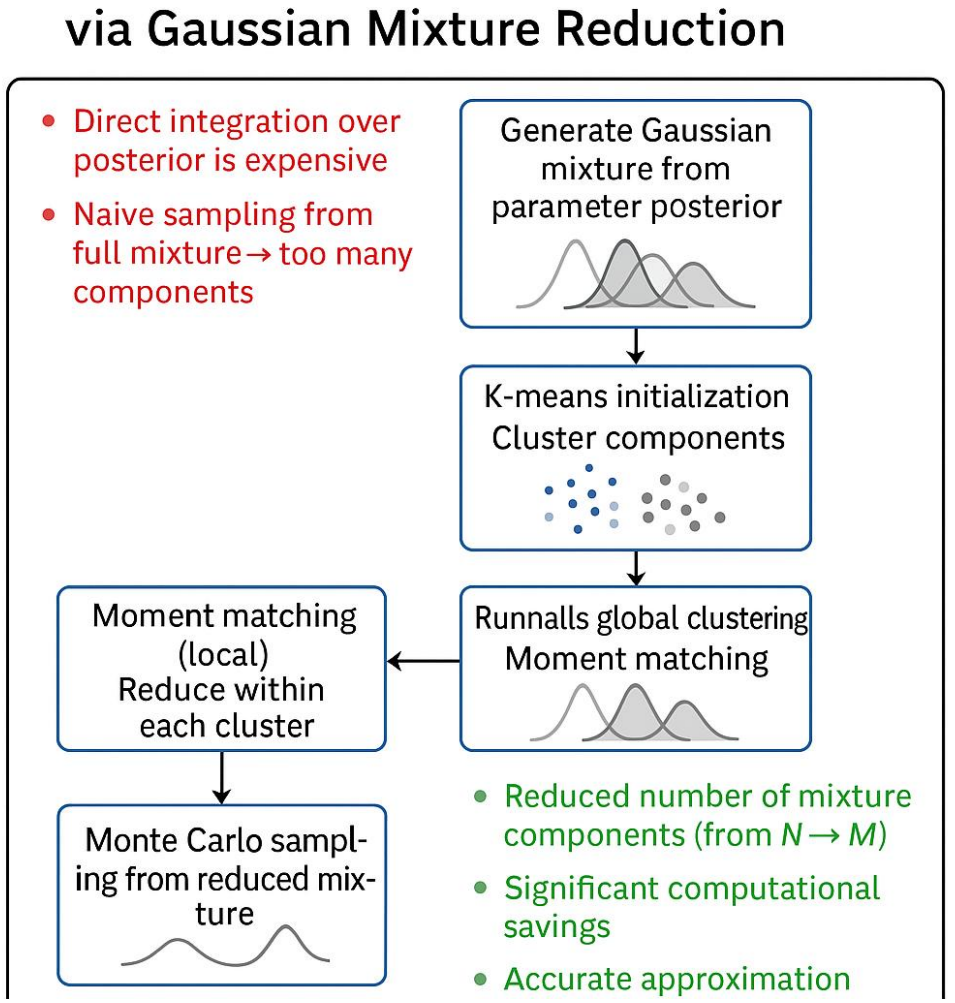
Gaussian Mixture Reduction:

If we have MCMC sample of 1000 sets of $\psi = (\theta, \phi)$

Each set of them will generate a predictive Gaussian distribution:

$$y^p(\mathbf{D}^{pred}) \mid y^p(\mathbf{D}), y^p(\mathbf{D}^{cand}), \psi \sim \mathcal{N}(\mu, \Sigma)$$

If 1000-component Gaussian mixture model can be reduced to 200,100,50….



