Application of oxygen in biofermentation engineering

I. The effect of dissolved oxygen on fermentation

In the fermentation process， the factors affecting oxygen consumption are as follows.

(1) the composition of the medium and bacterial concentration significantly affect oxygen consumption culture medium is rich in nutrients， the bacterium grows fast， oxygen consumption; high bacterial concentration， oxygen consumption; fermentation process replenishment or replenishment of sugar， microbial uptake of oxygen then increases.

(2) the age of bacteria affect oxygen consumption respiration is high， oxygen consumption is large. Later in the fermentation period， the bacterium is in the aging state， oxygen consumption naturally weakened.

(3) fermentation conditions affect oxygen consumption in the optimal conditions of fermentation， oxygen consumption is large.

During fermentation， the elimination of toxic metabolites such as carbon dioxide， volatile organic acids and excess ammonia is also beneficial to improve the oxygen uptake of the bacterium.

At 25°C， 0.10MPa， the solubility of oxygen in air is 0.25mmol/L in water and only 0.22mmol/L in fermentation broth， while a large number of microorganisms in fermentation broth consume oxygen rapidly (oxygen consumption rate is greater than 25~100mmol/L-h). Therefore， oxygen supply is very important for aerobic microorganisms. In aerobic fermentation， microorganisms have a minimum requirement for oxygen， to meet the minimum oxygen concentration of microbial respiration is called critical valueofdissolvedoxygenconcentration， expressed in c critical. Below the c critical threshold， the respiration rate of microorganisms decreases significantly with the dissolved oxygen concentration. The general aerobic microorganism c critical is very low， about 0.003 ~ 0.05mmol / L， oxygen demand is generally 25 ~ 100mmol / (L - h). Its c critical is about 1% to 25% of the oxygen saturation solubility.

When there is no other limiting substrate， the dissolved oxygen is higher than the c critical， the specific oxygen consumption rate of the cell remains constant; if the dissolved oxygen is lower than the c critical， the specific oxygen consumption rate of the cell decreases greatly， the cell is in a semi-anaerobic state and the metabolic activity is hindered. The oxygen required to maintain microbial respiration and metabolism in the culture fluid maintains a balance between oxygen supply and oxygen consumption to meet the use of oxygen by microorganisms. Microorganisms in the liquid can only use dissolved oxygen， microorganisms at the gas-liquid interface can also use the oxygen in the gas phase， so strengthening the gas-liquid interface will also be beneficial to oxygen supply.

Dissolved oxygen is one of the most important parameters for aerobic fermentation control. Since the solubility of oxygen is very small in water and even smaller in the fermentation broth， constant adjustment of ventilation and agitation is required to meet the oxygen demand of different fermentation processes. The amount of dissolved oxygen can have different effects on the growth of the bacteria and the formation and yield of the products. Such as glutamic acid fermentation， when the supply of oxygen is insufficient， the accumulation of glutamic acid will be significantly reduced， producing a large amount of lactic and succinic acid. Another example is the production of vitamin B12 in the fermentation of Propionibacterium Xue， the components of vitamin B12 cobinamide (also known as B-factor) of the biosynthesis of the two main enzymes in the early stage of oxygen blocked， limiting the supply of oxygen in order to accumulate a large number of B-factor， B-factor and only under the conditions of oxygen supply into vitamin B12， thus using a combination of anaerobic and oxygen supply facilitates the synthesis of vitamin B12. In the fermentation of asparaginase， the first stage is aerobic culture， while the later stage is changed to anaerobic culture， the vitality of the enzyme can be greatly improved. It is quite important to master the timing of the shift. According to experimental research， when the dissolved oxygen drops to 45%， it is changed from aerobic culture to anaerobic culture， and the enzyme activity can be increased 6 times， which shows the importance of using

control of dissolved oxygen to control the fermentation. For antibiotic fermentation， the supply of oxygen is even more important. As in the case of tunicamycin fermentation，stopping ventilation for a short time during the growth period may affect the sugar metabolism pathway of the bacterium during the production period， shifting from the HMP pathway to the EMP pathway and reducing tunicamycin production. Oxygen on tunicamycin C6 also comes directly from dissolved oxygen， so dissolved oxygen has an effect on bacteriophage metabolism and product synthesis.

In summary， aerobic fermentation is not the greater the dissolved oxygen the better. Although high dissolved oxygen is beneficial to the growth of the bacterium and product synthesis， but too much dissolved oxygen sometimes inhibit the formation of products. Because， in order to avoid fermentation in oxygen-limited conditions， need to check the c critical and optimum oxygen concentration of each fermentation product (optimumoxygenconcentration)， and make the fermentation process to maintain in the optimum oxygen concentration. The magnitude of the optimum dissolved oxygen concentration is related to the characteristics of the bacterium and the product anabolism，which is determined experimentally. It is reported that the c critical for secondary metabolism of penicillin fermentation is between 5% and 10%， below this value will bring loss to penicillin synthesis， and the longer the time， the greater the loss. While the primary metabolism of amino acid fermentation， the size of oxygen requirement is closely related to the synthesis pathway of amino acid. According to the different requirements of fermentation oxygen demand can be divided into three categories (see Figure 7-4): the first category has glutamic acid， glutamine， arginine and proline and other glutamic acid family amino acids， they are under the conditions of adequate respiration of the bacteria to maximize production， if the oxygen supply is insufficient， amino acid synthesis will be strongly inhibited， a large number of lactic and succinic acid accumulation; the second category，including isoleucine， lysine， threonine and aspartic acid， namely The second group，including isoleucine， lysine， threonine and aspartic acid， which are amino acids of the aspartic acid family， can obtain the highest yield with sufficient oxygen supply， but the yield is not significantly affected when oxygen supply is restricted; the third group，including leucine， valine and phenylalanine， can obtain the largest amount of amino acids only when oxygen supply is restricted and cellular respiration is inhibited， and product formation is inhibited if oxygen supply is sufficient.

The reason for these differences in the degree of oxygen demand for amino acid synthesis is caused by their different biosynthetic pathways， which produce different amounts of NAD(P)H and， of course， different amounts of dissolved oxygen required for reoxidation. The first group of amino acids is formed by two pathways， the glyoxalate cycle and the phosphoenolpyruvate carboxylation system， which produce the largest amount of NADH. Therefore， the amount of oxygen required for the oxidative regeneration of NADH is the most， and the more oxygen is supplied， the more smoothly the amino acid synthesis will be. The second type of synthesis pathway is the glyoxalate cycle that produces NADH or the phosphoenolpyruvate carboxylation system that consumes NADH， and the amount of NADH produced is small， so the relationship with the amount of oxygen supply is not obvious. The third category， such as the synthesis of phenylalanine， does not go through the TCA cycle， with little NADH production and excessive oxygen supply， but rather acts