

Agilent Case Study: XF Pro Analyzer for Drug Discovery Research

Consistency is Key

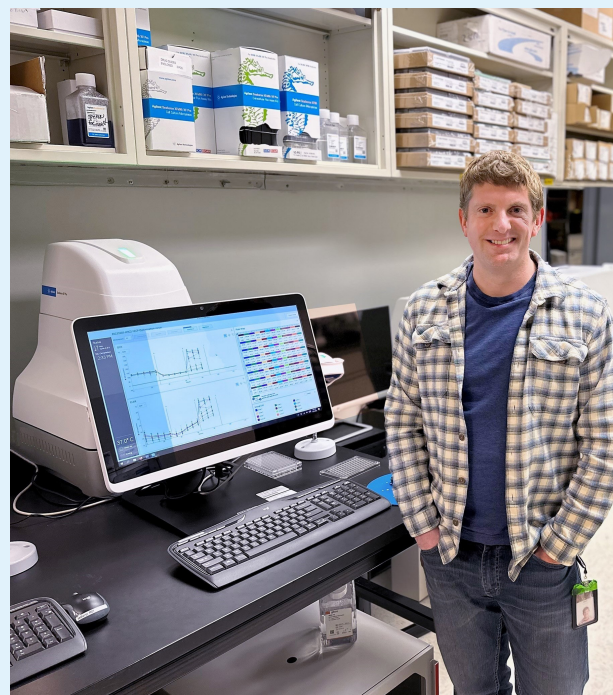
Improved intraplate reproducibility unlocks new levels of throughput – furthering therapeutic drug discovery research

"We want to provide our clients with the most up-to-date and best technology available for measuring cellular metabolism," proclaimed Dr. David Hoffman.

Dr. Hoffman is the scientific director for contract services at Cayman Chemical. His lab offers preclinical contract services for drug discovery and development, including identifying drug targets, confirming a gain or loss of biological functions, identifying a specific phenotype, and understanding mechanisms. Their mission is to help make research possible by supplying scientists worldwide with the resources necessary for advancing human and animal health.

Hoffman's team aims to provide insights into cellular energy metabolism. Energy metabolism plays a central role in a wide variety of cellular and physiological processes and is a key indicator of cell health. Many different disease states are associated with dysfunctional metabolism. Therefore, a deeper understanding of exactly what makes cells tick can help in therapeutic drug discovery and development.

"Many clients are interested in mitochondrial function using cultured cell models. These models are often more cost-effective than conducting *in vivo* studies. In my experience, the Agilent Seahorse Extracellular Flux (XF) analyzer is the best way to study mitochondrial function," explained Hoffman.



Dr. David Hoffman, PhD

Scientific Director
Cayman Chemical

The Seahorse XF analyzers simultaneously measure activity in the two main energy pathways in live cells, providing data on system-level cellular metabolic function. Hoffman, who has been an avid proponent of XF analyzers for more than a decade, added, "We use XF technology to help clients better understand metabolic disease models and the effects that their therapeutics have on these models."

After evaluating the latest Agilent Seahorse XF Pro analyzer, Hoffman could see the advantages for his laboratory within just a week. Despite not being in consideration for an XF Pro instrument at the beginning, the data on the XF Pro were so convincing that he traded in his current Agilent Seahorse XFe96 analyzer and purchased two new Seahorse XF Pro analyzers.

Most notably, Hoffman observed an increase in data consistency and reduced edge effects, especially when using the new Agilent Seahorse XF Pro M cell culture microplate. This plate has moat wells around the outer edge, which insulate the wells and improve intraplate data consistency. "The temperature control is fantastic. We saw very little variability between inner and outer wells. We typically throw out the outer wells for sensitive applications, but with the Pro, we don't have to," said Hoffman. For Hoffman's lab, their throughput significantly increased, taking their analysis from testing 90 to 120 conditions per day.

Hoffman was also pleased with the consistent assay signal between the older XFe96 analyzer and the new XF Pro. "Overall the data are very reproducible with both instruments with low CVs. It's great that we can compare data collected on this new analyzer to our historical data. However, the Pro really stands out because we can keep the outer wells and increase our throughput," described Hoffman.

Further efficiency gains are possible thanks to intelligent instrument features, such as the new automated data QC tool. "It's useful for flagging wells for a closer inspection—it's a huge timesaver. Before I would have to look at potential outliers manually by looking at oxygen and pH level data in the overview tab," stated Hoffman.

"New tools included in the Agilent Seahorse Wave Pro Controller software also improve efficiency. Easy-to-generate heat maps and concentration response generators are helpful when looking at dose dependency of experimental compounds. The heat map functionality is also beneficial when determining well-to-well variability and assay performance," explained Hoffman.

The XF assays in Hoffman's lab are further optimized through automation. His workflow also includes an integrated Agilent Bravo automated liquid handling platform for cell washing and Agilent BioTek Cytation 5 cell imaging multimode reader for cell normalization. "The wash protocol using Bravo is another huge timesaver and provides a consistent means to conduct a medium exchange," described Hoffman. He continued, "and, the Cytation 5 works great for normalizing cells, improving data quality and interpretability."

"In my experience, XF technology is the best platform for measuring bioenergetics in a cellular system. The XF Pro improves upon the XFe96, offering better sensitivity and temperature control and improved software—giving the user more options and improved data reproducibility. For the XF Pro, you can see some significant changes over the XFe96, such as the larger, temperature-controlled manifold. It's clear that a lot of thought went into the design of this instrument."

When asked if he would use fewer replicates per condition, Hoffman laughed, "Not yet. Old habits die hard!" But, that is the goal. The Agilent Seahorse XF Pro analyzer increases throughput over its predecessor by improving intraplate consistency and allowing more conditions to be tested per plate. A further increase in efficiency, driven by more confidence in results and fewer replicates needed, will continue to accelerate the drug discovery process—leading to faster and better therapeutics and delivering on Dave Hoffman and Cayman Chemical's goal of making research possible while advancing human and animal health.

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