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Next Level Scale-Up: How DOE and MVDA Improved Scale-Up Performance at a CDMO

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Abstract

Bioprocesses are usually developed in small scale bioreactors thanks to the utilization of less resources (media, cells, feeds, reagents) and the easiness and throughput of the smaller scale operation. Currently it is also a regulatory need as organizations such as the FDA stress the importance of establishing scale-down models (ICH Q11 Step 4). As bioprocesses are complex with several parameters to study, there is a requirement to consider robust data analysis enabled mainly via DOE and MVDA iterative approaches. Simply applying DOE is not enough as it mainly correlates with input of parameters and output of time-bound results, making it difficult to consider the timely nature of bioprocesses. Given that scale-up approaches lack a more holistic verification as they focus on the physical process parameters, there is an increasing need to consider key performance indicators and more variables criteria to assess whether a scale-down is indeed fit-for-purpose. This is where the application of MVDA in conjunction with DOE comes in, embedded into a QbD approach.

Find out more at:
www.sartorius.com/vaccine-development

Contents

This White Paper will focus on explaining how Sartorius supported this QbD approach with our Industrial CDMO Partner Labor Dr. Merk & Kollegen for a bioprocess scale up from 2L to 50L, while performing a minimum amount of experiments. The results here also enable further scale-up tech-transfers and are relevant for companies working with viral based therapies and recombinant protein production.

LABOR DR.MERK

Definitions

CQA. Control Quality Attribute. A physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality (ICH Q8).

KPI. Key Parameter Indicator. A physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure process economics, rather than product quality. For example, the product titer is economically relevant but DOEs not refer to the actual product quality.

CPP. Control Process Parameters. Parameter of the process that must be maintained in a defined range to ensure acceptable product quality.

Hotellings T2. "T square" represents the distance of a sample from the center of the modeled space. Samples with low T2 are similar to the average. Deviations of individual variables will impact the samples´ T2.

DModX. Distance to model in X space is an estimate of how far from the model plane the observation is positioned. This is a standard method to detect outlying observations. It is also used to detect differences in the interaction of variables. A new sample that differs from the training data set will have high DModX.

QbD. Quality by Design.

PCA | OPLS | PLS. Principal Component Analysis | Orthogonal Partial Least Squares | Partial Least Squares. Algorithms used for fitting the MVDA models.

PAT. Process Analytical Technology.

CDMO. Contract Development and Manufacturing Organization.

Introduction

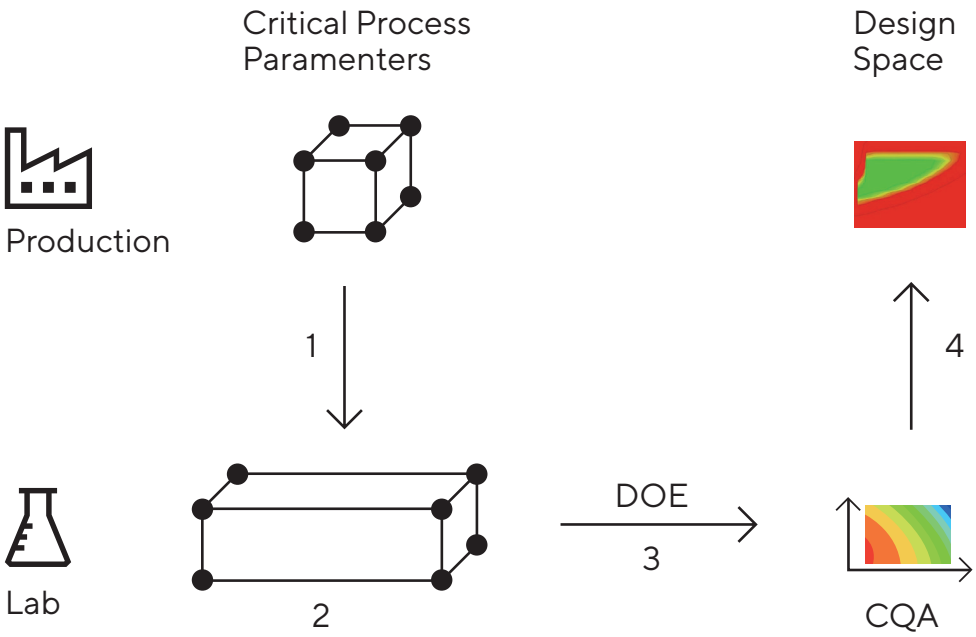
The development of commercial bioprocesses is very costly and time consuming. Therefore, process development is often performed in small scale bioreactors, which are operated in parallel. With a maturating project comes the point where it is necessary to transfer the process to an industrial relevant scale. This task is called scale-up and still represents one of the main challenges of bioprocess engineering.

During process development, design of experiments (DOE) is now a broadly applied technique to correlate the impact of certain critical process parameters (CPP´s) with the corresponding critical quality attributes (CQA´s), e.g. the relation between pO_2 and pH on product titer and impurities. Further, following this DOE approach thoroughly helps setting up adequate regression models, which then allow forecasting of quality attribute profiles already during the actual running process (Schmidberger, Posch, Sasse, Gülch, & Huber, 2015). Beside this, investigating the impact of process parameters and identifying critical parameters in a structured way, helps defining a so-called design space, within which a desired quality profile is maintained.

However, establishing the design space for a production system is not trivial, because the required DOE experiments cannot be performed at scale, due to time and resource restrictions. Hence, a predictive scale-down model must be available so that the design space can be derived and transferred to the production scale. Figure 1 below represents the basic workflow, considering the different operating ranges of various vessel sizes, with the aim to achieve one common design space.

The combined application of DOE and MVDA helps validating the predictability of scale-down models against the target scale in a very transparent manner and is therefore the object of the given work. It shall be mentioned that scale-up of a full design space is out of scope of this work, but the described approach may be extended to enable transfer of design space between scales.

Figure 1



Note. Design space definition requires large number of experiments, which are planned with DOE. The experiments are performed in small scale. For validated small scale models, the resulting design space is predictive for the production scale. The figure also considers the fact of different working anges. As an example, it would be meaningless to investigate operating conditions (e.g. very small mixing times), that are not accessible for the larger scale at all. Considering large scale restrictions results in more robust models in the small scale.

