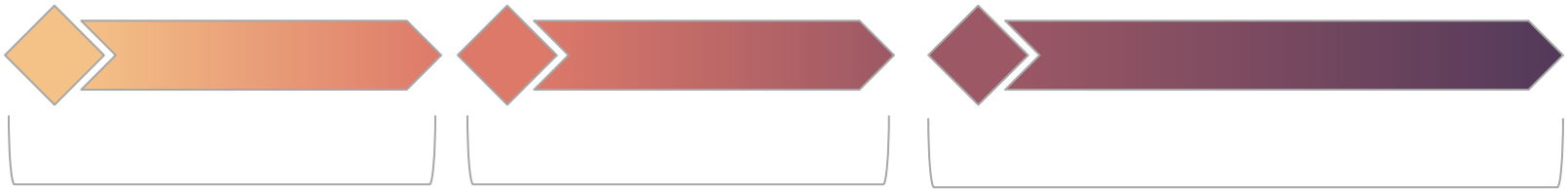
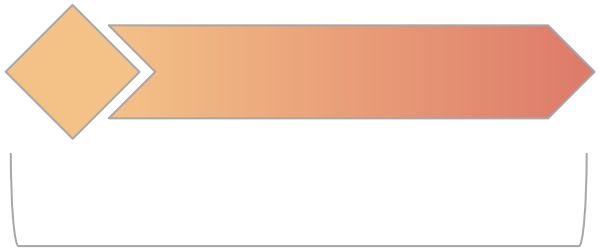
3DM Engineering

combining the Power of 3DM with AI for
Protein Engineering

Protein engineering pipeline with 3DM & AI



Finding a starting protein



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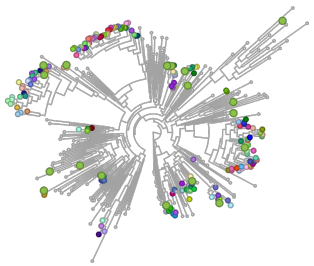


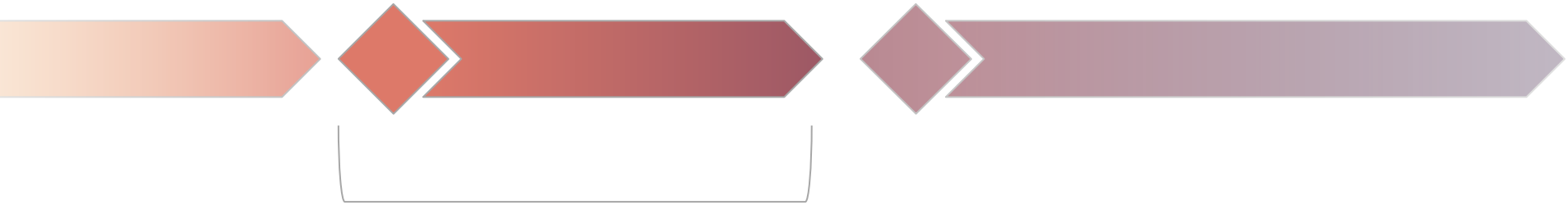
Number	50	54	58	113	207	Proteins
1.	D	H	V	N	S	28,639
2.	D	H	T	S	S	7,999
3.	P	H	C	S	S	4,471
4.	D	H	V	S	S	4,173
5.	D	H	C	S	S	3,492
6.	D	H	T	N	S	2,843

Intelligent in-silico panel design with 3DM

- Maximize hit rates with smart diversity
- FTO included
- Optimize for expression

Customers report an increase of protein expression from ~40% to >90%

Introducing diversity



Introducing diversity

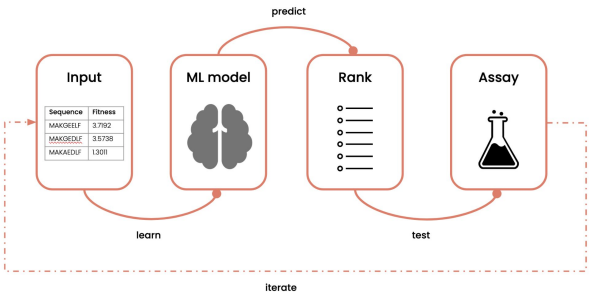
Smart diversity with 3DM & AI

- Smart hotspot selection
  - Literature review
  - Patents
  - Coevolution
- Exclusion of likely non-functional proteins

