Rapid Optimisations for Cell & Gene Therapy Applications

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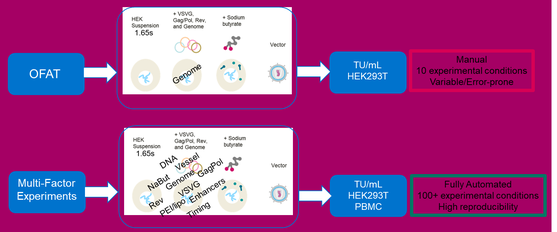
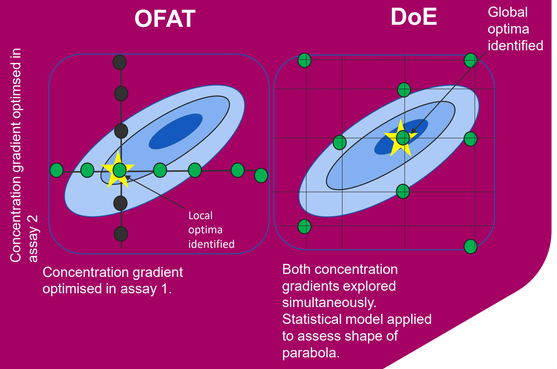
Design of Experiments (DoE)

A DoE is a multiple variable statistical method used to characterise and optimise systems quickly and efficiently. It has many advantages over one factor at a time approaches (OFAT). However, executed manually DoE methods can be time consuming and error prone.

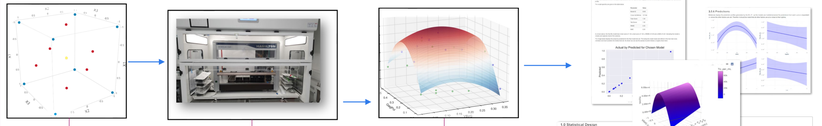


DoE methods have also been shown to identify global optimal conditions where OFAT might miss.



Overview of System

State-of-the-art automated optimisation platform with applications in automated DoE, synthetic DNA optimisations, small molecule optimisation, AQbD and high-throughput screening.



Instantaneous optimal design based on metadata or user specifications, full description and diagnostics.

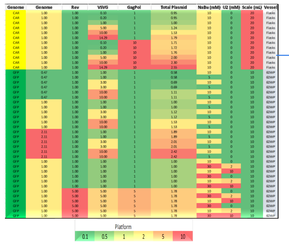
Robotic assay setup of up to 800 conditions and 20+ dimensions (per robot).

Optimal Machine Learning (ML) and Linear Model fit, refined and explained.

Automated statistical and robotics report, fully detailed tutorials.

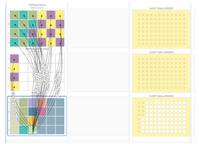
Case Study: Side-by-Side Optimisation of HEK293T Titre and Primary T Cell Transductions Using Optimal Plasmid Ratios and Proteomics

Optimal plasmid ratios for HEK293T titre may not represent the optimal ratios for target cell transductions, in this case primary T cell transductions.

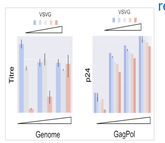


Ratios over Platform concentrations

DoE parsed into Synthace Cloud platform software and executed using a Hamilton STARLet liquid handler.

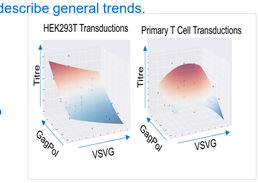


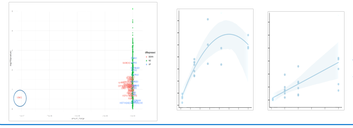
Data from multiple sources joined, modelled and reported



Linear modelling and ML used to characterise all optima.

Exploratory analysis carried out to describe general trends.



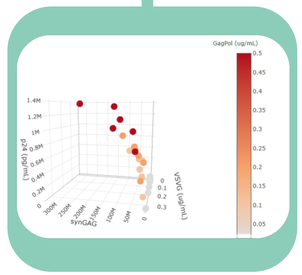


Proteomic analysis further characterised the system of interest.

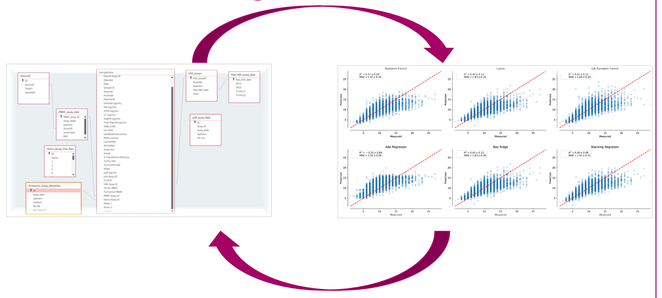
Interactive Multi-Response Optimisation Including Proteomic Augmented Models

Simultaneous optimisation of multiple responses i.e. Primary T Cell Transduction and HEK293T TU/mL

Exploratory proteomic enriched models allowing plasmid – protein – Titre interactions

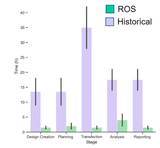


Machine Learning and Data Enrichment



- Explore non-linear trends with up to ten machine learning kernels and a flexible neural network architecture, automatically run, refined and fully reported.
- Draw upon high quality curated historical data and associated metadata to add power to your model, fill in blank design space, and extrapolate out of the design space.

Time, Accuracy & Precision



- Significant time saving in design, planning, analysis and reporting

- Full DoE repeated 2 times.
- Paired T test and REML run.
- Anonymized distributions shown on the right.

Test	Value	Result
T Test	0.9844	No evidence of difference
REML	0.68	High evidence of equivalence
Upper Bound P	<0.0001	>99.99% Probability that values differ by less than +/- 10%
Lower Bound P	<0.0001	

Conclusions

Enhanced High Throughput Optimisations
- 4000+ Runs (Flasks / Wells)
- 100+ Input Variables
- 10+ Response Variables
- Model responses as functions of other responses

Model Scale and Transgene Properties
- Multi Scale Systems
- Multi Transgene Optimisations

Flexibility
- Ability to characterise and optimise other measurable biological systems

Time and Reproducibility
- Reduction in wet lab work as well as analysis by over 80%
- Highly reproducible assays

Data Analysis
- State of the art linear and non-linear modelling
- Clear explanations and conclusions

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