Characterization of Xcellerex XDM and XDUO single-use mixers

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Introduction

Xcellerex single-use mixers (XDM and XDUO) are available in several different configurations and range in size from 50 to 2500 L. In common for all configurations is the robust mixing performance and ease of use. The mixers are designed for process development, commercial and clinical production of biopharmaceuticals, vaccines, and other biologics and they support upstream and downstream applications for preparation of buffer, media, product and intermediates, as well as other process fluids.

This performance guide contains mixing data and heating-cooling performance for XDM and XDUO mixers ranging in size from 50 to 500 L. XDM and XDUO mixers can be configured with the same basic functions and have the same basic dimensions. XDUO mixers, however, have more advanced pH and temperature control options including data-logging possibilities via the X-Station mobile control console. Further information regarding the features of XDM and XDUO mixers can be found in data files 29048367 and 29048366, respectively.

The information and experimental data found in this guide is essential for optimizing the mixing or heating-cooling protocol for bioprocess applications, and for effective scale-up.

Study outline

System setup

Mixers were equipped with their respective single-use mixer bags (XDM Plus bag ranging from 50 to 500 L) and the Xcellerex temperature probe. For the liquid-liquid mixing and the heating-cooling tests, a temperature control unit (TCU) was used (PolyScience: 3 kW for XDM 50 and XDM/XDUO 100; and 9 kW for XDM/XDUO 200 and XDM/XDUO 500). External pH (ProMinent), temperature (Ahlborn) and conductivity (Ahlborn) probes were connected to a data logger (Ahlborn) for data recording.

Table 1. The tested volumes for each mixer

Mixer size[1]	Minimum volume (L)	Nominal volume (L)
XDM 50	17	50
XDM/XDUO 100	30	100
XDM/XDUO 200	44	200
XDM/XDUO 500	110	500

[1] XDM/XDUO 1000 mixer characterization has not yet been performed. Details for the characterization of the XDUO 2500 are found in data file 29153543.

Heating-cooling study

The temperature range conditions chosen in the heating-cooling characterization of XDM/XDUO mixers were selected to represent the wide range of applications in modern bioprocessing.

The mixer bag was filled with 6 g/L NaCl in purified water to the nominal volume. During testing, the stirrer rate was constant at 125 rpm in counterclockwise (CCW) stirrer direction. The heating-cooling properties were assessed by calculating the time to reach 95% of the temperature step change (t_{95}), of four different temperature intervals: 5°C to 20°C; 20°C to 37°C; 37°C to 20°C; and: 20°C to 5°C. The temperature setting on the TCU was controlled manually by setting the temperature to 10°C above/below the intended set point and adjusting it to the set point when 95% of the step change had been reached. If using an XDUO mixer connected to an X-Station mobile control console, automatic temperature control with PID-regulation is possible. However, for the results to be applicable for both XDM and XDUO mixers, a manual approach was used in this case.

Liquid-liquid mixing study

Single-use mixers from GE's Life Sciences business allow for reduced working volumes in a wide range of bioprocess applications. To demonstrate this, a liquid-liquid mixing study was therefore performed to demonstrate the efficiency of the mixing characteristics at minimum and nominal volumes. Different liquid viscosities were also tested to mimic the range of viscosities encountered in bioprocessing.

The mixer bag was filled with liquid to the volume to be tested (minimum and nominal volumes, Table 1). For the tests at 1 cP, purified water with 0.1 M NaCl was used as liquid. Sucrose and NaCl dissolved in purified water was used to generate a liquid with a viscosity of 20 cP and a NaCl concentration of 0.1 M. The stirrer was set to CCW stirring at 175 rpm. Temperature was set to 20°C. For pH change induction, dilute acid (0.2 M HCl in purified water or 20 cP sucrose) was added at a ratio of 1:2667 for 1 cP and 1:1000 for 20 cP of the liquid volume in the mixer. For accurate pH mapping and mixing time measurement, nine probes were positioned strategically in the mixer bag (Fig 1). The probe distribution was arranged to cover all areas where poor mixing could be expected to occur. The number of electrodes was reduced as the liquid surface was lowered to the minimum volume. Mixing time was assessed by calculating the time to reach 95% of the pH step change (t_{m95}), Figure 2.

