

A New Orbital-Mixed 4L-12L Single-Use Bioreactor for Cell Culture Scale-Up and Bulk Protein Production

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Small-batch therapeutic protein production requires predictable scale-up to meet bulk delivery timelines. Here, an orbital-shaken 4L-12L bioreactor is presented as an alternative to stirred vessels for batch production and scale-up. Orbital-shaken bioreactors offer a low shear, technically conservative approach which preserves mixing hydrodynamics and kLa's from µl scale to volumes as large as 2,500L. Cultivation success at well-plate, tube or flask scales easily translates to larger volumes. kLa's, mixing times and CHO-K1 application data are shown here for the SB10, a 4-12L working volume orbital-shaken disposable bioreactor.

SHAKING MACHINES AVAILABLE TO ROUTINELY SCALE FROM 50µL TO 2,500L

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Sensors may be added to any of these

A Kühner touch panel ISF1-XC (up to 5L)

B Kühner SB10-X (4L-12L)

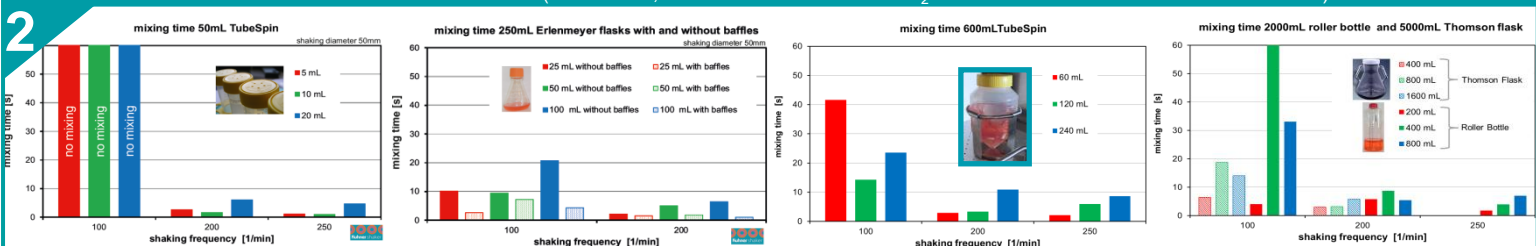
C Kühner SB50-X (10L-50L)

D Kühner SB200-X (40L-200L)

E Kühner SB2500-X (200L-2500L)

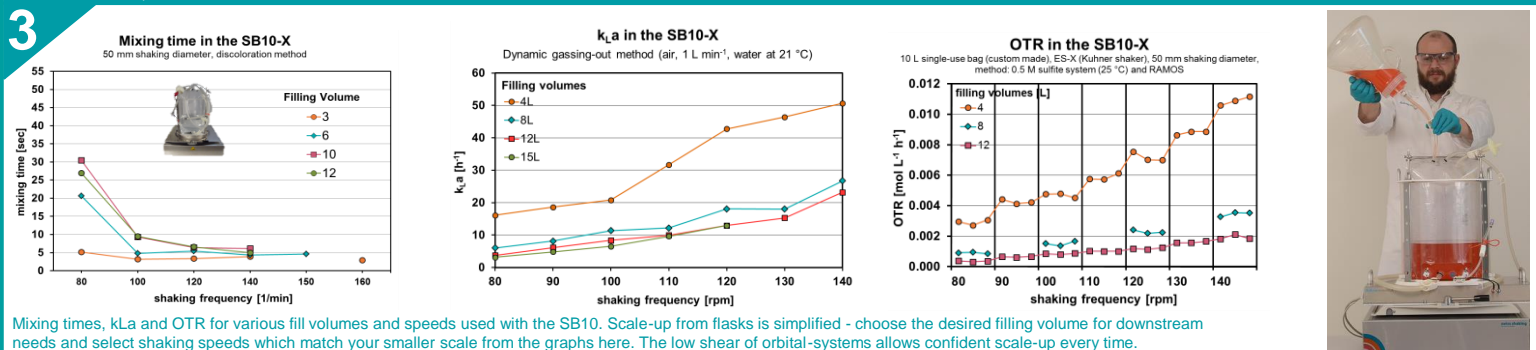
CO₂-controlled shakers (Kühner ISF1-XC (A)) handle cultures from 50ul to 5L. Known mixing times (Panel 2), kLa's and hydrodynamics are used to scale from well plates to tubes or flasks. Large orbital-shaken disposable bioreactors have working volumes of 4L-12L (SB10 – B), 10L-50L (SB50 – C), 40L-200L (SB200 – D) and 200L-2500L (SB2500 – E) and also have well-known mixing times and kLa's. Orbital-shaken single-use bioreactors offer straight-forward process scale-up. Panel 3 shows mixing times, kLa's and OTR's for the SB10-X. CHO-K1 cultivation comparison to a 1L stirred bioreactor is shown in panel 4.

