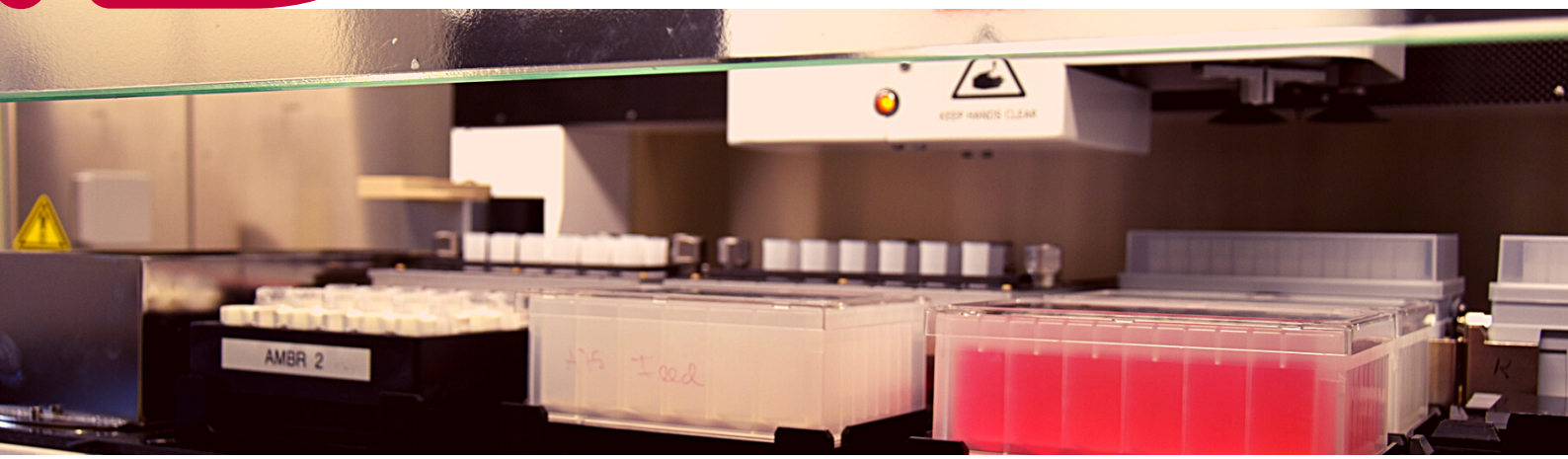
FyoniBio



Small Scale Perfusion Quick Facts

What's about?

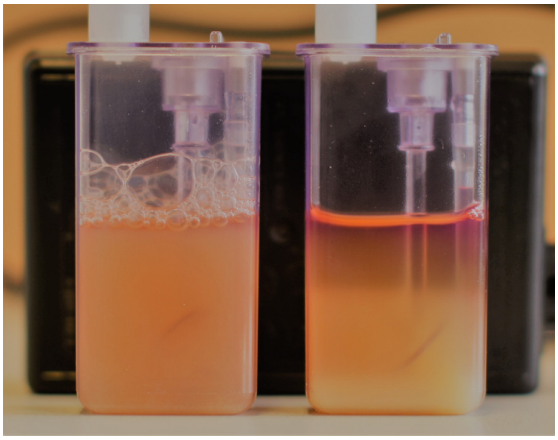
- Perfusion cultivation easily feasible from 300 mL culture volume up but not down. We show possibilites for downscaling

Why even needed?

- Downscaling saves resources in development

Which bioreactor system can be used?

- Mock perfusion in TubeSpin® or automated Ambr® 15 systems



COMPARING PERFUSION MIMIC IN DOWNSCALE SYSTEMS

What is perfusion and downscaling?

In a perfusion bioprocess cells are retained inside the bioreactor while product containing spent medium is removed continuously. To maintain steady conditions, fresh medium is replenished likewise continuously.
The need for downscaling, which includes reduction of cell culture volume and peripheral media, arises in process development, where multiple culture conditions, medium/feed combinations and further parameters are tested to get highest yields out of the process. Still, devices or methods to achieve high cell retention are not easily scaled down – mainly due to tubes which increase dead volume disproportionately.

