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LEVERHULME TRUST

>_Alchemy
AI FOR CHEMISTRY

GPSS 2025

Accelerating Chemical Discovery with Knowledge Guided Bayesian Optimisation

Xenofon Evangelopoulos

Computational/AI Lead
Leverhulme Research Centre for Functional Materials

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CLIMATE CHANGE

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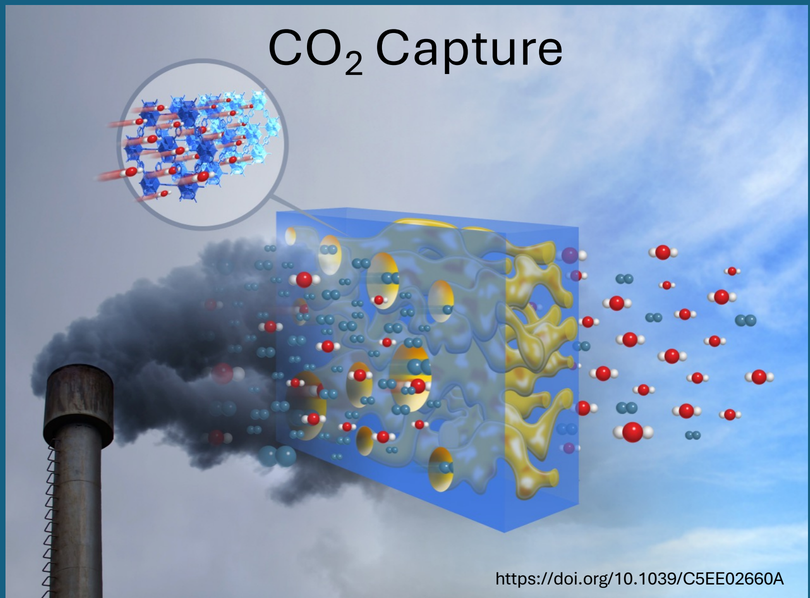
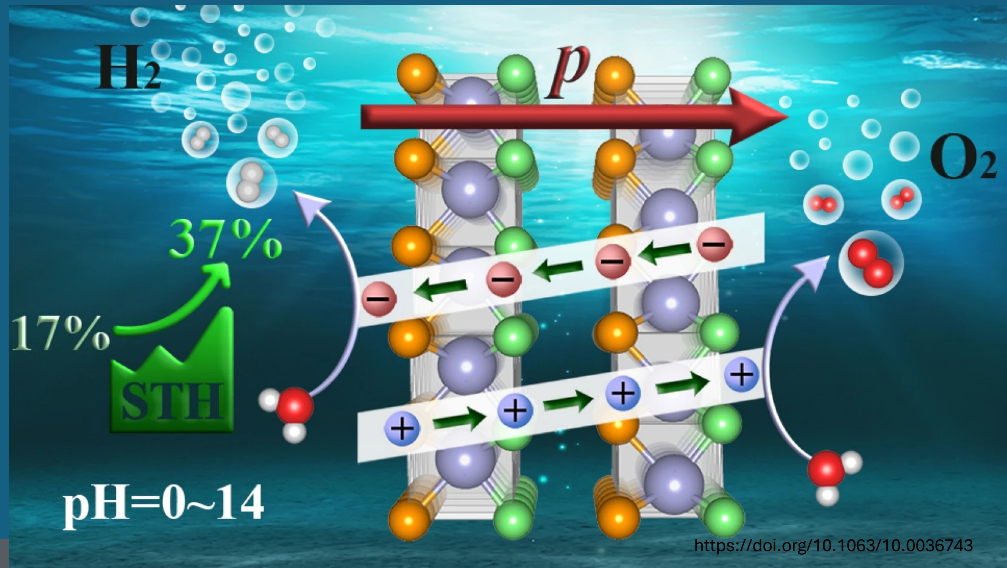
FUNCTIONAL MATERIALS





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MATERIALS MANUFACTURING TIMESCALE

Idea/Design → Synthesis → Testing → Manufacturing

> 10 Years

> £10M

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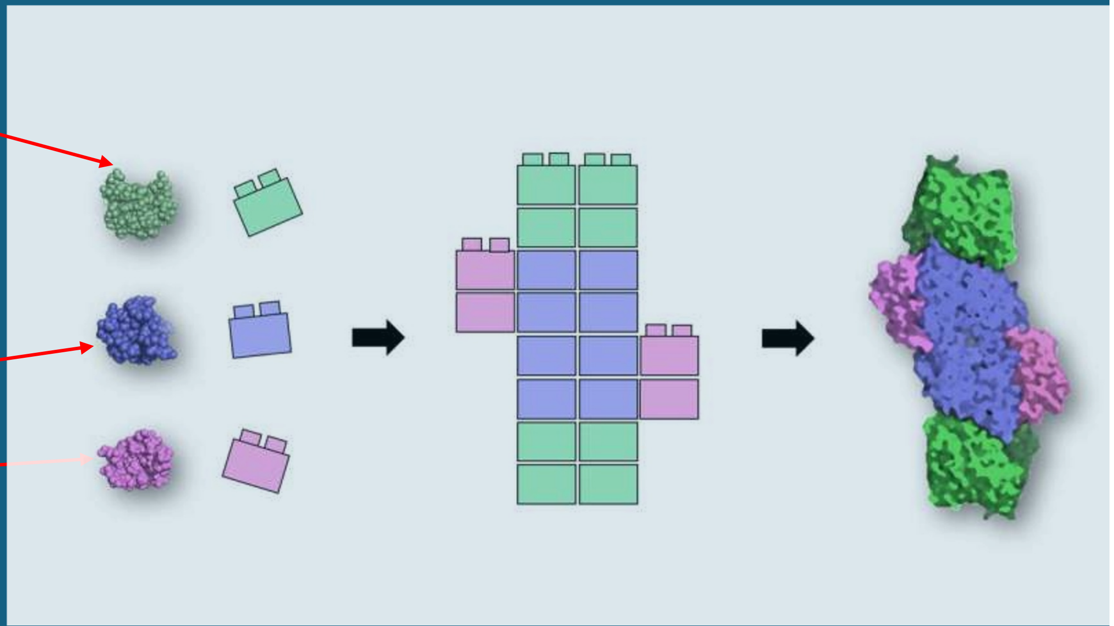
UNIVERSE OF MOLECULES

Building/Lego Blocks



 # Chemical Compounds = # Stars in the Universe x 2

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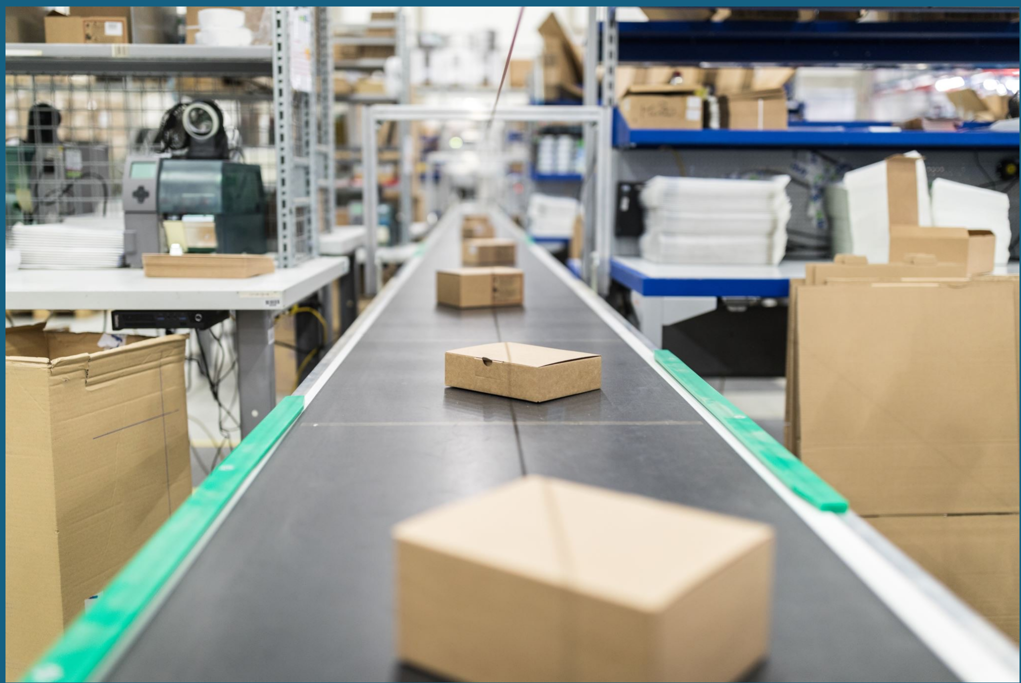
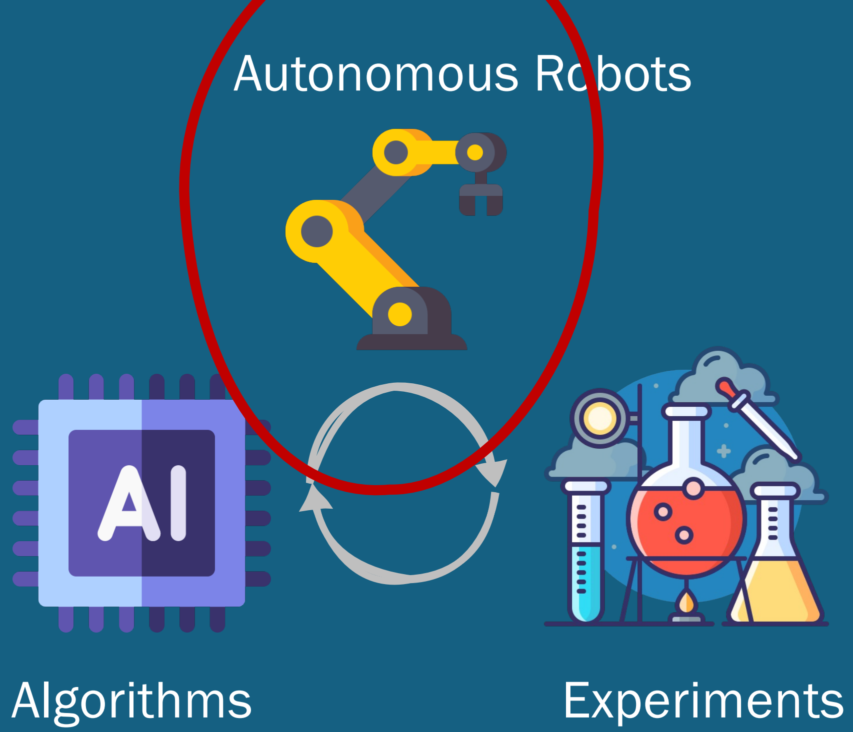
TECHNOLOGY INNOVATION