The QbD approach via Umetrics®, has the following key step-by-step as detailed below:
1. Scale down of physical process parameter from target production scale to lab scale bioreactor
2. Plan and run DOE in lab scale and create MVDA models, to establish small scale model based on target scale requirements
3. Identify process settings and design space in a scale down model that is predictive for the production scale
4. Final confirmation of design space at production scale

To make full use of the above advantages, it is feasible to follow a step-wise approach in a small scale system (Figure 2).

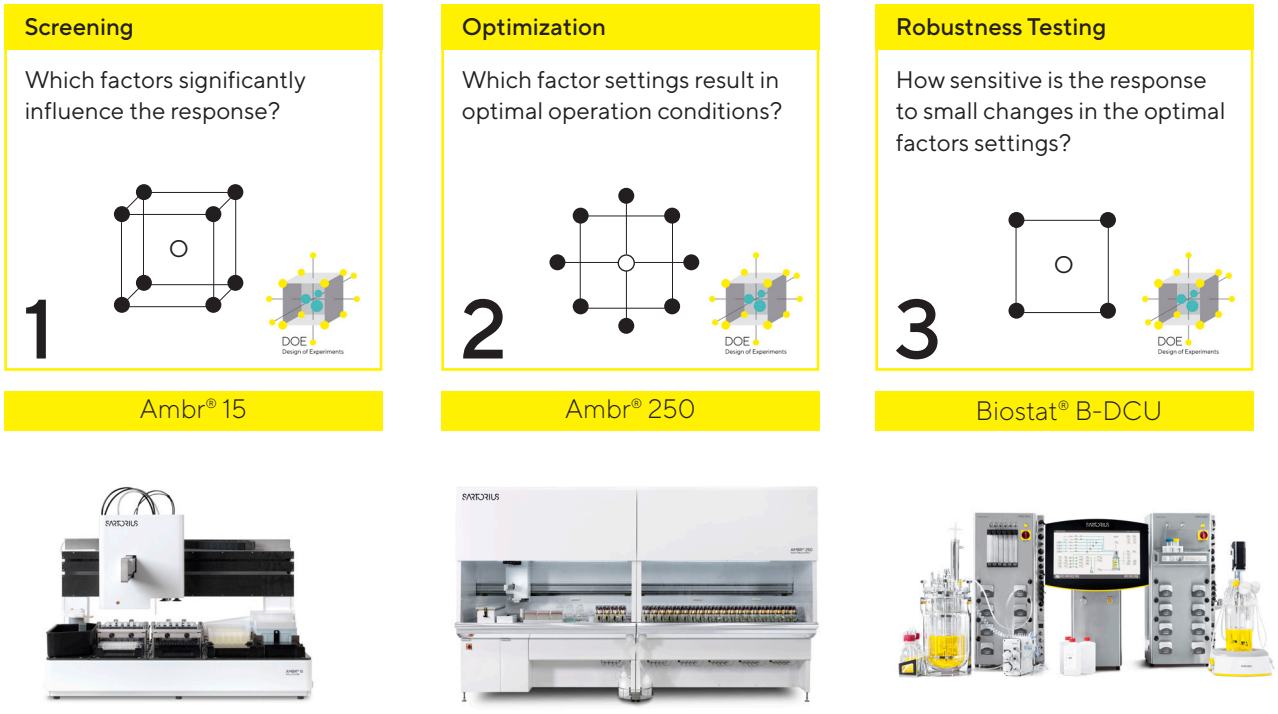
Screening. In the first set of experiments, a large number of process parameters are screened with low resolution experimental designs. The assessment will filter for the significant parameters that are then proven to have a direct impact on the target parameters, i.e. the CQAs. The significant parameters can now be considered as "critical" and hence, be defined as CPPs. Other parameters might still be controlled and monitored. However, the CPPs might differ for each CQA. Hence, the assessment must be applied to each quality attribute.

Optimization. While the screening design is supposed to investigate a broad range of parameters, the object of the optimization is to find the ideal working point of the process. Since optimization designs require a higher resolution, i.e. a larger number of experiments per parameter, this should only be applied to parameters that have before been identified as CPPs. Again, and similar to the comment about the screening, the optimum is specific for each CQA, i.e. there are usually multiple optima. It is then the task to balance out and compromise.

Robustness. In the last step, the newfound optimum is put in the center of another experimental design. If the CQA is highly sensitive to a corresponding CPP, it is very important to monitor and control this CPP very tightly. This assessment helps to maintain a robust process with a constant reliable quality profile.

Figure 2

Stepwise Application of QbD Principles at Different Stages During Process Development



Note. After identifying the relation between CPP´s and CQA´s comes the task of scaling it up to production scale.

Classical Scale-Up Approaches

Classical scale-up is based on trying to keep physical conditions constant across all scales. Next to others, common parameters are:

- (Specific) power input
- Impeller tip speed
- Oxygen transfer coefficient (kLa)
- Mixing time
- pCO_2 removal

It is well known that the main challenge lies in the different scale-dependency of relevant parameters. Therefore, it is not possible to maintain multiple scale-up factors constant across scales at the same time. It is then required to compromise between different factors. This inherent property of scale-dependency often results in measurable performance differences between small and production scale. For example, some authors describe a loss of productivity up to -40 % during scale-up (Mostafa & Gu, 2003).

