## ART: A machine learning Automated Recommendation Tool for synthetic biology

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## Project Goals: To develop machine learning methods to effectively guide bioengineering

Synthetic biology allows us to bioengineer cells to synthesize novel valuable molecules such as renewable biofuels or anticancer drugs. However, traditional synthetic biology approaches involve ad-hoc engineering practices, which lead to long development times. Here, we present the Automated Recommendation Tool (ART¹), a tool that leverages machine learning and probabilistic modeling techniques to guide synthetic biology in a systematic fashion, without the need for a full mechanistic understanding of the biological system. Using sampling-based optimization, ART provides a set of recommended strains to be built in the next engineering cycle, alongside probabilistic predictions of their production levels². We demonstrate the capabilities of ART on simulated data sets, as well as experimental data from real metabolic engineering projects producing renewable biofuels, hoppy flavored beer without hops, fatty acids, and tryptophan. We also discuss the limitations of this approach, and the practical consequences of the underlying assumptions failing. A fundamental part of using machine learning in synthetic biology involves the availability of large amounts of high-quality training data. We show how to use the Experiment Data Depot (EDD) to store, visualize and export data in a standardized fashion.

## References

- 1. Radivojević, Tijana, et al. "A machine learning Automated Recommendation Tool for synthetic biology." Nature communications 11.1 (2020): 1-14.
- 2. Zhang, Jie, et al. "Combining mechanistic and machine learning models for predictive engineering and optimization of tryptophan metabolism." Nature communications 11.1 (2020): 1-13.

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