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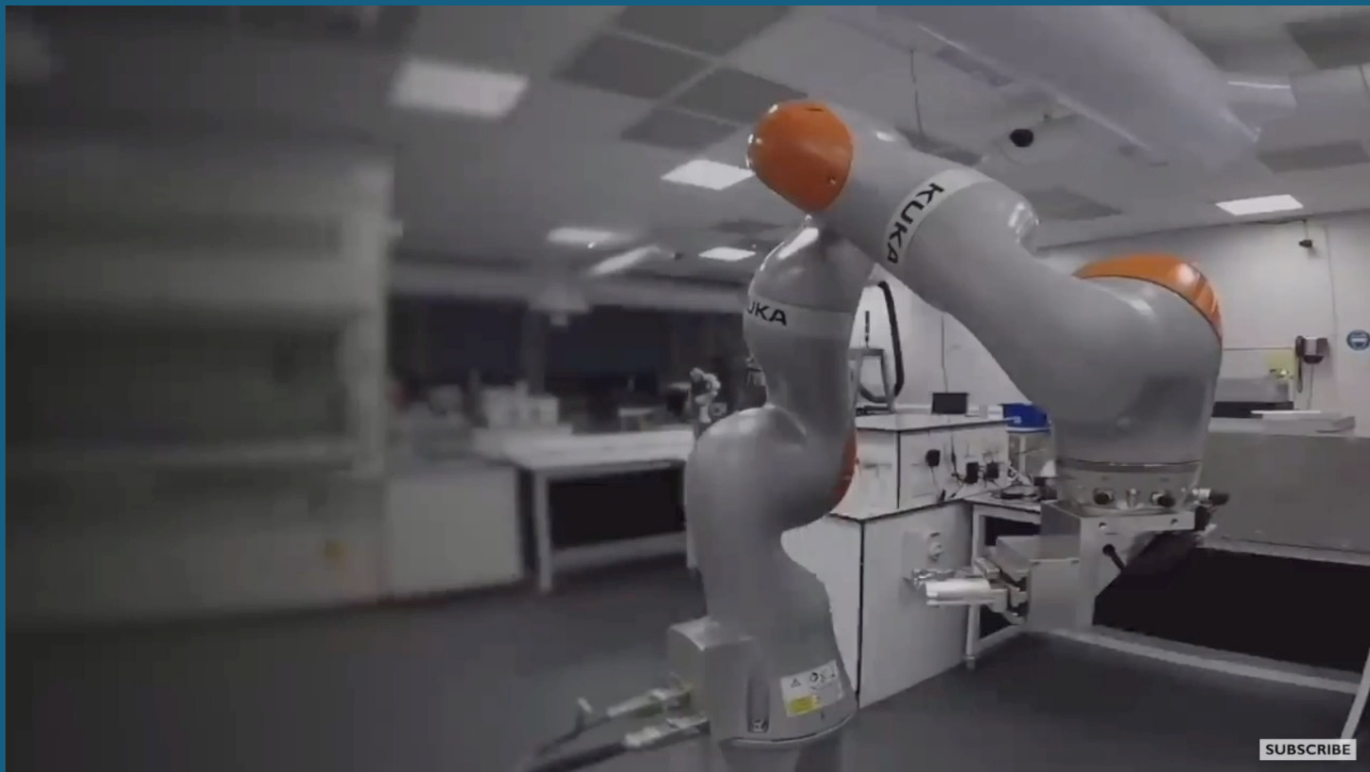
MOBILE ROBOTIC CHEMIST



BBC News Feature, July 2020: www.youtube.com/watch?v=WBwZp5Bg2L8

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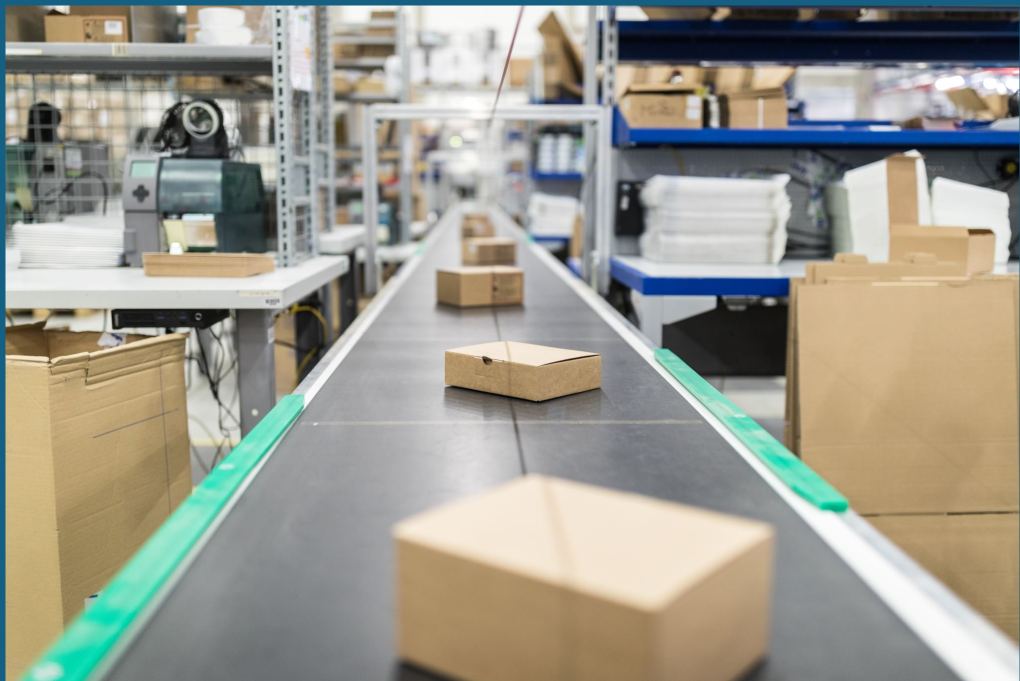
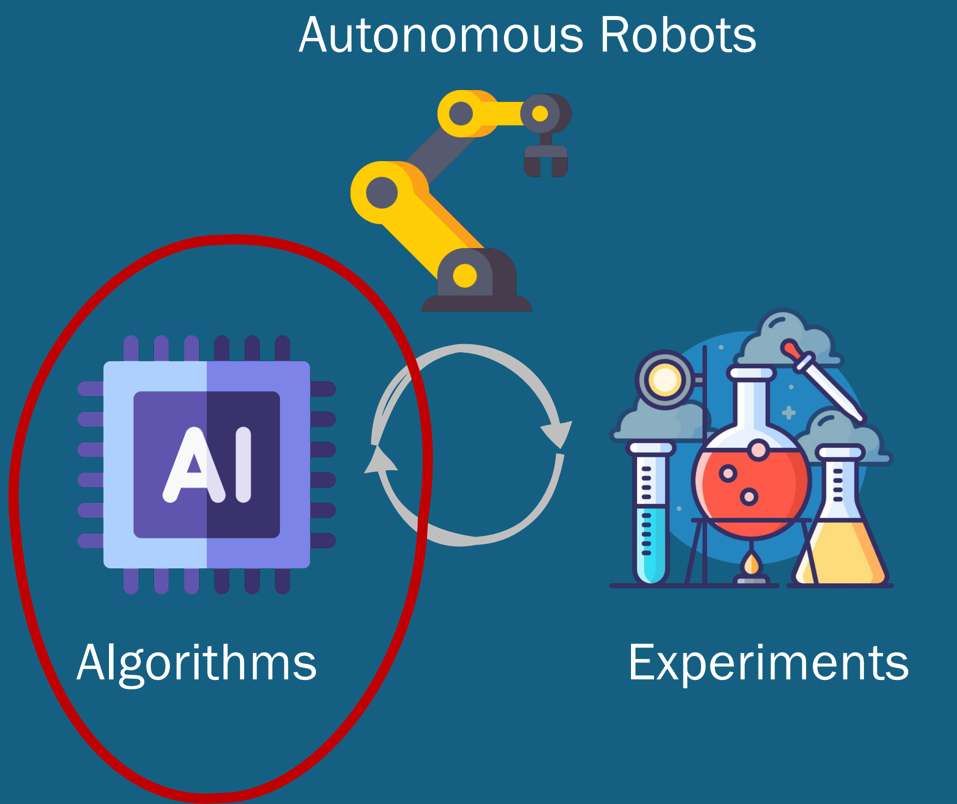
TECHNOLOGY INNOVATION





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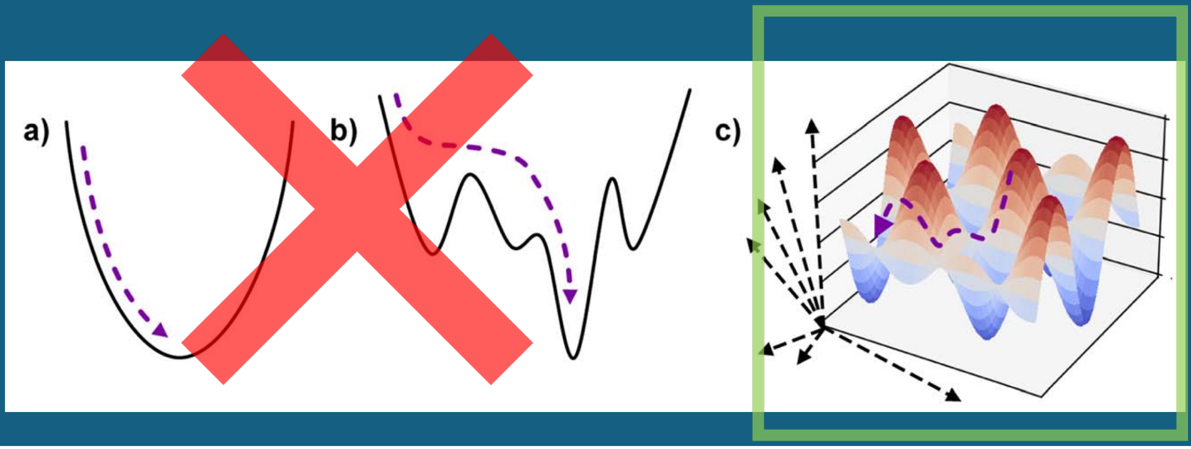
CHEMICAL DISCOVERY – OPTIMISATION

No analytic formula → Hydrogen production | Reaction yield | Organic solid-state lasers



- Non-convex
- Not continuous
- High-dimensional

→ Active Learning

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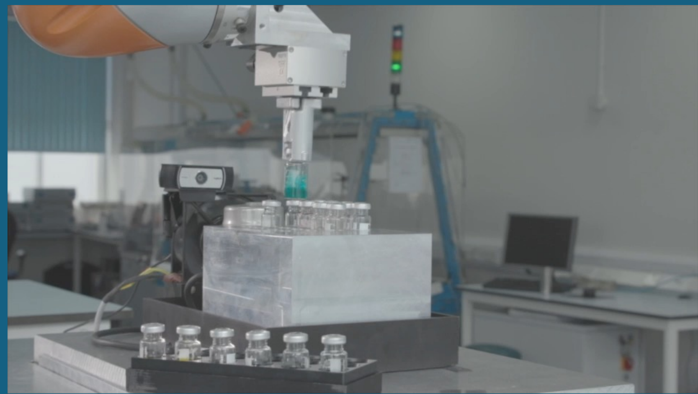
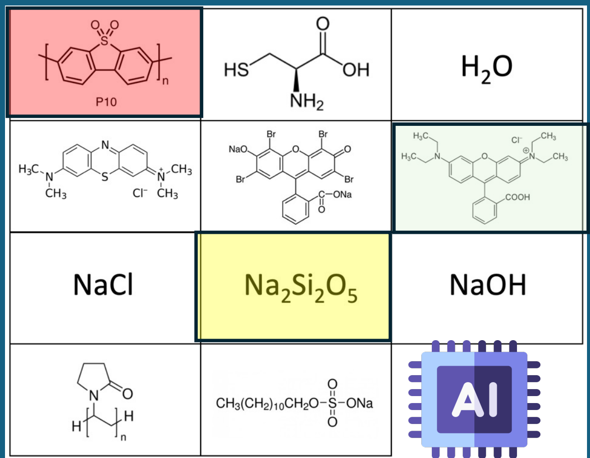
H_2 PRODUCTION OPTIMISATION



