

# Development of Bioreactor for Animal Cell Culture and Microorganism Culture



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## Introduction

We developed a bioreactor, so called the "VMF Reactor", which using vertical motion mixing. This reactor can perform high mixing performance with mild mixing to reduce shear stress, as well. Furthermore, with the combination of "SPG (Shirasu Porous Glass) Membrane Sparger" which was developed by JGC Corporation, we successfully developed the "VerSus Reactor", a next-generation bioreactor for highly efficient cell culture. In this work, we reported the outstanding performance of the novel bioreactor. Additionally, we also presented the high gas absorption performance impeller and Sparger which is most suitable for microorganism culture.

## Bioreactor for Animal Cell Culture

The "VMF Reactor", which using vertical motion mixing

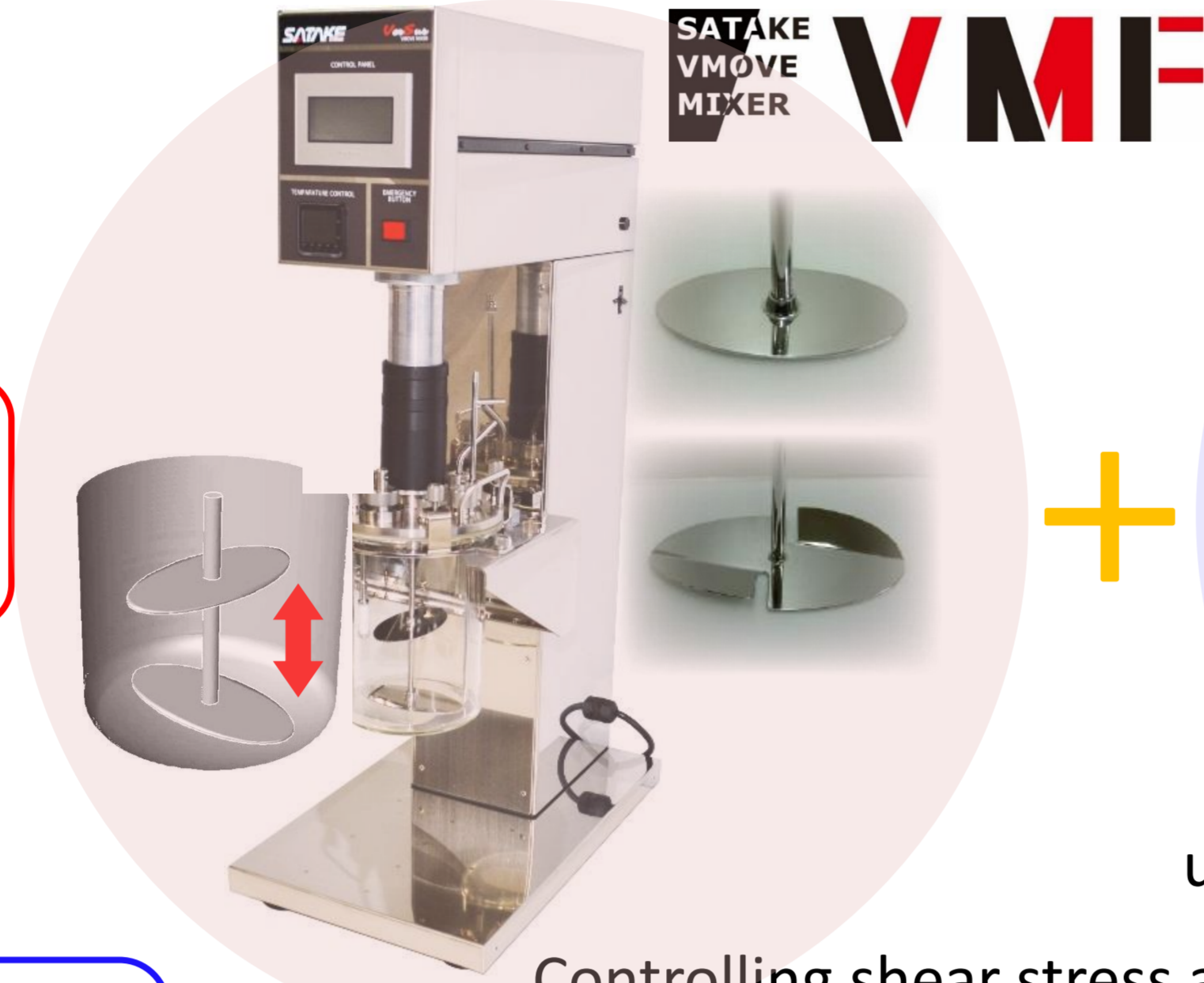
In regards to produce biopharmaceutical medicines efficiently

It is crucial to increase the production volume and maintain high cell density, as well.

Controlling shear stress

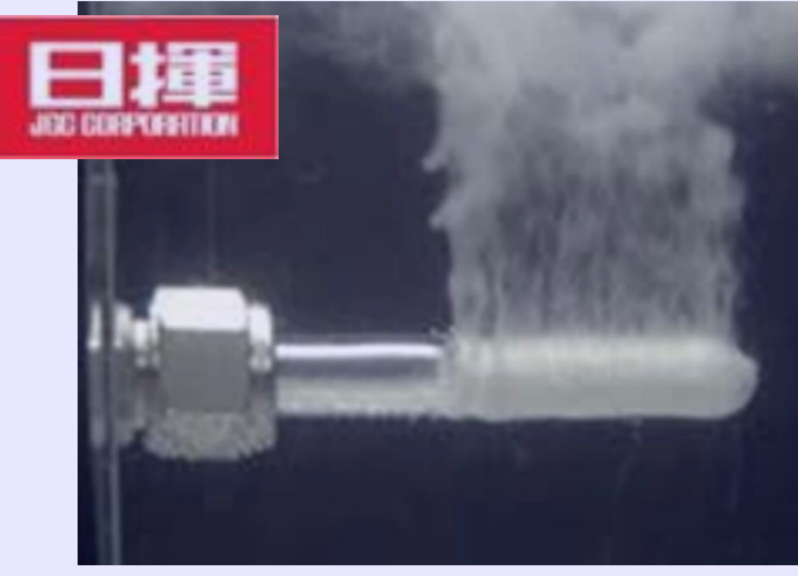
Oxygen supply

In conventional rotative mixing type of bioreactor, it is found difficult to provide ideal operational conditions to the cell culture, due to the trade-off relationship

