SARTORIUS

Raman Spectroscopy Analyte Prediction Models

A DOE Supported Workflow for Generating the Right Data with Ambr® and BioPAT® Spectro for Optimal Model Building

Technical Note

- Step by guide for Ambr® experimental set-up and statistical design for Raman BioPAT® Spectro integration
- Generate high-quality calibration datasets from Ambr® systems for use in MVDA tools such as SIMCA®, to create reliable analyte prediction models.
- Deploy models from Ambr® and transfer them to other scales with minimal additional calibration data to predict target analyte concentration in near real time

Overview

Sartorius Ambr® 15 Cell Culture, Ambr® 250 High Throughput and Biostat STR® systems can now integrate Raman spectroscopic measurement via the universal BioPAT® Spectro flow cell, for automated measurement of a range of analytes including glucose, lactate, glutamate, and glutamine in one sample, to generate calibration data which can be analyzed by multivariate data analysis (MVDA) to build a predictive analyte model.

Generating good quality data for model building requires specific set-up and data collection regimes of Raman spectra, as well as reference data. Data produced according to a statistical experimental design procedure such as DOE (Design of Experiments) generates potentially more accurate predictive calibration models with a larger range of validity. Scientists can then implement these models in the BioPAT® Spectro Ambr® application as a Process Analytical Technology (PAT) for rapid routine analyte predictions and real-time feedback control of several analytes at the same time, e.g. glucose and lactate concentrations. Difficult-to-measure analytes which would previously required a time and cost intensive sampling and laboratory analysis can also be measured by the technology. The models created, also provide the basis for a control strategy which users can transfer to larger scale manufacturing platforms, such as the Biostat STR®.

Introduction

Challenges Related to Building Predictive Analyte Models

Using non-invasive PAT tools such as Raman spectroscopy in bioprocessing means the acquisition of a spectrum, which consist of hundreds of data points per sample and time point. The spectrum is used to create a robust predictive Raman model by correlating the changes in the spectral information and analyte concentrations. Currently, to build this type of model requires measuring multiple analytes in a DOE approach to obtain statistically relevant data. Producing a predictive model can be time-consuming and costly in terms of media, reagents, and staff time, if the data is being collected manually from commercial scale bioreactors. Therefore, predictive Raman models are generally built by monitoring multiple production runs for variations or waiting for out of specification batches to occur.

However, utilizing automated mini bioreactors such as the Ambr® 15 and Ambr® 250 which mimic manufacturing scale cell culture with the Raman BioPAT® Spectro Ambr® application allows for cost-effective experimental design with induced variations and more efficient model building. Since one run can generate data from up to 24 bioreactor conditions, the design space is much larger than one provided by running hundreds of production batches with random variations, allowing acquisition of statistically relevant data to rapidly build lower-cost predictive Raman models.

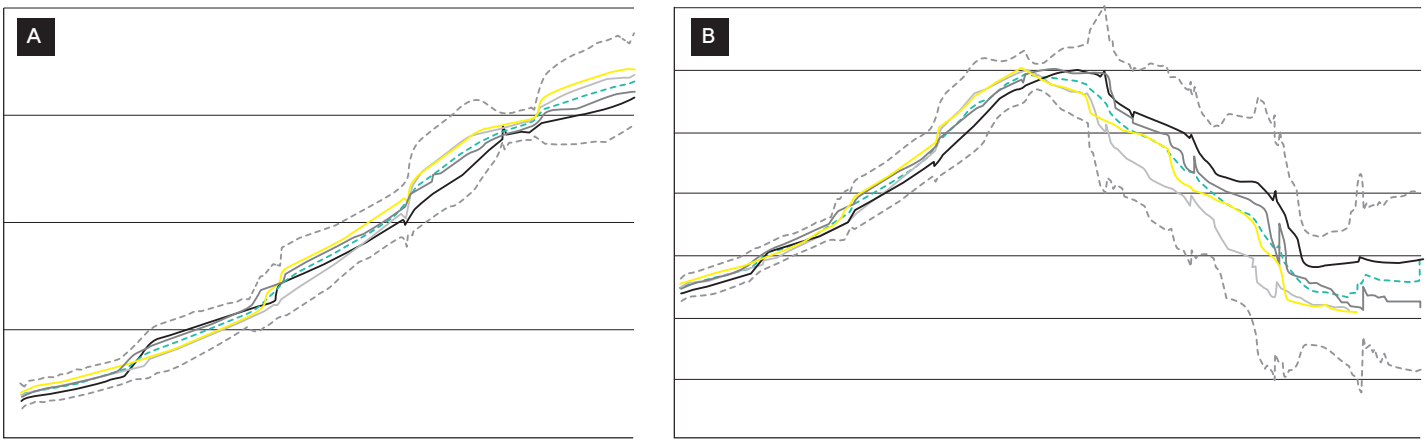
Why is a Planned DOE Better?

With the Ambr® 15 and Ambr® 250 systems and Raman BioPAT® Spectro, bioprocess scientists can undertake a planned DOE to collect their spectral data and corresponding analyte measurements. This is more efficient than using in-process variations from manufacturing bioreactors because:

- Easier to incorporate a range of typical and atypical process parameter values in the model building data set
- Easier to define the design space to span more variation than would be expected during production for clinical or commercial use
- Easier to have "golden batch" runs with "standard" parameter settings that help to identify inevitable process variations during production cycles (Figure 1a)
- Easier to include parameter variations which cause varying process trajectories (Figure 1b) and thus reduces the correlation between analyte trends
- Easier to include analyte spiking to induce a step change in analyte concentrations for either a single analyte or a range of analytes. This reduces correlations to other analyte trends and the range of analyte concentrations can be increased to ease the effect of a specific analyte on the spectra.

