Millipore®
Filtration, Separation
& Preparation

Application Note

Mobius® Power MIX: Scalability in Mixing

Executive Summary

The Mobius® Power MIX single-use systems provide an effective mixing platform for biopharmaceutical manufacturing in a range of sizes including 100, 200, 500, 1000 and 2000 L. Each unit is constructed based on the proven technology of our magnetically coupled NovAseptic® mixers, to deliver the high power necessary to incorporate buffer and media powders efficiently, while also showing capability for liquid-liquid mixing. Characterization of each size is complete, providing a comprehensive understanding of liquid-liquid mixing, and mixing of both sinking powders (buffers) and floating powders (media). Details of these studies can be found in individual notes for each size.[1] This document gives a summary of results, showing the scalability between sizes in the three main categories of mixing; liquid-liquid, sinking powders and floating powders.

Dimensional Scalability

Each of the Mobius® Power MIX units is designed with scalable dimensions; keeping the aspect ratio close to 1:1 at nominal volume, allowing for maximum volume at least 110% over nominal, providing sampling and real time monitoring at minimum volumes between 15-25%, with impellers and motors chosen to provide scalable mixing performance. **Table 1** summarizes the dimensional characteristics of each system.

Table 1. Key Dimensions in Mobius® Power MIX

Mixer	Min Sampling Volume (liters)	Max Volume (liters)	Diameter (inches)	Diameter (mm)	H/D (at nominal volume)	Impeller Diameter (mm)	Impeller Wing Height (mm)	Impeller Power Number	Motor Size	Max RPM
100	25	110	20.59	523	0.89	120	38.75	23	1/3 HP	380
200	40	220	25.75	654	0.91	120	38.75	23	1/3 HP	380
500	100	550	35.59	904	0.86	145	47	9	1/3 HP	375
1000	200	1100	43.50	1105	0.94	183	50	4	1/2 HP	380
2000	300	2200	53.50	1359	1.01	183	50	4	1/2 HP	380

Liquid-Liquid Mixing

In order to understand the capabilities of each Mobius® Power MIX unit, a comprehensive study of liquid-liquid mixing is performed. Mixing time at four volumes (25%, 50%, 75% and 100% of nominal) and four speeds (25%, 50%, 75% and 100% of maximum) are measured using the tracer method to track the change in conductivity when a small amount of highly concentrated salt solution is added to DI water. From these results, a mixing characterization map can be depicted, showing the relationships between mixing time and impeller speed, at key volumes within each vessel. These characterization maps are shown in **Figure 1**.