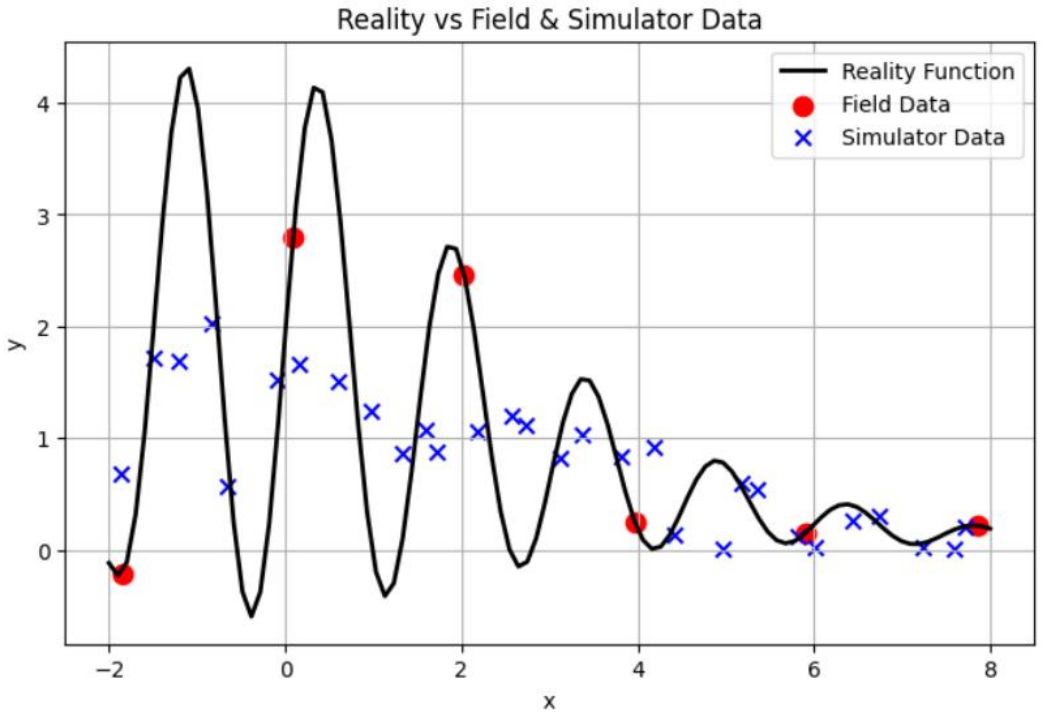
Schieferdecker, D., & Huber, M. F. (2009)

Simulation Example

One numerical example:

Computer model: $f(x;\alpha,\beta) = 10 \cdot Gamma(x + 2.2;\alpha,\beta)$ $\alpha: shape > 0, \beta: scale > 0$

Physical model: $f(x) = 10 \cdot Gamma(x + 2.2; 1.8, 2.0) + Gamma(x + 2.2; 1.8, 2.0) \cdot \sin(2\pi x) + \epsilon$



Data:
- Field data: 6 points
- Simulator data: 30 points

Input domain: $x \in (-2,8)$

Parameters:
- Shape α: True value 1.8
- Scale β: True value 2.0
- Kernel hyperparameters

Weakly informative priors

Gaussian process models:
1. Simulator data: stage 1 GP uses RBF kernel.
2. Discrepancy: stage 2 GP uses RBF kernel × periodic kernel.

Sequential & Adaptive Design

Sequential/Greedy (offline) and adaptive (online) design are both multi-round designs.

Initialize: set of selected design points $\mathbf{D}^* \leftarrow \emptyset$

For i (round) = 1,…,N:

1. **Evaluate criterion**: Compute $\boldsymbol{Criterion\,(d)}$ for all $d \in \mathbf{D}^{cand} \setminus \mathbf{D}^*$ using calibrated KOH Model.

2. **Select** $d^* = \arg\max \boldsymbol{Criterion\,(d)}$ (or $\arg\min \boldsymbol{Criterion\,(d)}$)

3. **Update:**
   If sequential (offline): $\mathbf{D}^* \cup \{d^*\}$
   if adaptive (online):
   1. Run experiment at d^*, obtain y^*
   2. Initial field data $\mathbf{D} \cup \{(d^*, y^*)\}$
   3. Recalibrate KOH model: update $\boldsymbol{\psi} = (\boldsymbol{\theta}, \boldsymbol{\phi})$
   4. $\mathbf{D}^* \cup \{d^*\}$

Setup

- Number of experimental rounds: 10 rounds

- Candidate design points $\mathbf{D}^{cand} = \{d_1, \ldots, d_J\}$ 50 points uniformly distributed over the interval (−1.98, 7.98).
- Prediction points DT: 100 points $\mathbf{D}^{pred} = \{d_1^{pred}, \ldots, d_K^{pred}\}$ uniformly distributed over the interval (−2, 8).