Figure 1

Examples of Cell Culture Batch Trajectories



Note. Both multivariate evolution plots show the scores of the processes over time, the teal dotted line is the average trajectory of all batches, the dotted grey line is the 3 sigma standard deviation delimiter. Plot (A) are "good batches" with low variability - even if we zoom in, the trajectories cover the average batch. Plot (B) shows trajectories with high variability due to parameter variations.

Method

How to Generate Good Raman Spectroscopy Data For Predictive Analyte Models

A sample DOE workflow for producing the optimum data to build predictive analyte models with Raman spectroscopy involves the following steps:

- Evaluate cell culture process and select areas where variations are likely to occur
- Set up Ambr® system for Raman measurements
- Create DOE based on process relevant factors, e.g. CPPs to obtain a wide spread in process trajectories
- Design an analyte spiking regimen
- Set-up spiked analyte sample plates
- Run Ambr® experiments in-parallel with and without spiking
- Consult with your Raman vendor to determine the ideal Raman measurement settings for your individual process
- Use the same measurement settings for the Raman spectra acquisition for all runs
- Transfer reference analyte and Raman data into MVDA analysis tools.

The workflow described in this application note can be used by scientists who strive to efficiently generate high-quality data to construct a predictive analyte calibration model. The description is an example workflow which users can adapt to best fit specific bioprocesses. How to pre-process data for MVDA analysis is not included in this note but is detailed in the Sartorius application note entitled "BioPAT® Spectro Ambr® calibration in SIMCA" which is available via the Sartorius web site.

Adapting the Ambr® System For Raman Spectroscopy Data Collection

To integrate Raman spectroscopy measurement into the Ambr® 15 Cell Culture and Ambr® 250 High Throughput systems, an Ambr® analysis module with BioPAT® Spectro (Figure 2), must be fitted to enable connection of a Raman BioPAT® Spectro flow cell to a sample cup and waste bottle. When integrated, the Ambr® system's liquid handler automatically takes samples from Ambr® bioreactors and dispenses them into the Ambr® analysis module sample cup. The sample is then transferred to the BioPAT® Spectro flow cell for Raman measurement. The Raman spectrometer with a dedicated optical probe is connected to the flow cell (Kaiser Optical Systems and Tornado Spectral Systems both offer suitable spectrometers and probes. Please contact your local representative for details).

Kaiser Optical Systems
https://kosi.com/products/kaiser-raman-analyzers/kaiser-raman-rxn2/

Tornado Spectral Systems
https://tornado-spectral.com/solutions/spectroport-raman-probe/

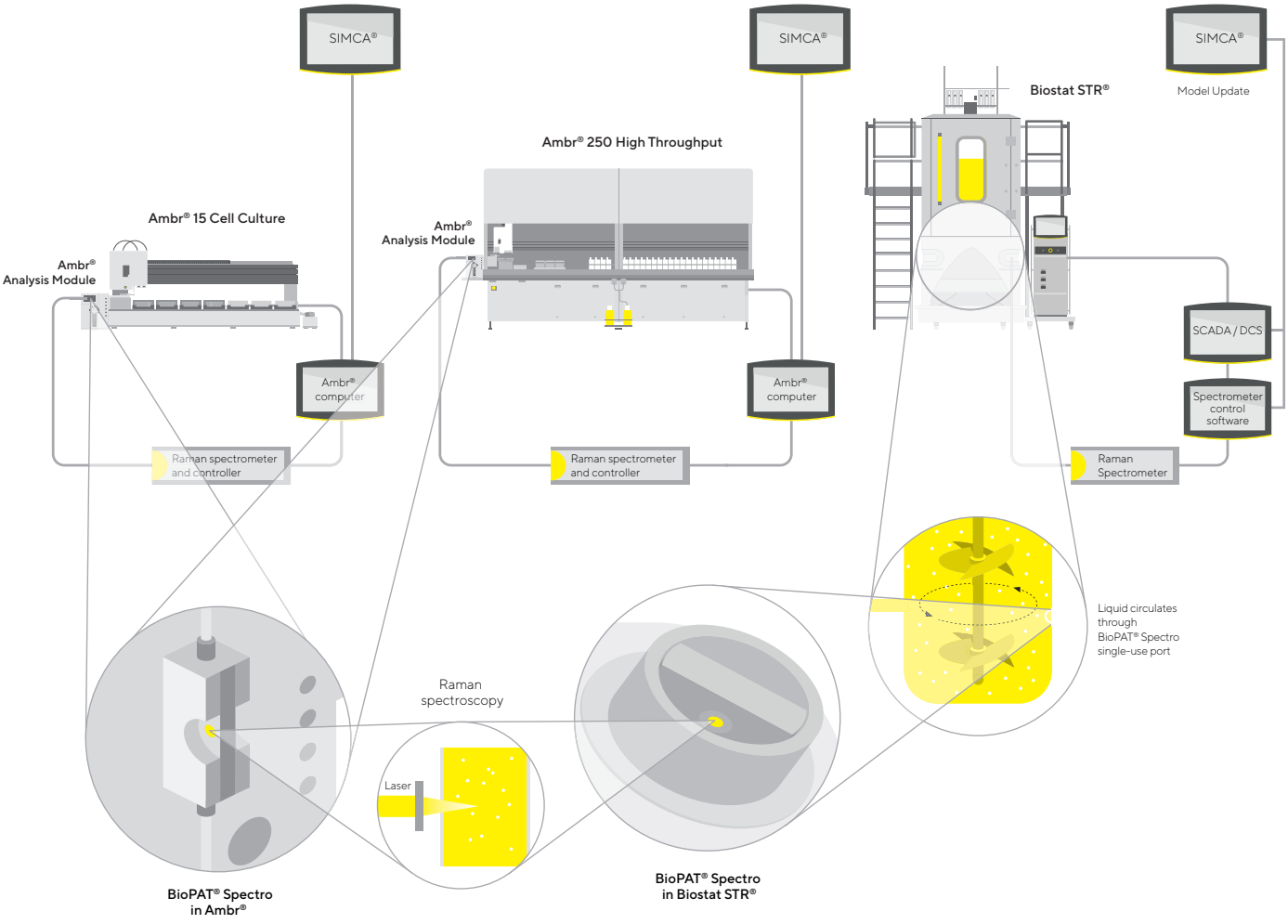
To build a good predictive model, a reference measurement method using an at-line integrated system such as the BioProfile® FLEX2 bioanalyzer (Nova Biomedical) can be used to measure analytes directly before Raman spectra collection to allow comparison of key analyte data for model calibration.