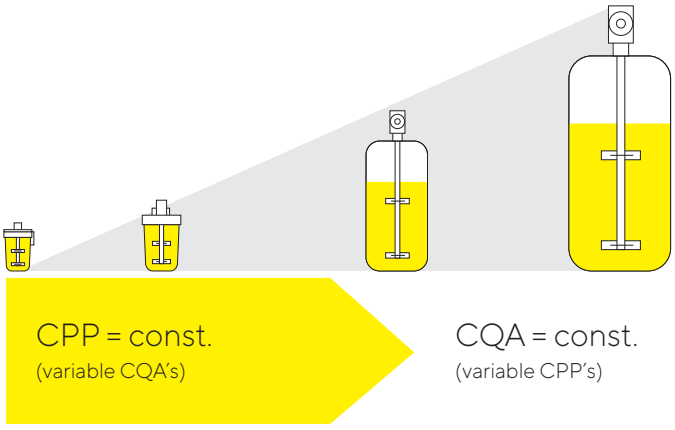
Especially for mammalian cell culture, carbon dioxide removal has been the object of many investigations and therefore is suitable to outline the issue. Small scale bioreactors have some superior pCO_2 stripping capabilities that are not available in large scale (Xing et al., 2009), mainly due to the much smaller height of the liquid column and the corresponding short gas residence time (Sieblist et al., 2011). Hence, instead of trying to transfer the very favorable pCO_2 profiles from small scale experiments, the challenge lies more in mimicking the worse process conditions present at the technical scale. This would mean to apply a pseudo scale-down approach taking into account the restrictions of the production scale compared to the small scale. With classical scale-up, it may be possible to maintain a certain pCO_2 profile, but with increasing number of parameters, this will make compromising necessary. Therefore, more advanced approaches must be applied that can cope with an elevated level of complexity.

Need for Advanced Tools During Scale-Up

Instead of keeping the CPPs constant and assessing the fluctuation on product quality afterwards, the target should be to aim for a CQA profile and adjust the CPPs accordingly (Figure 3). By following classical scale-up procedures alone, this goal may not be achieved.

However, by combining established scale-up strategies with readily available statistical methods, namely DOE and MVDA it will be possible to improve scale-up | down performance significantly. In this context, the very comprehensive work of (Ahuja et al., 2015) is recommended for further reading.

Figure 3



Note. Classical approaches aim to keep certain process parameters constant during scale-up. This often goes along with variable quality attributes and a general loss in process performance. Instead, the process parameters should be tuned in a way to maintain quality profiles across all scales. This is hardly achievable with given scale-up rules and thus, novel methods, such as MVDA, should be applied as a supplement.

Introduction to MVDA

Multivariate Data Analysis (MVDA) is a powerful technique for analyzing data, going beyond just looking at one variable at a time. MVDA takes a comprehensive overview, by utilizing correlations and patterns between parameters. This technique is used across disciplines, from research, development to manufacturing, for a variety of applications, including process monitoring, quality control and to support PAT and QbD strategies.

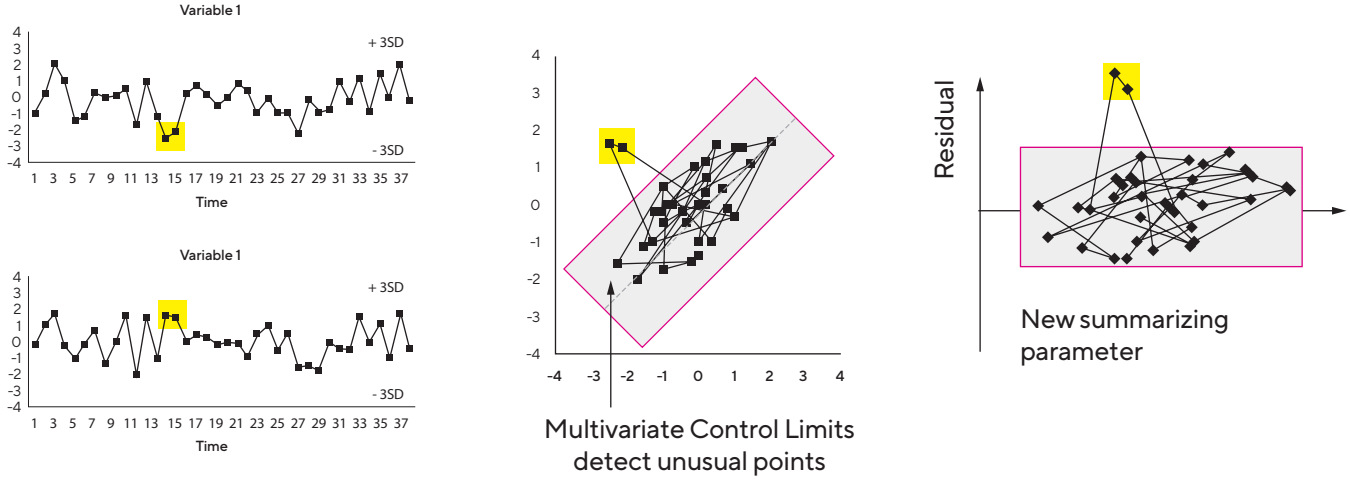
The key feature of MVDA is correlations and data compression. Data is often highly correlated meaning that large data sets do not necessarily contain an adequate amount of information.

By evaluating the underlying correlation patterns, the number of parameters to represent the data can be reduced, without losing any significant information, which finally simplifies data assessment.

A simple example shows the power of MVDA with just two (Figure 4) variables. Individually each variable show points within +/-3 standard deviation (SD). Close visual inspection shows that the parameters are correlated, when variable 1 is high, variable 2 is high, too. This pattern becomes clear when plotting the two variables against each other. From this representation, it's obvious that two points have broken the correlation. At this timepoint the process did go out of control, and the combined plot easily identifies these timepoints as different. Considering, for example, liquid flows and pump speeds, these should correlate and if the pump speed is high, but the flow is low, this would probably indicate an issue. Hence, following only one parameter, representing the correlation, would be sufficient to monitor the process. Multivariate compression of data reveals information which is not present in the single variables. In MVDA this summary of data results in a principal component.

Figure 4

Schematic Process of Aggregating Multidimensional Data into Principal Components (PC´s)



Note. The newly derived principal components don't have a physical meaning, but carry most of the process variation. Often it is easier to identify outliers based on the PC plots. In the next step, the origin of deviations can be identified.