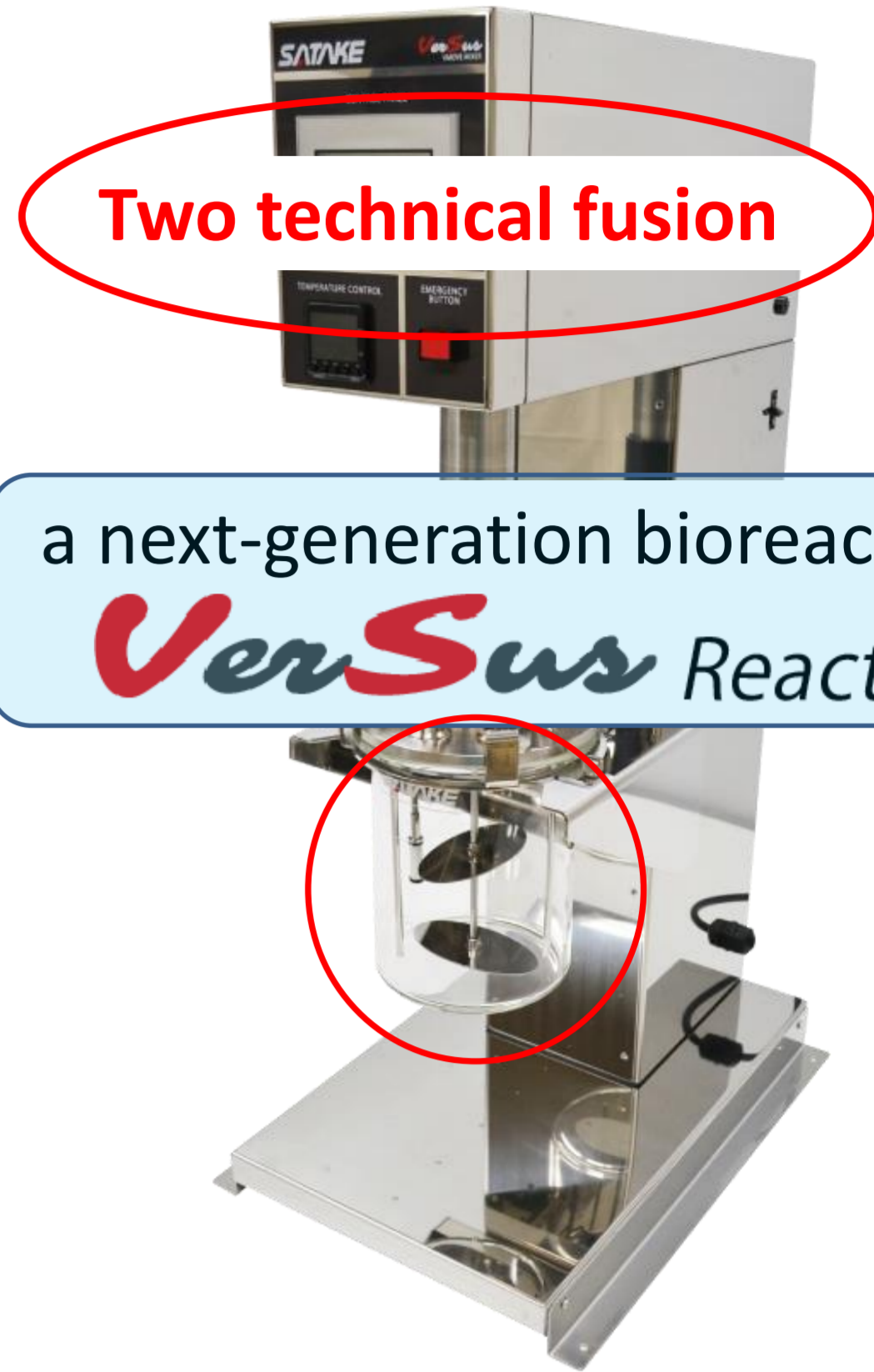


Controlling shear stress and high efficiency uniform mixture by using vertical motion mixing