Besides basing the recorded data on a DOE approach for maximized information output, it is also crucial to have highly accurate reference measurements The accuracy of the Raman prediction model can only be as accurate as the accuracy of reference analysis. The Ambr® software is able to use in-line, on-line, at-line and offline samples and comes with an integration and automatic data collection for some at-line sampling devices. More information on Integrated Cell Culture Analyzers is available on our website.

https://www.sartorius.com/en/products/fermentation-bioreactors/ambr-multi-parallel-bioreactors/ambr-analyzer

Figure 2

Schematic Diagram of BioPAT® Spectro Integration With the Common Port Geometry of the Ambr® and Biostat STR® Port



Evaluating the Cell Culture Process

To determine which analytes to monitor and control in Ambr® bioreactors using Raman spectroscopy, bioprocess scientists should consider where variation of critical process parameters (CPPs) will have the most impact on their product's critical quality attributes (CQAs). Table 1 details an example of how CPPs can vary in a cell culture process for production of a commercial monoclonal antibody (mAb).

Table 1

Typical Critical Process Parameters (CPP) and Related DOE Parameters

CPP	DOE parameter Type	Effort to control
Seed train	Qualitative arbitrary*	M
Media Lot	Qualitative arbitrary*	M
Cell line	Qualitative**	L
Molecule	Qualitative**	L
Inoculation density	Quantitative***	L
Glucose set point	Quantitative***	L
pH	Quantitative***	L
Dissolved oxygen	Quantitative***	L
Partial CO_2	Quantitative***	H
Glu	Quantitative***	H
Gln	Quantitative***	H
Lactate	Quantitative***	H

H = High M = Medium L = Low

***Qualitative** arbitrary this variation has an effect which cannot be influenced with the seed train and production media. The lots of these from both the same, and different suppliers will vary over time. Therefore, these parameters can be monitored but cannot be controlled and thus have no impact on DOE design but are being noted so they can be used as uncontrolled variables in the design if they prove to have a major impact.

****Qualitative** for each qualitative factor a dedicated DOE is required to cover all the variations and to improve model robustness with respect to this parameter.

*****Quantitative** this parameter can be controlled and set.
Our examples use a mAb cell culture process. Based on prior research and knowledge the scientist choses a set of process critical factors, or key process factors which can at the same time be set and controlled as DOE parameters. The resulting process values will show enough variation to build a stable multivariate calibration model for the Raman prediction.

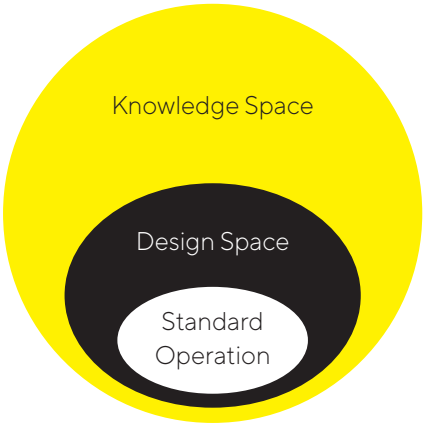
Creating a DOE

When the CPPs have been selected, scientists should create a DOE which minimizes sampling while maximizing data collection. The DOE should take into consideration the following points:

- Parameter variation – this should be larger than the expected process variation in standard operational batches (knowledge space) to obtain a large design space (see Figure 3).