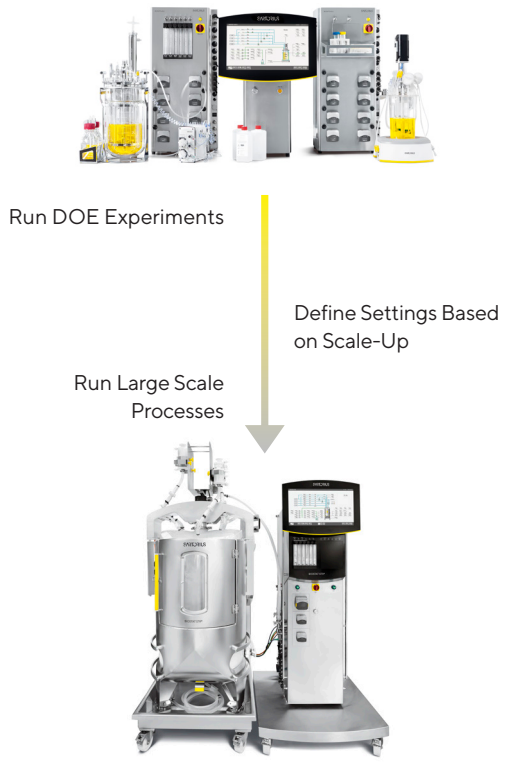
Application of MVDA to Scale-Up

The classical approach seems feasible for a broad range of processes. Nevertheless, most scale-up studies lack an actual re-assessment of the resulting process performance across the scales. It is then more of a one- way strategy (Figure 5).

It is a common observation that, by this approach, the technical scale would show a less favourable process performance compared to the small scale, e.g. because mixing becomes more difficult, or oxygen transfer capacity decreases. It is less common to really requalify scale-down models, and if done, often univariate methods are applied (Rouiller et al., 2012), e.g. ANOVA or t-tests. Another drawback is the missed chance to continuously acquire process knowledge by constantly feeding a process database: Even if a DOE has been applied to the small scale, subsequent DOE´s might not be fed into the same central database. This leads to isolated results, missing the opportunity to use this overall data for comprehensive process understanding. The same holds true for the production scale processes, where the data is again kept in isolated reservoirs, instead of feeding it back.

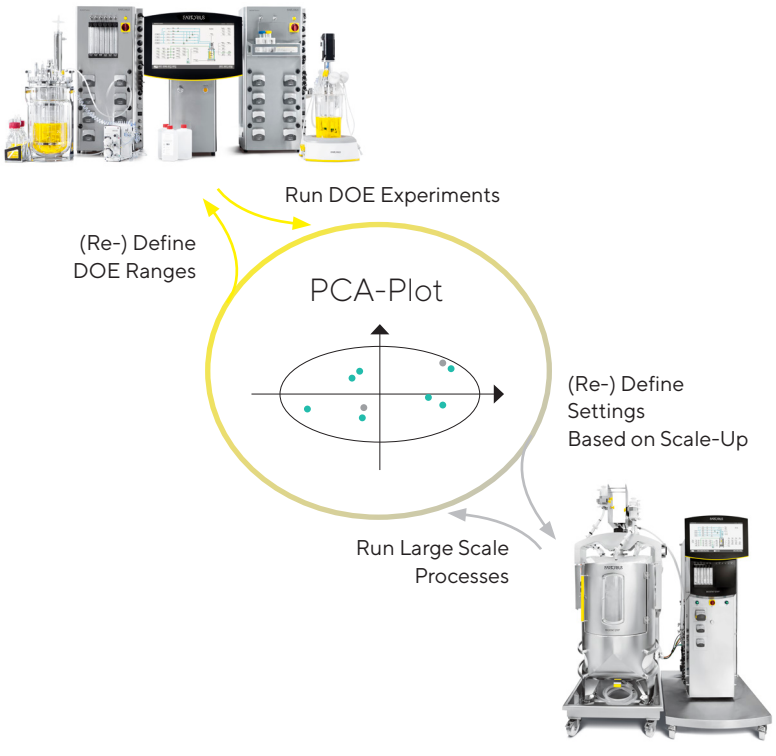
Usually the DOE aspect is of less importance in production scale, but since the amount of data derived from large scale runs, is by nature very limited, the value of each run is much higher, accordingly. However, the cost of neglected data usage is higher as well. A proposed alternative that shall overcome some of these drawbacks, is the application of PCA (Principal Component Analysis) indicated by Figure 6.

Figure 5



Note. Classical scale-up approaches define process parameters in a feed-forward mode. Large scale processes are then run under the once defined conditions and sometimes are never changed again. This approach tends to go along with variable quality profiles across scales.

Figure 6



Note. The application of MVDA allows readjusting of process parameters via a feedback-loop. A process data base is built up continuously. By this, the adequate parameter set can be identified that match the quality profiles across scales more accurately than classical scale-up approaches.

Partnership with Labor Dr. Merk & Kollegen

The objective of this study was to evaluate the scale up from 2L up to 50L by utilizing DOE and MVDA methodology in cooperation with Labor Dr. Merk & Kollegen GmbH for a common mammalian cell line process. Human cell lines such as HEK293 are recently gaining more interest for use in production of biotherapeutic proteins and viral or retroviral vectors for gene therapies. Some of these protein-based therapeutics are FDA and EMA approved by now (J. Dumont et al 2016).

As full CDMO, Labor Dr. Merk & Kollegen GmbH, offers end- to-end solutions from process development to GMP manufacturing at large scale. To ensure a frictionless transfer of the bench-top bioreactor process to the production scale, an initial scale-up study from 2L to 50L was performed. MVDA can benefit the predictability and the robustness of such tech transfers commonly performed by companies in the CDMO business.

For the scale-up, kLa (oxygen transfer rate coefficient) and P/V (power per volume) were kept constant. P/V defined the stirring speed. Given the kLa and a stirring speed, gassing rate was calculated according to the experimental data. Therefore during the actual processes, the stirring and total gassing rates were each kept constant, and only the oxygen portion in the inlet gas for DO control was manipulated in a very simple and straightforward manner.

