

# SonicMan

High Throughput Sonication System



## **SONICATION**

Sonication historically has had many general uses such as mixing, solubilization, driving chemical reactions, tissue homogenization, cell poration and lysis, shearing of biological macromolecules such as DNA, and many other uses like cleaning, plastic welding, etc.

Typically sonication in the life science industry has been performed in bath sonicators where water transfers the sonic energy from the transducer to the sample, or with probe sonicators where a metal probe immersed in the sample applies the sonic energy. However, bath sonication is limited in the amount of energy it transfers to the sample; probe sonication, while supplying substantial energy, is limited to one sample at a time. Other multi-probe sonicators have been manufactured, but these products have been designed for manual usage.

In today's laboratory where large numbers of compounds are stored in compound management systems, the need exists to apply sonication to high throughput processes used in drug discovery.

The **SonicMan high throughput sonication instrument** provides a platform to utilize sonic energy to accomplish high throughput solutions. Relying on a pinned lid placed on a microplate, the SonicMan provides simultaneous sonication of *all* wells of a 96, 384, or 1536-well (or custom formatted) plate. This tabletop instrument is ideal for scaling up to high throughput any application which uses a bath or single probe sonicator.

The user-friendly touchscreen interface with user-selectable program settings provides the reproducibility needed for a wide range of applications.

## **APPLICATIONS**

### **• Compound Resolubilization in Screening**

By sonicating precipitated samples just prior to liquid handling, those compounds which are capable of being dissolved will be driven back into solution, at least to the limit of their thermodynamic solubility.

### **• Compound Solubilization in Solubility Testing**

The SonicMan is an ideal adjunct to shake flask methods, as it provides a much faster method than shaking for driving compounds to the limit of their thermodynamic solubility.

### **• Small Volume Mixing**

Sonication provides a rapid mixing method which is independent of surface tension and wall effects in small wells.

### **• Bacterial and Mammalian Cell Lysis**

Sonication is a completely physicomachanical method of lysing cells, which can be performed in any buffer or medium. It can be fine-tuned for the cell type in question to provide just the right amount of energy to achieve lysis or release of a particular component, potentially resulting in cleaner extracts.

### **• DNA Shearing**

Sonication has been shown to break DNA into random small fragments.

### **• Tissue Homogenization and Disruption**

Sonication is an established method for homogenizing and disrupting tissues to release various components and can be done in any buffer, allowing cleaner extracts and homogenates to be produced.

### **• Potential Applications (in the process of being validated):**

Sonochemistry

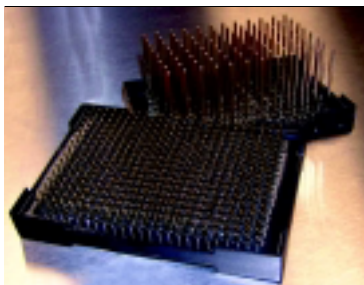
Sonoporation and loading of macromolecules

PMCA

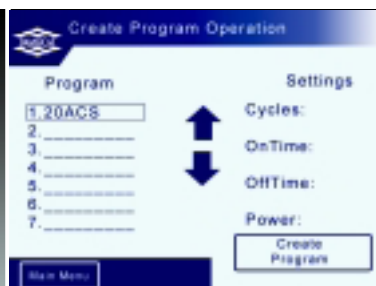


## **SONICMAN FEATURES**

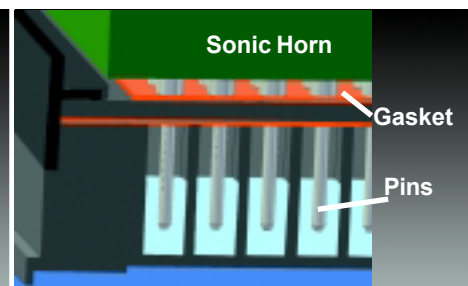
- Stand-alone or integrated bench-top instrument
- Interchangeable 96, 384, and 1536 format disposable pinned lids (custom labware upon request)
- Plate shuttle which allows for direct integration with pick and place robotics
- Touchscreen interface
- Variable power settings between 1 and 1,150 Watts
- Variable sonication time intervals from 0.1 to 20 seconds
- Gasketed pin lids to ensure sample integrity with no well-to-well cross contamination