SPG Membrane Sparger



High efficiency oxygen supply by the uniform dispersion of the microbubble



Two technical fusion

a next-generation bioreactor VerSus Reactor

## Comparison Result

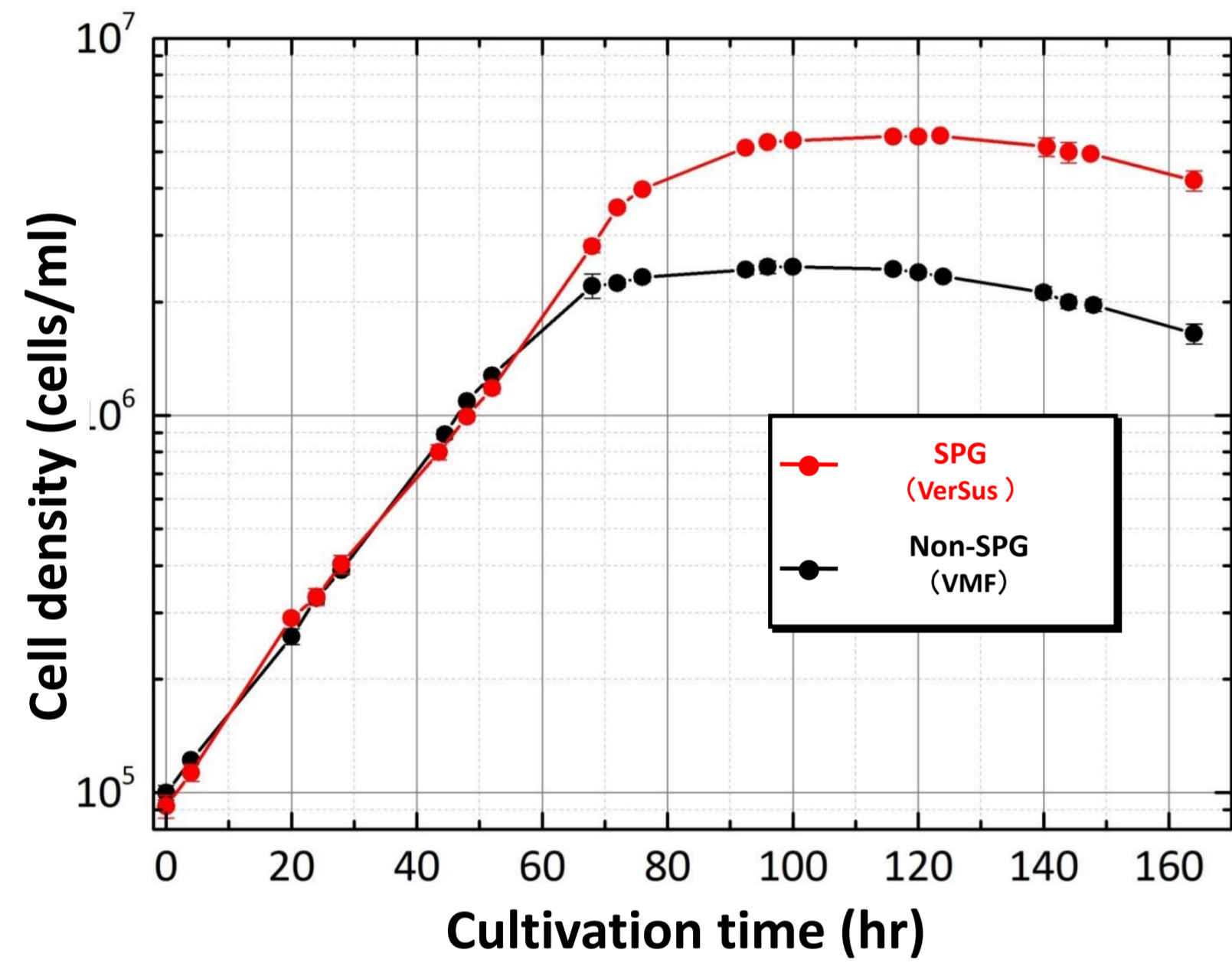


Fig.1 Growth curves of CHO-S cells

The arrival density of viable cell improved by using SPG Membrane sparger.

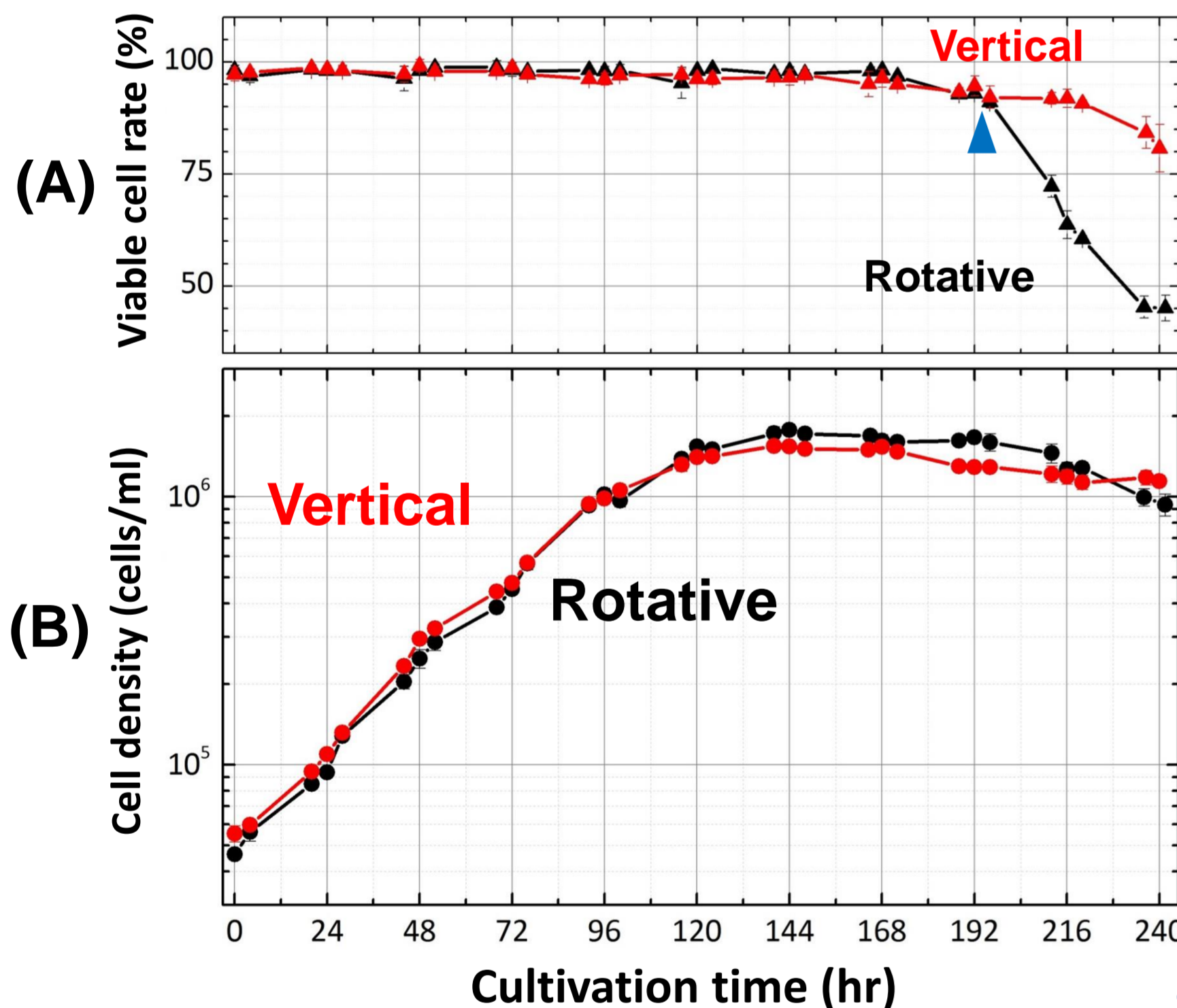


Fig.4 Growth curves of CHO1-15<sub>500</sub> cells  
(A) Viable cell rate, (B) Cell density.