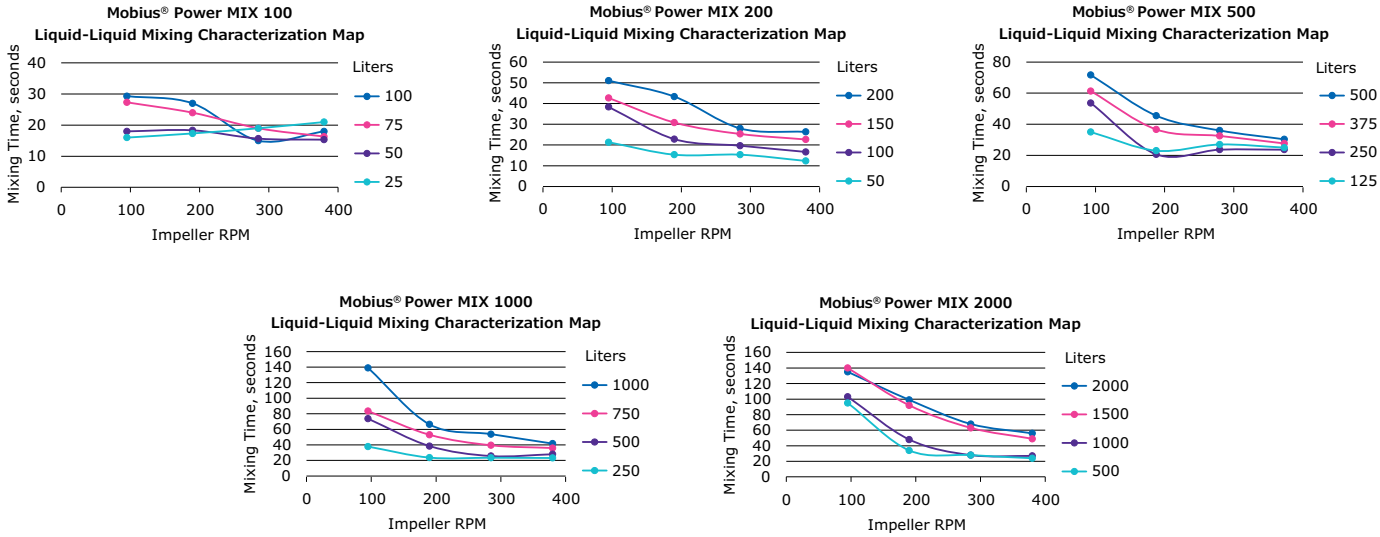

Figure 1. Liquid-Liquid Mixing Characterization Maps for Mobius® Power MIX.

Combining the characterization maps to show performance across the range of sizes is easily accomplished as shown in **Figure 2**.

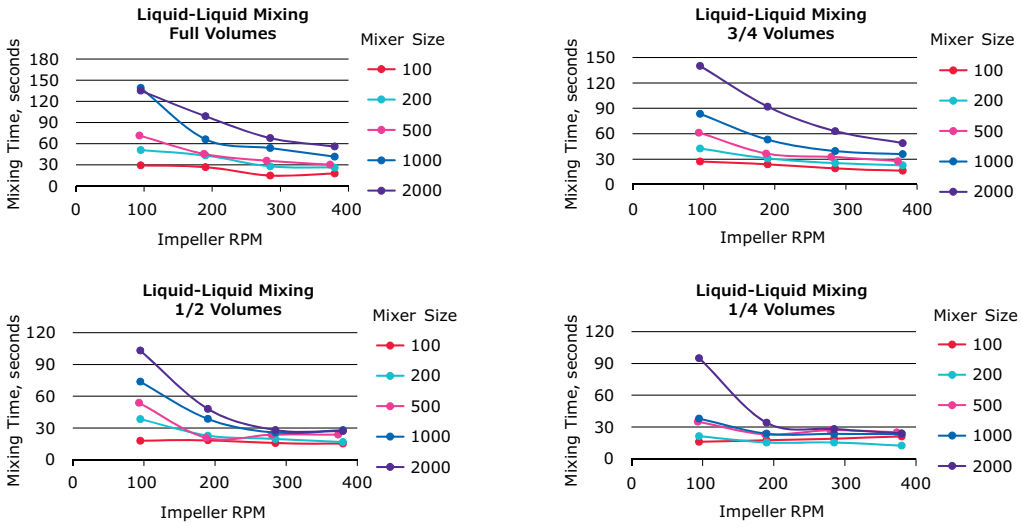

Figure 2. Liquid-Liquid Mixing Characterization grouped by relative volume in each vessel.

In order to compare performance across sizes, it is useful to normalize mixing time based on a consistent factor, such as power input per volume (Watts/m³). These characterization maps are shown in **Figure 3**.

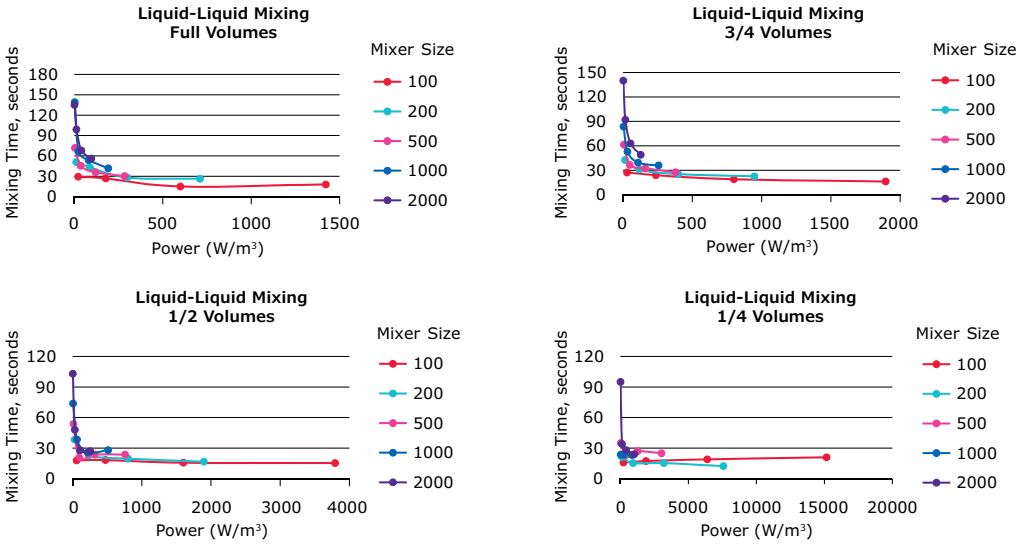

Figure 3. Liquid-Liquid Characterization at key volumes, normalized to power input.

