La Agente Optima – orchestrated Bayesian optimization and active learning for accelerated *in silico* compound discovery

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1. Abstract

Bayesian optimization (BO) plays a key role in data-efficient exploration and optimization for chemistry, materials science, and other scientific fields, particularly in settings where objective function evaluations are expensive [2, 3, 4]. Such evaluations are usually time-intensive and/or costly experiments, which can be noisy, asynchronous, and heterogeneous in fidelity, as encountered in physical experiments or high-accuracy computational simulations [5, 6]. BO formalizes closed-loop discovery as a problem of sequential decision-making under uncertainty, in which probabilistic beliefs over objective functions are updated via Bayesian inference and experimental actions are selected to optimize expected outcomes. In practice, BO encompasses a broad design space of models, priors, acquisition strategies, and optimization choices, whose effective coordination is critical in realistic closed-loop discovery settings [7].

At present, such workflows, where optimization algorithms are directly coupled to experimental evaluations, are typically realized through complex, manually assembled pipelines. This requires substantial technical expertise across multiple layers of the stack, spanning electronic-structure software, experimental platforms, and the coordination of optimization algorithms with orchestration engines [8, 9].

In parallel, recent advances in artificial intelligence (AI) agentic systems, driven by large language models (LLMs), have enabled the autonomous orchestration of complex scientific workflows by combining reasoning, tool use, and domain-specific execution modules, such as electronic-structure codes or laboratory automation interfaces [10]. As demonstrated in recent works from our lab with El Agente Q and more recently El Agente Gráfico, complex quantum chemistry (QC) workflows can be executed fully autonomously end-to-end through natural-

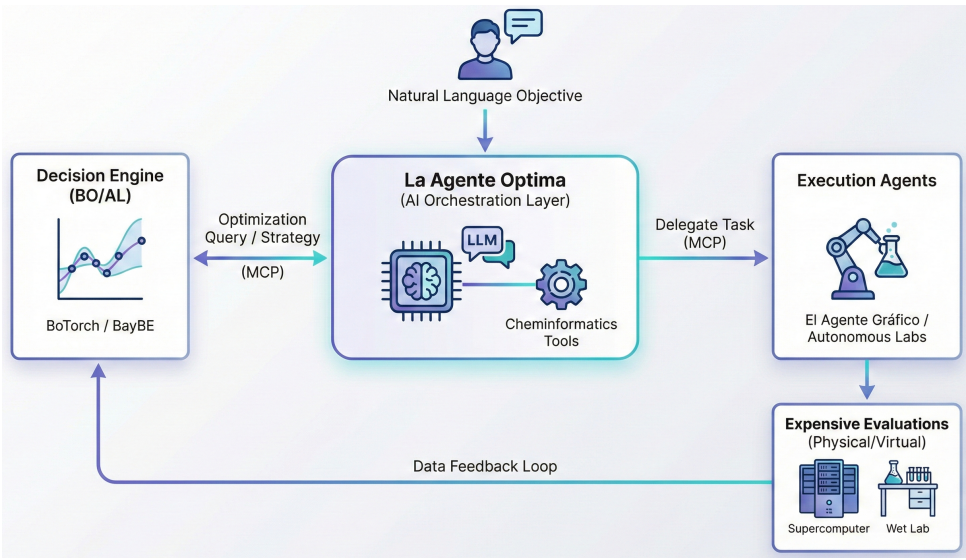

Fig. 1: Schematic of the La Agente Optima architecture [1], bridging Bayesian optimization (BO) and active learning (AL) frameworks through a central agentic artificial intelligence (AI) orchestration layer. The system translates natural-language objectives into closed-loop discovery workflows, delegating tasks to heterogeneous execution agents via model context protocol (MCP).

language interaction with a multi-agent system [11, 12]. This concept has since been extended to additional domains, including quantum computing [13], drug discovery [14], solid-state chemistry, and others.

Despite sharing a common abstraction of sequential decision-making under uncertainty, BO frameworks and agentic AI systems have largely evolved independently and have not yet been systematically integrated within unified discovery frameworks.

Here, we outline an early-stage concept to bridge these two paradigms (see Fig. 1). BO frameworks such as BoTorch [15] and BayBE [3], together with active learning (AL) algorithms [16], are integrated via a central agentic AI orchestration layer: La Agente Optima translates high-level scientific objectives into optimization and exploration queries handled by the BO/AL engines, while expensive function evaluations are delegated to execution agents such as El Agente Gráfico for electronic structure calculations. For the BO backend, we employ and compare BoTorch and BayBE, both exposed through in-house hosted Model Context Protocols (MCPs) servers. Results from expensive physical or virtual evaluations are asynchronously ingested by the decision engine via a dedicated data pipeline, allowing BO or AL models to update independently of the central agent, which only intermittently polls or supervises the feedback loop. By equipping La Agente Optima with cheminformatics and eletronic structure tools, the system can reason about appropriate (macro-)molecular representations and optimization strategies.

We demonstrate the capabilities of Optima through four diverse case studies. The first one is a fully autonomous, natural-language-orchestrated optimization of an emitter material, inspired by Ref. [8]. We further apply BO to conformer searches in small molecules, using a search space defined over internal coordinates. We then tackle a challenging catalyst optimization task that extends beyond standard optimization and routine electronic-structure calculations by requiring secondary, LLM-driven post-processing steps. In collaboration with a Human Organ Mimicry Self-Driving Laboratory at the Acceleration Consortium, we also demonstrate fully autonomous, multi-objective optimization of a biofabrication workflow using purely natural-language orchestration [17]. Beyond these case studies, Optima naturally extends to applications such as force-field and semiempirical method parameter calibration, as well as multi-objective materials screening [e.g., for metal–organic frameworks *aka* MOFs].

2. Conclusion

La Agente Optima enables closed-loop scientific discovery workflows by coupling agentic reasoning with Bayesian decision-making over domain-specific evaluation functions. While demonstrated here primarily in computational chemistry, we also present early-stage experimental orchestration, and the architecture is designed to generalize beyond a single scientific domain. This work marks an initial design and collaboration phase, laying the groundwork for broader validation, benchmarking, and joint development across multiple research groups, with the longer-term goal of enabling interconnected, AI-driven scientific workflows across institutions. As part of this effort, the El Agente ecosystem [11, 13, 14] will be made available through a shared platform, with community access and registration provided via elagente.ca.

3. Related work

LLMs have also been leveraged to warm-start BO workflows, for example, by improving candidate initialization strategies or by imposing structured priors on the search space [18, 19]. Han et al. showed accelerated BO using LLM-based multi-agent systems [20]. BORA integrates LLMs to enhance BO with domain knowledge and reasoning capabilities of LLMs [21]. As discussed in the main text, a growing body of work employs multi-agent or agentic AI systems to orchestrate scientific tools and workflows. Additional representative examples include Refs. [22, 23, 24].

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