Case Study: Applying MVDA for Scale-up of an Industrial Batch Process From 2L to 50L

The aim of this study was to define process settings for an industrially relevant batch process run in a Biostat STR® 50L. This represented a scale with the future prospect to increase the volume later in the project. As a small-scale system, a Biostat® B-DCU 2L system was used, which was set up in a way to ensure geometric similarity to the large scale. Since there was no prior process knowledge, two steps were performed: process development in small scale, followed by scale-up to large scale.

First, the feasible process settings were to be evaluated in the small scale. Therefore, a DOE was set up using MODDE 12.1 to investigate the two factors: gassing and stirring. The key point to consider when setting up a design for scale-up is how these values would transfer from small to a larger scale. For example, an impeller tip speed of 0.6 m sec^{-1} at 2L scale, would correspond to only 80 rpm at 50L scale. This is especially relevant when defining the factor levels. Often, settings are defined very conservatively, i.e. at the lower range. However, this strongly limits transferability to a larger scale. For example, stirring rate decreases with increasing scale for most of the classical scale-up rules. If the investigation is performed, with these settings already too low, there will be no room to move into either direction during scale-up.

A mixed factorial design was set up, giving the following structure of design (Figure 7). The ranges of the CPP´s were set as follows:

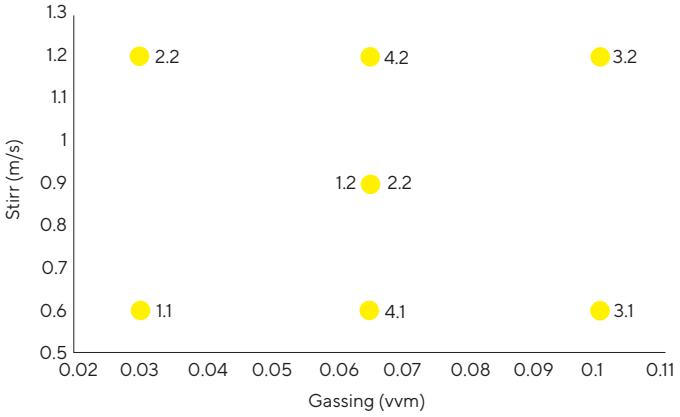
- Stirring (m sec^{-1}): 0.6, 0.9 and 1.2
- Gassing (vvm): 0.03, 0.065 and 0.1

As quality attributes, CQA´s1, the following parameters were defined:

- Growth rate
- Viable cell count after 48 h of inoculation
- Viability

Figure 8

Graphical Display of the Experimental Design. Numbers Indicate Exp. Number as Indicated in Table 1



The results of the DOE are listed in Table 1. Although it is out of scope for this work, the statistical analysis already gives insight into how CPP´s impact KPI´s. For example, in this case gassing had a strong negative impact on the viability. This knowledge can be used to characterize the interrelation between cell biology and physical conditions. Regression models can be derived, based on these results that enable the optimization towards certain quality profiles. Ultimately, such analysis is crucial for the definition of a design space (cp. Figure 1).

Table 1

Results of the Experiments Run in the Small Scale

Exp. name	Gassing, (vvm)	Stir speed, (m sec^{-1})	µmax, (d^{-1})	VCC at 48h, (E06 Cells mL^{-1})	Viability, (%)
1.1	0.030	0.6	0.71	1.6	98.2
1.2	0.065	0.9	0.63	1.5	98.1
2.1	0.030	1.2	0.62	1.3	97.0
2.2	0.065	0.6	0.61	1.2	95.5
3.1	0.100	0.9	0.68	1.6	92.8
3.2	0.100	1.2	0.62	1.4	94.0
4.1	0.065	0.6	0.74	1.8	97.0
4.2	0.065	1.2	0.67	1.6	97.0
2.1.2	0.030	1.2	0.65	1.4	97.3
2.2.2	0.065	0.9	0.53	1.1	93.9

Note. These parameters would usually be considered as KPI´s. For simplification, it was not distinguished between real CQA´s and KPI´s in this work, because there was no production phase. The described approach is independent of this definition.

Since this was the first iteration of scaling up to a larger scale, no practical experience was available to be used as a guidance. Therefore, it was decided to transfer the center point from the DOE performed in small scale, based on a classical approach. First, the stirring rate was defined by keeping the power input per volume constant. Next, the gassing was defined by the kLa. Since the stirring rate was already defined by ppv=const., the second degree of freedom acting on the kLa, i.e. the gassing rate, could be read directly from an internal database of experimentally derived process engineering parameters. Gassing and stirring rate were then kept constant throughout the whole process. Oxygen control was performed by increasing the oxygen ratio, while maintaining the overall gas flow rate. Keeping these parameters on a constant level simplified data evaluation. Variable parameters used in pO_2 cascades are more difficult to assess with standard DOE methods.

Considering the above scale-up strategy, the following values were maintained:

- ppv = 44.0 W m^{-3}
- kLa = 7.9 h^{-1}

Both bioreactors, Univessel® 2L MU and Biostat STR® 50, were operated with maximum working volume. As impeller, a two-stage three-blade segment impeller without baffles was used. Air was introduced via a ringsparger. The corresponding process settings are given in Table 2.

The described approach was very basic, but was considered to be a sound starting point for further investigations. Future process optimizations may manipulate the gassing and stirring in cascade mode. Two runs were performed at 50L scale. The results are listed in Table 3. The first run (50.1.1) showed issues related to inoculum and pH, so only a single run was available for further analysis (50.2.1).