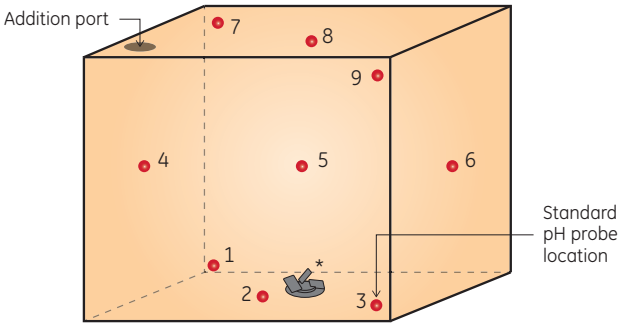

Fig 1. Distribution of the nine pH probes (red points) in the XDM/XDUO mixers. *The impeller assembly is welded to the bag. The impeller shown is for XDM/XDUO 100, 200, and 500. The equivalent impeller for XDM 50 is not shown.

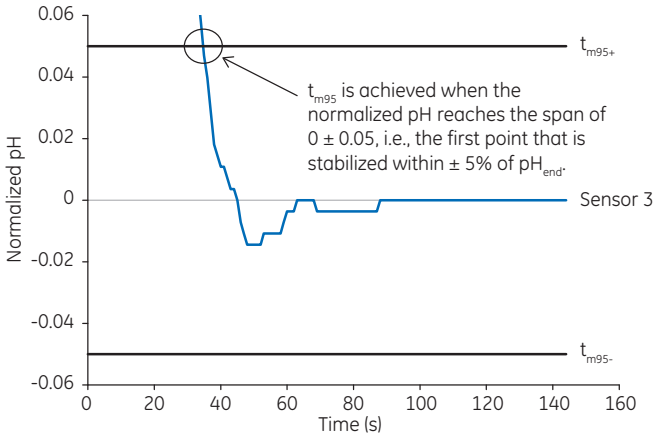

Fig 2. An example of t_{m95} determination. The graph shows normalized pH data from one sensor. The black lines indicate the interval where t_{m95} is achieved.

Solid-liquid mixing study

Solid-liquid mixing was tested on XDM 50 and XDM/XDUO 200.

PBS

The mixer was filled with water to the tested volume, minimum and nominal. The stirrer was set to 100 rpm for the minimum volume and 200 rpm for the nominal volume. The temperature of the liquid was 20°C. Salts to produce a 20 mM phosphate-buffered saline (PBS) buffer with 150 mM NaCl (pH 7.4) were added through the funnel mounted on top of the mixer bag whilst stirring in clockwise (CW) mode. Conductivity was measured and the mixing time was assessed by calculating t_{m95} on the conductivity step change. The conductivity probe was placed in position 9 (Fig 1).

HyClone™ HyCell™ CHO

The medium was prepared according to the medium rehydration protocol (see data file 29128610), hence the medium powder was added to purified water at 90% of the final volume. For XDM 50, this was 17 L (minimum volume) and 45 L (90% of nominal volume), respectively. For XDM/XDUO 200, the volumes were 44 L (minimum volume) and 180 L (90% of nominal volume), respectively. These volumes were chosen to display the minimum and maximum volume of medium that is possible to produce in each mixer. The stirrer was set to 100 rpm for the minimum volume and 200 rpm for the nominal volume. The temperature of the liquid was 20°C. HyCell CHO powder medium was added using a single-use powder bag whilst stirring in CCW mode. Conductivity was measured and the mixing time was assessed by calculating t_{m95} on the conductivity step change. The conductivity probe was placed in position 9 (Fig 1).

Results

Rapid heating-cooling

Heating-cooling was tested at the nominal volume. An example of a heating curve from 5°C to 20°C is seen in Figure 3.

Heating from 5°C to 20°C and 20°C to 37°C was generally achieved within 2 h for all mixer sizes. Cooling from 37°C to 20°C and 20°C to 5°C was achieved within 2 h except for XDM/XDUO 500, where the cooling times were 2.8 and 3.8 h, respectively.

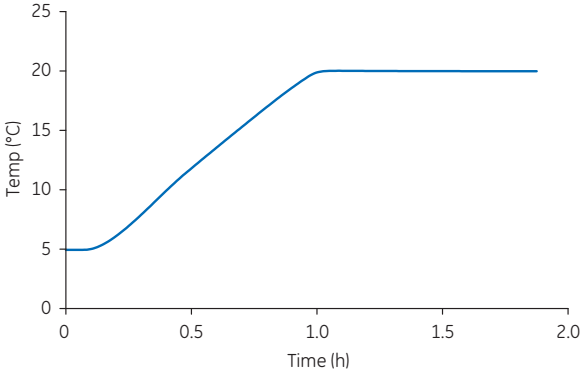

Fig 3. An example of a temperature curve when heating from 5°C to 20°C, in this case XDM/XDUO 200 at 200 L.

