YPSO Ionic®

IMPACT OF KEY OPERATING PARAMETERS IN A COMPLEX PROCESS

PREDICTION OF IEX OLIGONUCLEOTIDE PURIFICATION

PROCESS: CHROMATOGRAPHY, ION EXCHANGE, SINGLE COLUMN, SMALL MOLECULE
PRODUCT: OLIGONUCLEOTIDE

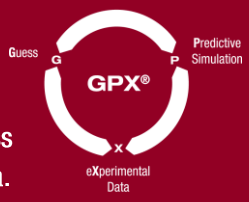
CHALLENGE

Designing a **chromatographic process** requires **selecting numerous operating parameters** (column dimensions, number of steps, step duration, buffer type, eluent pH, flowrates, gradient slope…)

There is a high interest in **using predictive simulation to predict the impact of key operating parameters** and thus reduce the experimental burden and development times.

No satisfactory **model for oligonucleotide purification** was found in the literature, so we took the challenge to build one!

METHODOLOGY

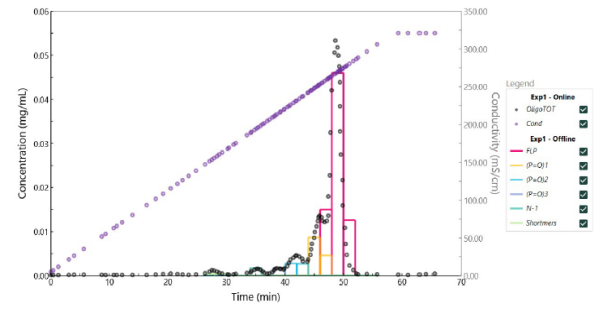


Based on the GPX® Concept : in order to address your challenges, we capitalize on the **Guess ability** of different experts, the possibility of **Predictive simulation** and the use of **eXperimental data.**

❑ Acquisition of few experimental data

Building a mechanistic model requires few well targeted experiments.

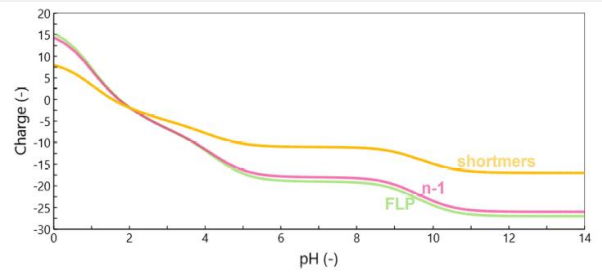
This case study is inspired by the experimental data reported in Deshmukh et al. OPRD (2002) 4, 205-213. It deals with the purification of Alicaforsen on a strong anionic resin.

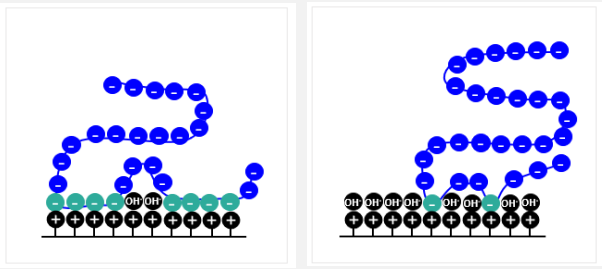


❑ Presentation of the model

The model embedded in Ionic accounts for a certain number of physical phenomena:

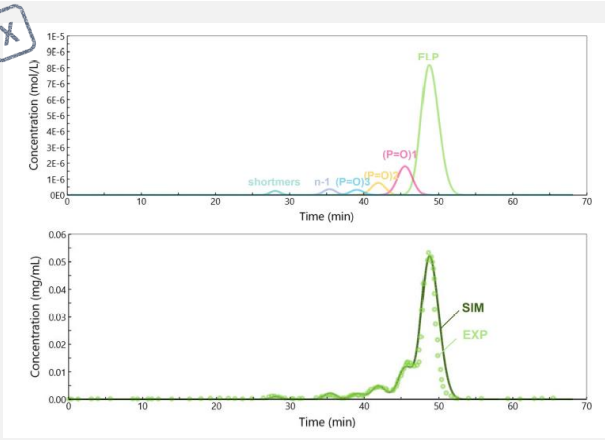
- The variable **charge of the oligonucleotide with pH**
- The possibility for the oligo **to interact with the resin with a number of charges lower than its charge in solution** (e.g., the oligo may bear 28 negative charges at basic pH but interact only with 8 of them)
- The possibility for the oligo **to interact with the resin in different ways** (e.g., with 6, 7 or 8 charges)
- **The competition between the oligo and the other Species in solutions** (e.g., OH-, phosphate) at the surface of the resin





❑ Comparison experiments / simulations

The model parameters were determined by **fitting model simulations to experimental data.**
A good agreement was obtained between experiments and simulations.



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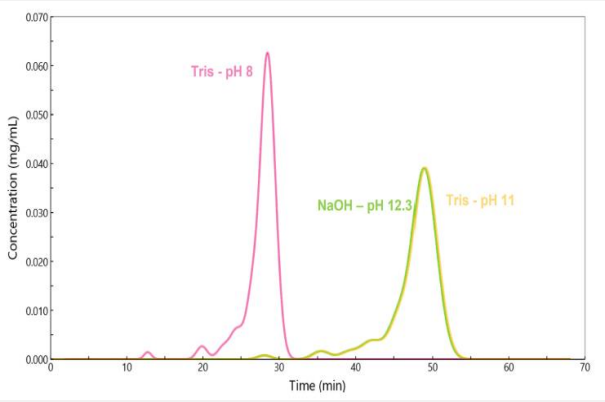
RESULTS

After determining model parameters, simulations were performed to predict the impact of key operations parameters. The observed trends are well in line with those reported experimentally in Deshmukh et al. OPRD (2002) 4, 205-213.

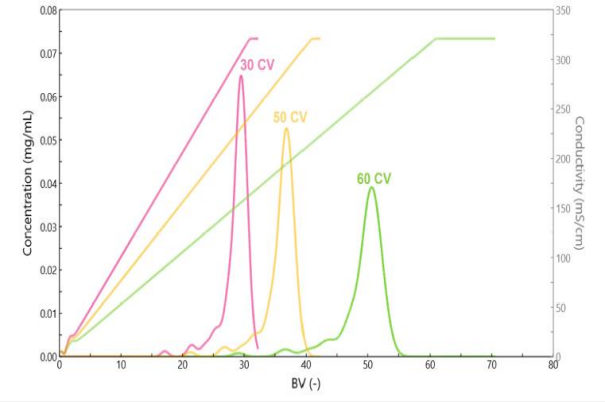
❑ Impact of buffer type and pH

- The model correctly predicts an increase in the retention time when increasing the pH from 8 to 11 or 12.
- This is due to the higher number of negative charges on the oligo molecule at higher pH.



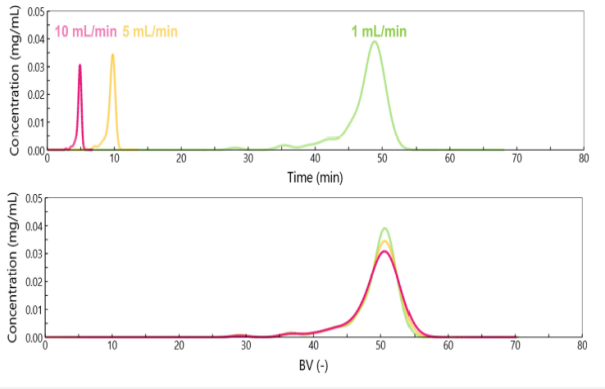
❑ Impact of gradient slope

- The model correctly predicts an increase in peak retention time, peak width and peak resolution when decreasing the gradient slope.



