

A High-Dimensional Space-filling DOE for Assay Development

How SPT Labtech created an efficient and robust solution to reduce assay development cycles with automated DOE execution and data aggregation.



CASE STUDY



Overview

SPT Labtech, a leading lab automation solutions provider, wanted to push the boundaries in physical execution of sophisticated Design of Experiment (DOE) campaigns to increase the optimization of many inputs and parameters simultaneously. The goal was to shorten pharmaceutical assay development cycles for rapid production of robust assays that could be transferred into high-throughput screening workflows.

The solution to this challenge was combining the speed and accuracy of SPT Labtech's dragonfly® discovery dispenser with the flexible planning and data aggregation capabilities of Synthace, which allowed for the physical execution of a 6-factor space-filling DOE campaign to comprehensively characterize the design space for an enzymatic assay in a single rapid experiment.

94%

Total Time Savings

Over typical assay development cycles

75%

Time Savings

In execution planning

98%

Savings in Liquid Handling Time

Compared with an average pipetting robot

99.9%

Savings in Tip Usage

Compared with an average pipetting robot



Challenge

Pharmaceutical assay development groups work under constant time pressure and face increasing complexity without a commensurate increase in resources. As a result, these groups often adopt powerful statistical approaches such as DOE to shorten assay development cycles. DOE investigations enable the rapid optimization of many inputs and parameters simultaneously, offering the ability to quickly and easily execute and analyze higher-granularity, multifactorial characterizations of biological processes.

Yet conventional DOE campaigns executed by hand still require weeks of iterative cycles, as the number of runs possible per cycle is limited by the need to minimize the complexity of manual calculation, liquid handling, and data collection tasks to avoid human error. The challenge for assay development is **to increase the speed and accuracy of DoE campaigns by reducing time spent on planning, data aggregation, protocol execution, and liquid handling.**

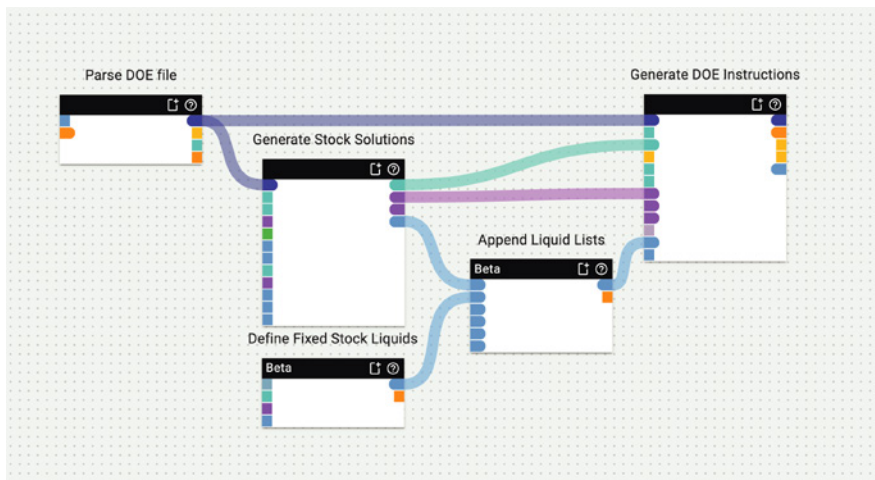


Figure 1. A simple, rapid and flexible DOE execution planning using Synthace's workflow builder.



Solution

SPT Labtech combined dragonfly® discovery dispenser capabilities with Synthace experiment platform to increase speed, accuracy, and flexibility to execute a 6-factor space-filling DOE.

Synthace experiment platform allows users to rapidly prototype complex automated liquid handling workflows by providing modules that can be easily rearranged and customized (Figure 1). Synthace could rapidly and flexibly generate an automated liquid handling protocol from the input DOE design file to send instructions to execute that campaign on the dragonfly® discovery, reducing the need for physical dry-runs to validate the protocol. (Figure 2)

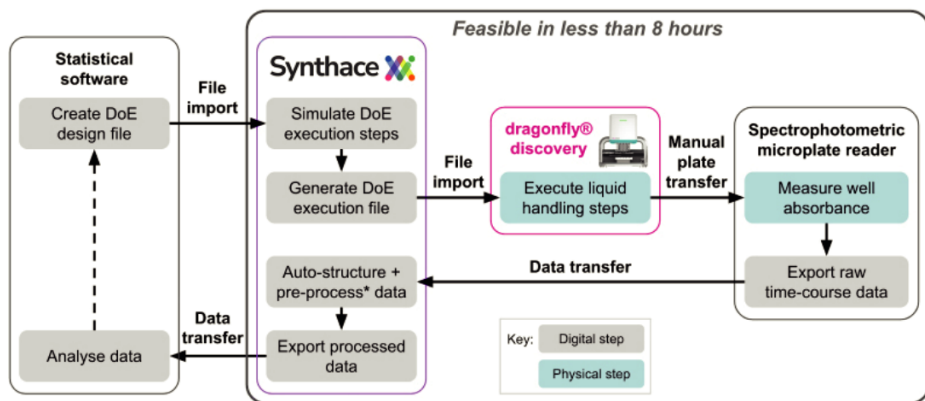


Figure 2.