Table 2

Process Parameters as Being Scaled-Up from the Center Point in Small Scale to the Large Scale, Based on Const. ppv and kLa

	Scale	Gassing, (vvm)	FG, (Lpm)	utip, (m sec^{-1})	N, (rpm)
center	Univessel® 2L	0.065	0.13	0.9	318
scale-up	Biostat STR® 50	0.052	2.60	1.4	187

Table 3

Results of the Large-Scale Runs

Run Order	Scale	µmax, (d^{-1})	VCC at 48h, (E06 Cells mL^{-1})	Viability, (%)
50.1.1	Biostat STR® 50	0.53	0.8	93.8
50.2.1	Biostat STR® 50	0.62	1.3	95.8

Scale-Up Using MVDA - Results and Discussions

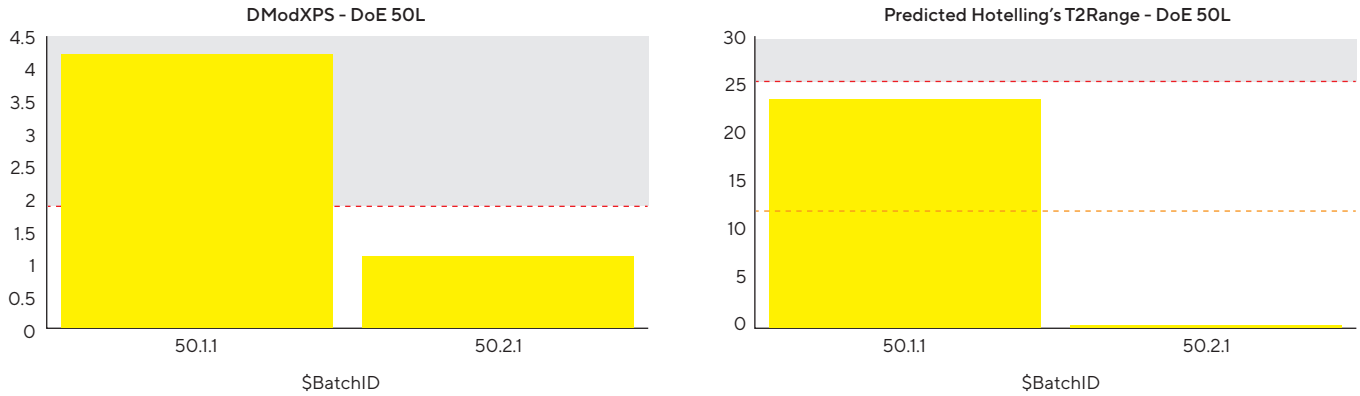
The data from the small-scale DOE were imported to SIMCA® 16.0. An OPLS batch model was created with this data to show how these batches changed over time. Using this model, the 50 L data could also be imported and used as a 'prediction set' to demonstrate if the 50L batches had similar profiles or not.

The first of the tools that can be used to demonstrate how well the data fits the model are DModX and Hotellings T2 plots. Controller settings of run 50.1.1 differed from the settings used in the small scale. This led to different pO_2 and gassing profiles. This was easily detected as strong outliers by using Hotellings T2 and DModX plots (Figure 8). These plots also show how well large-scale data fits a model from the small scale, the larger the bar, the larger the distance to the model. This demonstrates that the second run 50.2.1 fits well with the data from the 2L batches, which is in good accordance to the expectations.

The added value of this analysis, is that we can find the outliers via the T2 and DModX. For GMP and larger scale processes, at the commercial stage, the advantage here, is being able to identify issues at a very early stage of tech transfer.

Figure 8

DModX (left) and Hotellings T2 (right) Plots Indicating the Difference Between Run 50.1.1 and 50.1.2



Note. The first run had no comparable settings regarding the pO_2 control loop, leading to deviating process parameter profiles. This deviation is indicated by high value in both, DModX and Hotellings T2. Hence, for further analysis, run 50.1.1 was considered an outlier and not analyzed further.

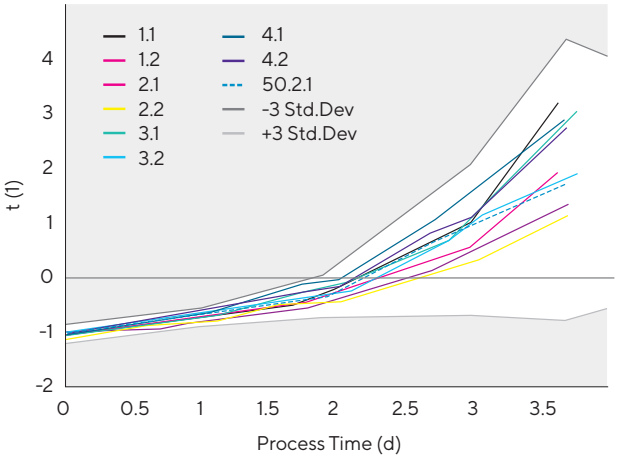
MVDA-based methods allow comparing data across batches easily by summarizing it into a few principal components. The score plot below shows the small scale runs and the larger 50L together. In general, the score plot summarizes the profile of the batches, which appear to be similar, i.e. the plot reduces each batch with its containing data into a single time course (Figure 9).

Condensing the data further, a batch level model is created that reduces a batch with all its containing data into one single data point. The resulting PCA model allows easy visual interpretation (Figure 10). The origin in the plot relates to the overall average of all batches. Well established production processes should therefore scatter closely around this point. However, in the context of scale-up it is interesting to see how data points of different scales cluster. The closer points are in the score plot, the more similar they are. In the given case, the small scale run 3.2 corresponds most closely to the large scale run 50.2.1. Nevertheless, it shall also be noted that the repetition of the center points, i.e. run 1.2 and 2.2, show a certain spread. Ideally, repetition runs should fall closely together in the plot. Although this reduces the overall model validity, the general approach as described here, is still considered as valid.

By looking at the viability and VCC for both of these runs it can be demonstrated that similar profiles were achieved across the scales (Figure 11).

Figure 9

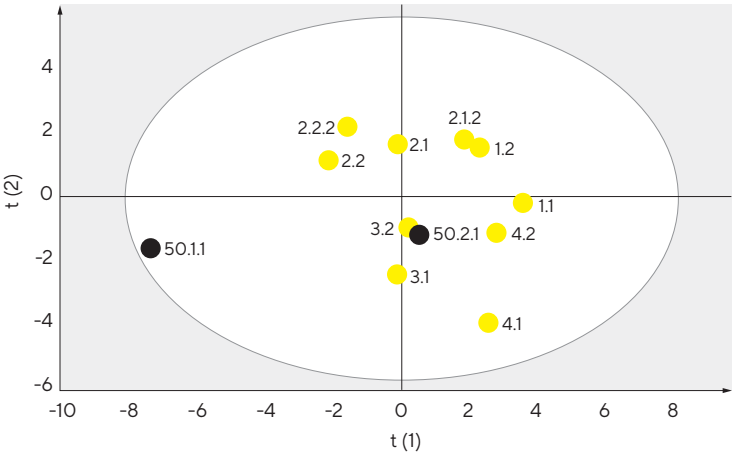
Time Courses of Principal Components of the Performed Batches



Note. The graph condenses the multi-dimensional batches into a single parameter, already allowing simplified interpretation even for a large number of processes.