MIXING TIME DATA FOR SMALL SCALE CULTURES (5ml – 2.5L, COMMONLY USED IN CO₂-CONTROLLED SHAKER INCUBATORS)



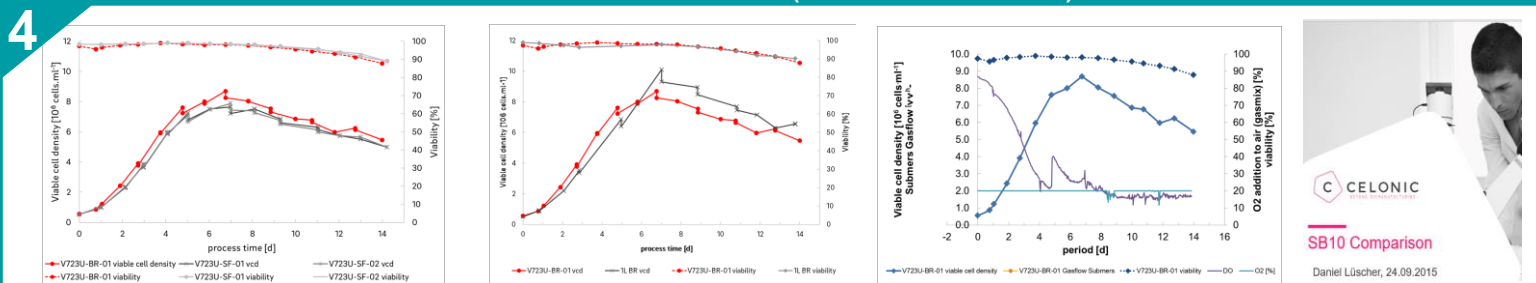
Mixing times for commonly used vessels: 50ml Tubespin®, 250ml Corning Flasks, 600ml Tubespin®, and 5L Thompson Optimum Growth® flasks. At smaller scales, mixing times of <10 seconds are accepted as sufficient. Though not reported here, mixing hydrodynamics are available for each of these scales and are conserved with the hydrodynamics of the larger scales shown below.

MIXING TIME, kLa and OTR for the SB10 BIOREACTOR AT VARIOUS FILLING VOLUMES



Mixing times, kLa and OTR for various fill volumes and speeds used with the SB10. Scale-up from flasks is simplified - choose the desired filling volume for downstream needs and select shaking speeds which match your smaller scale from the graphs here. The low shear of orbital-systems allows confident scale-up every time.

CULTIVATION OF CHO-K1 IN THE SB10-X AND COMPARISON TO A 1L STBR (DATA FROM CELONIC AG)



CHO-K1 Stable mAb expressing cell line from a fully established production process. Initial volume 6.5L, final volume 8.3L. 80-90rpm, headspace aeration at 0.5-0.75 slpm air with 5% CO₂, temp shift from 37C to 32C at day 5.

Conclusions:

- Mixing time data is available for commonly used small scale shaker-incubator vessels.
- Small scale mixing time data may be used to select shaking speeds and fill volumes of larger shaken Single Use Bioreactors.
- kLa data from the 10L, 50L, 200L and 2500L supports their use for CHO and low-OTR microbial cell culture production processes.