Disposable 96 & 384 pinned lids



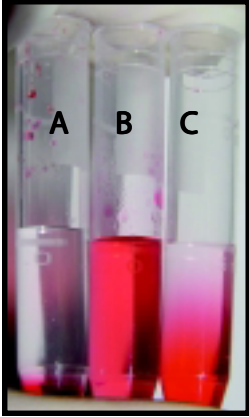
Touchscreen interface



Gasketed lid design ensures airtight seal during sonication to eliminate cross-contamination

## MEASUREMENT OF SONICATION-INDUCED MIXING

The SonicMan uses sonic energy to speed mixing in small volumes as well as to remove air bubbles trapped in wells. In low volume 384 or 1536 well plates, sample mixing is achieved in just a few seconds of sonication. The following experiments demonstrate the measurement and visualization of sonication-induced mixing:

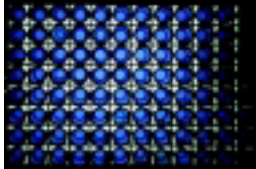


### Diffusion vs. Sonication

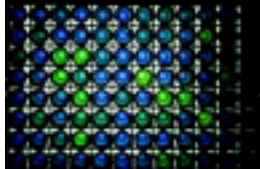
Simple experiment: 50uL of concentrated sucrose colored with red dye was placed in 1.5mL microtubes, allowed to dry to a solid film and then covered with 500uL of DI water (Tube A). Even in the presence of plate shaking for eight hours (Tube C) mixing is not complete. By contrast, the SonicMan achieves complete mixing in 10-20 seconds (Tube B).

### Measurement of Mixing

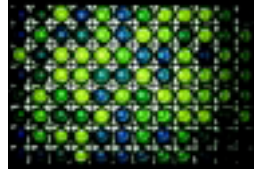
The evenness of mixing can be visualized in a 96-well plate (see series of figures below) using a two-component system, using a pH-sensitive dye (bromothymol blue, BTB) and selecting the starting pH and buffering capacity of the two components. The dye starts out in the blue form, but quantitatively converts to the yellow form on mixing. After 9 seconds of sonication, all but one well are completely mixed, and after 12 seconds, all wells are mixed.