❑ Impact of flowrate

- The model correctly predicts a decrease in retention time and an increase in peak width when increasing flowrate.



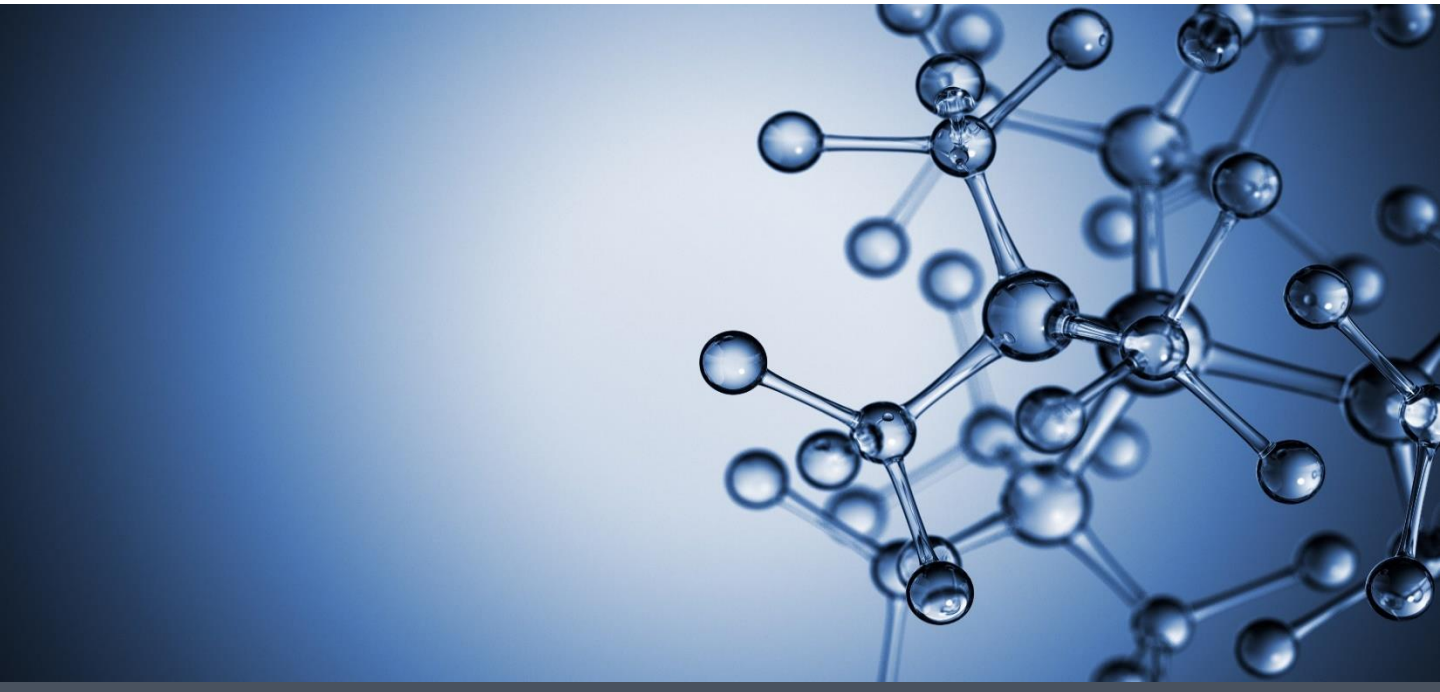
Conclusion

Take home messages

1. **Predictive simulation** can be used with **complex molecules**
2. **Only few well targeted experiments are sufficient** – no need of a heavy experimental program!
3. **The impact of a wide variety of operating parameters** like buffer pH, gradient slope or flowrate, but also crude composition, loading volume, or wash time **can be predicted**

Visit our website and contact us for a demo or more information!

contact@ypso-facto.com



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