- Design criteria to compare:
  1. MI (mutual information maximization)
  2. MI-complexity hybrid
  3. IMSPE (Integrated mean squared prediction error minimization)
  4. IMSPE-complexity hybrid
  5. D-optimality: better calibration of model parameters θ
  6. Maximin distance: space-filling benchmark, greedily add the candidate whose minimal Euclidean distance to the existing design set is largest.

Pseudo Bayesian

Setup

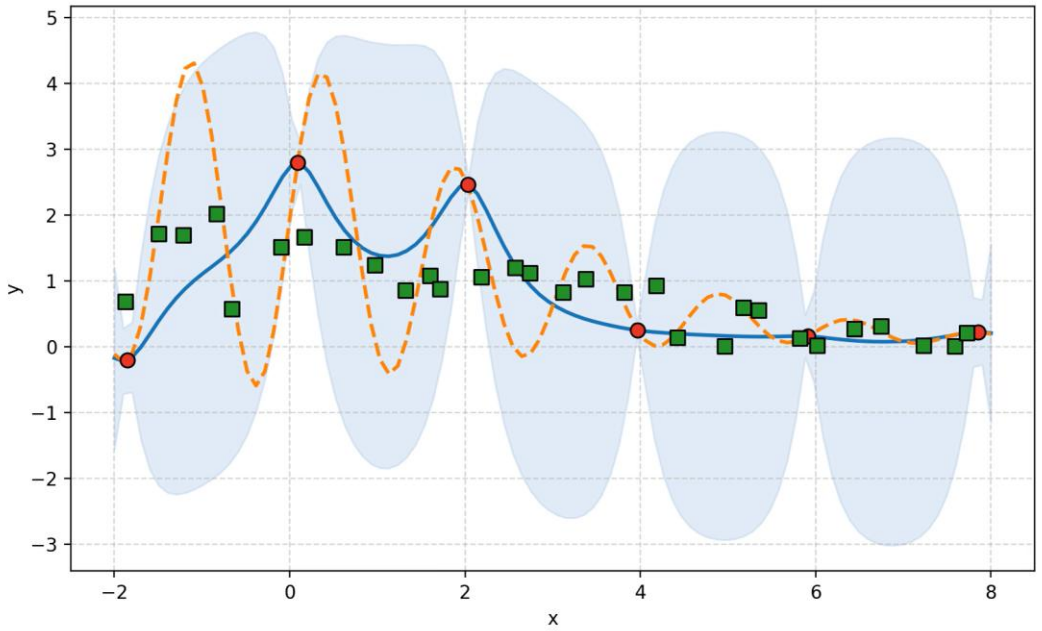
- Software:
  Pytorch, Pyro

- MCMC:
  NUTS HMC algorithm
  1000 posterior parameter samples of hyperparameters and calibration parameters $\psi = (\theta, \phi)$