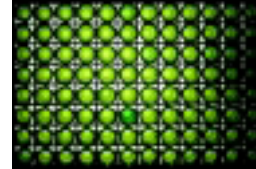
T=0 Seconds



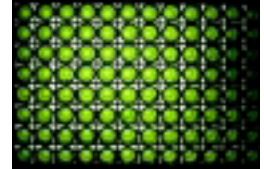
T=3 Seconds



T=6 Seconds

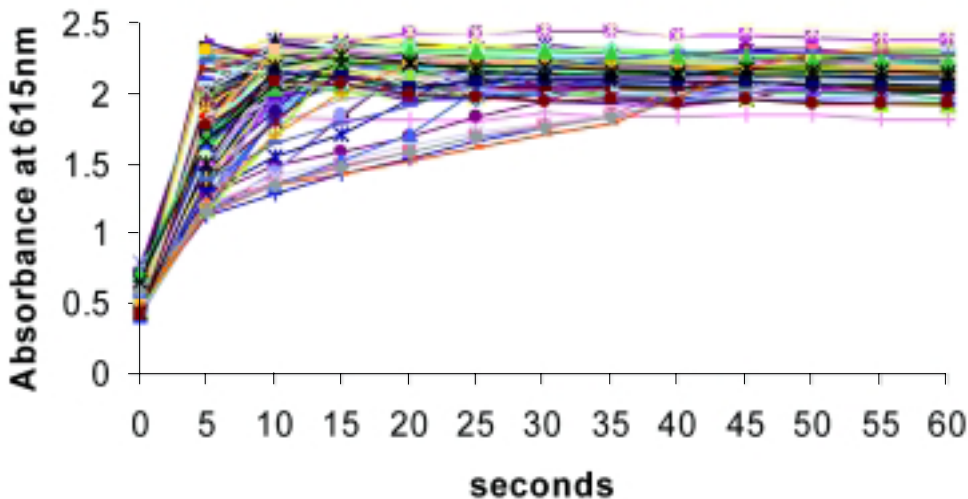


T=9 Seconds



T=12 Seconds

### Time Profile of Sonication-Induced Mixing



The figure to the left shows the time profile of the absorbance at 615nm (blue dye form) for a 384-well plate with 70 uL per well. 20uL of pH=5 buffer, 50% sucrose, BTB (yellow form) was overlain with 50uL of a pH=10 buffer. Upon sonication, 98% of the wells are fully mixed within 10 seconds from the onset of sonication with all wells being fully mixed within 40 seconds. Differences in final signal are due to errors in pipetting the 50% sucrose solution.



## ENHANCEMENT OF BIOASSAY RESULTS

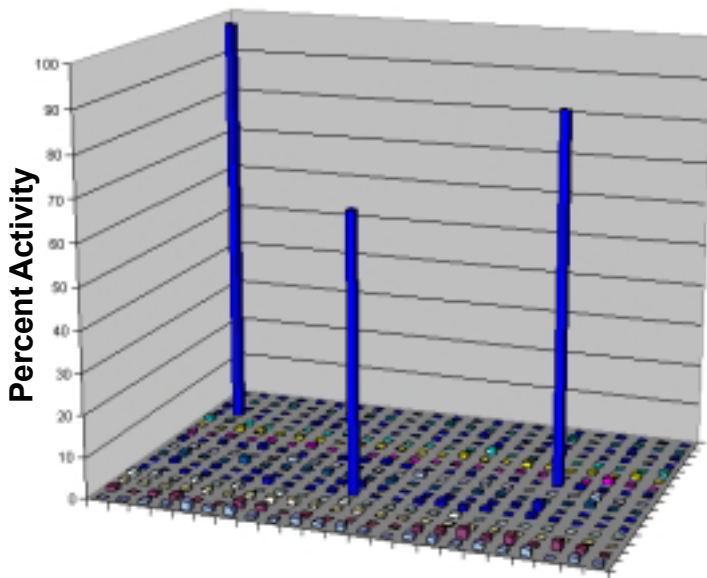
Data shows a 384-well plate pre and post-sonication. 384-well plate containing related compounds and tested in a biological assay.

Data provided courtesy of Aventis Pharmaceuticals, Bridgewater, NJ.

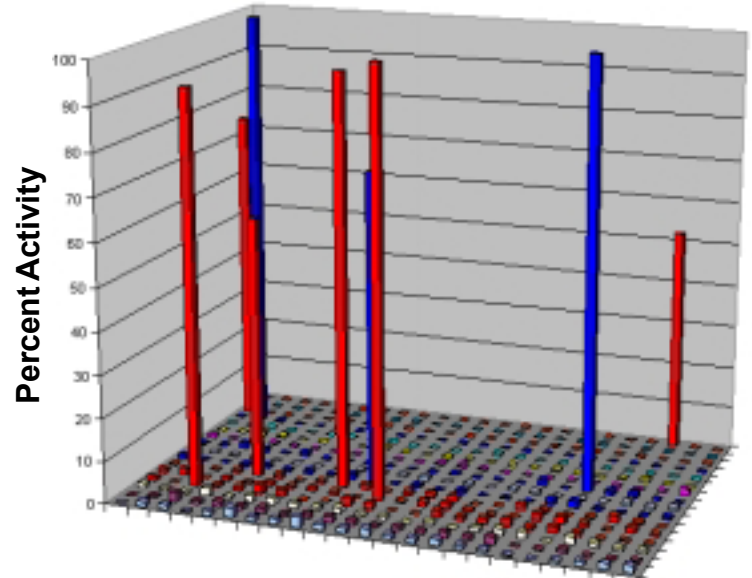
Compounds in **BLUE** show biological activity pre-sonication.

Compounds in **RED** show significant activity post-sonication with the **SonicMan**.