Figure 3

Effect of Parameter Variation on Design Space



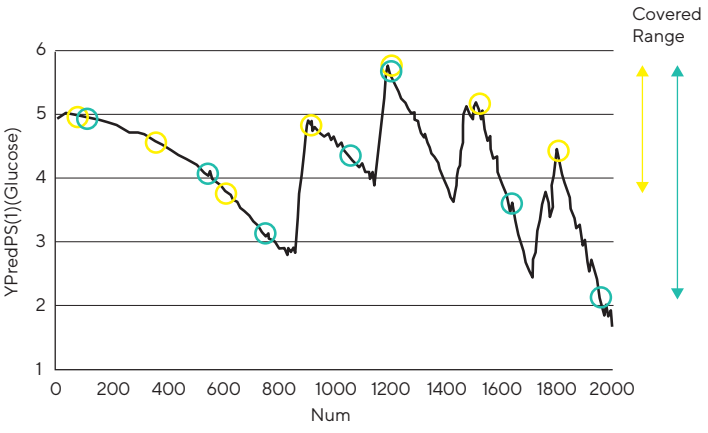
- Sampling frequency: is determined by:
  - Ambr® bioreactor type (15 or 250)
  - Sum of the sampling volume, considering how much volume all the reference and spectroscopy samples will require, as well as the remaining volume in the bioreactor.
  - Available liquid handler time, taking into consideration the time that the liquid handler is not in use for routine process control.

- Sampling workflow: Scientists using the FLEX2 bioanalyzer as the analytical method for reference values must sample these first using the automated Ambr® workflow in this sequence:
  1. Sampling for Flex2 (non-spiked)
  2. Sampling for spectroscopy (non-spiked)
  3. Optional sampling for spectroscopy (spiked)

- Sampling time points: Users should design these to increase the variation of analyte concentration. For example, scientists should not take samples directly after glucose monitoring or addition but at different time points during the experimental run, (see Figure 4 for an example of the benefit of varying sample timing). Users should also carefully consider sampling priority and whether they want the system to prioritize control actions above sampling schedule.

Figure 4

Effect of Varying Sample Timing on the Range of Glucose Concentration Measured by Raman Spectroscopy



Timing of sampling:

Goal: equally distributed samples covering a large range:
e.g. 1 sample a day

Example A: 11 am (5 min after feed
Example B: Varying time points

- Sample volume: Ambr® 15 bioreactors have a working volue of 10 mL, therefore it can be benefecial not to sample every day. As an alternative, multiple similar process conditions (see Table 2) can be set up to increase the possible volume for sampling, when operating with a limited working volume.

Table 2

Typical CPPs Which Can Be Duplicated to Increase Sample Volume

CPP	DOE parameter Type	Effort
Seed train	Qualitative arbitrary	M
Media Lot	Qualitative arbitrary	M
Inoculation density	Quantitative	L
Glucose set point	Quantitative	L
pH	Quantitative	L
Dissolved oxygen (dO)	Quantitative	L

Note: Glucose has a significant impact on the process trajectory, therefore different glucose set point levels have been chosen.

Example DOE

Taking parameter variation, sample frequency, workflow, time point and volume into consideration, a DOE set-up to generate Raman spectroscopy data from a cell culture process for production of a commercial mAb was constructed and is detailed in Table 3.

In this example, the DOE has:

- Four center points, ("golden batches" in bioreactor experiments assigned 9 to 12)
- Eight parameter variations (in bioreactor experiments assigned 1 to 8).
- Randomized vessel numbers
- Two kinds of seed train (designated A and B) and media lots (assigned X And Y) used in the runs (qualitative arbitrary factors) to maximize variability.

Points to note about this DOE set-up are the following:

- Where sampling volume is not sufficient with one vessel per setting, scientists can duplicate or use multiples of bioreactor experiments assigned from 1 to 8
- Users can duplicate, or even multiply center point bioreactor experiments designated from 9 to 12 if required.
- If necessary, scientists can reduce sampling times per vessel to one time every three days. Additional guidance and suggestions can be found in Ambr® 15 Sample Volume Solved application note.
- For each cell line and/or molecule combination (qualitative factors) users can repeat this DOE and analyze the combined data set
- For Ambr® 250, scientists can use the same experimental design and increase sampling frequency to the maximum, to make use of all available liquid handler time.

Table 3

Example of a Best Practice DOE Set Up of an Ambr® 15 | 250 For Optimum Raman Spectroscopy Data Generation

Exp No	Exp Name	Vessel number	Incl/Excl	Seed train	Media lot	Inoculation density (10×10^6 cell/ml)	Glucose set point (g/l)	pH	dO
1	N1	3	Incl	A	X	0.3	4	6.8	20
2	N2	10	Incl	B	X	0.7	4	6.8	80
3	N3	5	Incl	A	Y	0.,3	7	6.8	80
4	N4	6	Incl	B	Y	0.7	7	6.8	20
5	N5	11	Incl	A	Y	0.3	4	7.2	80
6	N6	4	Incl	B	Y	0,7	4	7.2	20
7	N7	7	Incl	A	X	0.3	7	7.2	20
8	N8	8	Incl	B	X	0.7	7	7.2	80
9	N9	1	Incl	A	X	0.5	5.5	7	50
10	N10	2	Incl	B	X	0.5	5.5	7	50
11	N11	9	Incl	A	Y	0.5	5,5	7	50
12	N12	12	Incl	B	Y	0.5	5.5	7	50

Designing an Analyte Spiking Regimen

After creating a DOE set-up, users should design a spiking regimen where analytes of known concentration are added to the cell culture sample before Raman spectroscopy measurement. In contrast to univariate regressions, multivariate calibration models cannot extrapolate a concentration beyond the calibrated concentration range. Therefore spiking is recommended to extend the ranges of the calibration model. Spiking also breaks correlations between analytes, which can cause cross-sensitivity that could interfere with model building, such that, future predictions of the analyte of interest would fail where previously seen correlations change or do not remain valid.