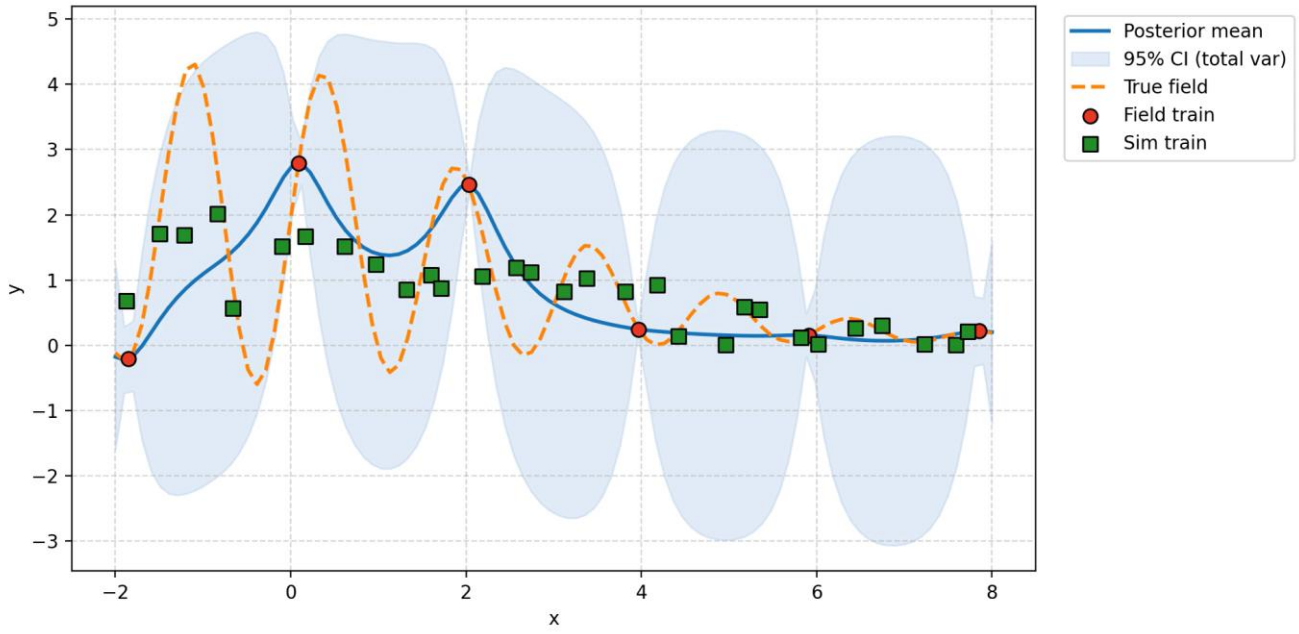
- Outer sample for y: 10000

- Computation:
  1. Use **vectorized operations** to avoid explicit for loops
  2. Cache big matrices and pre-computations in sequential (offline) design (e.g. Schur complement)
  3. **Gaussian Mixture Reduction via clustering**
  ….

