Yield Prediction

Introduction

Manufacturing in the modern pharmaceutical era has become increasingly challenging to control, especially when dealing with live organisms. This increase in process complexity has resulted in high variability experiments and unexpected outcomes that result in significant production inefficiencies. Being able to anticipate the performance of a process before it has ended can be of immense value for any manufacturing team. This can enable pharmaceutical companies to significantly improve yield output and drastically reduce manufacturing costs for any given process.

Aizon's AI-powered, GxP-qualified platform offers a range of functionalities that allow for the creation of a fully adaptable, real-time solution to help production teams anticipate bioreactors' poor performance and as a result, achieve higher product quality.

Anticipating yield decrease during a batch

Aizon's algorithm helps operators anticipate low-performing batches, and provides hints on how to regulate the process in case of poor performance. These hints help operators understand the algorithm's decisions, and hence improve decision-making in critical situations. The algorithm works by augmenting the operator's ability to make the right decision at the right time.
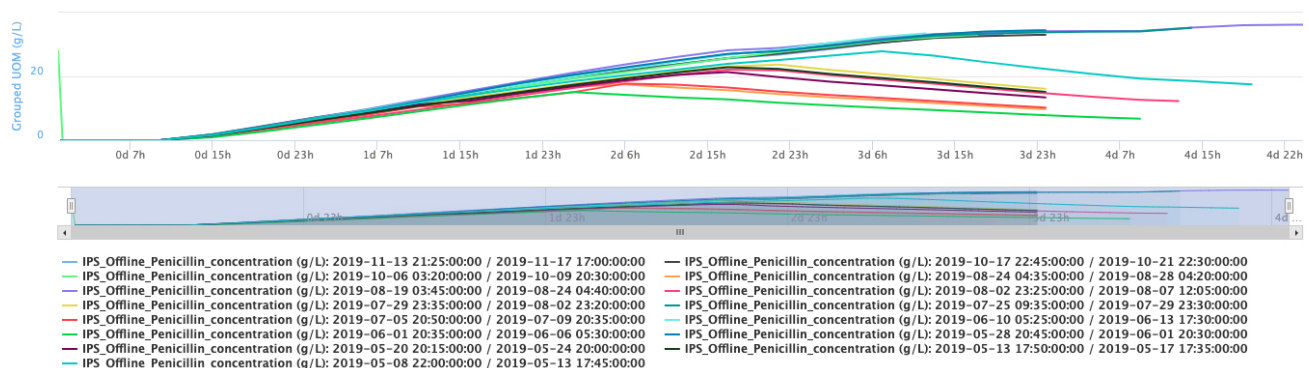

— IPS_Offline_Penicillin_concentration (g/L): 2019-11-13 21:25:00:00 / 2019-11-17 17:00:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-10-06 03:20:00:00 / 2019-10-09 20:30:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-08-19 03:45:00:00 / 2019-08-24 04:40:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-07-29 23:35:00:00 / 2019-08-02 23:20:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-07-05 20:50:00:00 / 2019-07-09 20:35:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-06-01 20:35:00:00 / 2019-06-06 05:30:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-05-20 20:15:00:00 / 2019-05-24 20:00:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-05-08 22:00:00:00 / 2019-05-13 17:45:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-10-17 22:45:00:00 / 2019-10-21 22:30:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-08-24 04:35:00:00 / 2019-08-28 04:20:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-08-02 23:25:00:00 / 2019-08-07 12:05:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-07-25 09:35:00:00 / 2019-07-29 23:30:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-06-10 05:25:00:00 / 2019-06-13 17:30:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-05-28 20:45:00:00 / 2019-06-01 20:30:00:00
— IPS_Offline_Penicillin_concentration (g/L): 2019-05-13 17:50:00:00 / 2019-05-17 17:35:00:00

Fig. 1: Penicillin concentration of 15 batches: we can clearly see high and low performance

To build a solution to this technical challenge, Aizon leverages an open source simulated data set[1] that represents a penicillin fermentation process, with a total of 70 batches of data (containing 30+ high frequency continuously monitored variables). Performance is varied across all batches, ranging from very low yield to quite optimal penicillin concentration (g/L) outputs.