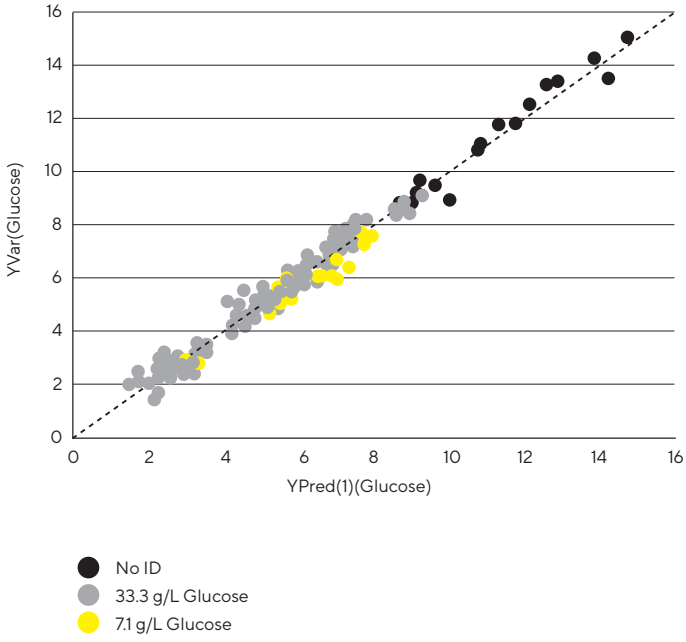
The spiking sampling regimen should consist of one reference measurement per vessel followed by Raman spectroscopy measurements from a non-spiked sample, and a spiked sample. Samples can be automatically spiked with concentrated analyte stock solutions prior to Raman analysis. Please note that glucose spiking may not be required for fed batch processes where the glucose concentration is highly increased by the feed solution.

The sampling protocol should include the following:

- non-spiked samples equally distributed over the increased range
- two stock spiking solutions per analyte to avoid correlation to a simple dilution.

Figure 5

The Effect on Analyte Concentration Range of Spiking Different Concentrations Compared to No Spiking, Measured by Raman Spectroscopy