PRINCIPAL THOUGHTS

Extensive work has shown that scaling down while changing the cultivation method from perfusion to batch, fed-batch or chemostat does not always predict outcome in a perfusion process correctly, putatively due to comparable lower cell counts.
The goal is therefore to reach high cell concentrations which can be achieved by replenishing medium often. To prevent losing cells when removing the spent medium, there are two main methods: separating cells from spent medium via sedimentation or centrifugation.

Figure: Ambr® 15 vessel before (left) and after (right) sedimentation in small scale mock perfusion, culture volume is 12 mL.

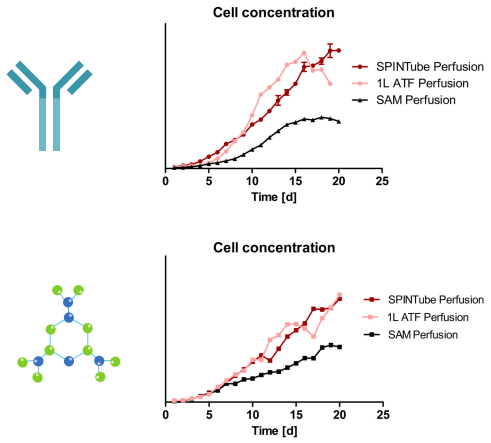
Process Development

TECHNICAL APPROACH

At FyoniBio, we use SAM [1], a fully automated mock perfusion approach in the Ambr® 15 – a microbioreactor system with a working volume of only about 10 mL. Cells are separated from spent medium by simply stopping stirring which leads to cell sedimentation and allows removal of a fraction of spent medium from top of the liquid. Programming the Ambr® to run this discontinuous process 4 times per day mimics a perfusion rate of 2 volumes per day in a continuous matter. This system allows to run up to 24 experiments in one run!
When only a few experiments are needed, centrifugation in TubeSpin® bioreactors proves to be a more simple approach. Here, cells are cultivated on a shaking platform in small tubes (working volume up to 20 mL) and centrifuged to replenish medium. One centrifugation step per day mimics a continuous perfusion rate of around 2 volumes per day.

[1] sedimentation in an automated microbioreactor

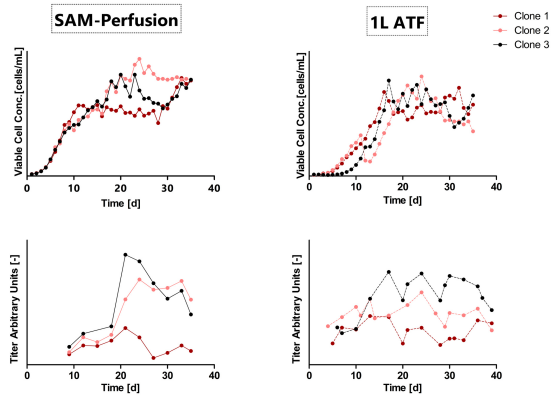
Comparison of 1L ATF vs small scale perfusion of GEX cell line



RELIABILITY

At FyoniBio, we successfully selected clones and medium compositions out of a 12 mL SAM approach which transferred greatly to the 1 L scale.
While comparison between media, process parameters, and clones proved to be great in the discussed systems and even post-translational modifications matched, absolute outcomes should be taken with a grain of sand. We showed that cell concentration and overall yields still differ between small and larger scales which makes downscaling a perfusion process a versatile tool, but it still needs to be complemented by experiments using continuous perfusion methods.

SAM perfusion in clone screening uncovers best productive clones



FyoniBio SERVICES

FyoniBio has many years of experience in clone development, bioprocess development and bioanalysis for the manufacturing of biopharmaceuticals. All steps are performed according to the current ICH, FDA and EMA guidelines in our ISO 9001 certified and GCLP compliant laboratories.

THE FyoniBio TEAM IS GLAD TO SUPPORT YOU THROUGHOUT YOUR PROJECTS.

FyoniBio
www.fyonibio.com
Robert-Roessle-Str. 10
13125 Berlin, Germany
+49 (0) 30 9489 2500
contact@fyonibio.com

02/2022