Accelerating Drug Discovery in the Matter Lab: From Agentic AI to Automated Experimental Validation

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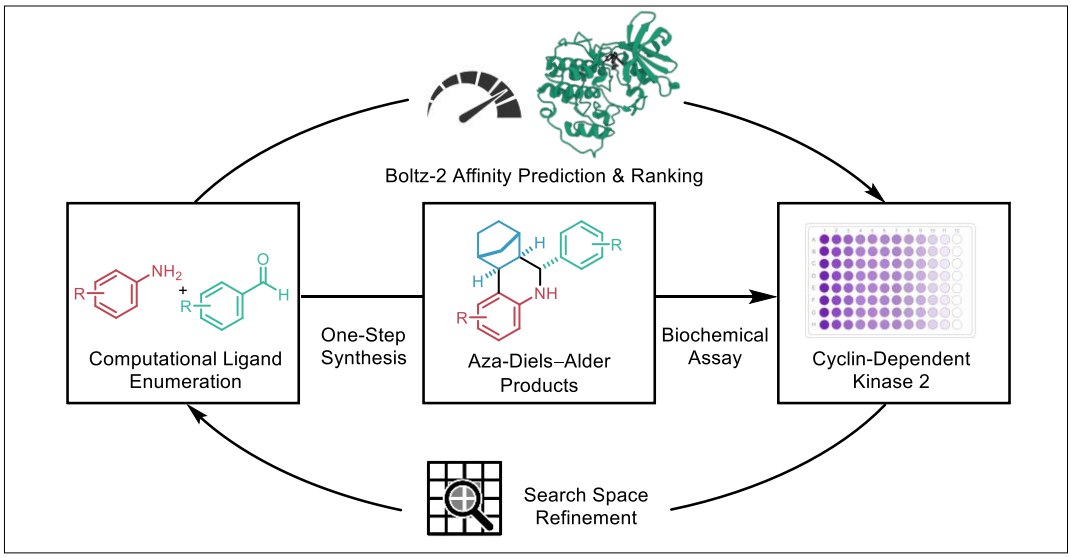
Part 1. Agentic Drug Discovery with Fármaco

The Matter Lab has pioneered the *el agente* ecosystem, a modular framework of AI-driven agents designed to autonomously orchestrate complex scientific workflows. Here, we introduce its most recent addition: *Fármaco*, an agent engineered specifically for computational drug discovery. By unifying predictive modeling with operational autonomy, *Fármaco* executes end-to-end *in silico* campaigns with minimal human intervention. Its core capabilities center on generative models for small molecule design paired with rapid binding affinity estimation. Equipped with a versatile toolkit to navigate large chemical spaces and formulate hypotheses, *Fármaco* is designed to effectively bridge the gap between early-stage computational design and downstream experimental validation, serving as a powerful new engine for discovery.

Part 2. Rapid Discovery of Potent CDK2 Inhibitors Using Boltz-2



Translating advanced *in silico* predictions into physical molecules remains a major bottleneck in drug development. To bridge this gap, we developed a streamlined platform coupling Boltz-2 affinity predictions with automated experimental validation, and showcased the platform for cyclin-dependent kinase 2 (CDK2), an important therapeutic target in oncology. We first curated a large virtual library of structurally diverse tetrahydroquinolines and utilized Boltz-2 to efficiently prioritize the most promising candidates. These *in silico* hits were then directly synthesized via a single-step aza-Diels–Alder approach. The resulting compounds underwent rapid evaluation through miniaturized chemiluminescence-based kinase assays. While automating the bioassay workflow at a 10 µL scale on Opentrons liquid handlers posed initial challenges, overcoming them ultimately drove significant improvements in precision and reproducibility. This seamless pipeline successfully yielded novel, single-digit micromolar inhibitors of CDK2.