Figure 10

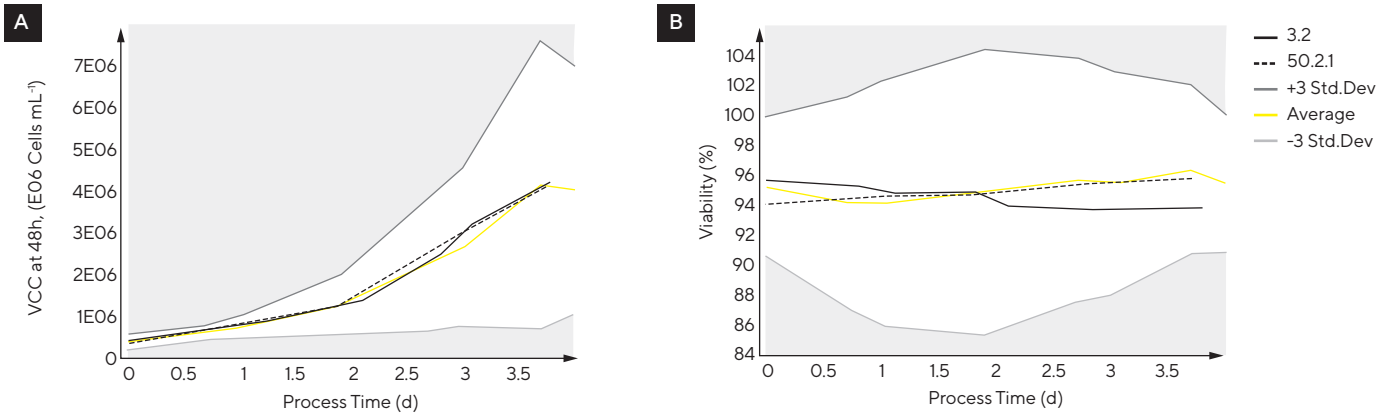
PCA Plot Summarizing the Small-scale Experiments (Yellow) and Large-scale Runs (Black) Each As One Single Point in the Graph



Note. Points being close to each other are considered similar based on the relevant quality attributes.

Figure 11

Detail View, Comparing the Time Course of Quality Attributes of Experiment 3.2 and 50.2.1



Note. The profiles are well aligned, allowing the interpretation of both runs being very similar.

The model helps understand the correlation between scales. Although the center point was scaled-up based on well-established parameters, i.e. ppv and kLa, the objective statistical assessment, which takes all available data into account, revealed that the "high-high" setting (3.2) in the small scale, corresponds much more closer to the run performed in the 50L scale.

With the classical approach, there would have been no straightforward way of applying scaling rules leading to the above result, because the main physical parameters such as ppv, kLa and mixing time do differ, as is indicated by Table 4.

Despite the already good agreement, the process can be expanded further. As mentioned earlier, multiple iterations can be undergone before an ideal alignment is achieved. In the next step the results of the large-scale run were mapped into the small scale. With other words, the model tried to match the parameters that must be set, to achieve the exact results as seen in large scale. This calculation can be easily performed via MODDE's optimization algorithm. The result is shown by Figure 12.

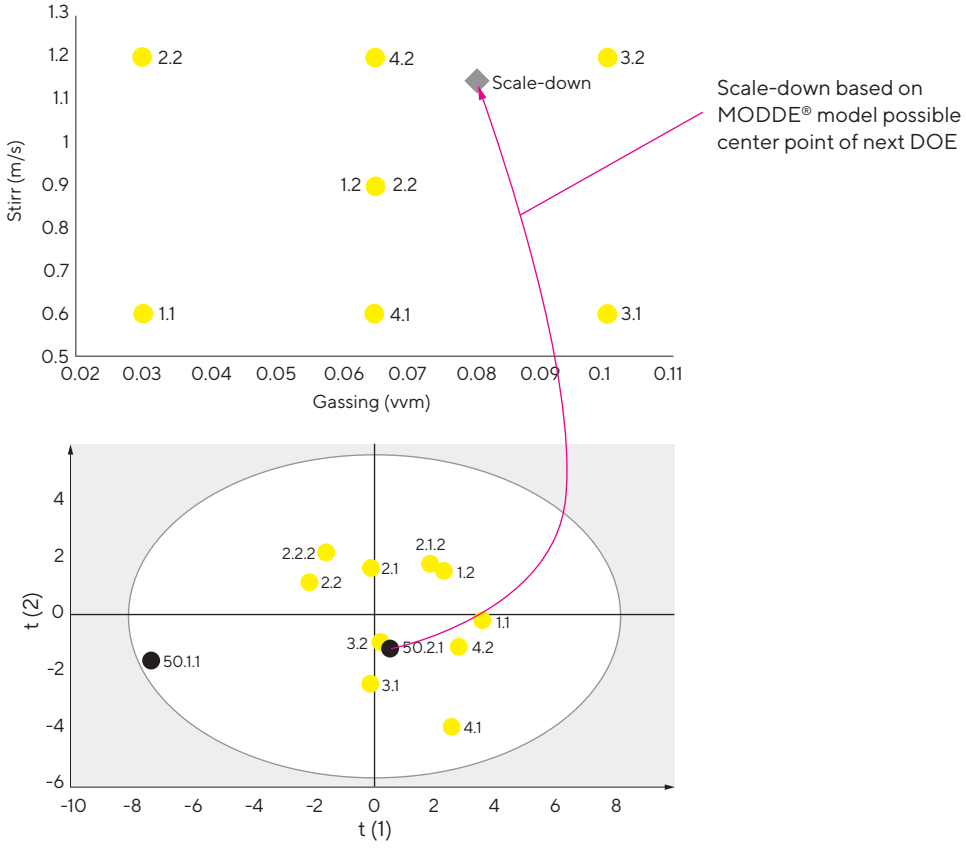
Table 4

	Exp. name	Gassing, (vvm)	FG, (Lpm)	kLa, (h^{-1})	utip, (m sec^{-1})	N, (rpm)	Mixing time, (s)	ppv, (W m^{-3})
UV2L	3.2	0.100	0.20	15.5	1.2	424	3.0	91.2
STR50	50.1.2	0.052	2.60	7.9	1.4	187	9.2	44.0

Note. Summary of Corresponding Physical Process Parameters regardless of the matching quality profiles. Unique scale-up approach for matching quality criteria instead of the traditional scale up approach based only on physical engineering parameters. High and low ranges are defined for the DOE, however as a second step the key performance indicators criteria approach was utilized.