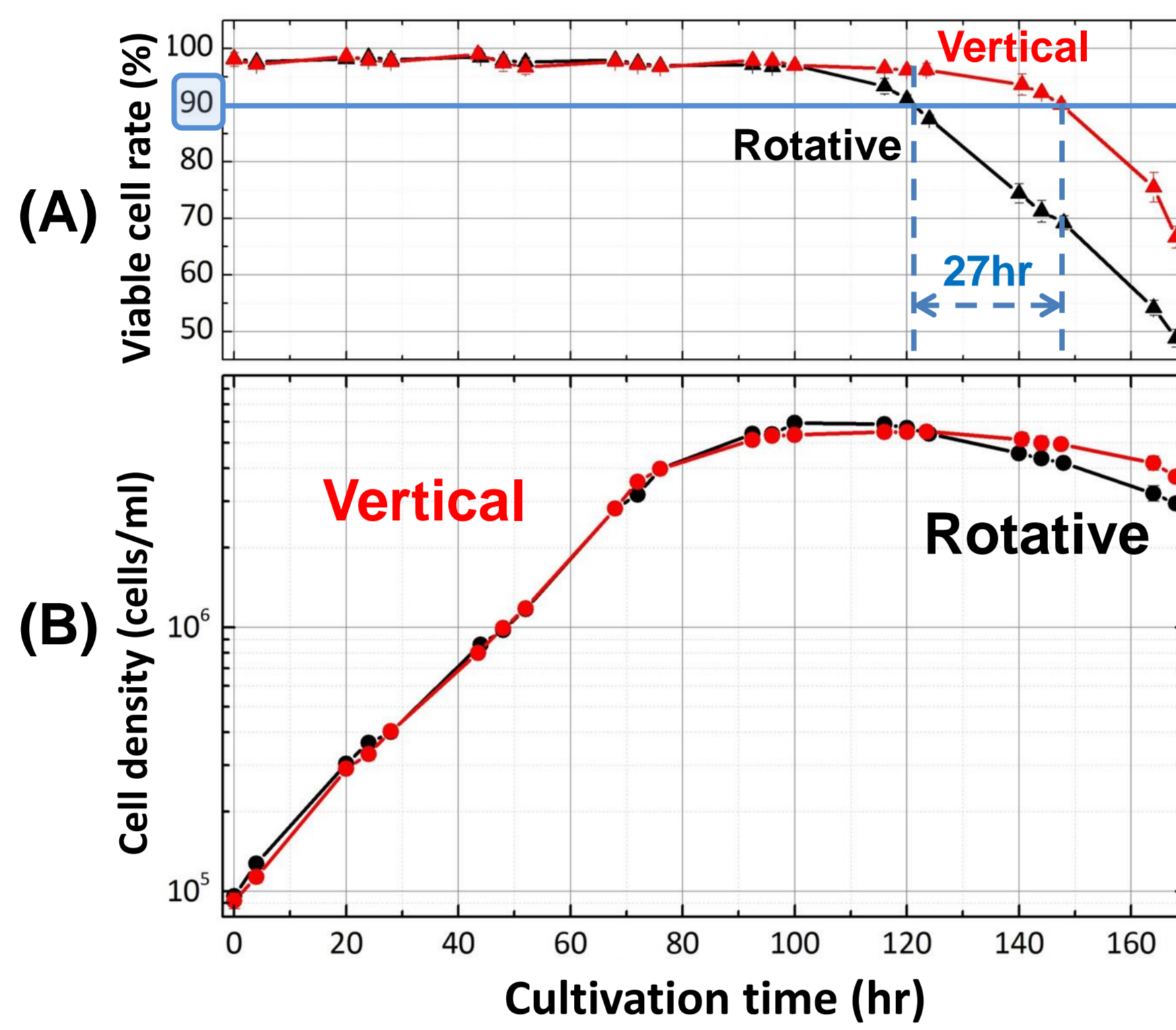


Fig.2 Growth curves of CHO-S cells  
(A) Viable cell rate, (B) Cell density.

The Vertical motion type can maintain the viable cell rate highly at stationary phase.

