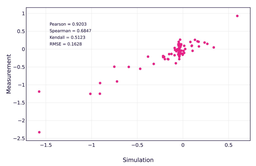
Our Cellular Simulations toolkit

OncoSim©

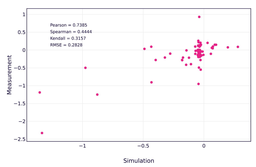
OncoSim is our Cellular Simulations toolkit and contains our model library. It comprises **mechanistic models**, **machine learning models** and a pipeline to **parameterize** these models using various data repositories. We can efficiently create models for **>1000 oncology cell lines.**

Performance of our Mechanistic and ML based models

100 gene mechanistic pathway model

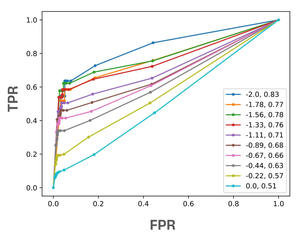


Performance on an example cell line when **fitting to all available data**.



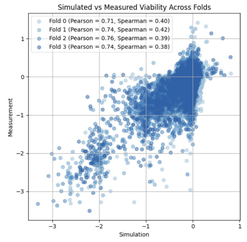
Performance on the same example cell line in 5-fold **cross-validation** (combined folds shown).

1700 gene metabolic model



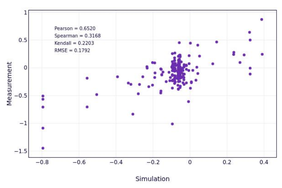
Viability **classification** performance.

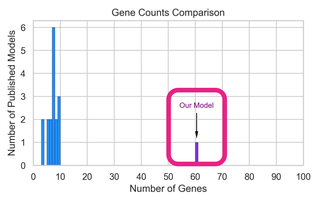
400 gene ML pathway model



4-fold **cross-validation** performance.

60 gene mechanistic pathway model. **Order of magnitude larger** than published models of same pathway.





Discovering Novel Synthetic Lethal Pairs With Large-Scale Cellular Simulations

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At Deep Origin we help scientists solve disease and extend healthspan by building tools that simplify R&D, simulate biology, and untangle the complexity of life.

The challenge of synthetic lethality

- **400M** possible pairwise gene combinations.
- Exponentially more with **conditional biomarkers**.
- We virtually screen this space with **cellular simulations**.

Aims of this work

- Identify novel **synthetic lethal** pairs.
- Identify **conditional biomarkers**, to:
  - **Stratify** patient populations.
  - Predict **resistance** mutants.
  - **Prioritize** pairs.

Progress

- Predicted **>100 novel synthetic lethal pairs**.
- Multiple **known pairs** predicted.
- Some predicted **novel** pairs have been **validated** in-house.

We are interested in partnering on our platform and our pairs.

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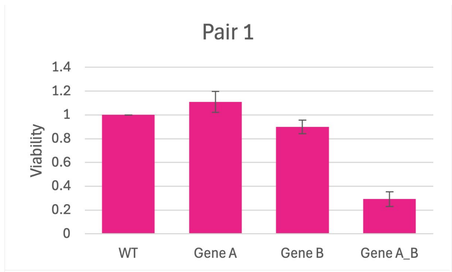
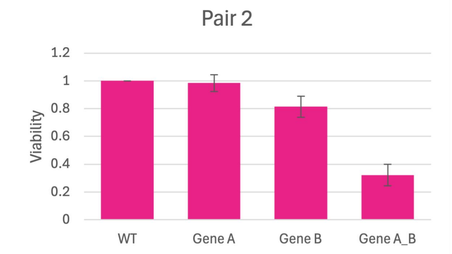
Validation of some predicted pairs

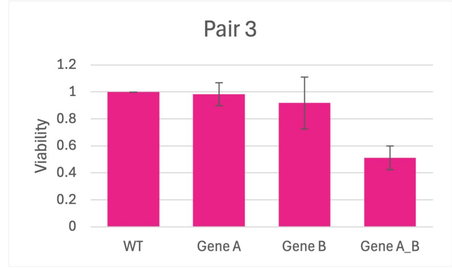
Validation of three of our predicted synthetic lethal pairs from our metabolic model, in a single line.



GI: Mean: -0.72 SE: 0.08

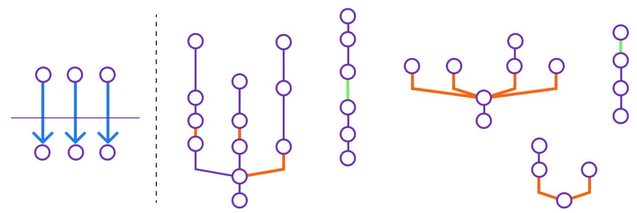


GI: Mean: -0.48 SE: 0.06



GI: Mean: -0.39 SE: 0.2

Our toolkit can uncover conditional biomarkers



Anonymized example of a predicted conditional biomarker in metabolism. Nodes are metabolites and lines are reactions. All reactions are in a downwards direction. Blue arrows are import reactions. Blue and orange reactions are driven by synthetic lethal genes, the green reaction is driven by a biomarker that strengthens the relationship when deleted. Orange and green reactions are in the same subdomain of metabolism.