The results for the whole range of mixers can be seen in Figure 4.

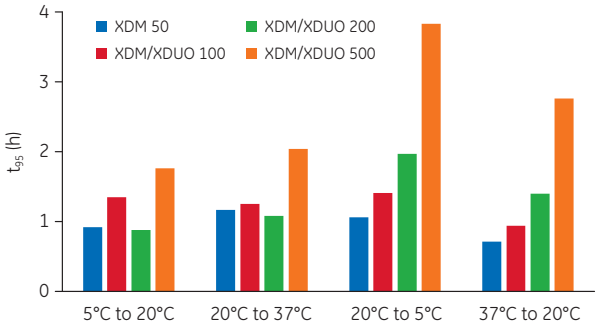

Fig 4. Results from the heating and cooling tests at the nominal volume. Stirrer speed = 125 rpm.

Effective liquid-liquid mixing

Liquid-liquid mixing was tested at minimum and nominal volumes and at two different viscosities; 1 cP and 20 cP. In Figures 5 to 8, results are shown from the probe position with the longest t_{m95} determined for each run, that is, the worst-case scenario. The pH data has been normalized to determine t_{m95}. Mixing was achieved within 30 s for all mixer sizes at the tested conditions.

The results of the liquid-liquid study are summarized and plotted as a bar chart in Figure 9.

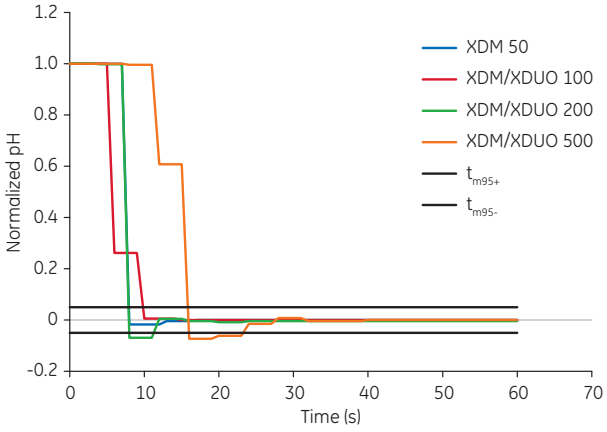

Fig 5. Normalized pH data from liquid-liquid mixing in XDM/XDUO mixers at 1 cP, 175 rpm, and nominal volume. The black lines indicate the range for t_{m95}.

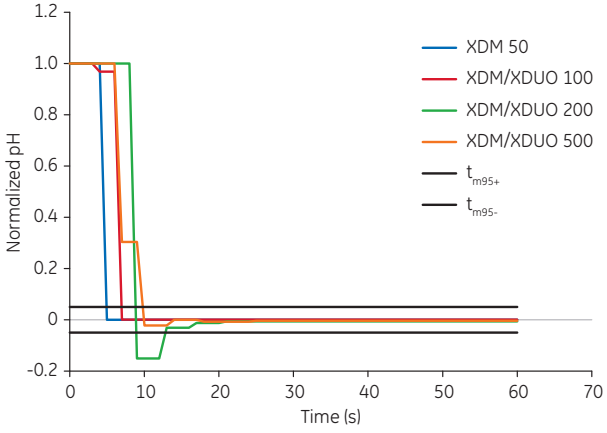

Fig 6. Normalized pH data from liquid-liquid mixing in XDM/XDUO mixers at 1 cP, 175 rpm, and minimum volume. The black lines indicate the range for t_{m95}.

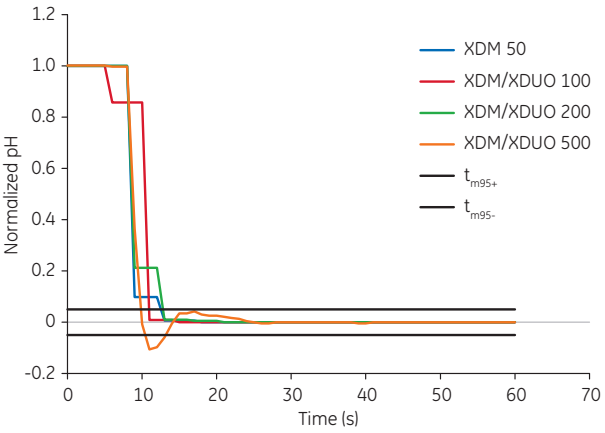

Fig 7. Normalized pH data from liquid-liquid mixing in XDM/XDUO mixers at 20 cP, 175 rpm, and nominal volume. The black lines indicate the range for t_{m95}.