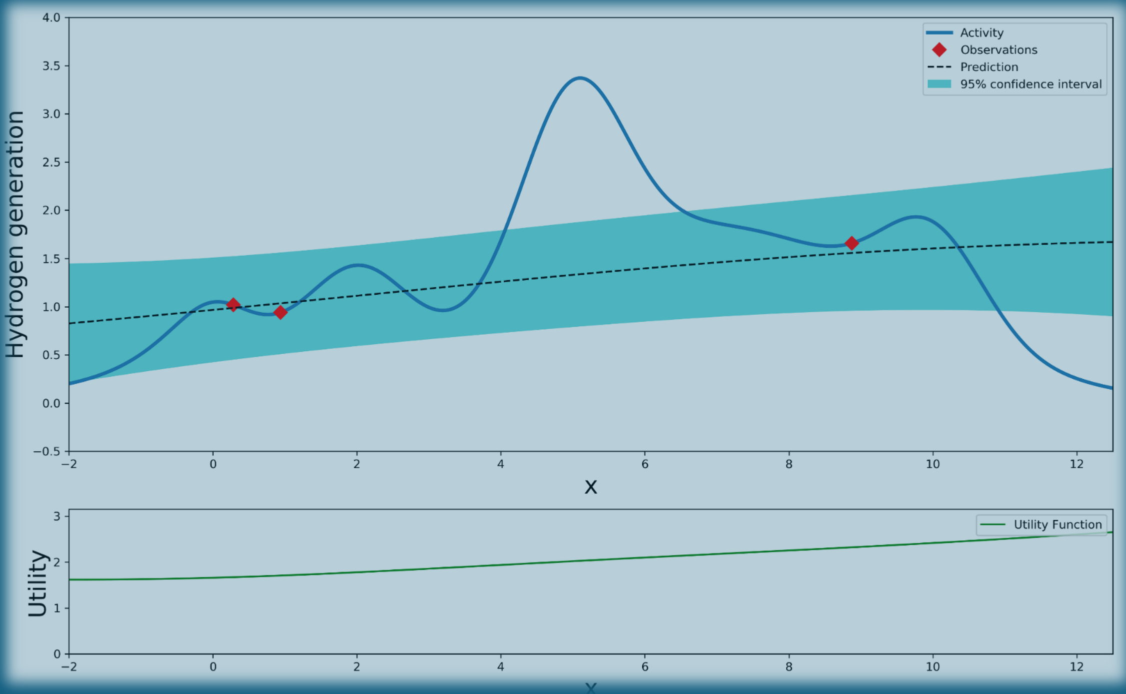
11 catalyst formulation components
→ 98.4 M possible combinations



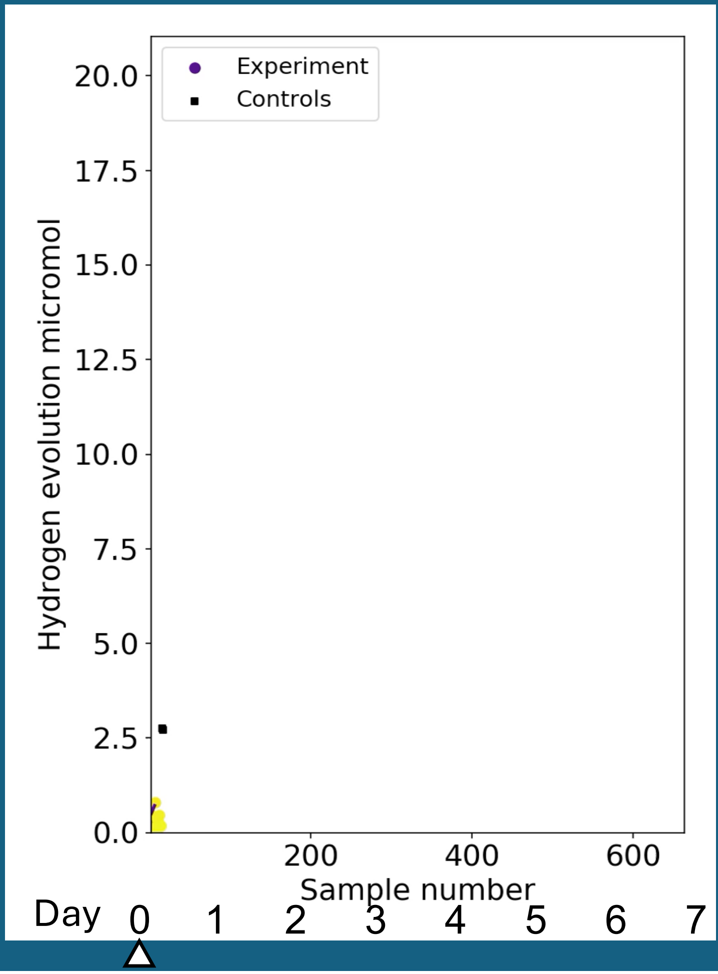
GP-BASED BAYESIAN OPTIMISER

How it works

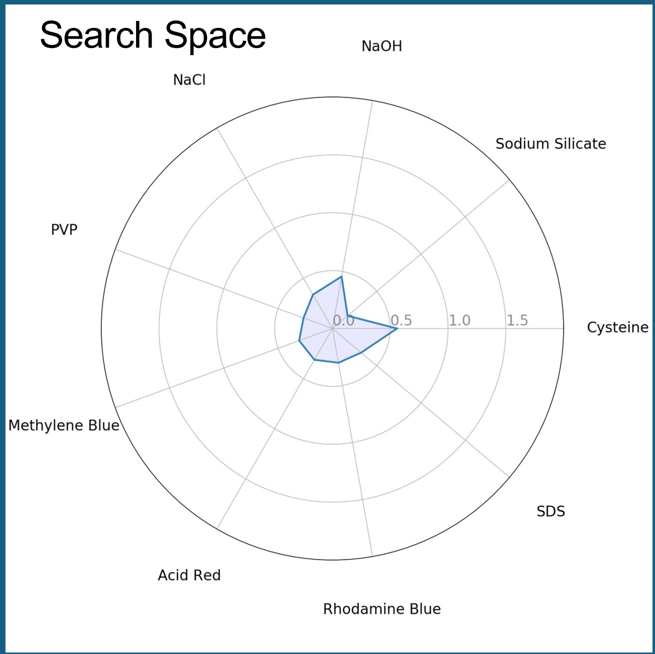
1. Prescribe a prior belief (Gaussian)
2. Calculate the posterior probability
3. Use an acquisition function based on the posterior
4. Sample the acquisition function according to the batch size



BAYESIAN OPTIMISER



Did a PhD (in experimental load), within a week!



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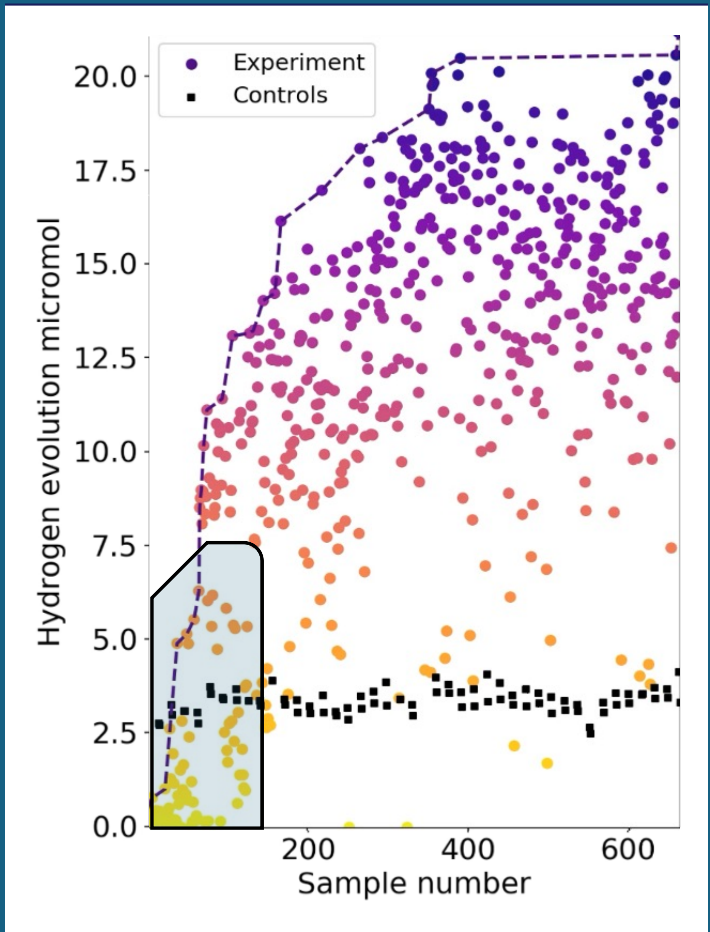
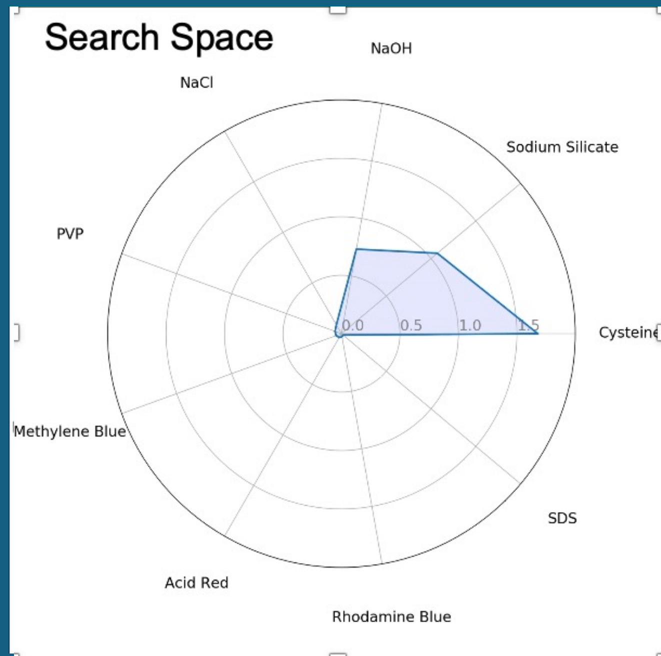
BAYESIAN OPTIMISER