AI based optimization

AI based optimization

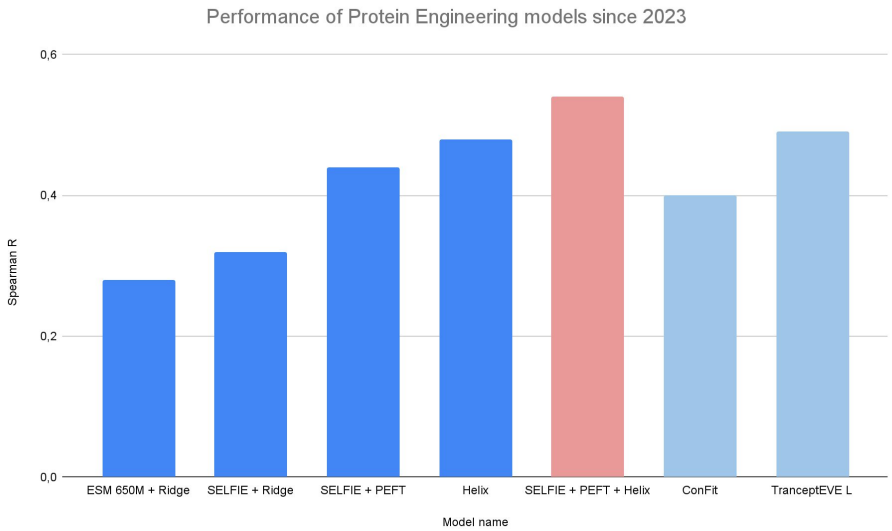
AI optimization cycle



Best in class in-silico engineering pipeline

- Iteratively improve protein fitness
- AI models tuned to any fitness
- Explore vs. exploit sequence space

AI based optimization



Spearman Correlation (ranking performance) with true fitness of variants in 56 test sets

AI based optimization

AI based optimization

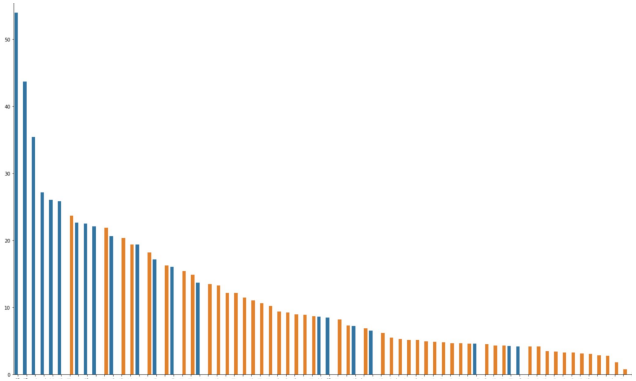
AI based optimization

Winner in Big-Pharma in-house evaluation

- Blind evaluation by a large pharma company to find real value
- Already developed In-house enzyme (multiple rounds) as target
- 165 single variants with measured activity as starting point

Results

- First Round Results: Our best variant was 53 times more active than the best training variant (5 variants introduced).
- Second Round Achievement: An enzyme 30% more active than the pharma company's best variant.
- Helix engineering offers **real value:**
    - **Efficiency**: Superior results with just 2x96 sequences compared to tens of thousands.
    - **Cost-Effectiveness**: Achieving a better enzyme with a fraction of the time and costs.

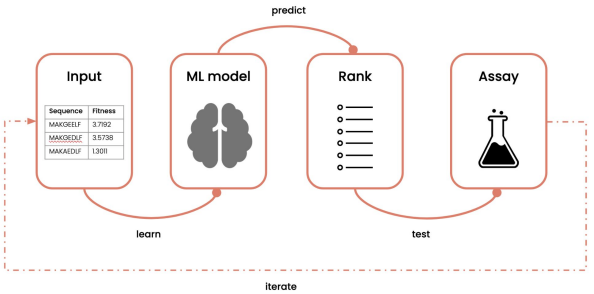


AI based optimization

AI based optimization

Faster and better protein engineering results

- Low number of quality mutations needed (even 50 to 100 works) for the prediction of a high quality second round of evolution.
- Can be applied to different protein features, such as activity, stability, co-factor binding, and many others.
- We evaluate on dozens of datasets and outcompete state-of-the-art competitors in most scenarios
- Demonstrated in real-world cases



Conclusion

- We offer a full-service package for protein engineering with **low turnaround times and low overhead**
- Applying 3DM for panel design results in faster and superior protein candidate identification
- Hotspot selection for initial diversity leads to more effective libraries and sets the process up for success
- Our AI based protein optimization is extremely efficient and cost-effective
- In a **collaborative approach** we combine domain expertise to get the most out of each evolutionary run using a minimum of mutations to measure.
- The result: **Faster, cheaper and more successful protein engineering projects**

Q&A

More information:
www.bio-prodict.com
helixlabs.ai

Whitepaper: https://arxiv.org/abs/2104.01033