Adaptive Design for MI and MI-Complexity Hybrid Criteria

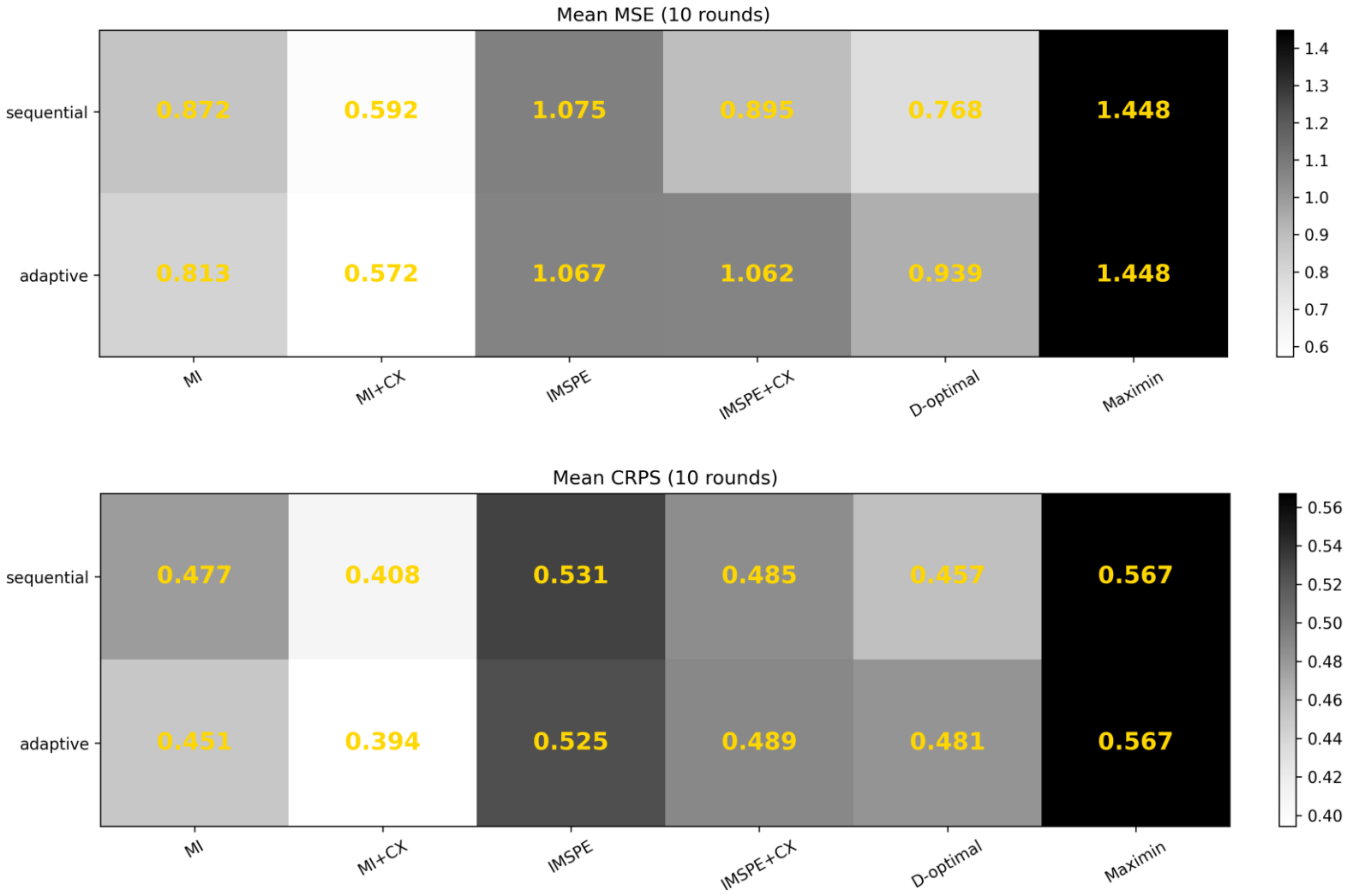


MI

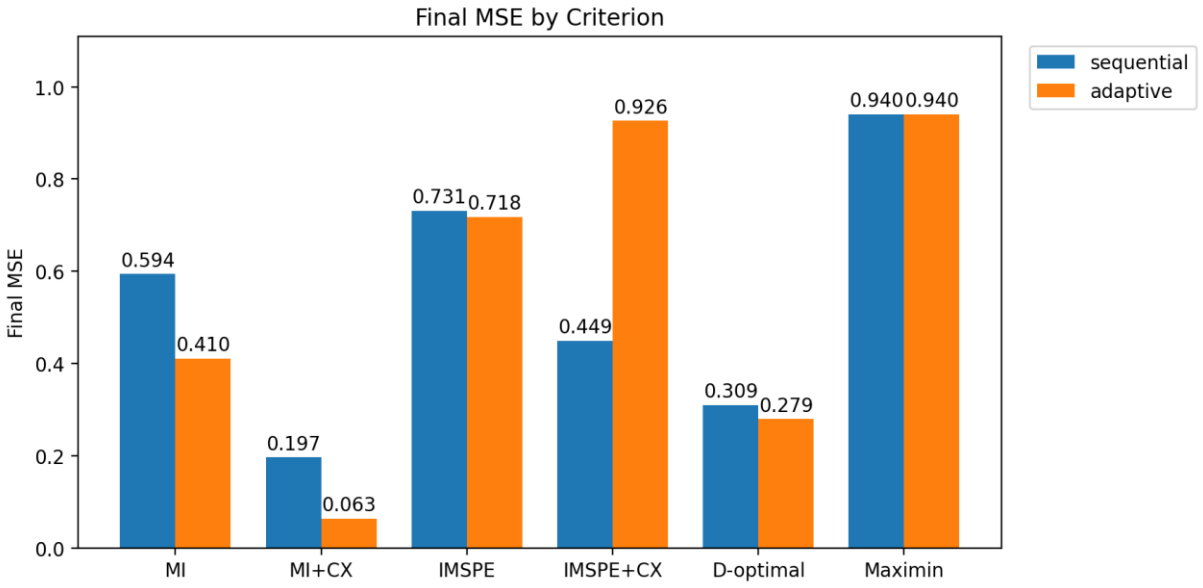


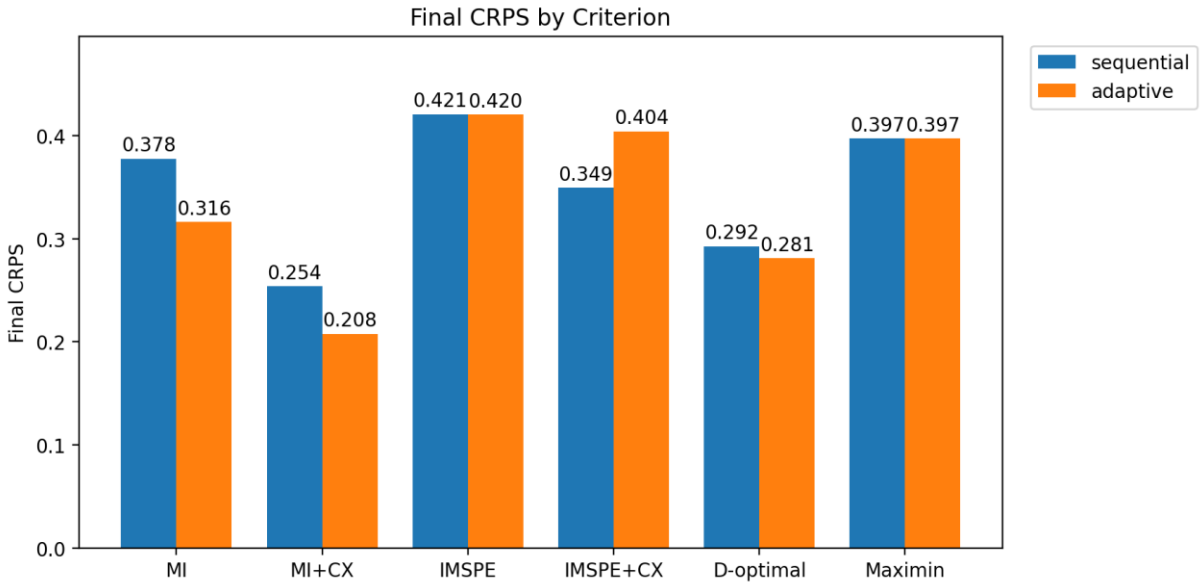
MI-Complexity hybrid

Average Performance Across Multiple Criteria



Final-Round Performance Across Multiple Criteria





Criteria	Running Time (10 rounds sequential design)
MI (naive NMC)	901.4012s
MI (Gaussian mixture reduction)	142.0512s
MI-complexity hybrid (naive NMC)	902.8288s
MI-complexity hybrid (Gaussian mixture reduction)	143.1869s
IMSPE	10.0309s