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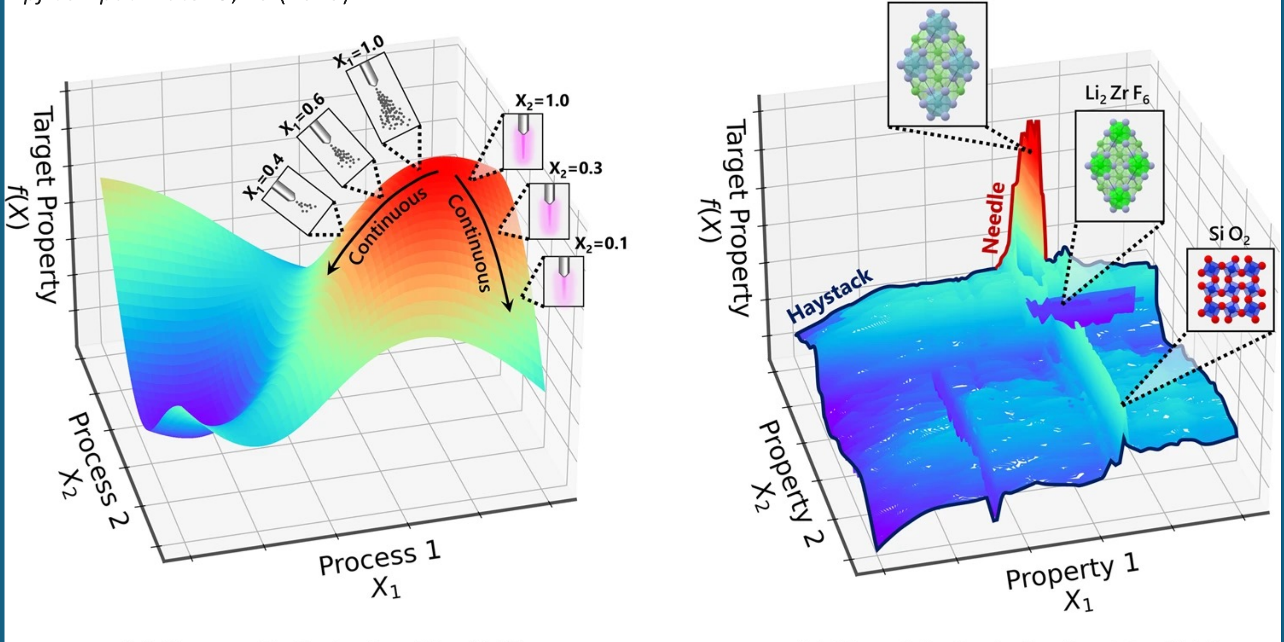
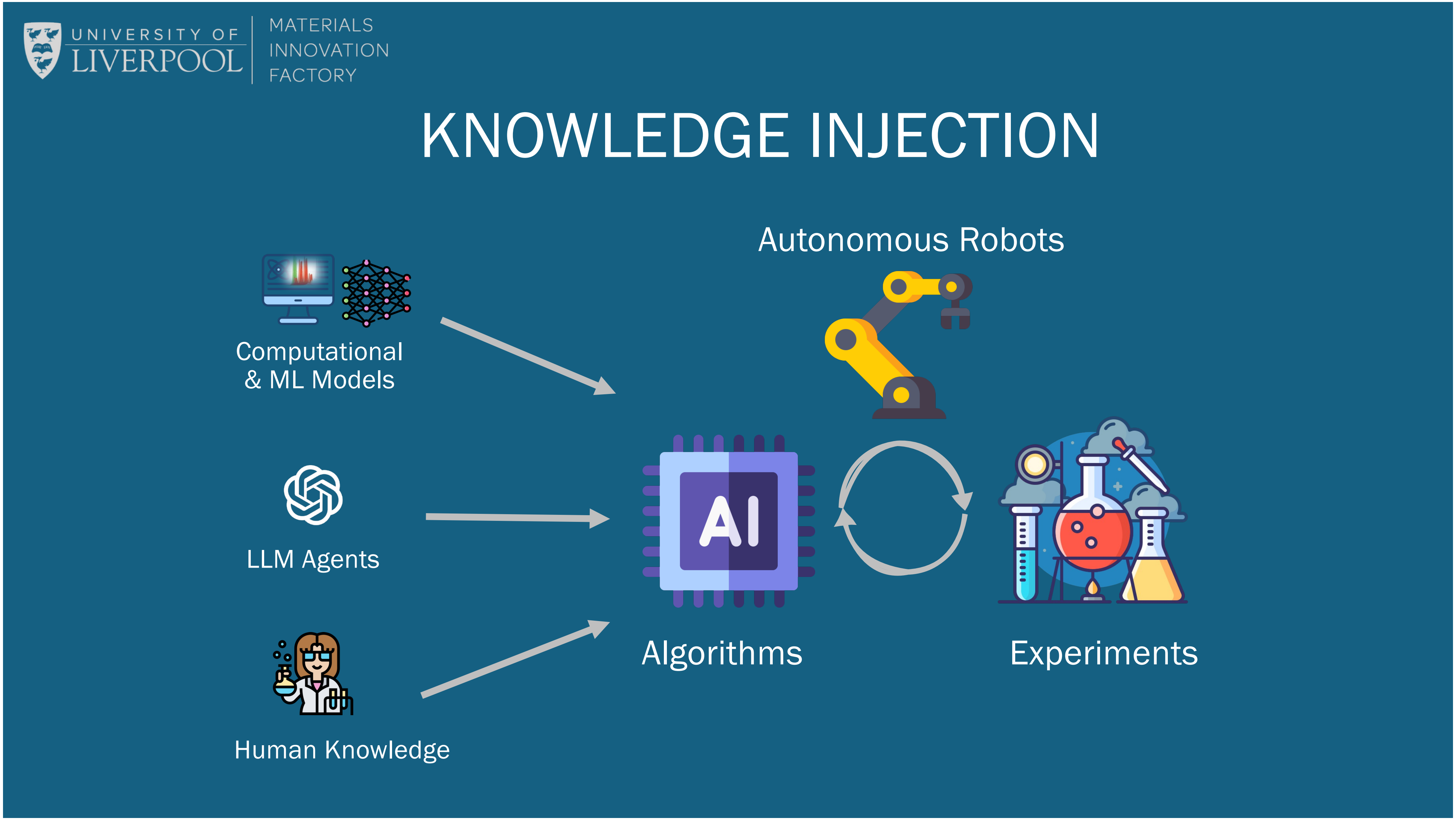
LOOKING FOR NEEDLES IN A HAYSTACK

npj Comput Mater **9**, 79 (2023)



(a) Process Optimization Manifold (b) Materials Optimization Manifold

Smoother Representation of Exploration Space → Focus on Fruitful Regions → Faster Navigation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KNOWLEDGE INJECTION
Autonomous Robots
Computational & ML Models
LLM Agents
Human Knowledge
AI
Algorithms
Experiments

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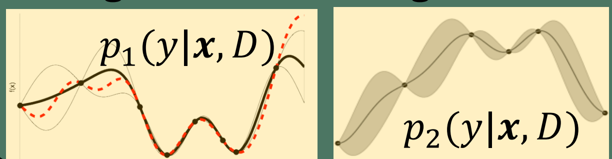
ECAI '23

ML-ENRICHED RESPONSE SURFACES

Sequential Multi-Model-based Optimisation

Dataset

Surrogate Model 1 **Surrogate Model 2**



Acquisition Function

$$\boldsymbol{x}_i = argmax_{x\in X}\ a(\boldsymbol{x}, p_1(y|\boldsymbol{x}, D), p_2(y|\boldsymbol{x}, D))$$

$$\{\boldsymbol{x}_i, y_i\} \cup Dataset$$

dynamic weight

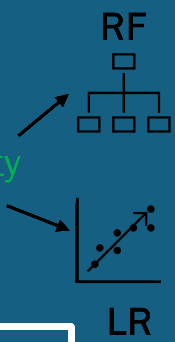
$$\mathbf{x}^\star = \arg\max_{\mathbf{x}\in\mathcal{X}} \alpha(\mathbf{x}, \mathcal{D}) + \gamma\xi(\mathbf{x}, \mathcal{D})$$

BO acquisition

domain knowledge acquisition

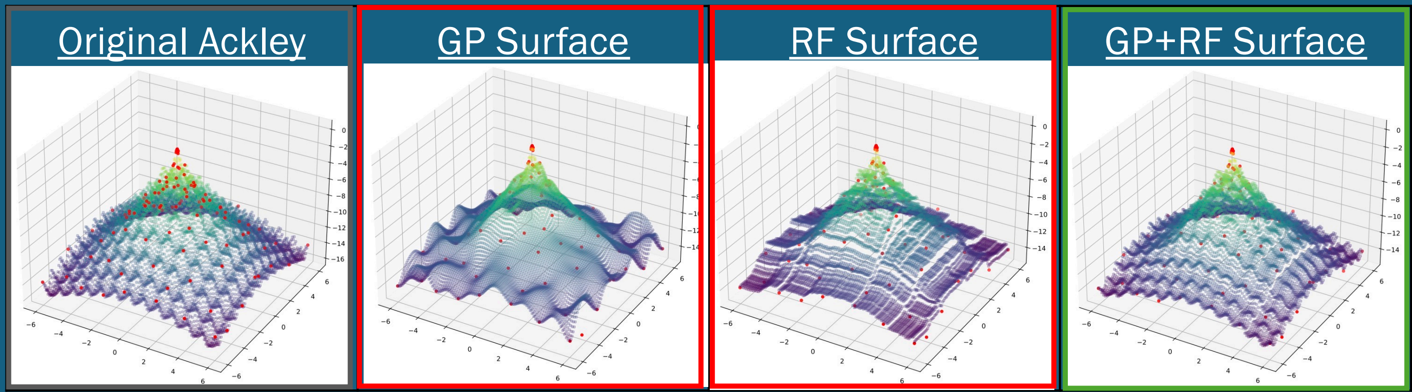
$$\mu(\mathbf{x}) + \kappa\sigma(\mathbf{x})$$

mean and uncertainty of ML model

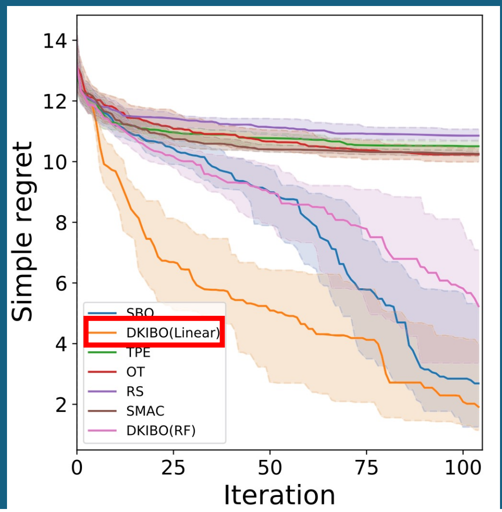


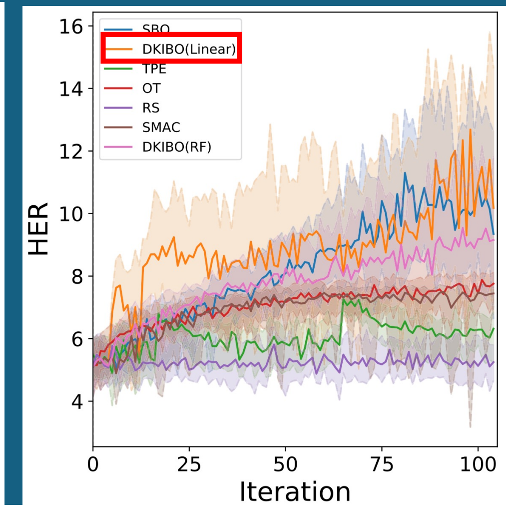
Different ML models capture different underlying structure of the function landscape