Iterative DOE user flow with Synthace, the SPTLabtech dragonfly(R) discovery and third party statistical software empowers scientists to be able to design, plan, execute, structure data and analyse within a single working day.



The dragonfly® discovery allows teams to develop their assays using the same dispenser and high-density plates (384 or 1,536-well) as would be used in subsequent high-throughput workflows. Synthace automatically generates a detailed, digital record of every liquid handling and data aggregation step in that process, which significantly reduces risk of assays failing when transferring protocols into HTS. The 6-factor space-filling DOE required 3,456 runs in total for two sets of triplicates of 384 runs and the corresponding blanks. This amounts to 20,745 liquid handling steps, 2,305 for each of nine 384-well plates (*Figure 3*). Synthace guides users on required reagents, volumes, and labware with detailed schematics of how to set up the liquid dispenser and reagent reservoirs, and when to swap out the dispensing heads.

The in silico simulation allows the user to validate the experimental workflow prior to physical execution. All low-level decisions are taken care of by Synthace so that the user isn't required to manually determine plate maps and reservoir set-up before conducting a physical run in the lab, thereby reducing risk of human error or the need for repetitive dry-run physical testing in the lab before executing with valuable reagents. Synthace prompts the user to change the reservoirs when necessary, allowing more than 10 liquids to be layered onto the experiment plate. In the last step of the simulation, the user can select any well to inspect all the details of the liquids added during the protocol.

Using Synthace massively cut down on time needed to complete an assay cycle. The initial workflow set-up and simulation took 30 minutes, a quarter of the time it takes to manually create an equivalent instruction file in spreadsheet software. Synthace then auto-structures raw time-course data from the microplate reader and applies a suite of pre-processing steps such as replicate grouping and blank correction to eliminate all manual data handling steps. A single data table that can be easily mined is ready within 30 minutes of exporting data from the plate.



Figure 3.

Visual preview of the 2,305 liquid handling steps onto a 384-well plate as simulated by Synthace. Interrogate your *in silico* simulation from (A) the perspective of source liquid transfers or (B) all transfers made to a destination well.



Results

The combination of SPT Labtech's dragonfly® discovery dispenser with Synthace allowed for the characterization of a spectrophotometric enzymatic assay using a space-filling DoE with a total of 3,456 runs for three sets of triplicates of 384 runs and the corresponding controls. (Figure 4).

Synthace reduced time spent on planning the 20,745 liquid handling steps and data aggregation from the microplate reader by 75% and 94% respectively. The dragonfly® discovery reduced liquid handling time by 98% compared with an average pipetting robot, as well as eliminating 99.9% of the number of tips needed. This success demonstrates the ability to run thousands of runs of assay optimizations in a single day, opening up new experimental possibilities.

Synthace and dragonfly® discovery combine to create an efficient and robust solution to reduce assay development cycles with automated DOE execution and data aggregation. This approach can prevent future bottlenecks in assay transfer by enabling digitization of assay protocols and use of the same liquid handler from assay development through to high-throughput screening, reducing the need to miniaturize or re-optimize assays when proceeding into HTS campaigns.

Proven ability to run thousands of runs of assay optimization in a single day

A single data table that can be easily mined is ready within 30 minutes of exporting data from the plate.

94% total time-savings by programming over 20,745 liquid handling steps in a 6-factor DOE campaign.

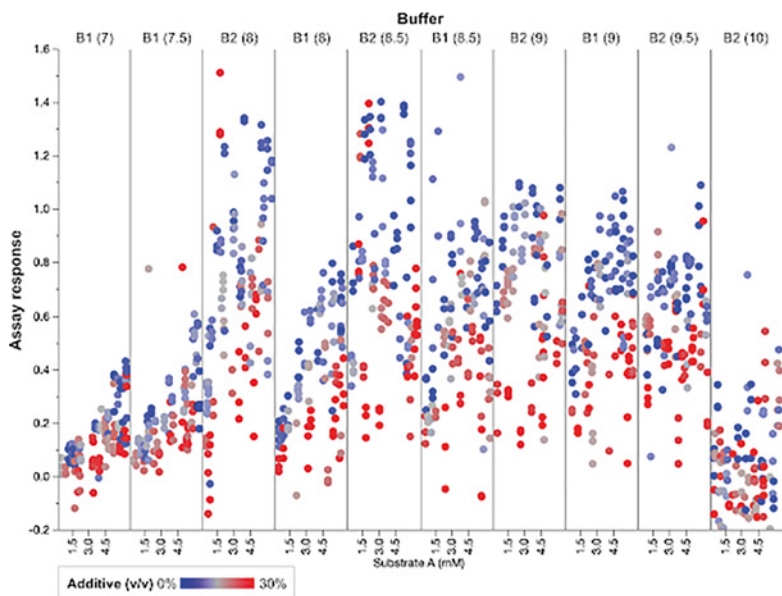


Figure 4.

Full characterization of a spectrophotometric enzymatic assay using a space-filling DOE achieved using Synthace & the SPT Labtech dragonfly(R) discovery.

About Synthace

Synthace is a cloud-based experiment platform that enables life science R&D teams to do experiments that would otherwise be impossible. It helps scientists innovate faster by executing high throughput experiments, structuring complex datasets, and allowing them to use powerful methodologies—like Design of Experiments—all within their browser.

To find out more about our platform or to book a demo please visit www.synthace.com.