Impact of Elevated Pressure on k_La and Oxygen Transfer with the BioXplorer 400P

Abstract

Oxygen transfer is a critical limitation in aerobic fermentations directly impacting cell growth, productivity and bioprocess efficiency. The addition of pressure to a bioreactor contributes to increasing the Oxygen Transfer Rate (OTR) and therefore gas solubility in the fermentation broth. More bioprocess scientists are turning to pressurized systems to increase the availability of dissolved gases and accelerate gas-dependent bioprocesses.

This application note demonstrates how operating at elevated pressure significantly enhances dissolved oxygen availability and OTR (k_La), using the Bioxplorer 400P high pressure parallel bioreactor system. By increasing pressure, oxygen solubility in the fermentation broth improves, enabling faster and more efficient bioprocesses. The Bioxplorer 400P allows precise control of dissolved oxygen via pressure offering a powerful alternative to traditional agitation-based strategies.

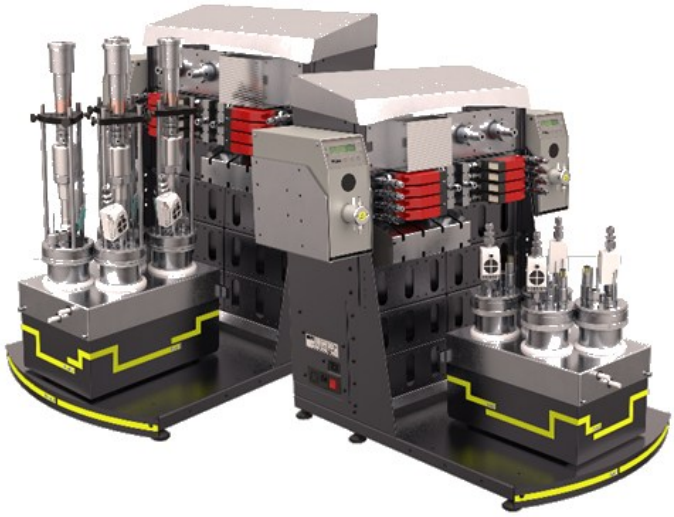

Figure 1. H.E.L Group's BioXplorer 400P

Key Benefits of the BioXplorer 400P

- Accelerates fermentation by improving oxygen availability
- Enables higher productivity without increasing shear stress
- Provides a scalable route to optimize oxygen transfer
- Allows precise dissolved oxygen control via pressure
- Reduces reliance on agitation for oxygen transfer lowering shear stress and protecting sensitive cultures.

What is k_La? And why is it important in fermentations?

k_La is the volumetric oxygen mass transfer coefficient, measuring the efficiency of oxygen transfer from bubbles to liquid in the bioreactor. In practical terms, k_La determines how quickly oxygen becomes available to cells, making it a critical parameter for aerobic fermentation performance, productivity, and scale-up.

Higher operating pressure increases oxygen solubility in the fermentation broth, which can enhance oxygen transfer and improve overall process efficiency.

Previous studies using the H.E.L bench-top bioreactor systems (BioXplorer 100 & 400) have shown that a constant k_La can be used as a basis for scale-up, as the values obtained can be accurately reproduced in conventional scale bioreactors (Gill *et al.*, 2008). In these studies, k_La is used as a measure of how well oxygen is transferred to the liquid under pressure.

The BioXplorer 400P

The BioXplorer 400P is an automated 4-zone parallel pressure bioreactor system used for the discovery and optimization of novel bioprocesses.

Designed for applications ranging from syngas fermentation to cell-free enzymatically catalyzed processes, the BioXplorer 400P uses pressure and precise gas feed control to accelerate bioprocesses that depend on the availability of dissolved gases.

Materials and Methods

Experiments were designed to evaluate the impact of pressure on oxygen transfer under controlled conditions.

- Reactor: 500 mL stainless steel reactor
- Working volume: 300 mL w/v dilute solution of sodium sulphite.
- Gas: 1 vvm (300 sccm) air gas blend containing H2.
- Temperature: 37 °C.
- Stirring: 1500 rpm.

