

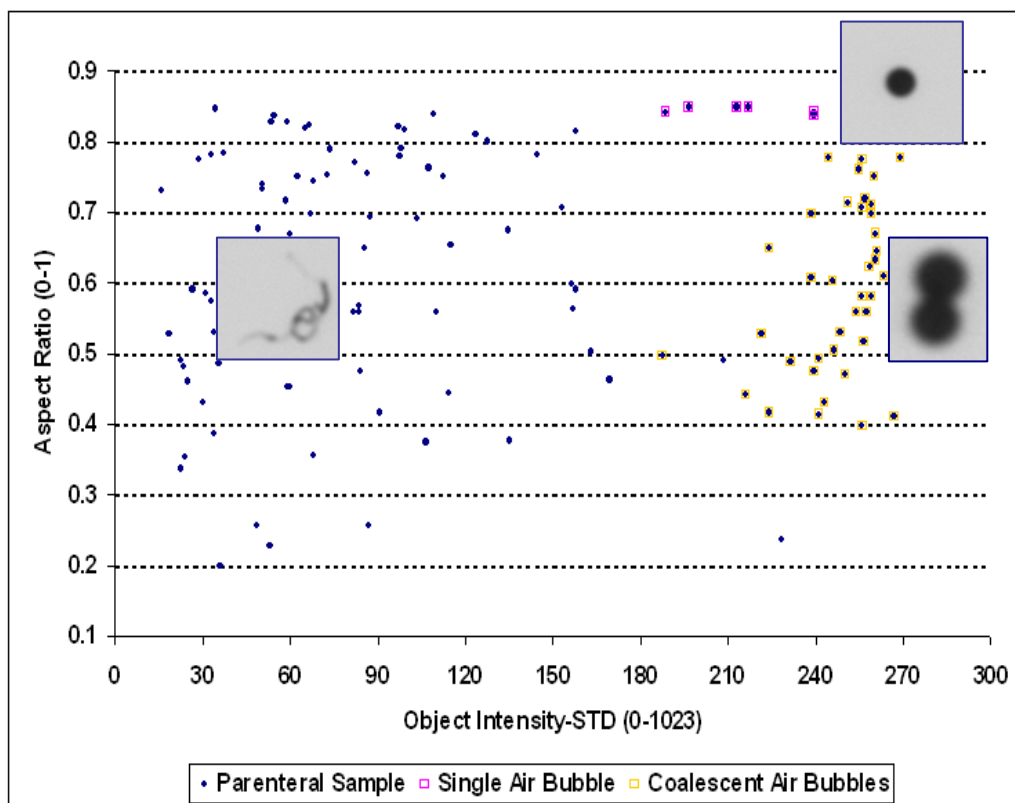
Detecting and Counting Air Bubbles Using MFI™

Bubbles can be introduced in pharmaceutical formulations as a result of handling or manufacturing processes. This is particularly the case with reconstituted lyophilized products. Regardless of how they are created, it is desirable to eliminate bubbles wherever possible (using sonication or other degassing techniques). However, it may be impractical or impossible to completely remove them. The remaining bubbles will then interfere with particle measurements since they cannot be reliably distinguished from real particles using conventional particle counting methods such as obscuration. The result is measurements which may indicate a higher number of particles in various size ranges than actually exist.

Micro-Flow Imaging (MFI) uses morphology-based software filters to identify and quantify bubbles. To demonstrate, a sample with high particle counts in the ≥ 10 and $\geq 25\mu\text{m}$ size ranges (as measured by obscuration) was analyzed with MFI. Using the MFI software, bubbles were visually identified and an appropriate software filter, based on aspect ratio, was created. This filter was then applied to the database representing the complete sample to isolate single bubbles from the total particle population.

A subsequent inspection of the filtered database revealed the presence of bubble clusters (coalescent air bubbles). An additional software filter, based on intensity, was then created and applied to the remaining images to isolate these clusters.

Using the morphology-based software filters, 98% of the 3796 particles/ml $\geq 10\mu\text{m}$ detected in the original sample were identified as air bubbles or bubble clusters with an error rate of 0.05%.



How Does MFI Work? MFI captures images of suspended particles in a fluid sample. Images are displayed on the system monitor in real-time and are analyzed to produce a particle database including count, size, transparency and shape parameters. Morphology-based software filters can be created and applied to this database to produce particle size distributions and isolate sub-populations. Native images are also stored for further investigation and analysis.