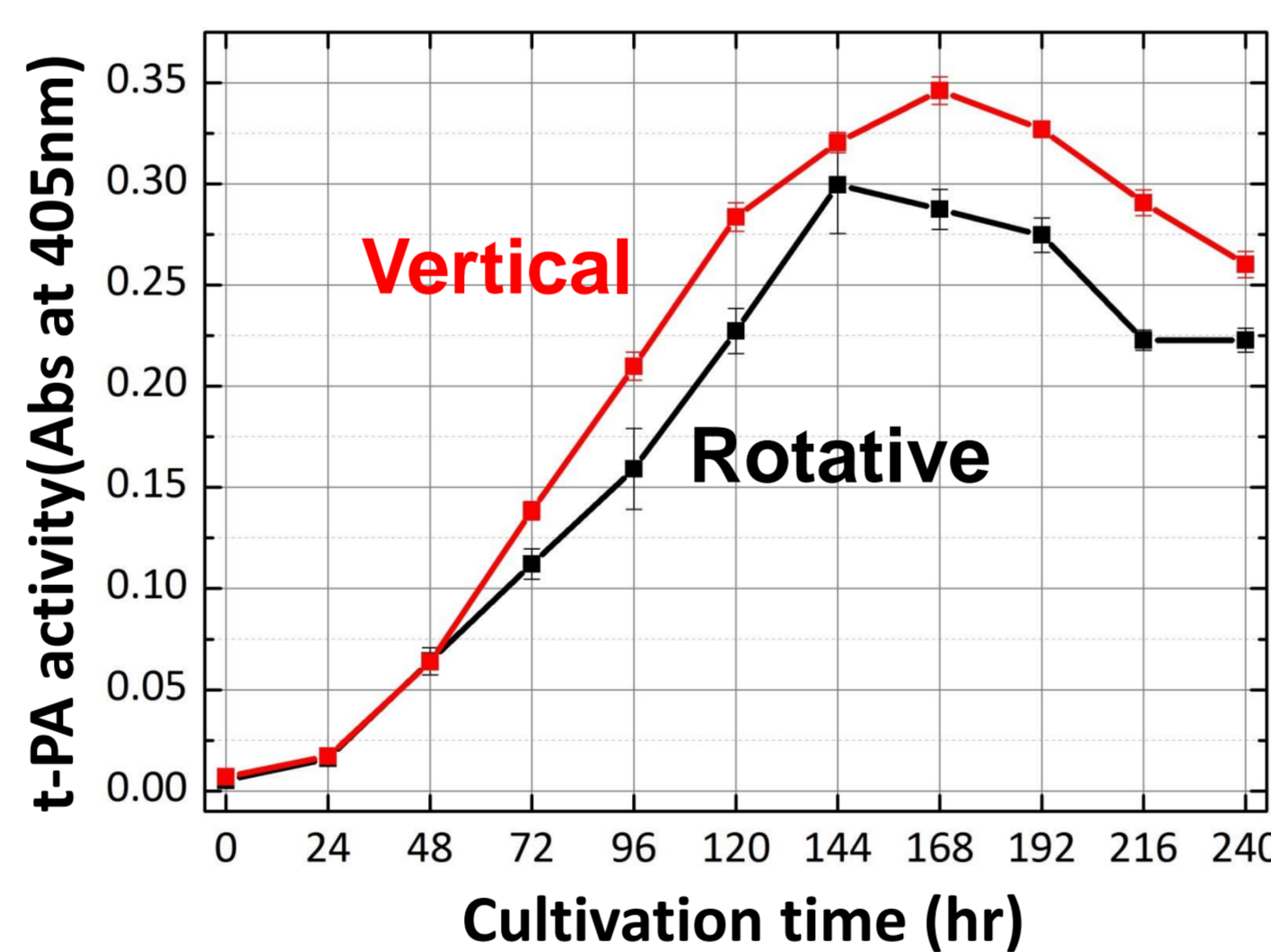


Fig.5 Production of tPA by CHO1-15<sub>500</sub> cells

The Vertical motion type can maintain the viable cell rate highly at stationary phase. Furthermore, this type is suitable for effective production of target protein.

Vertical (VerSus)



Rotative (EE)

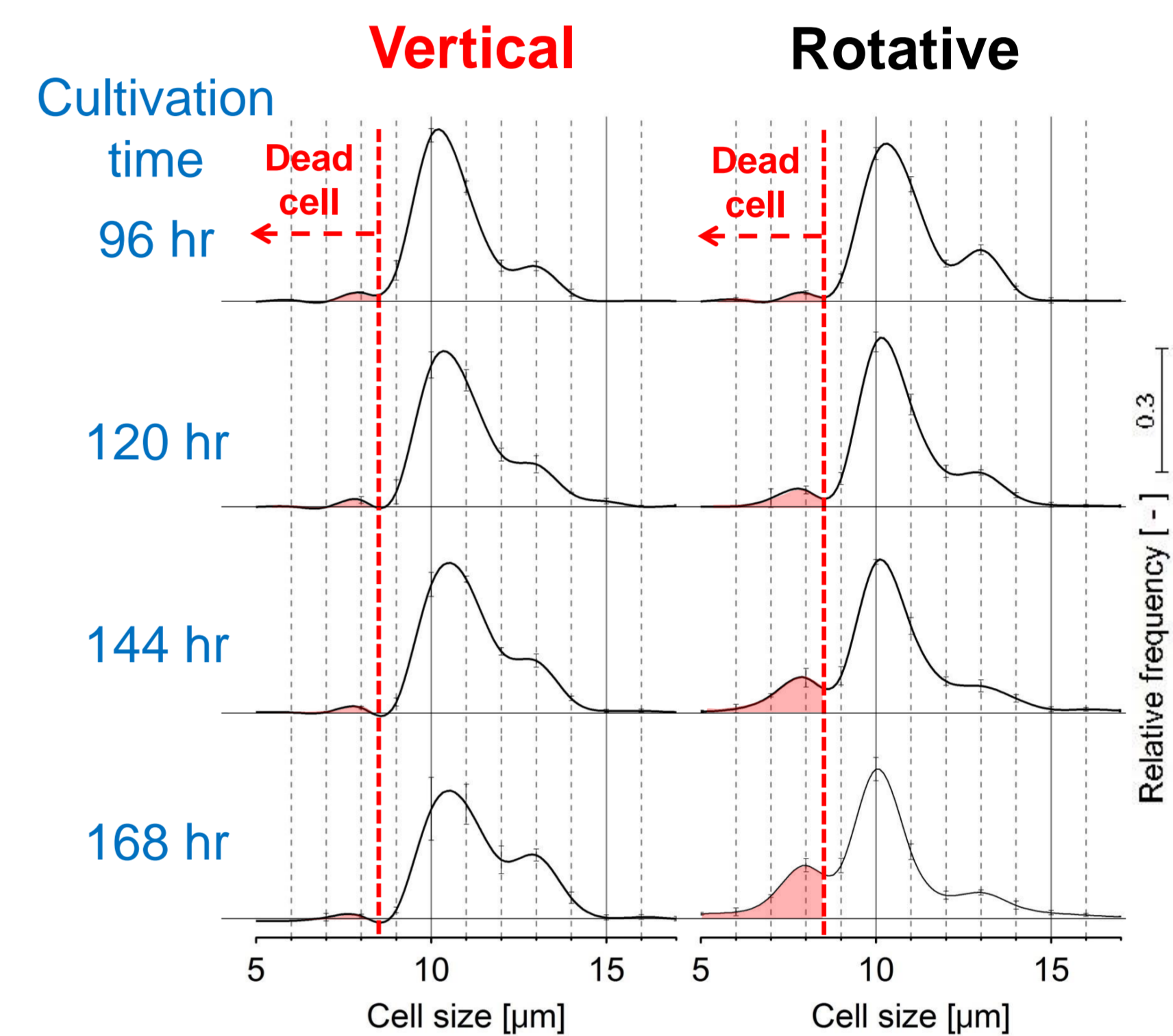
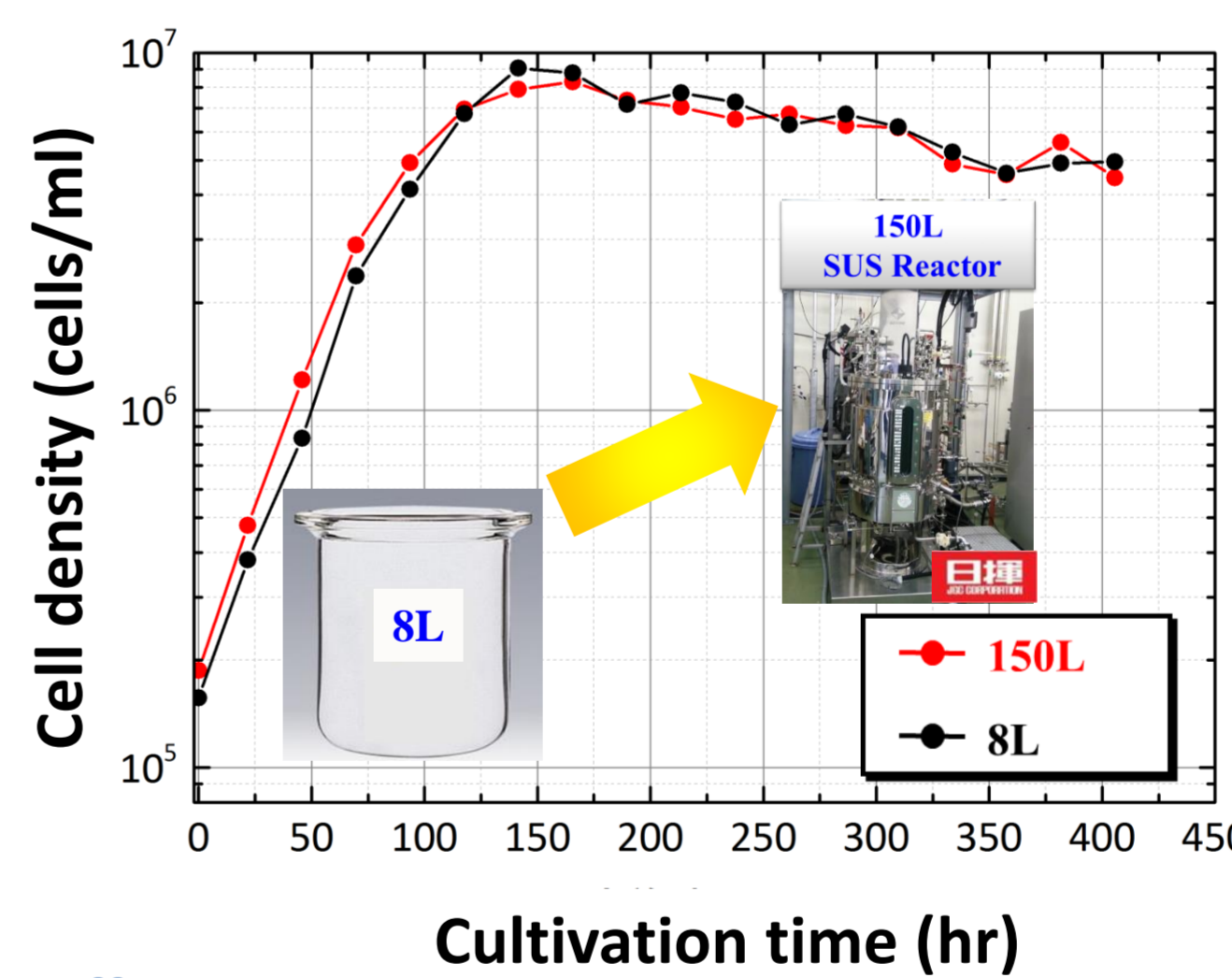