IMSPE-complexity hybrid	10.7311 s
D-optimality	295.0461s
Maximin distance	0.0168s

Comparison of running time of 10 rounds sequential/greedy (offline) design for each criterion

Real-World Example

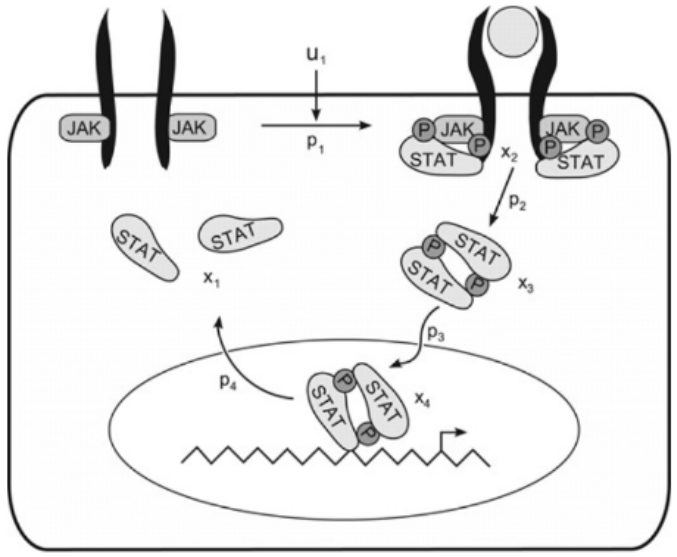


Fig. 2. Model of the JAK-STAT pathway. In this model u_1 serves as driving input, while the total concentration of STAT ($x_1+x_2+2x_3$) and the total concentration of phosphorylated STAT in the cytoplasm (x_2+2x_3) were measured. Note that the step from x_4 back to x_1 is associated with a delay.