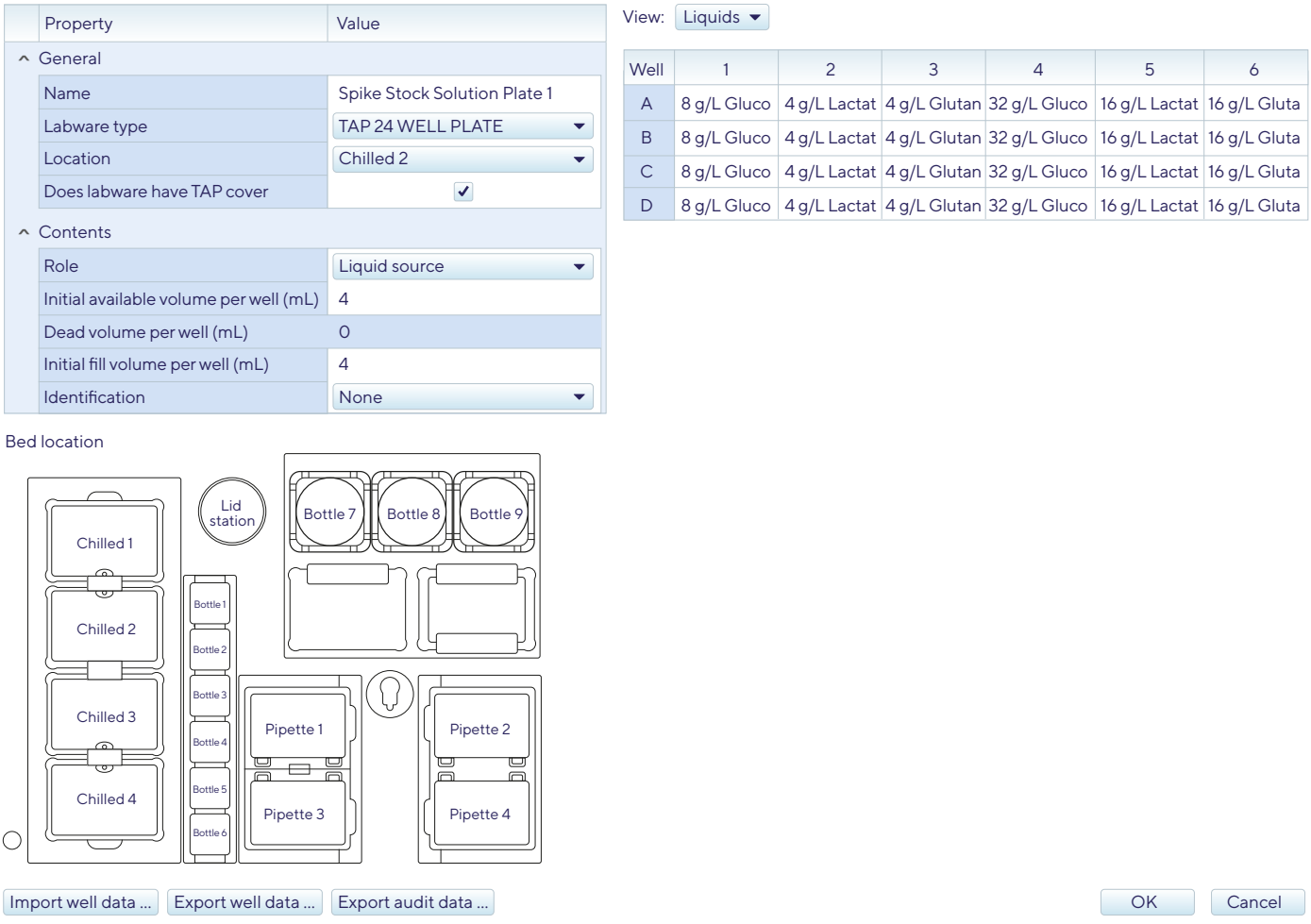
Preparing Spiked Analyte Sample Plates

As stated above it is advisable to prepare two different spike stock solutions, one with a low and one with a high concentration per analyte (see Table 4 for example concentrations). Stock solutions should be refreshed as frequently as possible (ideally daily). The locations of each stock solution within the stock solution plate are configurable by the user within the Ambr® software (see Figure 6 for an example of 3 stock solutions at 2 concentrations). Once stock solutions are defined (name of analyte, concentration, and location within the plate), spectroscopy specific liquid handling template scripts allow the user to automatically combine a defined volume (20-60 µL) of the predetermined stock solution with a 140 µL cell culture sample aspirated from a selected bioreactor. The Ambr® system will then mix these solutions in a mixing plate and dispense the mixture into the Ambr® AM sample cup for spectral analysis, automatically calculating the new concentration of specified analyte within the spiked sample (spiking set-up methods in Ambr® 15 and Ambr® 250 differ in detail, see Ambr® 15 BioPAT® Spectro and Ambr® 250 BioPAT® Spectro user guides respectively).

Using these stock solutions, an example of the range of working concentrations that scientists can use to spike two microwell plates over a 12-day run is shown in table 5. To calculate working concentrations when using a sample size of 140 µL and for example glucose in 50 µL of stock solution 2 (32 µg/µL) added to the cell culture sample, results in a working concentration of 8.42 µg/µL (50 x 32 µg / (140+50) µL).

Figure 6

Defining Stock Solution Plates



Mixing of the spike stock solution and cell culture sample takes place in a dedicated 96 well mixing plate. Each spiking event will use one unique well location, configurable by users within the Ambr® software when setting up the spiking step. Table 5 illustrates how a scientist may design mixing plates over the course of a 12-day process, while spiking with five different analytes, glucose, lactate, glutamine, glutamate, and the product being generated such as a mAb. Each column represents a different bioreactor and each row represents a different day i.e. this regimen contains one spiked sample per bioreactor per day (days 0-5 and 10-12) and two spiked samples per bioreactor per day (days 6-9). The spike volume and analyte occur in blocks for a given concentration (low or high) due to ease of set-up in the Ambr® software. These blocks are randomized and deliberately staggered to avoid the same combination of volume, analyte and concentration occurring with the same bioreactor repeatedly.

Table 4

Example Of Typical Low and High Analyte Concentrations to Use For Spiking Samples When Constructing a Predictive Raman Model

	Glucose	Lactate	Glutamine	Glutamate	Product
Stock solution 1 (µg/µL)	8	4	4	4	4
Stock solution 2 (µg/µL)	32	16	16	16	16

Table 5

Example of a Typical Analyte Working Concentration Range Used For Spiking Samples Over a 12-Day Cell Culture Run to Construct a Predictive Raman Model