Once normalized, these data can be combined, to provide an all-inclusive relationship between mixing time and power input, across all five Mobius® Power MIX systems, as shown in **Figure 4**.

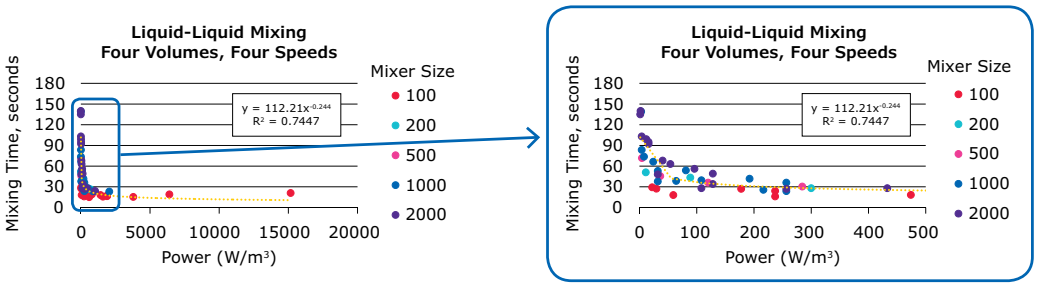

Figure 4. Relationship between Mixing Time and Power Input across five sizes of Mobius® Power MIX.

Focusing on maximum capability of the systems, a similar relationship between mixing time and power input is observed, translating to a linear relationship between mixing time and mixer volume, as shown in **Figure 5**.

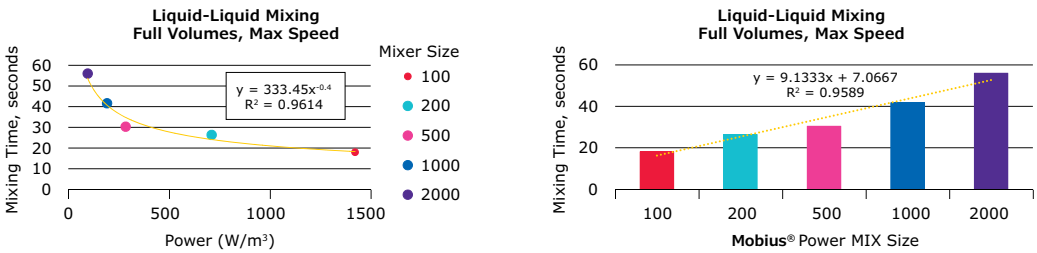

Figure 5. Scalability in maximum capability of liquid-liquid mixing in Mobius® Power MIX from 100 L to 2000 L.

Sinking Powder (Buffers) Mixing

Evaluation of buffer mixing in the Mobius® Power MIX systems is accomplished by mixing a 1X DPBS (Dulbecco's Phosphate Buffered Saline) solution in each size, according to typical process conditions; 90% starting liquid volume, at maximum impeller speed. Mixing time is determined when conductivity reaches a stable value (within +/- 1% variation). Conductivity traces and summary of mixing times are given in **Figure 6**.

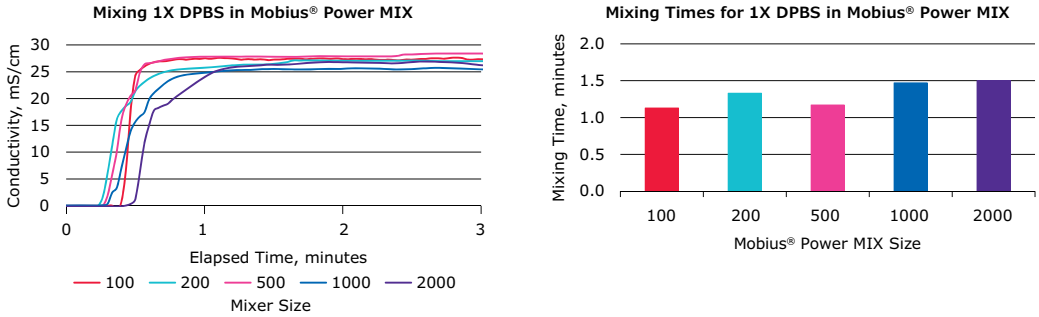

Figure 6. Mixing 1X DPBS in all sizes of Mobius® Power MIX complete in less than 2 minutes.