Swameye et al. 2003

Biological background:

We study the JAK–STAT5 signalling pathway (Swameye et al. 2003) in which

$$v_1, v_2, v_3, v_4$$

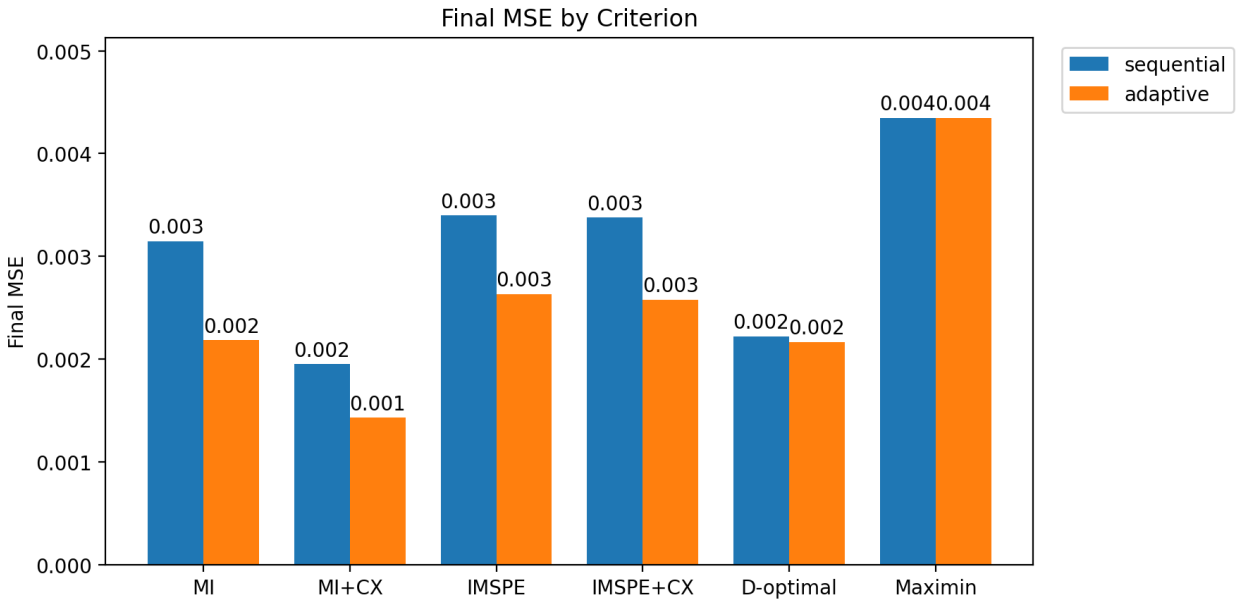
are cytoplasmic unphosphorylated STAT5, phosphorylated STAT5 monomer, dimer, and nuclear STAT5, respectively.