The BioXplorer 400P stainless steel pressure vessel was fitted with gas sparger, pH probe, DO probe, overhead motor and magnetic drive with Ruston impeller (Figure 2). The system was cycled between gassing with air and scrubbing with nitrogen with increasing pressure.

Figure 2. BioXplorer 400P SS bioreactor

Results and Discussion

The Figure 3 shows the dissolved oxygen (DO) profile of a reactor while being cycled between gassing with air and with nitrogen. DO in the liquid increases as pressure increases within the reactor.

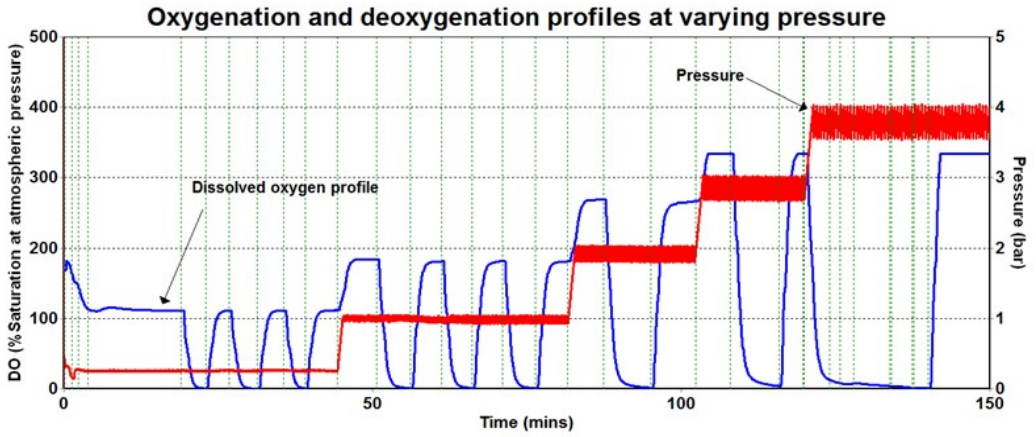

Figure 3. Oxygenation and deoxygenation profile at various pressures over time.

The gradient of the DO profile represents the rate of change of oxygen concentration, which is a measure of oxygen flux (Figure 4). By using the fact that 100% saturation corresponds to an oxygen concentration of ~9 mg/L (at room temperature), the corresponding oxygen flux profile (in grams per liter per minute) can be generated.

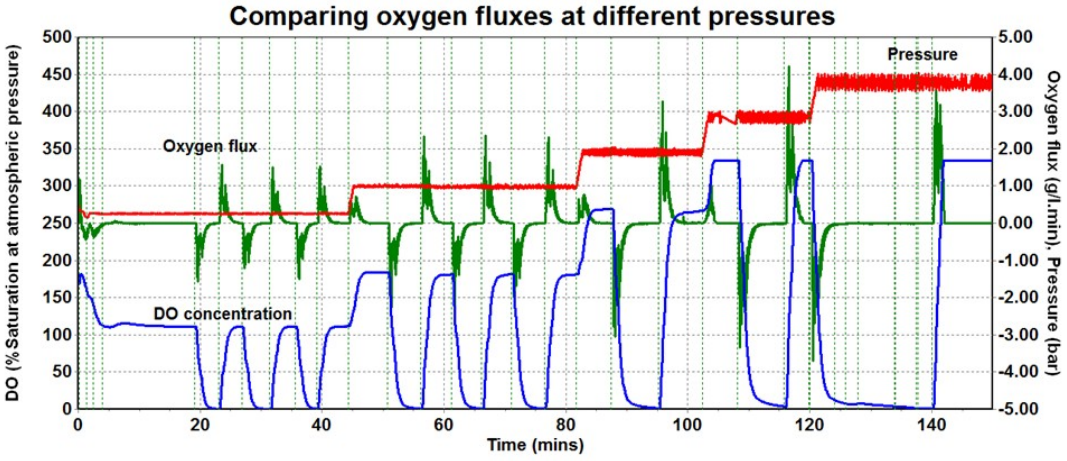

Figure 4. Comparison of O_2 flux at different pressures.