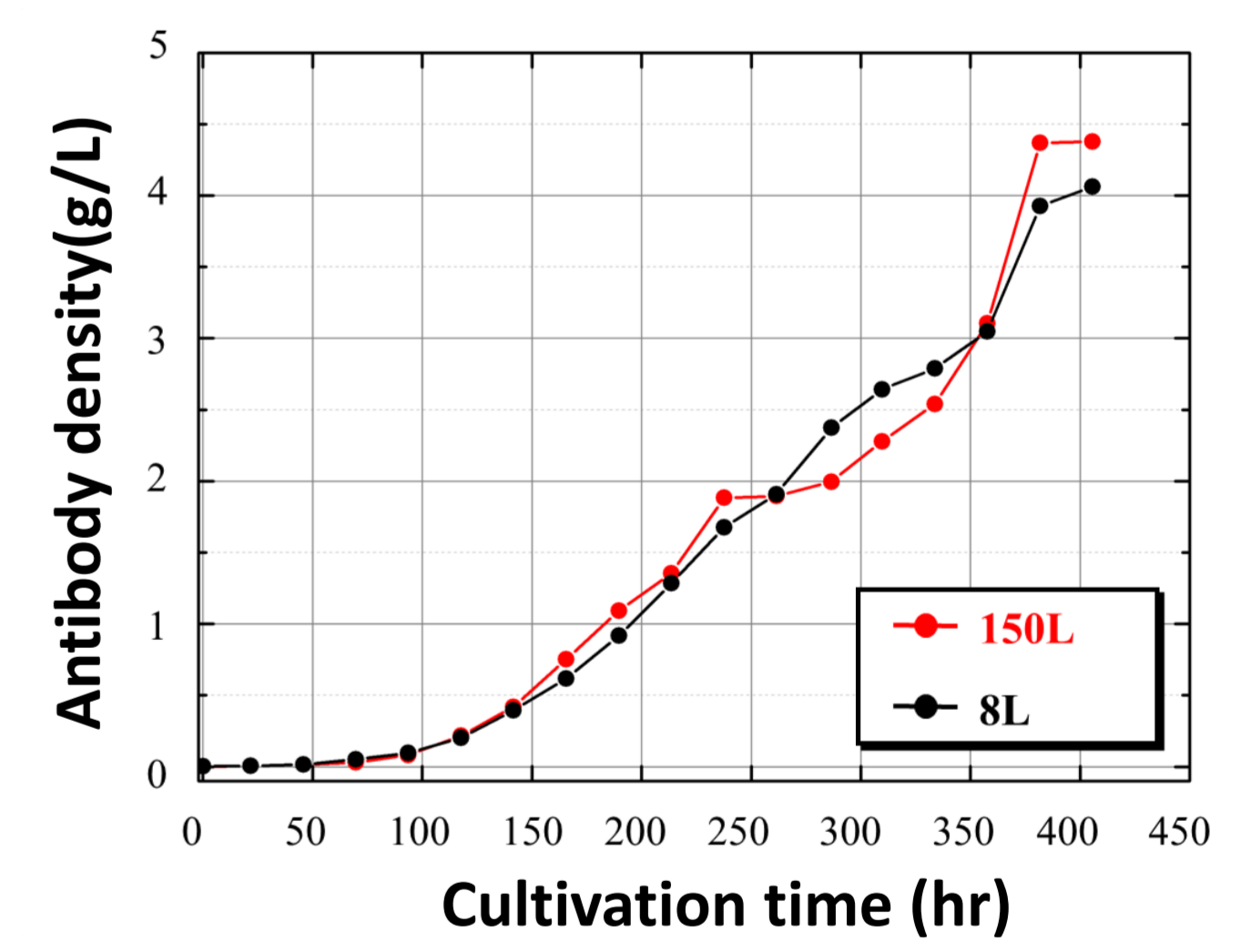
Fig.3 Change of cell size distribution

The Vertical motion type has few dead cells at stationary phase.