**Assay Results Without Sonication**



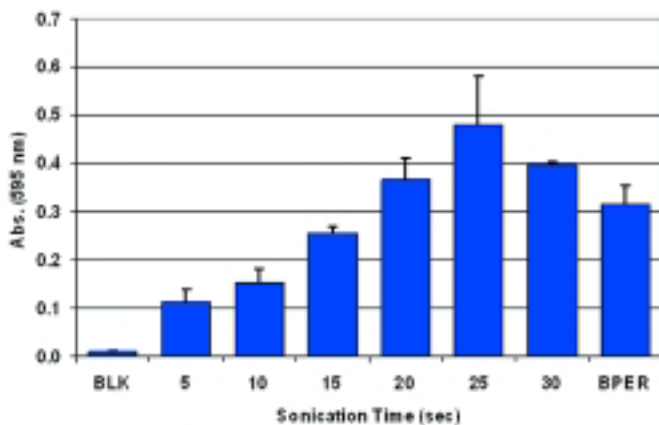
**Assay Results With Sonication**



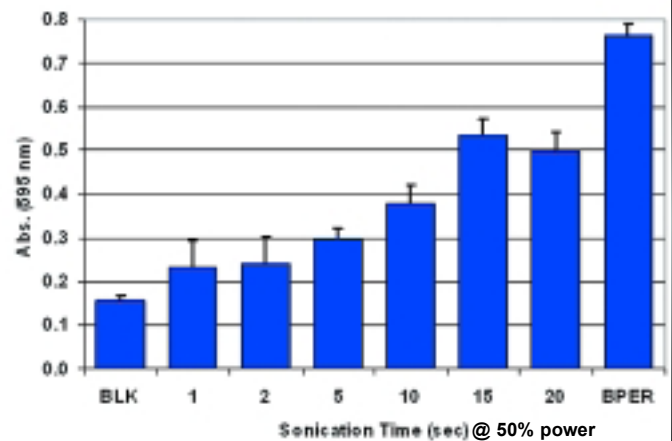
## BIOLOGICAL APPLICATIONS

The figures below show the effect of increasing sonication on suspended mammalian and bacterial cells as measured by the protein released into medium. In both cases, the amount of protein increases up to a limit which is consistent with the amount of protein released by a commercial protein release agent. Maximal protein release is accomplished in less than 25 seconds.