Pressure can be used to manipulate the oxygenation level. This would traditionally be achieved by manipulating stirrer speed. However, this is not an option for more fragile organisms, for example, algae, amoeba, etc., due to shear forces that affect cell integrity. In the experiment, represented by the data below (Figure 5), a control loop has been created that links a requested DO set point with the control output to a back-pressure regulator (BPR). The pressure in the system will vary because of the automatic regulation of the BPR, which is not, however, explicitly manipulated.

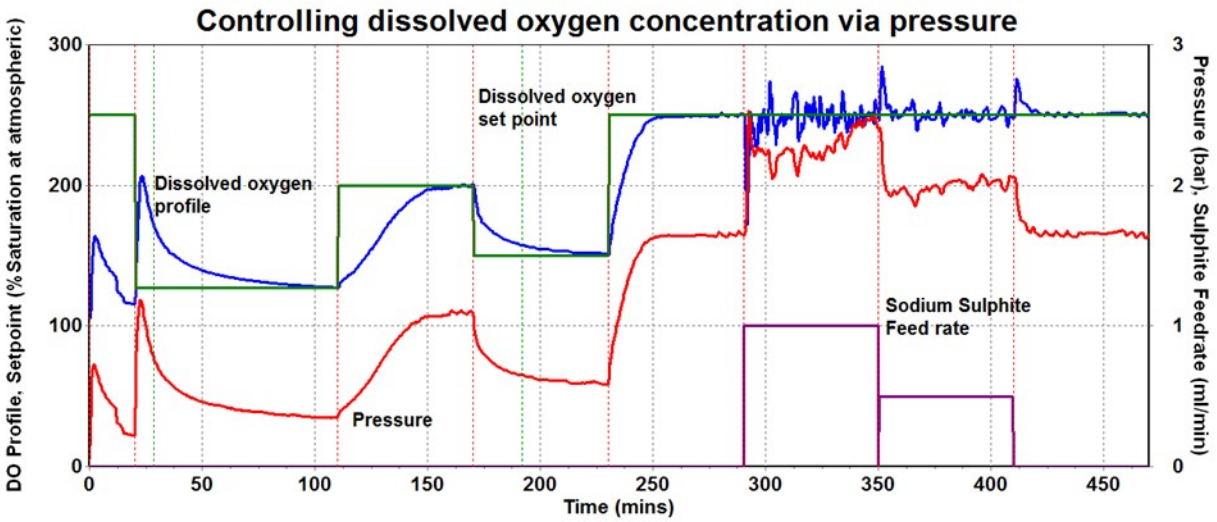

Figure 5. Control of dissolved oxygen via pressure over time using an automatically controlled BPR. Oxygen concentration increases stepwise with pressure showing clear correlation between pressure and oxygen transfer rate.

Data was processed by H.E.L analysis tools. Here, each different coloured section represents a separate curve fitted region. Markers represent measured data points. Each fitted curve yields a separate estimate of k_La. Each

In the first 250 minutes of the experimental run, the DO set point varied between 120 and 250%. These DO intervals within the reactor were easily reached and maintained automatically with the help of the BPR, regulating pressures between 0.4 and 2.5 bar. The DO set point was kept stable after 250 minutes and the stability of DO was tested with the addition of sodium sulphite, which removes oxygen from the liquid in an oxygen scavenging reaction. Once sodium sulphite was fed, the BPR effectively increased the pressure in the reactor to keep DO at the set point until the end of the experiment.

Conclusion

According to Henry's Law, the DO concentration (but not k_La) scales approximately linearly with oxygen partial pressure. In our high-pressure experiments, the DO value improved several-fold and showed a near-proportional relationship with applied pressure.

Operating a bioprocess at elevated pressure (e.g. up to 10 bar) using the BioXplorer 400P can therefore deliver substantial improvements in oxygen transfer. Achieving similar gains through k_La optimization alone would be significantly more challenging, due to the influence of additional factors such as gas–liquid interfacial area, bubble size, and agitation. By using pressure instead of increased agitation, the risk of shear stress can be minimized, helping to protect sensitive cultures.

Our results demonstrate that applying pressure in the BioXplorer 400P bioreactors increases DO levels and enhances gas transfer rates, providing a robust approach to improving yield, productivity, and biomass growth in bioprocesses.

For further information on our BioXplorers, visit our **Automated Bioreactor Systems** on our website, where you can download full brochures.

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