## Scale-up



Cultivation time (hr)



Cultivation time (hr)

It is confirmed that scale-up is possible to make the assumed scale-up factor fixation.

## Bioreactor for Microorganism Culture

In regards to produce enzyme and biopharmaceutical medicines efficiently

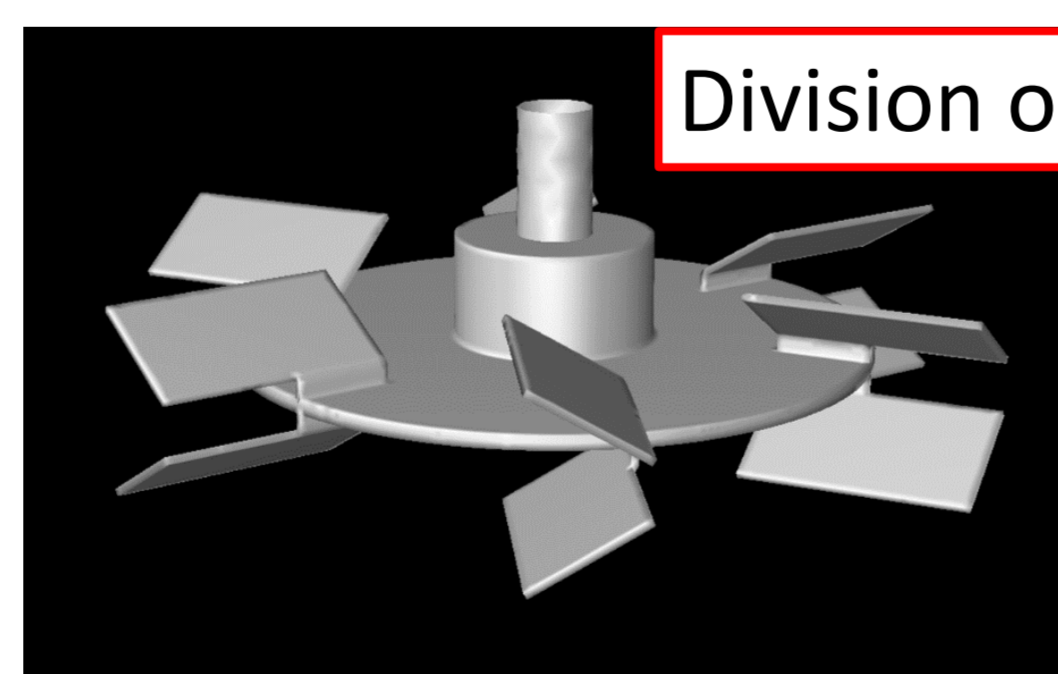
It is crucial to increase the production volume and maintain high cell density, as well.

Oxygen supply (High OTR)

In conventional Impeller type, If air flow rate is increased Accumulation of gas bubbles at the back surface of the blade

- Decrease liquid discharge performance
- Decrease gas bubbles break-up performance

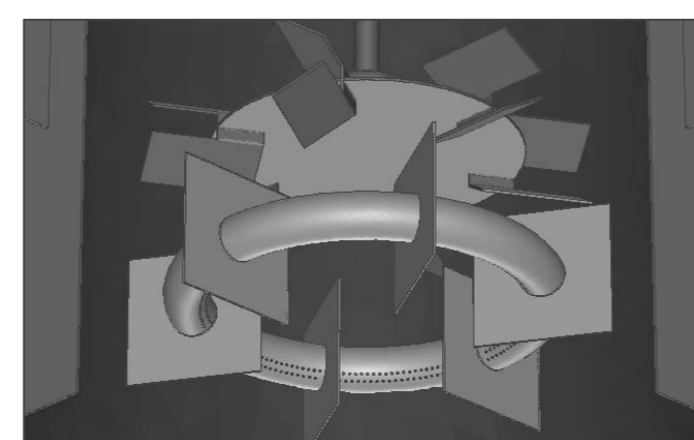
## Supermix® HS100 Turbine



Division of effect

Flow effect by the main blade. Shear and break-up effect is provided by flow gradient and pressure fluctuation at the discharged area.

## SATAKE Sparger



Increase the gradient of fluid flow by locating the stationary impeller blade to the ring.