ML-ENRICHED RESPONSE SURFACES



H_2 Production Optimisation





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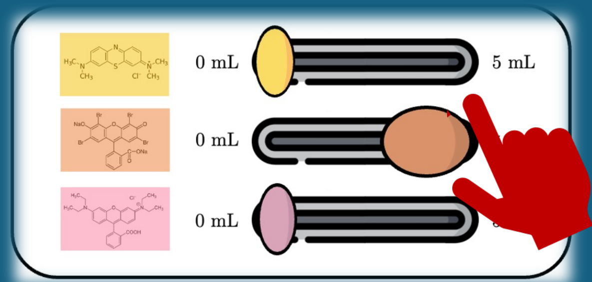
BO DOES NOT UNDERSTAND CHEMISTRY

- Serendipity
- Gut feeling
- Experience
- Creativity
- Wisdom
- Context



- Dyes will have a positive effect
- AR87 was successful with other related photocatalysts [Wang et al., 2018]

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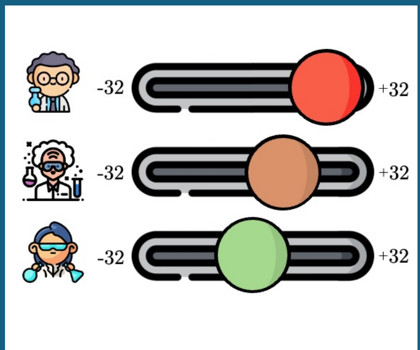
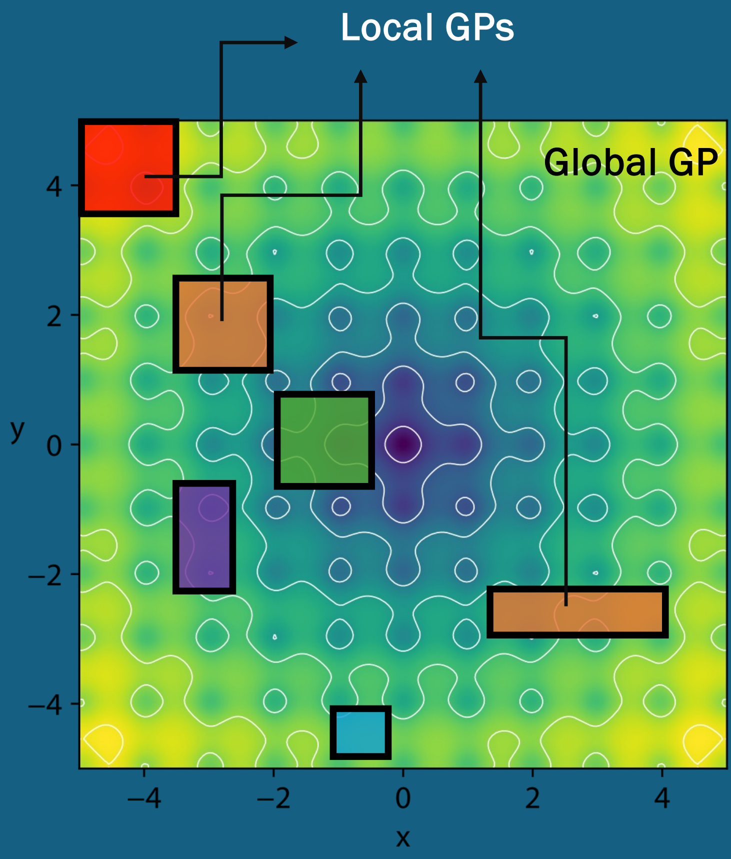
IJCAI ‘24

HYPOTHESIS BAYESIAN OPTIMISATION

‘Tapping’ into promising regions in the parameter space





Hypotheses Subspaces $\mathcal{H}$

▼

‘Soft’ box constraints

f is approximated in each hypothesis subspace by a local GP model:

$$\phi_j \sim \mathcal{N}(\mu_j(x), k_j(x, x'))$$

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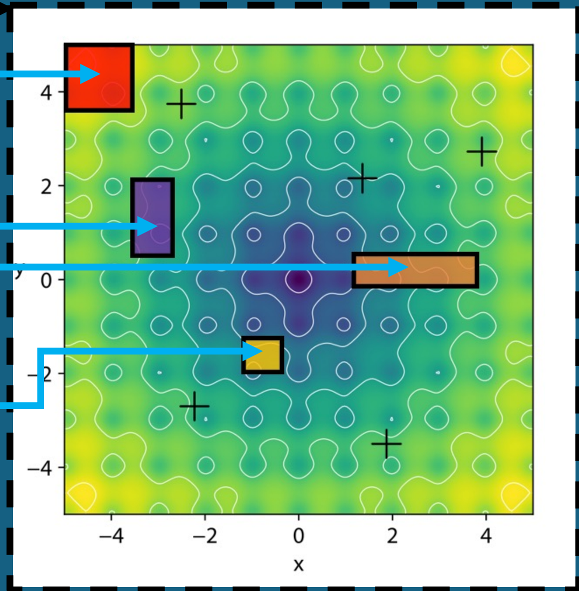
BI-LEVEL OPTIMISATION

Key Concept: Use of expert hypotheses to generate improved seed points.

Upper Level: Global search using vanilla BO to find the maximum of the target function

Lower Level: Local search within hypothesis subspaces to find the promising seeds.



$$x^* = \underset{x\in\mathcal{X}}{argmax}\, \alpha(x, \mathcal{D}\cup\{(s_t, f(s_t))\}_{t=1}^{T}) \qquad \text{(Upper)}$$

s.t

$$\{s_t\}_{t=1}^{T} \in \underset{s\in\bigcup_{j=1}^{J}\mathcal{H}_j}{argmax}\{\underset{s\in\mathcal{H}_j}{max}\, \alpha_{\phi_j}(s,\{\mathcal{D}\cup\{x^*, f(x^*)\}\}\cap\mathcal{H}_j)\}_{j=1}^{J}. \qquad \text{(Lower)}$$

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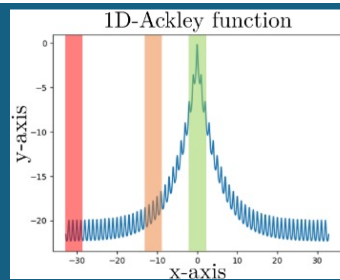
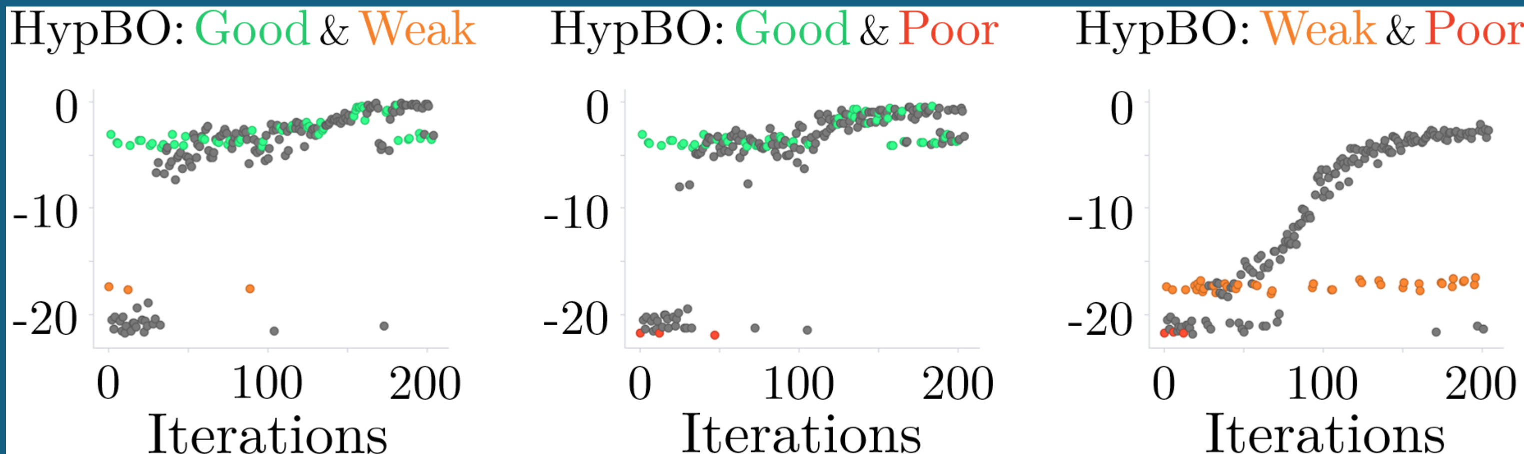
MATERIALS INNOVATION FACTORY



HypBO

- HypBO on $Ackley_{d9}$ with three different mixtures of hypotheses of various qualities.
- Colored sample points came from the hypotheses (lower level) while the grey ones came from the upper level.