Aizon leverages a combination of a process expert's knowledge and a data scientist's analytical expertise, to fully understand the data and bring direct business value. Through the use of Aizon's Bioreactor Application, a solution designed to monitor and discover the intricacies of any process, 7 relevant factors were identified. These parameters carry most of the relevant information to achieve accurate predictions of the yield.

Once relevant factors are identified, Aizon's platform trains several models with this selected and cleaned data, using an adapted data preprocessing pipeline to tackle the low number of events' challenge. After this process, the LASSO algorithm is selected over other regression algorithms for two reasons:

→   High accuracy achieved on the data set (R2 over 0.9)

→   Easily explainable predictions due to the algorithm's nature

Interpretability of the predictions is a crucial element of any AI-powered solution, to help ensure the end-user's correct use and encourage adoption of the solution.

These models are then deployed and automatically trigger predictions at regular intervals from 25% completion of the batch up to its end. At this point, it is straightforward to implement alarms and triggers to alert users in case of potential drop in yield.
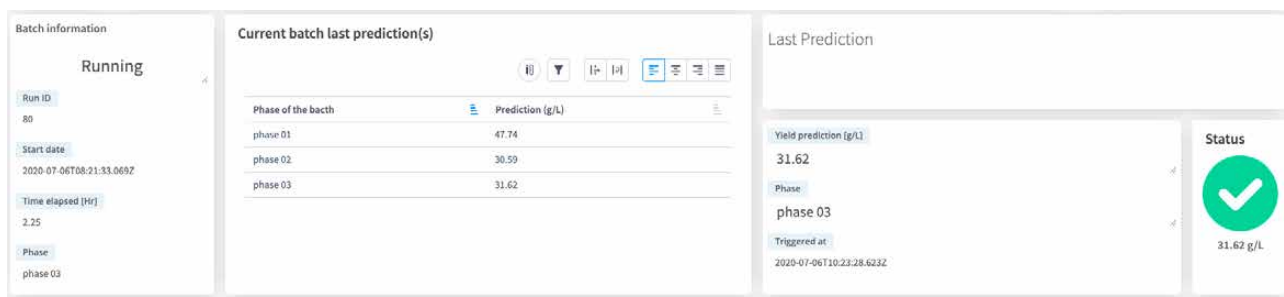

Fig. 2: Screenshot of a Yield Prediction dashboard on the Aizon platform

Conclusion

The use of state of the art technologies in process monitoring can have a huge impact on any pharmaceutical manufacturing operation. In this specific situation, the prediction of yield in the early stages of a fermentation procedure allows process experts and manufacturing teams to not only ensure high quality results

for every batch, but also learn from the process and improve the current best performing batches.

Nevertheless, it is important to note that the use of Artificial Intelligence will not render outstanding results by itself, it is necessary to leverage process experts' knowledge of the process to take full advantage of this kind of technology.

The benefits of using Industry 4.0 technologies in pharmaceutical manufacturing, however, can be extremely positive, not only from an economic standpoint but also from a Quality Assurance situation. Being able to fully control the state of a process allows for a faster and better Process Performance Qualification and ensures the capability of the manufacturing team to maintain stage 3 of the FDA's Validation Process Guidelines. This promises a significant evolution in the way medicines are made, and will help write the future of drug manufacturing as a whole.

About Aizon: Aizon is a software provider that transforms manufacturing operations with the use of IoT, cloud, advanced analytics, artificial intelligence, and pharma 4.0 technologies focused on optimizing pharmaceutical and biotech companies. The Aizon analytics platform seamlessly integrates unlimited sources of structured and unstructured data to deliver actionable insights across all manufacturing sites. Aizon offers an intuitive way to gain meaningful operational intelligence with data by enabling real-time visibility and predictive insights in a GxP compliant manner with end-to-end data integrity. Founded in 2014, the company is based in San Francisco, California and also has a European office in Barcelona, Spain.