A 1X DPBS solution contains 9.86 g/L solute. To more fully differentiate the mixing performance in the Mobius® Power MIX vessels, a more challenging sinking powder test is performed; mixing 90 g/L NaCl powder into 80% volume of DI water. Mixing time is determined not solely by conductivity trace, but also through visual record and a measure of particles in solution with the Mettler-Toledo FBRM® (Focused Beam Reflectance Measurement) particle probe. Details of experimental setup and records of each trial are found in the Mobius® Power MIX Characterization Notes.[1] Summary of mixing time for each system is given in **Figure 7**. Sinking powder mixing generally follows the same trends as liquid-liquid mixing, when relating mixing time to power input. Once again, scaling to mixer size gives a nearly linear relationship between mixing time and mixer size. Additionally, comparing the sinking powder mixing time to the liquid-liquid mixing time (at 75% volume) confirms the scalability relationship.

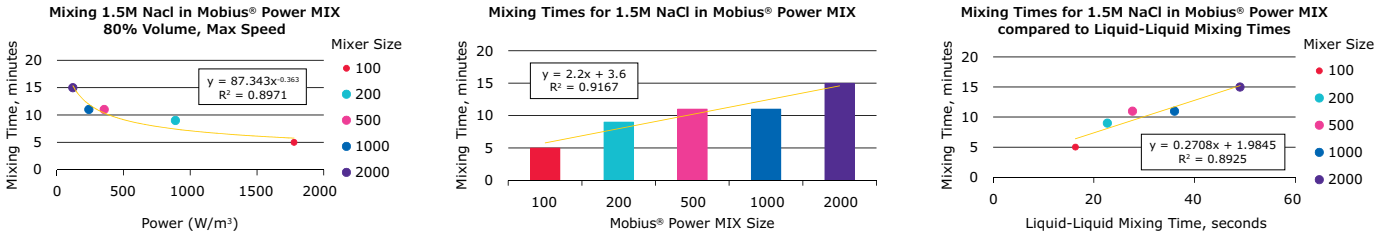

Figure 7. Scalability in mixing 1.5M NaCl in Mobius® Power MIX from 100 L to 2000 L.

Floating Powder (Media) Mixing

To demonstrate scalability of floating powder mixing, two sets of media mixing trials are performed in the Mobius® Power MIX; mixing DMEM (Dulbecco's Modified Eagle's Medium) powder into solution and mixing a chemically defined CHO medium (Custom MilliporeSigma CHO Medium). DMEM powder is one of the easier floating powders to mix, while the chemically defined media can be more difficult, including a pH adjustment step to bring particles into solution. Evaluation of media mixing in the Mobius® Power MIX systems is done according to manufacturers' recommended process conditions at 80% starting liquid volume, at maximum impeller speed. As with the sinking powder trials, mixing time is determined not solely by conductivity trace, but also through visual record and a measure of particles in solution with the FBRM® particle probe. Details of experimental setup and records of each trial are found in the Mobius® Power MIX Characterization Notes.[1]

Results for DMEM mixing are summarized in **Figure 8**. Using power input alone to scale floating powder mixing results in two distinct relationships; one for the 100/200/500 mixers and one for the 1000/2000. A secondary factor is needed to describe the mixing potential for floating powders. In mixing floating powders, the vortex is key to wetting out and breaking up the powder on the surface of the liquid. A factor relating vortex volume to total liquid volume can be used to rescale power input. Evidence of vortex size is shown in **Figure 9**. Based on the new factor of power input times relative vortex size, there is once again a predictable, scalable relationship across all volumes of Mobius® Power MIX.