y



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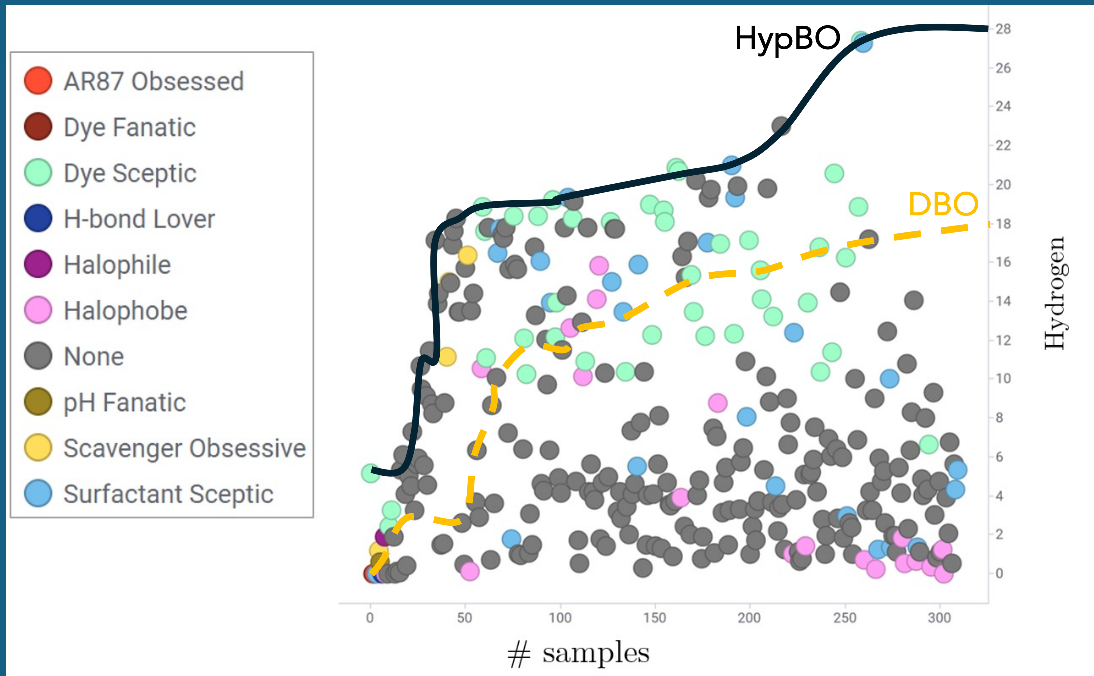
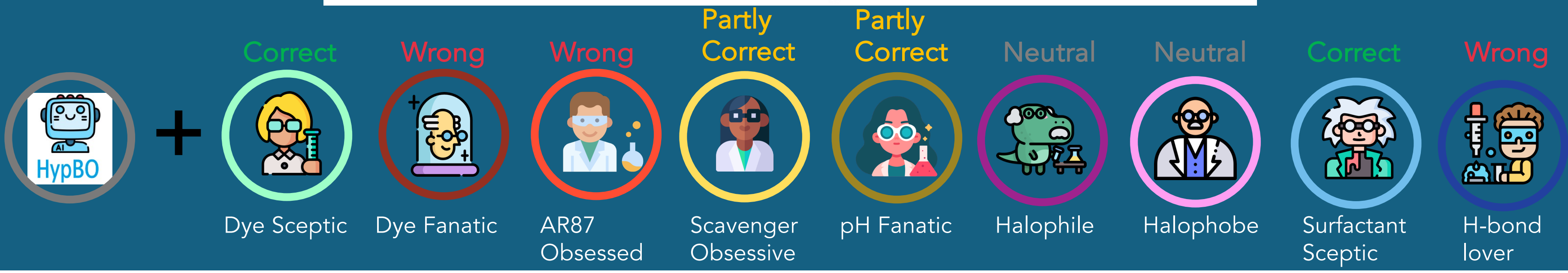
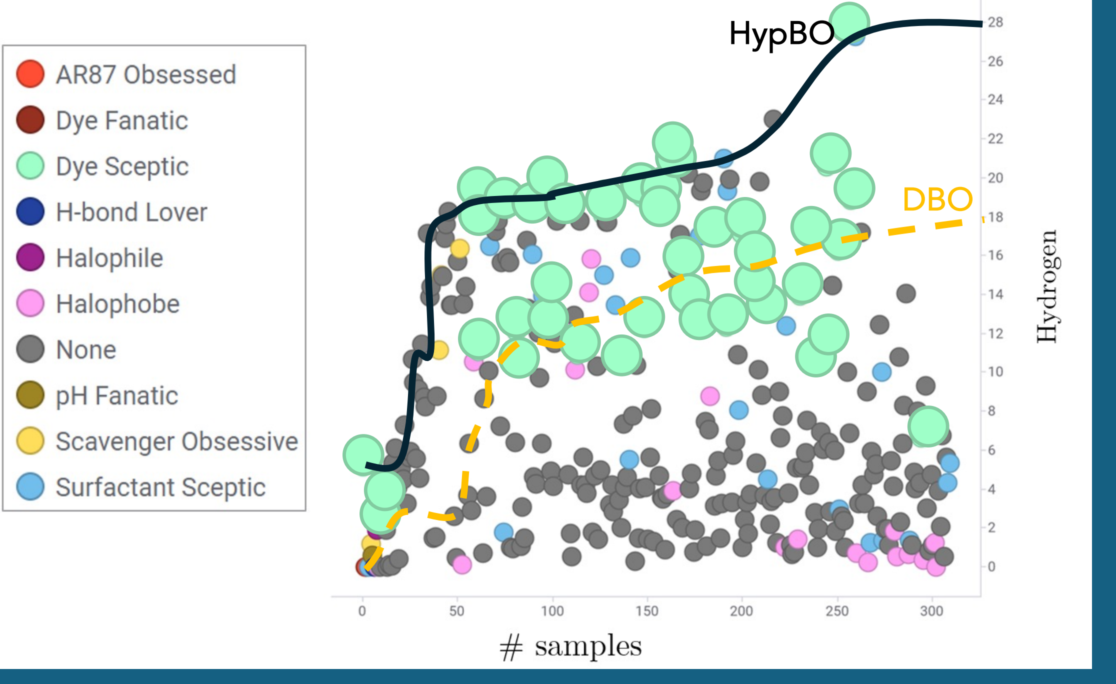
H_2 EXAMPLE





MATERIALS
INNOVATION
FACTORY

H_2 EXAMPLE



+

Correct

Dye Sceptic

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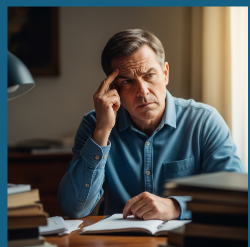
GPT GENERATED HYPOTHESES

Hypotheses

Patterns

Literature



Database

Chat GPT

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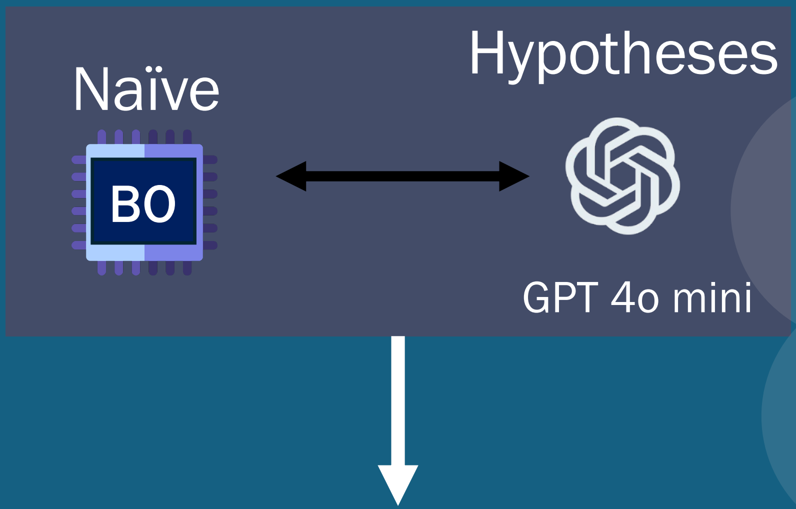
IJCAI ’25

LANGUAGE BO ASSISTANT (BORA)

Hybrid Optimisation



Next experiment

Experiment card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 "domain": "chemistry",
 "description": "The experiment is about maximizing the rate of hydrogen production from a photocatalyst mixture of different chemicals in water. The mixture is exposed to ultraviolet and visible light to generate hydrogen, and the amount produced is measured using gas chromatography. The goal is to enhance the hydrogen evolution rate (HER) through modifying the quantity of the chemicals such as adjustments to pH, ionic strength, addition of dyes and surfactants and so on, in the mixture.",
 "constraint": "the sum of all parameters excluding P10-MIX1 should not exceed 5 to fit inside the vial."
 "parameters": [
   {"name": "AcidRed871_0gL", "description": "A dye that could be used as a photosensitizer or to study dye degradation efficiency under photocatalytic conditions", "bounds": [0, 5], "type": "discrete", "step": 0.25},
   {"name": "L-Cysteine-100gL", "description": "An amino acid that can act as a hole scavenger in photocatalytic processes, potentially enhancing hydrogen production by improving charge separation efficiency", "bounds": [0, 5], "type": "discrete", "step": 0.25},
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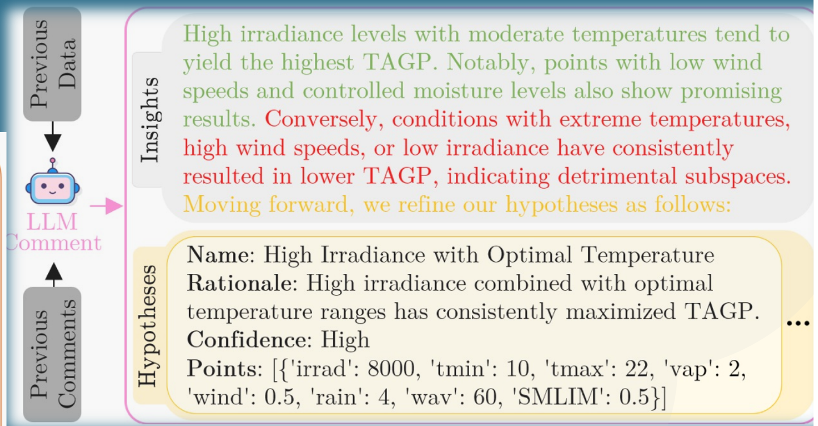
LLM Hypothesis



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LANGUAGE BO ASSISTANT (BORA)

Actions

1. Naïve BO
2. LLM Comments and Suggests new points
3. LLM Comments and Selects points from BO

Adaptive Heuristic Policy

If $\sigma_{t,\text{mean}}^{\text{GP}} < \sigma_{t,\text{lower}}$ or 'no plateau' $\rightarrow$ **action** a_1,

Else if $\sigma_{t,\text{mean}}^{\text{GP}} > \sigma_{t,\text{upper}} \rightarrow$ **action** a_2,

Else $\rightarrow$ **action** a_3.

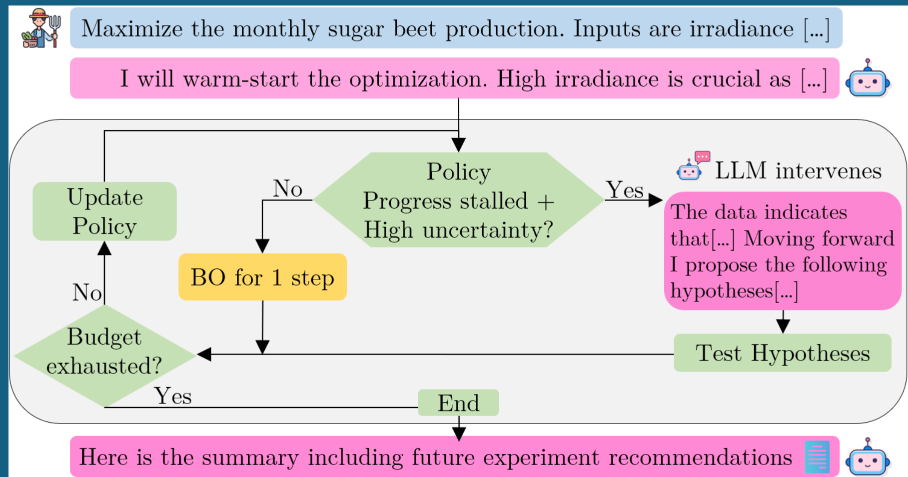
Subject to LLM Trust

$$\sigma_{t,\text{mean}}^{\text{GP}} = \frac{1}{q} \sum_{i=1}^{q} \sigma_t(x_{\text{mon}}^{(i)})$$

$$\sigma_{t,\text{upper}} = 0.5 \times \sigma_{t,\max}^{\text{GP}} \text{ and } \sigma_{t,\text{lower}} = 0.3 \times \sigma_{t,\max}^{\text{GP}}$$

$$\sigma_{t,\max}^{\text{GP}} = \max\left(\sigma_{t-1,\max}^{\text{GP}}, \max_{1 \le i \le q} \sigma_t(x_{\text{mon}}^{(i)})\right)$$