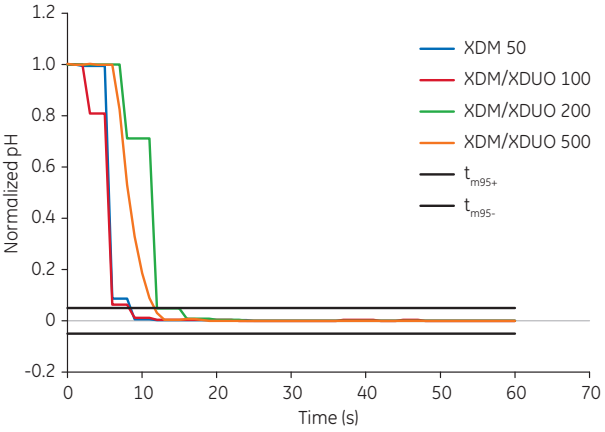

Fig 8. Normalized pH data from liquid-liquid mixing in XDM/XDUO mixers at 20 cP, 175 rpm, and minimum volume. The black lines indicate the range for t_{m95}.

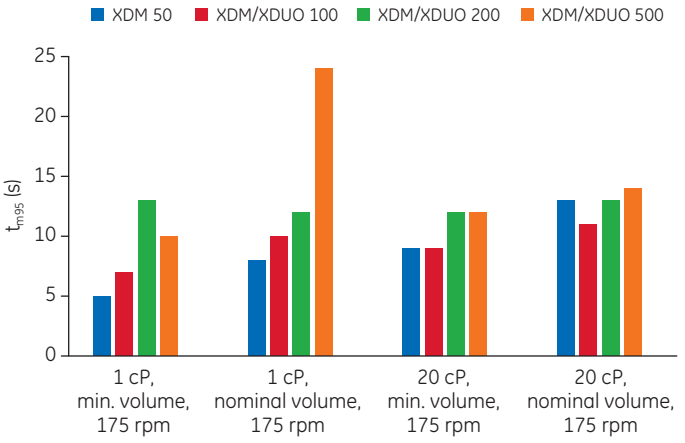

Fig 9. t_{m95} results from the liquid-liquid mixing study.

Solid-liquid mixing

PBS mixing in less than 2 min

Mixing times for PBS at minimum and nominal volumes in XDM 50 and XDM/XDUO 200 are given in Table 2. Stirrer rates of 100 and 200 rpm, which are representative of mixing speeds used in bioprocessing, were used at the minimum and nominal volumes, respectively. Normalized conductivity data for the PBS mixing for XDM 50 and XDM/XDUO 200 at minimum and nominal volume is shown in Figure 10.

t_{m95} for the minimum and nominal volumes of XDM/XDUO 200 and the nominal volume of XDM 50 was reached within 1 min. The t_{m95} for the minimum volume of XDM 50 was achieved within 2 min.

Table 2. Mixing times for PBS in XDM 50 and XDM/XDUO 200 at minimum and nominal volumes. Each test was performed in duplicate

Mixer size	Volume (L)	Stirrer rate (rpm)	Average t_{m95} (s)	Standard deviation (s)
XDM 50	17	100	113	2
XDM 50	50	200	17	1
XDM/XDUO 200	44	100	48.5	4.5
XDM/XDUO 200	200	200	34	3

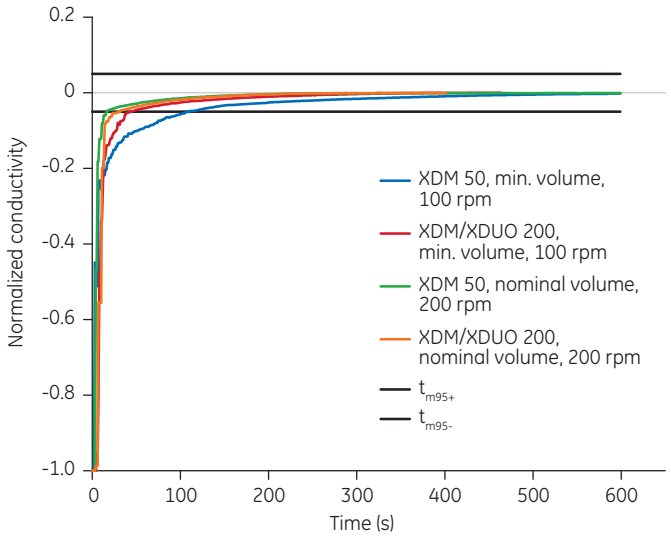

Fig 10. Normalized conductivity data from mixing of PBS in XDM 50 and XDM/XDUO 200. CW stirrer direction. The black lines indicate the range for t_{m95}. Only one of each replicate is shown.