## Comparison Result

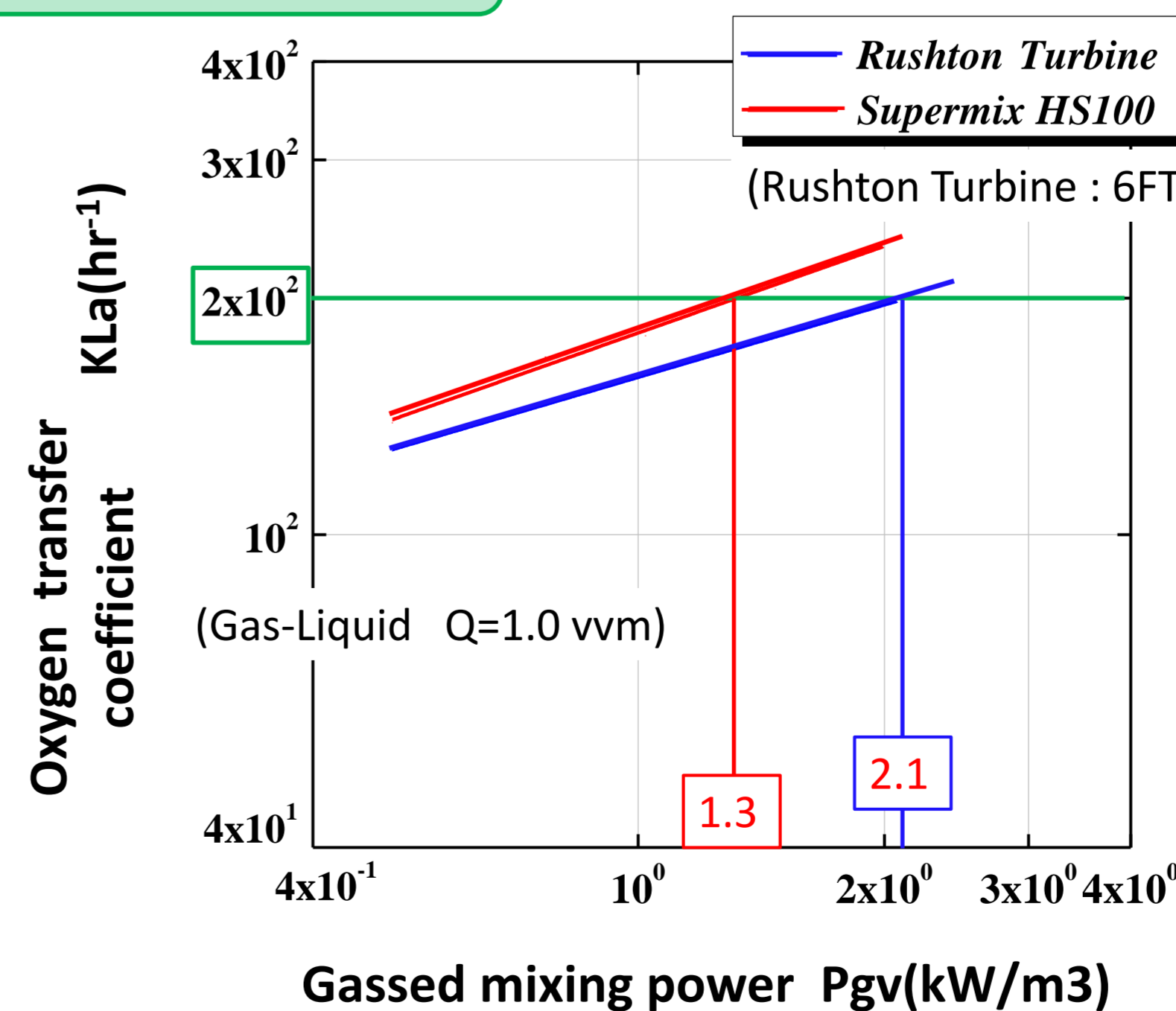


Fig.1 Comparison between HS100 and 6FT at KLa

"HS100" can considerably improve gas absorption Performance.

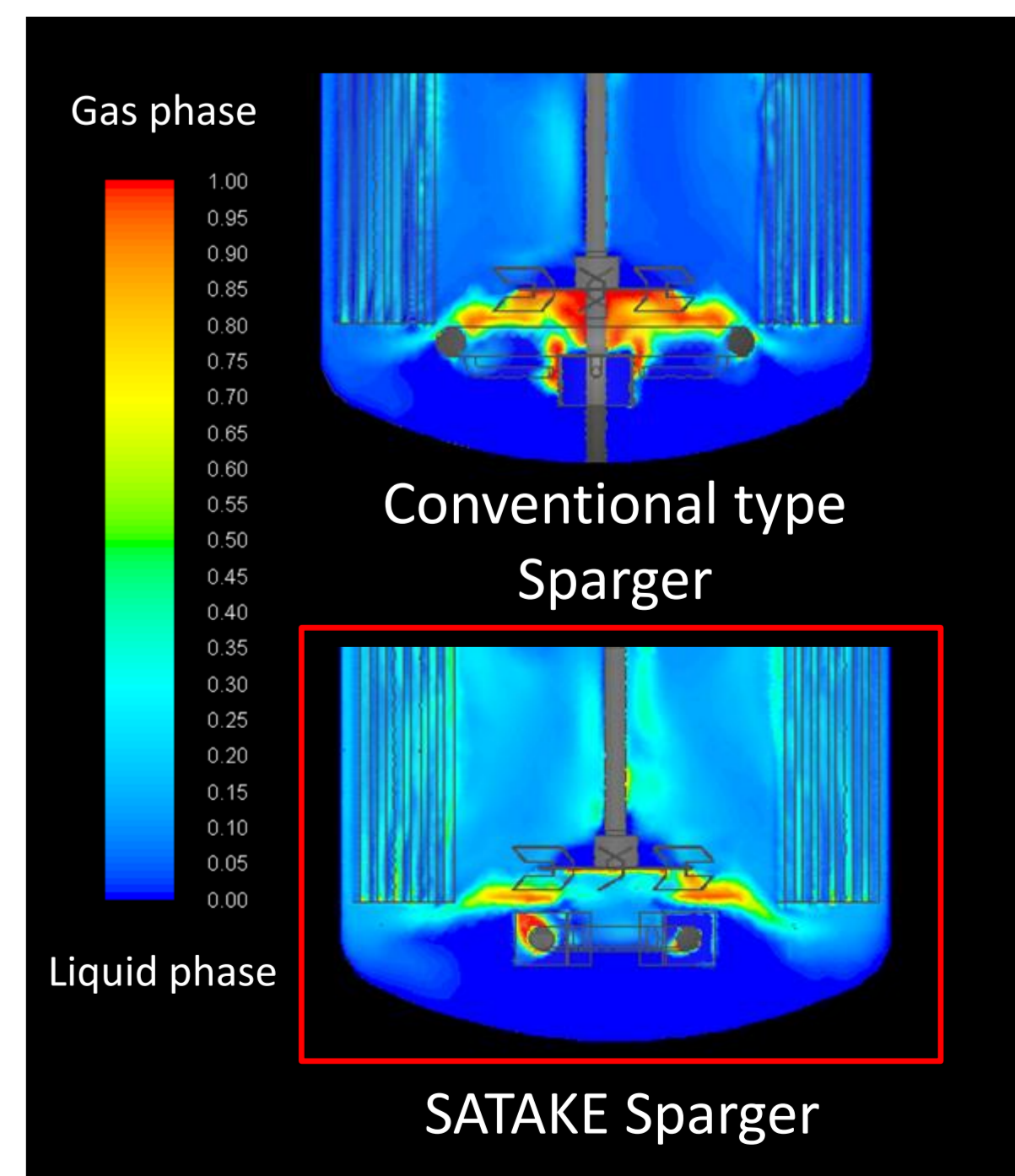


Fig.2 Comparison between Conventional type and SATAKE type at volume fraction of gas

"SATAKE Sparger" can disperse with gas uniformly