Workflow



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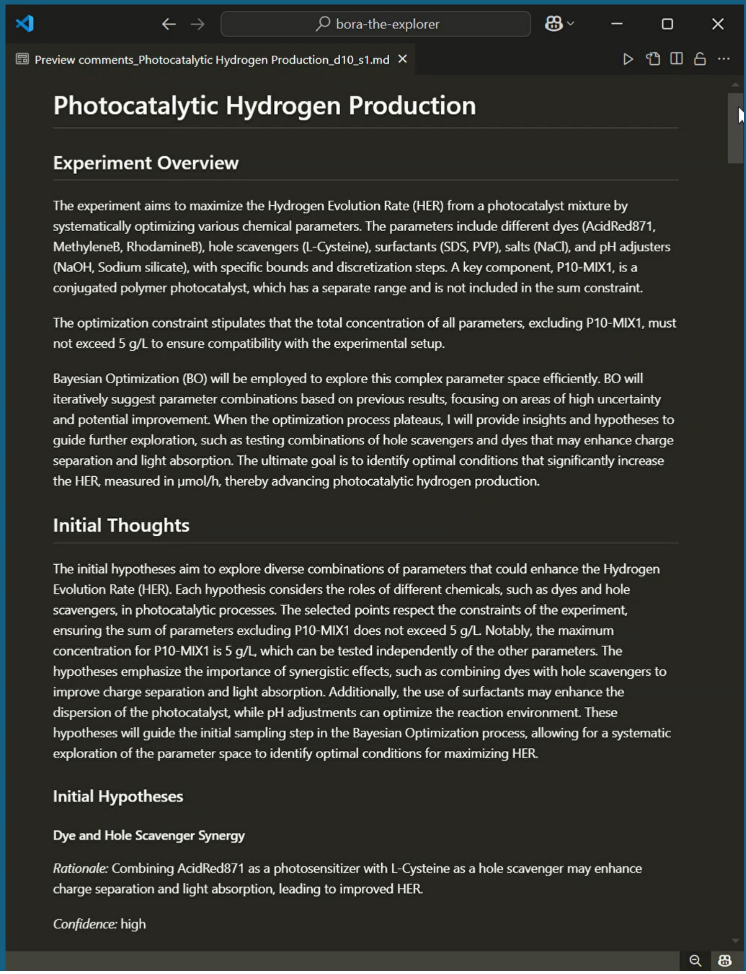
LANGUAGE BO ASSISTANT (BORA)


bora-the-explorer

Preview comments_Photocatalytic Hydrogen Production_d10_s1.md

Photocatalytic Hydrogen Production

Experiment Overview

The experiment aims to maximize the Hydrogen Evolution Rate (HER) from a photocatalyst mixture by systematically optimizing various chemical parameters. The parameters include different dyes (AcidRed871, MethyleneB, RhodamineB), hole scavengers (L-Cysteine), surfactants (SDS, PVP), salts (NaCl), and pH adjusters (NaOH, Sodium silicate), with specific bounds and discretization steps. A key component, P10-MIX1, is a conjugated polymer photocatalyst, which has a separate range and is not included in the sum constraint.

The optimization constraint stipulates that the total concentration of all parameters, excluding P10-MIX1, must not exceed 5 g/L to ensure compatibility with the experimental setup.

Bayesian Optimization (BO) will be employed to explore this complex parameter space efficiently. BO will iteratively suggest parameter combinations based on previous results, focusing on areas of high uncertainty and potential improvement. When the optimization process plateaus, I will provide insights and hypotheses to guide further exploration, such as testing combinations of hole scavengers and dyes that may enhance charge separation and light absorption. The ultimate goal is to identify optimal conditions that significantly increase the HER, measured in μmol/h, thereby advancing photocatalytic hydrogen production.

Initial Thoughts

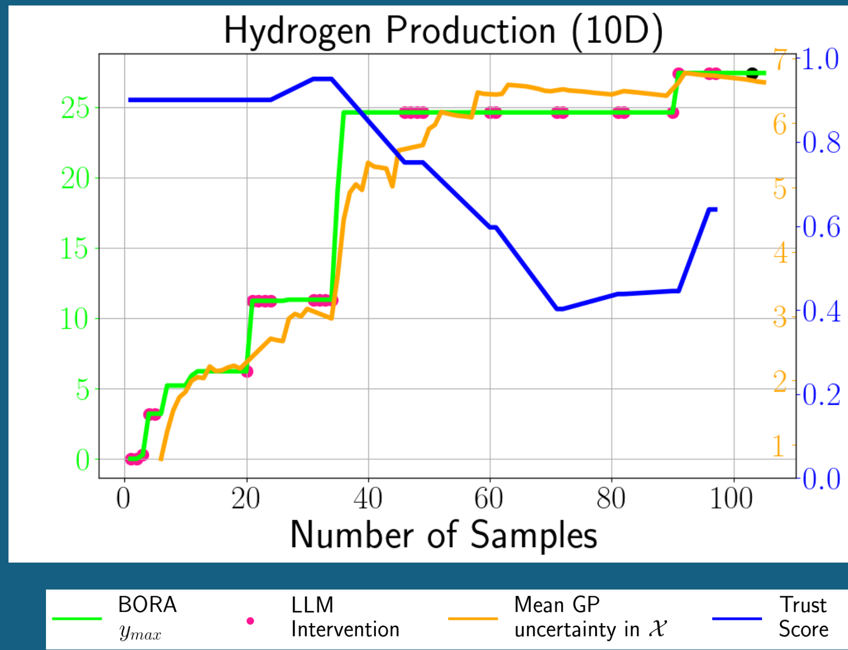
The initial hypotheses aim to explore diverse combinations of parameters that could enhance the Hydrogen Evolution Rate (HER). Each hypothesis considers the roles of different chemicals, such as dyes and hole scavengers, in photocatalytic processes. The selected points respect the constraints of the experiment, ensuring the sum of parameters excluding P10-MIX1 does not exceed 5 g/L. Notably, the maximum concentration for P10-MIX1 is 5 g/L, which can be tested independently of the other parameters. The hypotheses emphasize the importance of synergistic effects, such as combining dyes with hole scavengers to improve charge separation and light absorption. Additionally, the use of surfactants may enhance the dispersion of the photocatalyst, while pH adjustments can optimize the reaction environment. These hypotheses will guide the initial sampling step in the Bayesian Optimization process, allowing for a systematic exploration of the parameter space to identify optimal conditions for maximizing HER.

Initial Hypotheses

Dye and Hole Scavenger Synergy

Rationale: Combining AcidRed871 as a photosensitizer with L-Cysteine as a hole scavenger may enhance charge separation and light absorption, leading to improved HER.

Confidence: high



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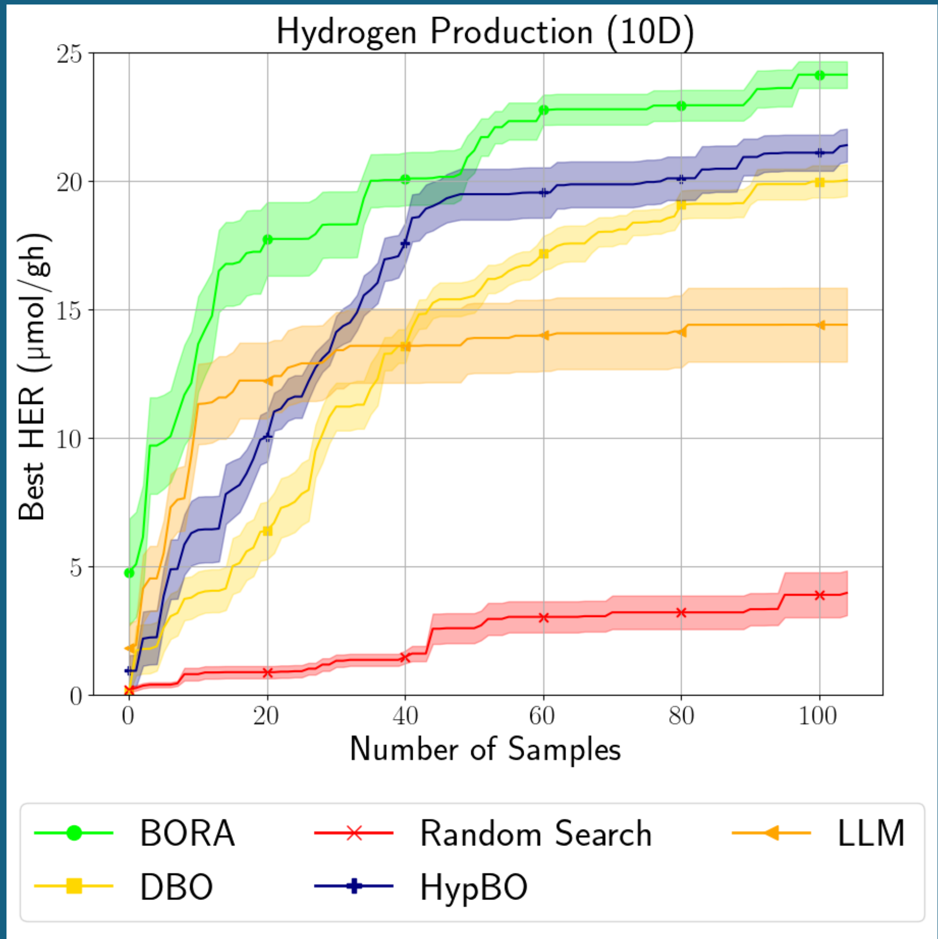
H_2 PRODUCTION



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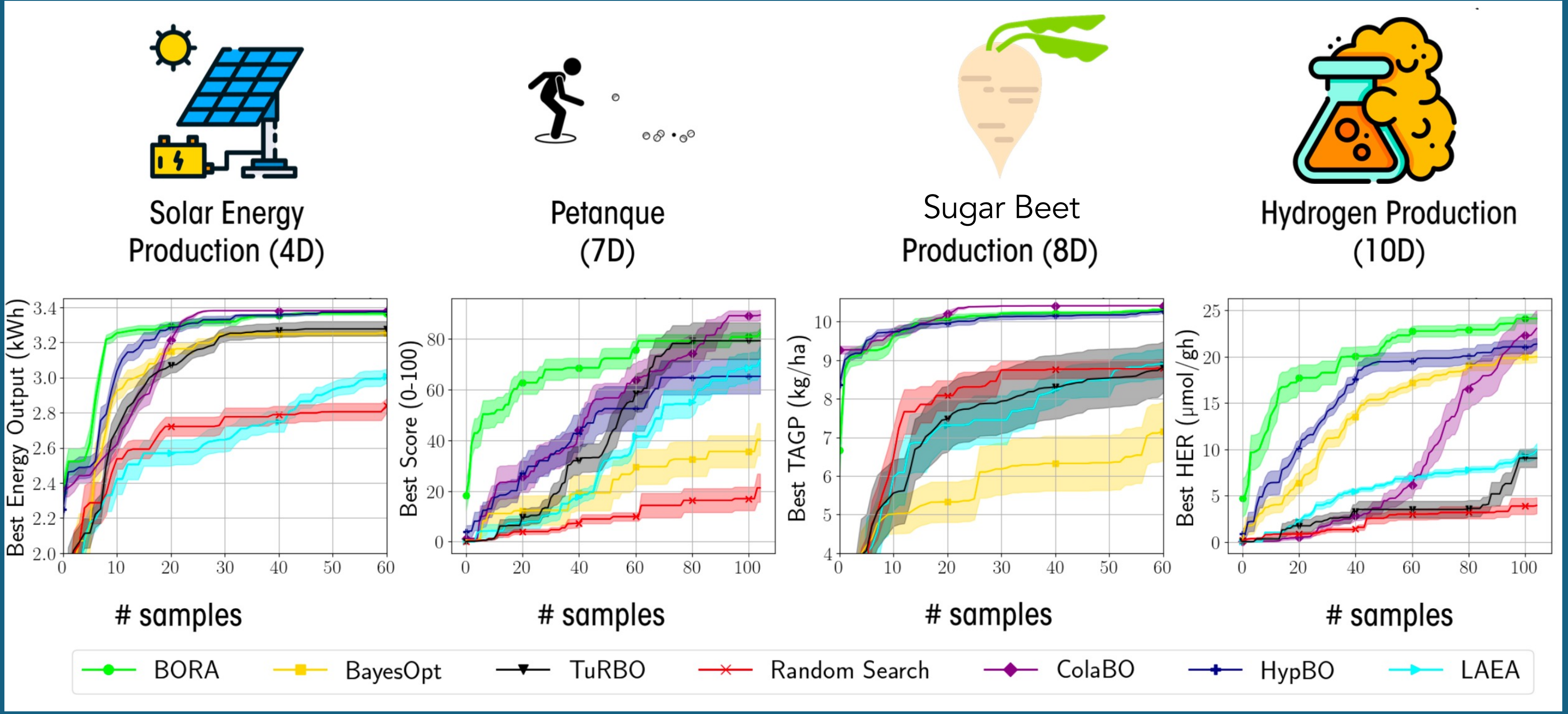
BORA AS A SCIENCE OPTIMISER



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HOW TO AUTOMATE CHEMISTRY?