HyCell CHO mixing in 4 min

Mixing times of HyCell CHO at minimum and 90% of the nominal volumes in XDM 50 and XDM/XDUO 200 are shown in Table 3. Stirrer rates of 100 and 200 rpm were used at the minimum and nominal volumes, respectively. The normalized conductivity data from the mixing is shown in Figure 11.

Conductivity t_{m95} was achieved in 3 min or faster for both the minimum and 90% of the nominal volumes on XDM/XDUO 200 and 90% of the nominal volume on XDM 50. The t_{m95} for the minimum volume on XDM 50 was achieved within 4 min.

Table 3. Solid-liquid mixing times for HyCell CHO in XDM 50 and XDM/XDUO 200 at 100 and 200 rpm stirring rates

Mixer size	Volume (L)	Stirrer rate (rpm)	t_{m95} (s)
XDM 50	17	100	216
XDM 50	45	200	180
XDM/XDUO 200	44	100	139
XDM/XDUO 200	180	200	181

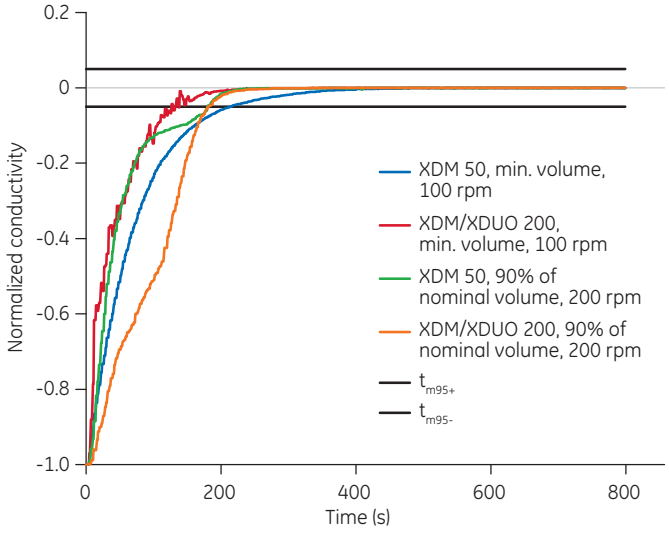

Fig 11. Normalized conductivity data for solid-liquid mixing of HyCell CHO medium in XDM 50 and XDM/XDUO 200. CCW stirrer direction. The black lines indicate the range for t_{m95}.

Conclusions

This characterization study demonstrates the performance of Xcellerex single-use mixers in the preparation and handling of solutions in multiple applications and conditions. Heating of liquid from 5°C to 20°C and 20°C to 37°C was generally achieved within 2 h; cooling from 37°C to 20°C and 20°C to 5°C was also achieved within 2 h for mixer sizes up to 200 L. Cooling times for XDM/XDUO 500 varied between approximately 3 and 4 h. Robust and consistent liquid-liquid mixing was achieved within 30 s for all mixer sizes and liquid viscosities tested. In the solid-liquid mixing, effective t_{m95} mixing of PBS was achieved within 2 min while HyCell CHO powder was mixed in under 4 min. The results of these studies should aid in the implementation of single-use mixers in new facilities and help in process optimization and scale-up.

Ordering information

Product	Product code
Xcellerex XDM-T Jacketed Stainless Steel Mixer (50 to 500 L volumes)	29054862
Xcellerex XDUO-T Jacketed Stainless Steel Mixer (100 to 500 L volumes)	29054863
XDM 50 Plus bag	888-0351-C
XDM 100 Plus bag	888-0154-C
XDM 200 Plus bag	888-0155-C
XDM 500 Plus bag	888-0156-C

For more information on Xcellerex XDM and XDUO mixing systems, please contact your local sales representative.

Related literature	
Application note: Characterization of Xcellerex XDM 50 single-use mixer	29237878
Application note: Characterization of Xcellerex XDM and XDUO 100 single-use mixers	29242783
Application note: Characterization of Xcellerex XDM and XDUO 200 single-use mixers	29242788
Application note. Characterization of Xcellerex XDM and XDUO 500 single-use mixers	29242789
Data file: Xcellerex XDM Mixer	29048367
Data file: Xcellerex XDUO Mixer	29048366
Data file: Xcellerex XDUO 2500 Mixer	29153543

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