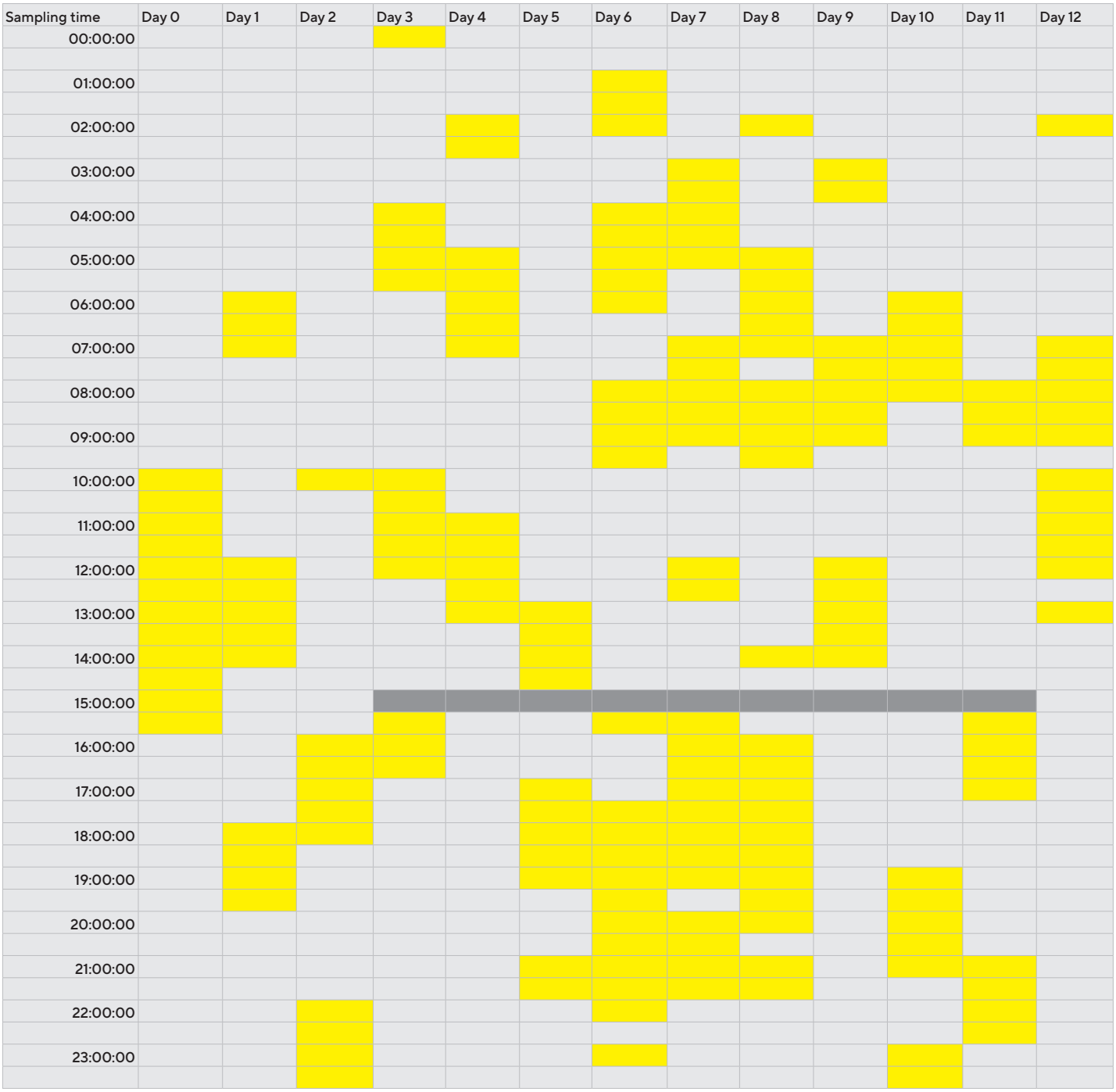
Mixing Plate 1														
		1	2	3	4	5	6	7	8	9	10	11	12	
A	Vol added	20 Glc	20 Lac	20 Gln	20 Glu	20 Prod	60 Glc	60 Lac	60 Gln	60 Glu	60 Prod	25 Glc	25 Lac	Day 0
	Effective conc	1.00	0.50	0.50	0.50	0.50	2.40	1.20	1.20	1.20	1.20	4.85	2.42	
B	Vol added	25 Gln	25 Glu	25 Prod	20 Glc	20 Lac	20 Gln	20 Glu	20 Prod	30 Glc	30 Lac	30 Gln	30 Glu	Day 1
	Effective conc	2.42	2.42	2.42	4.00	2.00	2.00	2.00	2.00	5.65	2.82	2.82	2.82	
C	Vol added	30 Prod	40 Glc	40 Lac	40 Gln	40 Glu	40 Prod	40 Glc	40 Lac	40 Gln	40 Glu	40 Prod	25 Glc	Day 2
	Effective conc	2.82	1.78	0.89	0.89	0.89	0.89	7.11	3.56	3.56	3.56	3.56	1.21	
D	Vol added	25 Lac	25 Gln	25 Glu	25 Prod	60 Glc	60 Lac	60 Gln	60 Glu	60 Prod	30 Glc	30 Lac	30 Gln	Day 3
	Effective conc	0.61	0.61	0.61	0.61	9.60	4.80	4.80	4.80	4.80	1.41	0.71	0.71	
E	Vol added	30 Glu	30 Prod	20 Glc	20 Lac	20 Gln	20 Glu	20 Prod	40 Glc	40 Lac	40 Gln	40 Glu	40 Prod	Day 4
	Effective conc	0.71	0.71	4.00	2.00	2.00	2.00	2.00	1.78	0.89	0.89	0.89	0.89	
F	Vol added	60 Glc	60 Lac	60 Gln	60 Glu	60 Prod	30 Glc	30 Lac	30 Gln	30 Glu	30 Prod	25 Glc	25 Lac	Day 5
	Effective conc	9.60	4.80	4.80	4.80	4.80	1.41	0.71	0.71	0.71	0.71	4.85	2.42	
G	Vol added	25 Gln	25 Glu	25 Prod	60 Glc	60 Lac	60 Gln	60 Glu	60 Prod	25 Glc	25 Lac	25 Gln	25 Glu	Day 6
	Effective conc	2.42	2.42	2.42	2.40	1.20	1.20	1.20	1.20	1.21	0.61	0.61	0.61	
H	Vol added	25 Prod	30 Glc	30 Lac	30 Gln	30 Glu	30 Prod	20 Glc	20 Lac	20 Gln	20 Glu	20 Prod	40 Glc	Day 6
	Effective conc	0.61	5.65	2.82	2.82	2.82	2.82	1.00	0.50	0.50	0.50	0.50	7.11	