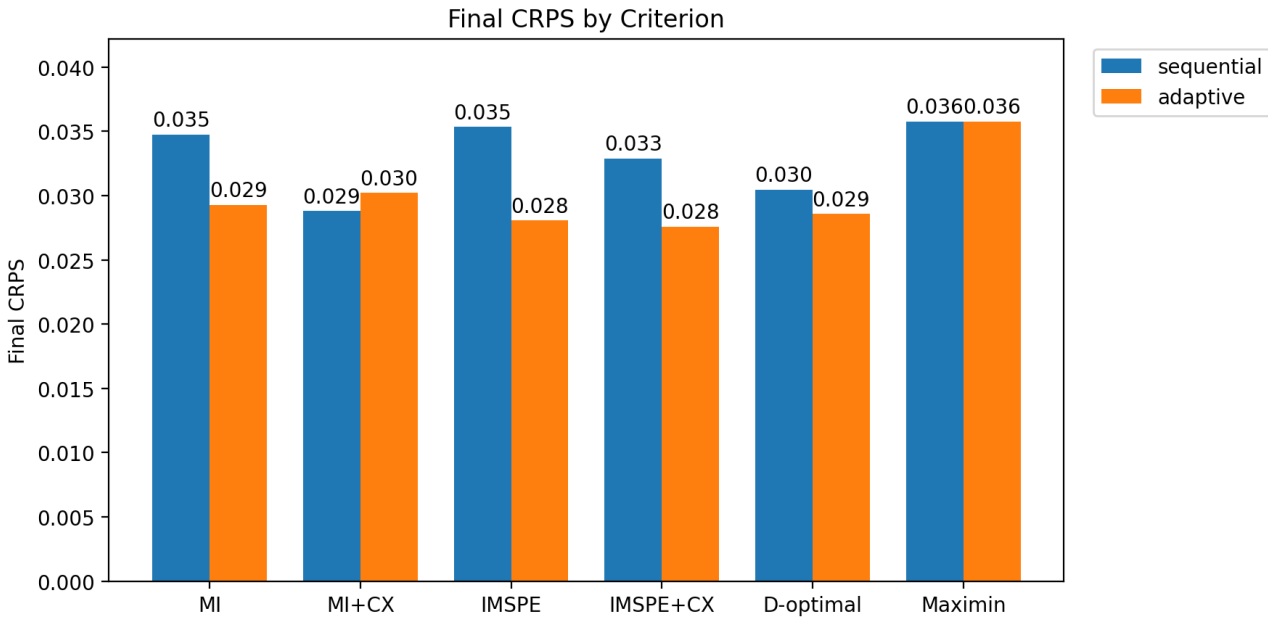
ODE system (simulator):

$$\frac{dv_1}{dt} = -p_1\, u_1\, v_1 + 2\, p_4\, v_4,$$
$$\frac{dv_2}{dt} = p_1\, u_1\, v_1 - p_2\, v_2^2,$$
$$\frac{dv_3}{dt} = -p_3\, v_3 + 0.5\, p_2\, v_2^2,$$
$$\frac{dv_4}{dt} = p_3\, v_3 - p_4\, v_4,$$

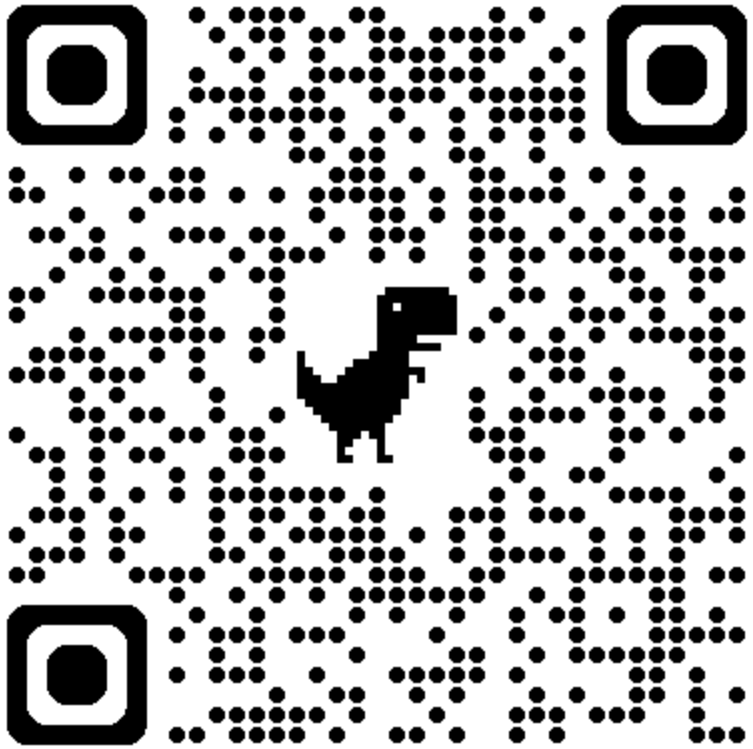
Here u_1 is the cytokine input, and $\theta = (p_1, p_2, p_3, p_4)$ are calibration parameters.

Final-Round Performance Across Multiple Criteria





Scan for Full Paper



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