**Protein Released by Sonication of E Coli**

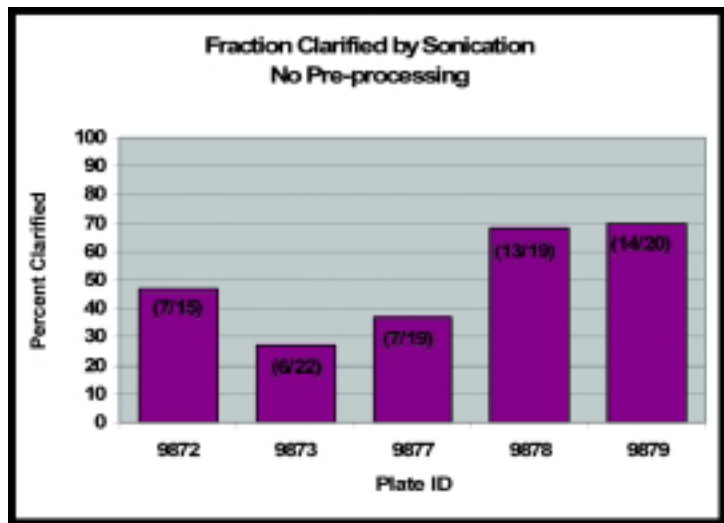


**Protein Released by Sonication of Mammalian Cells**



## ENHANCING SOLUBILIZATION

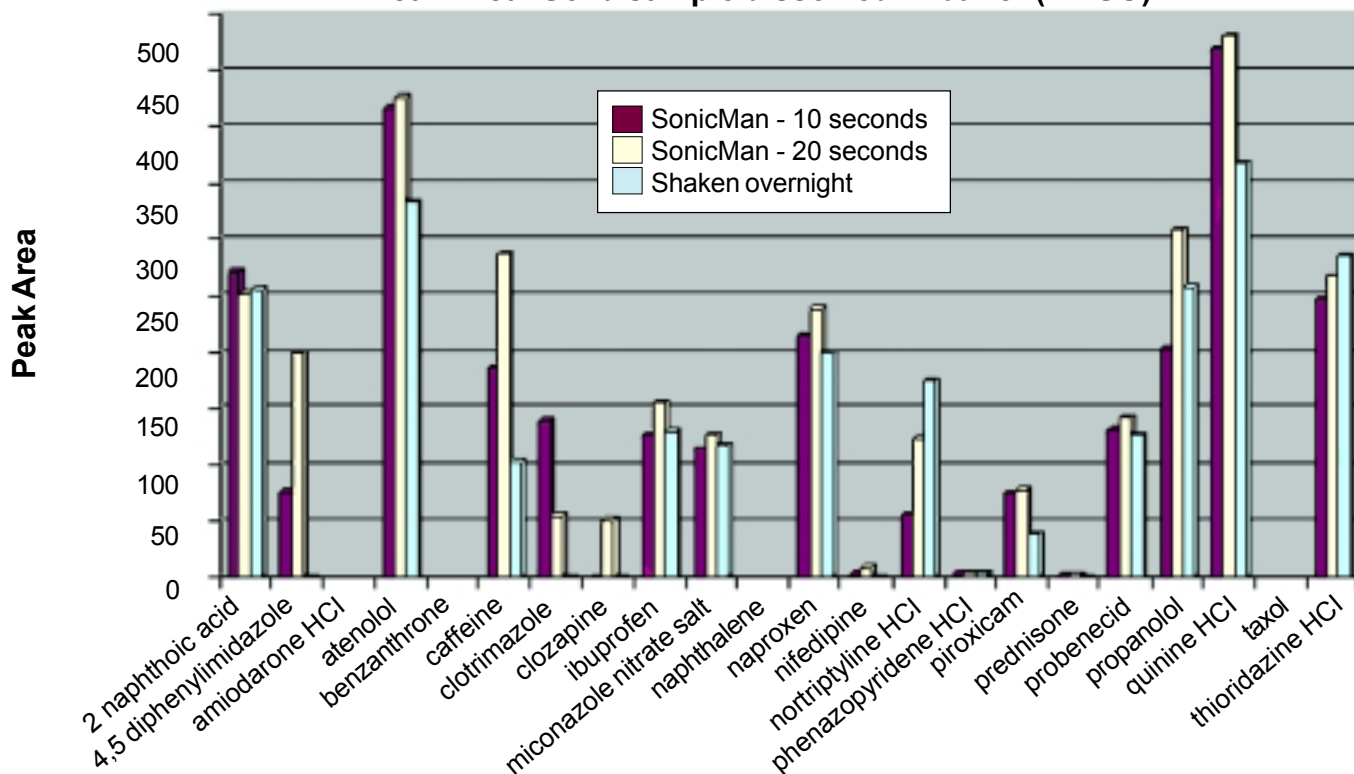
Dissolving compounds in DMSO prior to liquid handling is common practice in the setup of assays. An unknown but significant fraction of those compounds may not go into solution, or may go into solution only to precipitate out at a later time as a result of water pickup from multiple freeze-thaw cycles or extended time on the bench. Sonicating those samples just prior to liquid handling drives the compounds which are capable of being dissolved back into solution. Typically, such samples need to be shaken overnight to accomplish mixing and solubilization of compounds. The SonicMan shortens that process to a matter of seconds, turning a time consuming process into a reliable automated process.



The figure to the left shows results from five selected 96-well storage racks (80 compd/plate) out of a large number which were being prepared for screening. Each sample tube in each rack was individually inspected for precipitation. The racks were then sonicated using SonicMan, and reinspected. The graph shows the percentage of precipitated samples which were clarified by sonication. The improvement in solubilization ranges from around 25% up to 70%. (Data courtesy of Chiron Corp.)