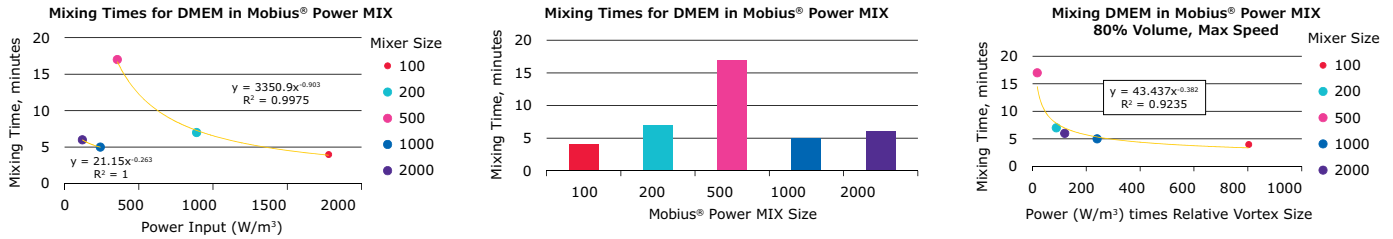

Figure 8. Scalability in mixing DMEM in Mobius® Power MIX from 100 L to 2000 L.

Figure 9. Vortex at 80% volume, maximum speed in Mobius® Power MIX from 100 L to 2000 L.

Results for mixing Custom MilliporeSigma CHO medium are shown in **Figure 10**. As with the DMEM, scalability based on power input alone shows two distinct relationships for 100/200/500 and 1000/2000. However, by using the relative vortex factor, there is a scalability trend through all sizes.

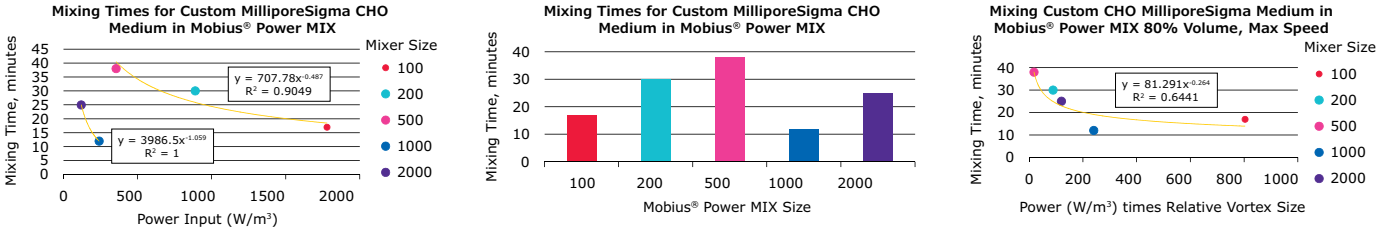

Figure 10. Scalability in mixing Custom MilliporeSigma CHO Medium in Mobius® Power MIX from 100 L to 2000 L.

Conclusion

The Mobius® Power MIX systems are designed for effective mixing of buffers and media in scales from 100 L to 2000 L. Starting with systems designed for scalability in liquid-liquid mixing, effective performance in buffer and media mixing has been confirmed. Results of trials with a typical buffer solution demonstrate mixing times of less than 2 minutes for all sizes. In a more difficult sinking powder trial, with concentration 10 times typical buffer solutions, mixing times for all sizes are still below 15 minutes, with predictable relationship between mixing time and mixer size. Mixing efficiency for media is highly dependent on media type, but even the most challenging media are mixed in less than 40 minutes, in all sizes. A model can be developed to show a scalable relationship between mixer size and mixing time for a variety of media powders. The Mobius® Power MIX systems have proven effective in meeting the needs for buffer and media preparation in a single-use system at scales from 100 L to 2000 L.

For more information on the Mobius® Power MIX, refer to Mobius® Power MIX Data Sheets and Specification Sheets.

References

1. Mobius® Power MIX 100 Mixing Characterization for Buffer and Media Preparation
   Mobius® Power MIX 200 Mixing Characterization for Buffer and Media Preparation
   Mobius® Power MIX 500 Mixing Characterization for Buffer and Media Preparation
   Mobius® Power MIX 1000 Mixing Characterization for Buffer and Media Preparation
   Mobius® Power MIX 2000 Mixing Characterization for Buffer and Media Preparation

To place an order or receive technical assistance

In the U.S. and Canada, call toll-free 1-800-645-5476

For other countries across Europe and the world, please visit: **EMDMillipore.com/offices**

For Technical Service, please visit: **EMDMillipore.com/techservice**

MilliporeSigma.com

Lit. No. AN5096EN00 Ver. 1.0
2017-03798
05/2017