Figure 12

Graphical Assessment of the Scale-Up Approach



Note. Showing the "high-high" (3.2) setting in the DOE corresponding closely to the run performed in 50L (50.2.1) in the plot. However, by using the model it is easily possible to map the results of the 50L run back into the corresponding parameter set that was required to match these values in small scale. This mapped scale-down model may be the center point of a follow-up DOE.

To match the large-scale attributes, the estimated scale-down model lies in-between experiment 4.2 and 3.2, represented by following process parameters:

- Stirring (m sec^{-1}): 1.14
- Gassing (vvm): 0.08

which correspond to

- ppv = 80.2 W m^{-3}
- kLa = 11.8 h^{-1}

The predicted results of CQA´s, that are derived from the MLR model, are listed in Table 5.

The study ended at that point, but it is now generally possible to feed the database with further experiments, e.g. if a new DOE was set up around the estimated scale-down model as a new center point or with new data derived from production scale runs at different settings. However, the basic protocol of the process must prevail. This approach would allow identifying representative and predictive settings for the scale-down, that correspond to various possible working points at the technical scale. This iterative strategy allows constant improvement of process understanding, making best use of the data derived from experiments and production runs.

Table 5

Comparison of Large-Scale Run Results vs. Predicted Results of the Mapped Scale-Down Model

Scale	**50L**	**2L**
Exp. name	50.2.1	scale-down
	Measured values	**Predicted values**
µmax, (d^{-1})	0.62	0.64
VCC at 48h, (E06+ Cells mL^{-1})	1.3	1.5
Viability, (%)	95.8	95.8

Conclusions

The described procedure of applying statistical methods represents a versatile and universal tool in the context of scale-up, where it supplements the classical approach with another perspective on data evaluation and assessment of experiments. It enables the build-up of knowledge, by an iterative feedback loop joining data pools from different scales into one single graph.

The above method may be extended, to consider more key parameters and quality attributes, especially related to the product itself. Nevertheless, the results will still be accessible for interpretation in the same manner as described, while non-multivariate methods tend to become confusing with added complexity.

Finally, the described method will lead, in many cases, to process settings that would not have been found using classical scale-up rules, and bring added value for commercial early stage process and product assessment of scale-up and tech transfer success.

For Labor Dr.Merk & Kollegen, these experiments and the data evaluation support by Sartorius, were highly important not only to scale-up confirmation to the large scale, but also to achieve very comparable cell densities and viabilities between 2L and 50L at point of induction for the product synthesis.

For the client, Sartorius was able to assist bringing the Data Analytics´ strong knowledge with a unique field vendor support, enabled by the QbD approach from Umetrics®. This can be further utilized for larger production scales eg.: 200L like Figure 1. suggests.

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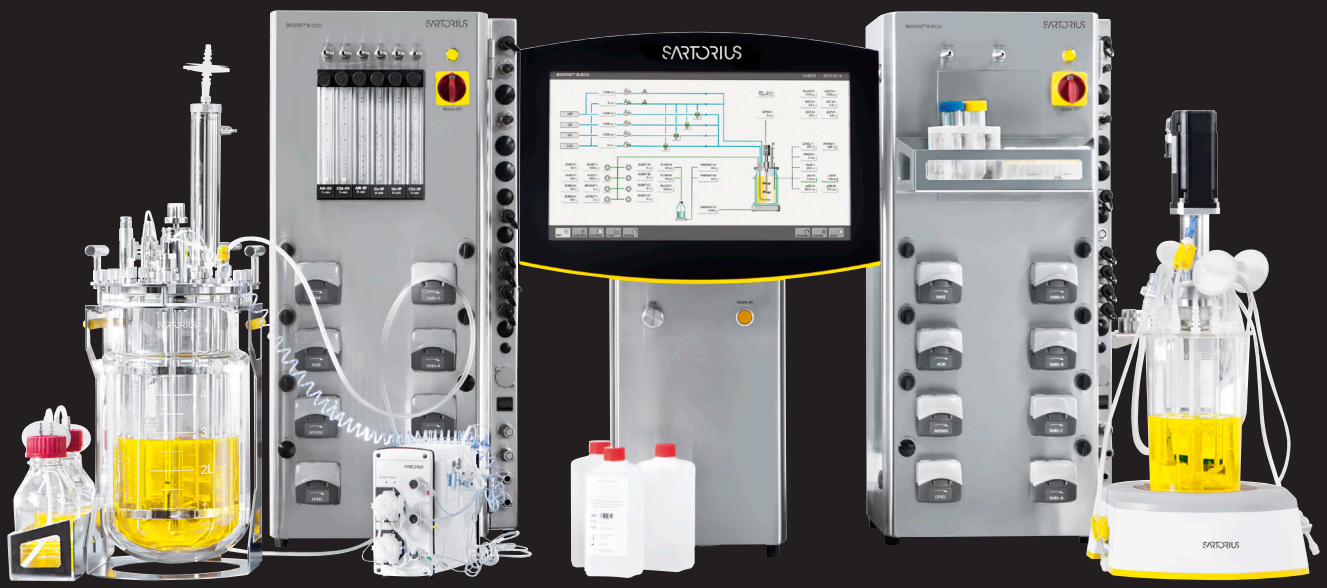

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