WHAT CHEMISTRY TO AUTOMATE?

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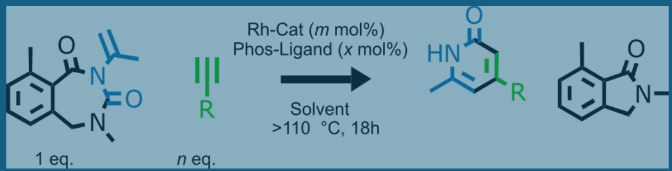
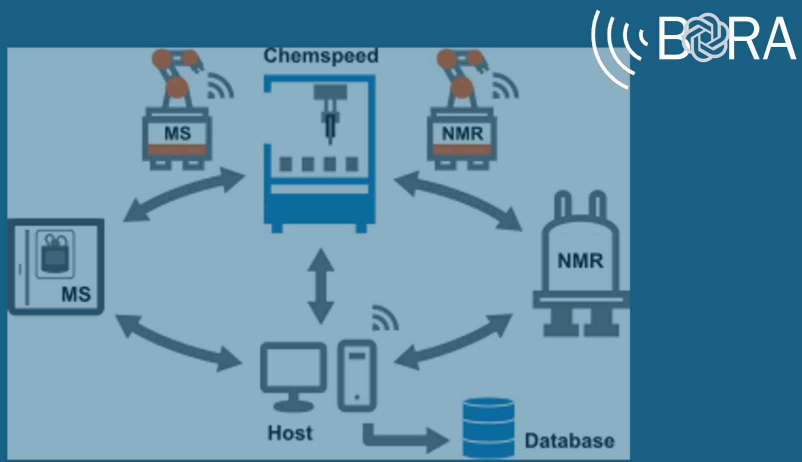
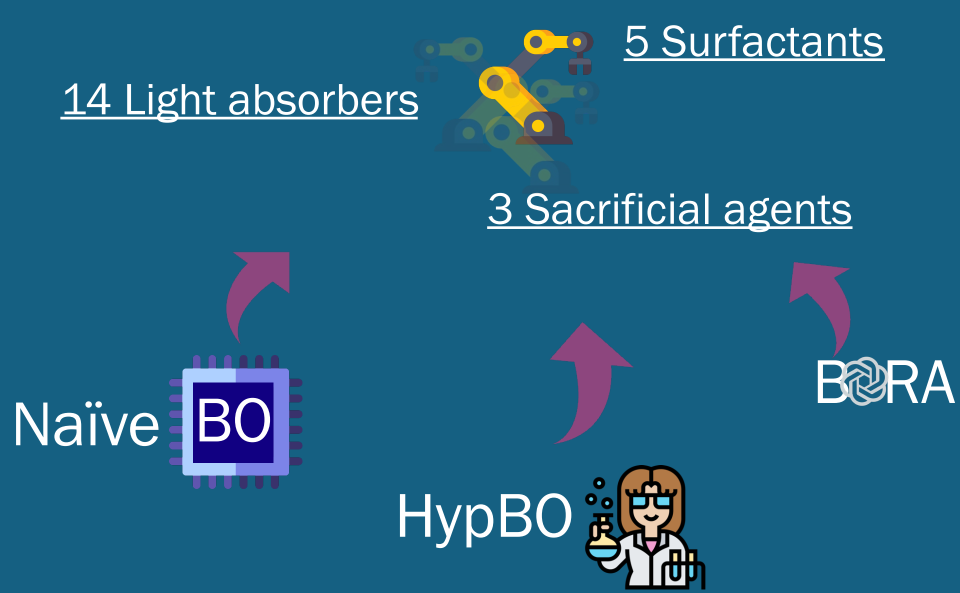
BORA AS A GENERAL TOOL

Reaction Generalisation





Hydrogen Production 22-D



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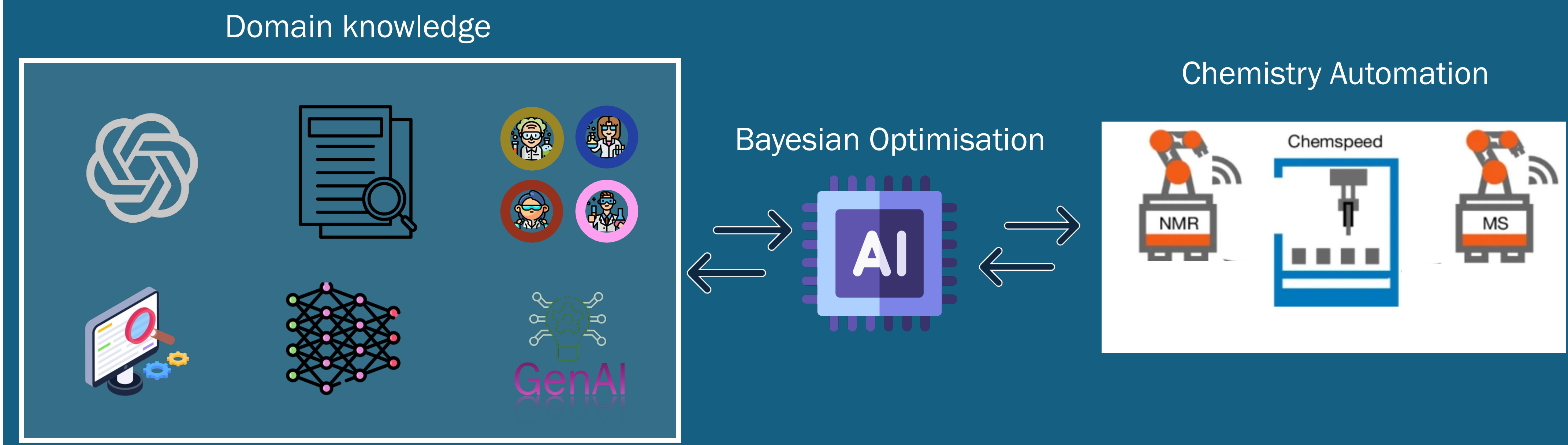
HYBRID INTELLIGENCE



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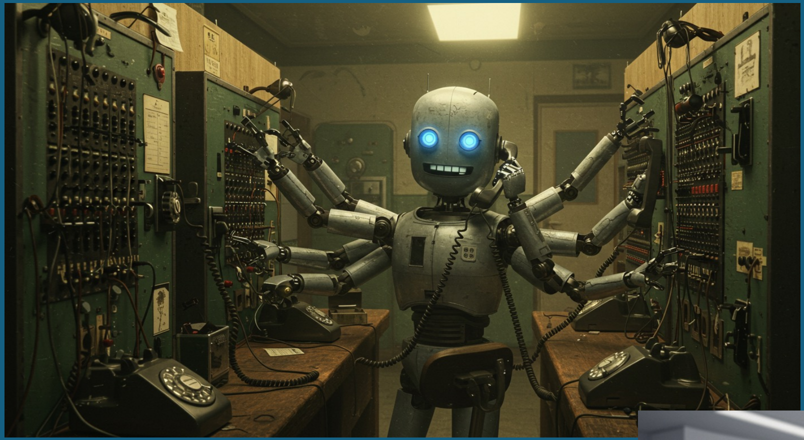
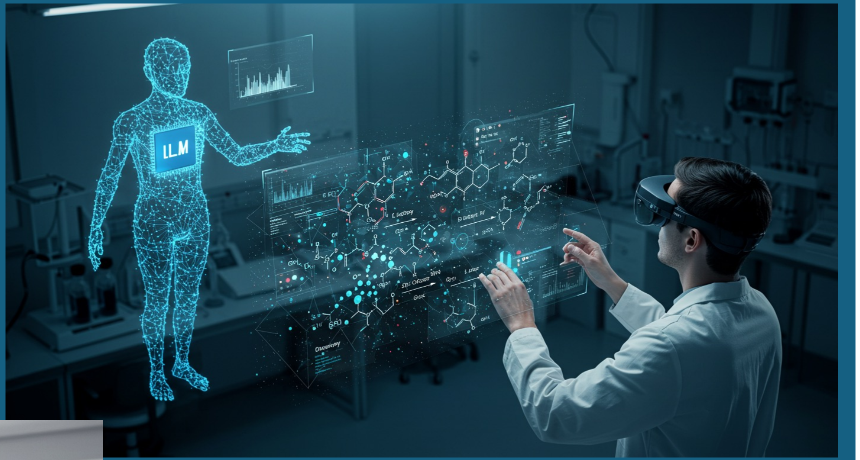
OPEN CHALLENGES

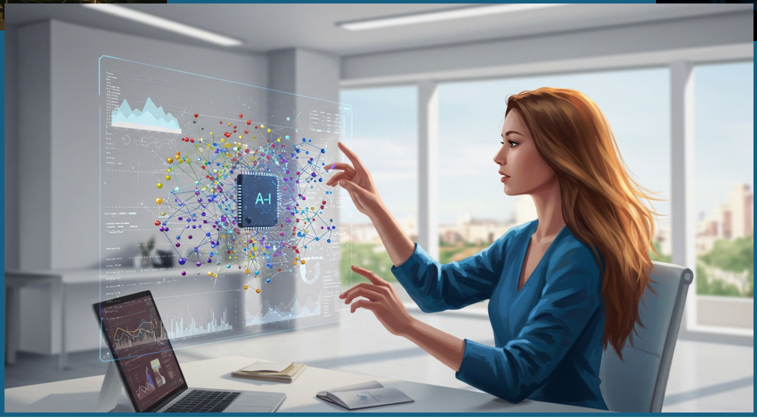
Multi-fidelity BO



LLM Chemistry Conceptualisation



HITL Data Visualisation



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ACKNOWLEDGEMENTS

Prof. Andy Cooper

Cooper group

LEVERHULME TRUST

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THANK YOU FOR LISTENING ☺

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