In the experiment described below, three different methods of mixing are compared for 22 biologically active compounds of varying aqueous solubility. The amount of compound in solution in each case was measured using the NanoStream Veloce system. Results for the three methods are comparable for each compound, showing that sonication can achieve solubilization within seconds. (Data courtesy of Nanostream)

### Peak Area: Solid sample dissolved in buffer (DMSO)



## SYSTEM SPECIFICATIONS

### Modes of Operation

- continuous
- timed
- pulsed
- timed/pulsed

Pulse on and off time is adjustable in 0.1 second increments from 0.1 to 20 seconds. Sonication power settings are variable from 1 to 1,150 Watts. This combination of intermittent operation and variable amplification permits application specific, high-intensity sonication while avoiding heat build-up in the processed sample.

### Remote Control

Ethernet port and command set

### Plate Shuttle

The plate shuttle is in landscape presentation and allows for direct integration with pick and place robotics. Plate shuttle extends 115mm/4.5" (to center of plate) and is 140mm/5.5" above bench top

### Sonic Horn

Constructed from titanium with carbide coating

CE Certified

### Physical Dimensions

Height: 787mm/31"

Width: 356mm/14"

Depth: 432mm/17"

Weight: 125lbs/56.7kg

### Required System Components

SonicMan instrument: Part#SCM1000

Integration Software Package: Part#SCM1000-IS

### Other System Requirements

Compressed air: 100psi/7bar

### Electrical Requirements

208-240 VAC, 50/60 Hz, 10 amps

### Environmental Requirements

Operating ambient temperature: 50-95°F/15-35°C

Operating relative humidity: 0-90% at 85°F/30°C

Altitude: 0-2000 meters

### Accessories

Portable air compressor: Part#PAC-01

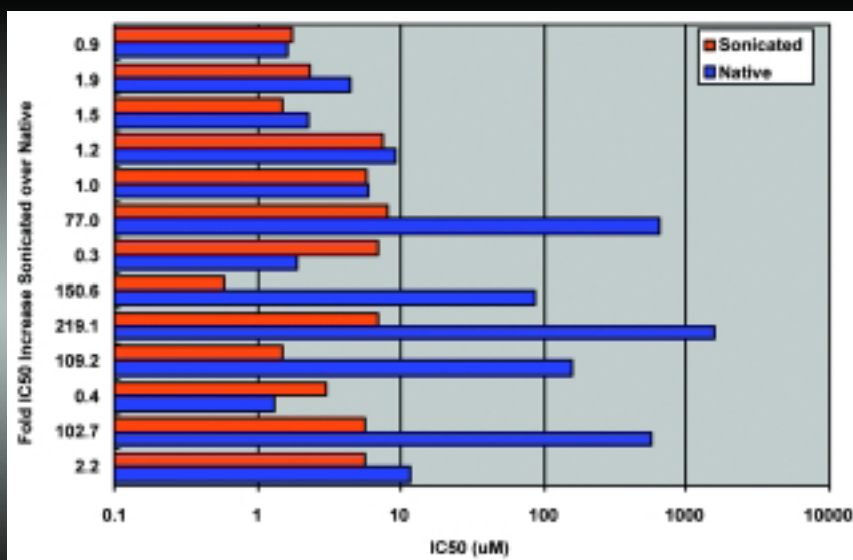
Disposable Sonic Lids (80/case):

- 96-format pinned lid Part#SL0096
- 384-format pinned lid Part#SL0384
- 1536-format pinned lid Part#SL1536

Step down transformer: Part#SDT-01 (110V)

## COMPOUND RESOLUBILIZATION IN SCREENING

Resolubilization just prior to screening eliminates one major source of false negatives. It can have a noticeable impact on the quality of hits by facilitating better, more consistent data for structure-based screening data analysis software and SAR models.



The figure to the left shows the comparison of IC50s determined before and after sonication of the stock DMSO solution for randomly chosen hits from a screen. Five of the thirteen compounds (38%) showed approximately two orders of magnitude improvement in measured IC50 if the stock compound solution was sonicated prior to aliquotting for the concentration-response experiment.

## RELATED PRODUCTS

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- eliminate vapor lock

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### Compound Storage System

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