Mixing Plate 2														
		1	2	3	4	5	6	7	8	9	10	11	12	
A	Vol added	60 Glc	60 Lac	60 Gln	60 Glu	60 Prod	20 Glc	20 Lac	20 Gln	20 Glu	20 Prod	20 Glc	20 Lac	Day 7
	Effective conc	2.40	1.20	1.20	1.20	1.20	4.00	2.00	2.00	2.00	2.00	1.00	0.50	
B	Vol added	20 Gln	20 Glu	20 Prod	60 Glc	60 Lac	60 Gln	60 Glu	60 Prod	40 Glc	40 Lac	40 Gln	40 Glu	Day 7
	Effective conc	0.50	0.50	0.50	9.60	4.80	4.80	4.80	4.80	1.78	0.89	0.89	0.89	
C	Vol added	40 Prod	40 Glc	40 Lac	40 Gln	40 Glu	40 Prod	25 Glc	25 Lac	25 Gln	25 Glu	25 Prod	25 Glc	Day 8
	Effective conc	0.89	7.11	3.56	3.56	3.56	3.56	1.21	0.61	0.61	0.61	0.61	4.85	
D	Vol added	25 Lac	25 Gln	25 Glu	25 Prod	30 Glc	30 Lac	30 Gln	30 Glu	30 Prod	30 Glc	30 Lac	30 Gln	Day 8
	Effective conc	2.42	2.42	2.42	2.42	1.41	0.71	0.71	0.71	0.71	5.65	2.82	2.82	
E	Vol added	30 Glu	30 Prod	60 Glc	60 Lac	60 Gln	60 Glu	60 Prod	30 Glc	30 Lac	30 Gln	30 Glu	30 Prod	Day 9
	Effective conc	2.82	2.82	9.60	4.80	4.80	4.80	4.80	1.41	0.71	0.71	0.71	0.71	
F	Vol added	60 Glc	60 Lac	60 Gln	60 Glu	60 Prod	40 Glc	40 Lac	40 Gln	40 Glu	40 Prod	20 Glc	20 Lac	Day 10
	Effective conc	2.40	1.20	1.20	1.20	1.20	7.11	3.56	3.56	3.56	3.56	1.00	0.50	
G	Vol added	20 Gln	20 Glu	20 Prod	20 Glc	20 Lac	20 Gln	20 Glu	20 Prod	30 Glc	30 Lac	30 Gln	30 Glu	Day 11
	Effective conc	0.50	0.50	0.50	4.00	2.00	2.00	2.00	2.00	5.65	2.82	2.82	2.82	
H	Vol added	30 Prod	40 Glc	40 Lac	40 Gln	40 Glu	40 Prod	25 Glc	25 Lac	25 Gln	25 Glu	25 Prod	25 Glc	Day 12
	Effective conc	2.82	1.78	0.89	0.89	0.89	0.89	1.21	0.61	0.61	0.61	0.61	4.85	

Glc=Glucose Lac=Lactate Gln=Glutamine Glu=Glutamate Prod=Product

Table 6

A Typical Sampling Frequency Schedule for Collecting Data Over a 12-Day Process Run To Construct a Predictive Raman Model of Glucose as an Example Analyte



Collecting Raman and Reference Data

When the sampling schedule is set, the Ambr® software automatically collects all key data from the Ambr® bioreactors, Raman spectrometer and any other analyzers (such as the BioProfile® FLEX2 by Nova Biomedical) integrated with the Ambr® system. The software merges this analysis data with relevant bioreactor data including vessel number, ID, batch ID, sampling time, batch age, reference data and exports all merged data in one CSV file.

Pre-Processing Raman Spectral Data

Before generating a calibration model with SIMCA®, users must pre-process the entire data set (spectroscopic and reference data) and check for consistency. Samples with missing or questionable reference values or extremely different spectral features caused by air bubbles, fluorescence etc. should be excluded.

The raw spectra usually show a strong baseline shift from beginning until the end of the cultivation. This is mainly caused by an increasing number of cells. The signal-to-noise of a spectrum can vary depending on the analyte concentrations. SIMCA® incorporates different pre-processing methods to compensate for these effects and normalize the spectrum. SIMCA® 17 has a built-in calibration wizard to guide the user during the spectra pre-treatment process. One unique feature is the water-band normalization. The water band at around 1.650 cm^{-1} is used to compensate the signal intensity between different probes, fibers and spectrometers of one vendor. This feature is also included in SIMCA® 16, but the implementation requires to use a Python script.

For more detailed information on pre-processing methods in SIMCA® please contact our Data Analytics specialists or check out our Sartorius application note entitled "BioPAT® Spectro Ambr® calibration in SIMCA®".

Conclusion

Planning experiments to generate good Raman spectroscopy data from Ambr® systems using the BioPAT® Spectro application is important for building robust predictive analyte models. This will help to avoid typical pitfalls and ensure that only consistent data is used for the model building process. Utilizing the example DOE workflow which scientists can modify to best fit their specific cell culture processes will help guide Ambr® users to generate Raman data of the right quality. This data can be automatically transferred into MVDA analysis tools without the time and effort and potential errors of manually copying and pasting data across, enabling scientists to develop a robust predictive Raman model covering a wide concentration range.

Due to the identical optical design of the BioPAT® Spectro flow cell in Ambr® and in the Biostat STR® single-use bioreactors, it is possible to use Raman multivariate calibration models which were developed in the Ambr® and transfer those to the STR®. This ensures full scalability from Ambr® 15 up to a 2000 L Biostat STR® single-use bioreactor where it enables a real-time process monitoring and control at a commercial scale.

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen
Phone +49 551 308 0

USA
Sartorius Stedim North America Inc.
565 Johnson Avenue
Bohemia, NY 11716
Toll-Free +1 800 368 7178

For further contacts, visit
www.sartorius.com