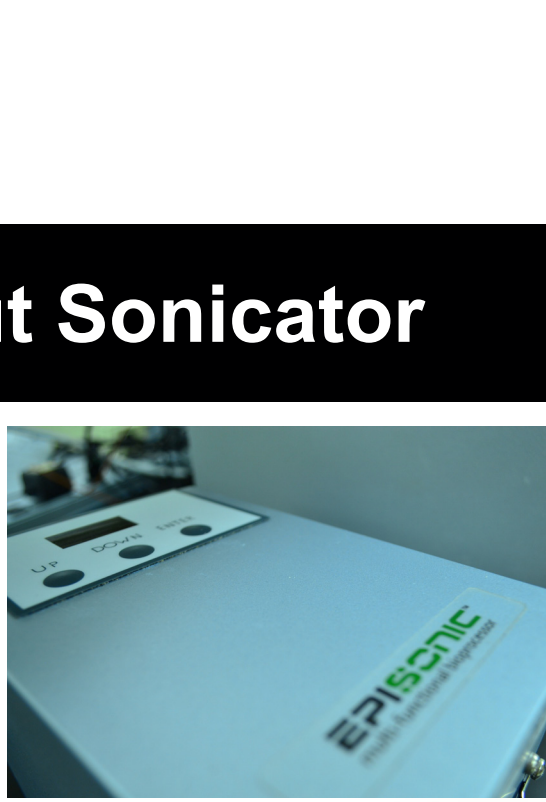
EpiSonic™ Hi-Throughput Sonicator



DNA Shearing
NGS Library Preparation
Chromatin Shearing
Cell Disruption/Lysis

INTRODUCING BETTER SONICATION

The EpiSonic™ Multi-Functional Bioprocessor 1100 system, or simply the EpiSonic™ 1100, is a high-throughput capable sonication instrument of the latest generation for use in a wide range of biological applications, in particular for DNA and chromatin shearing. This completely digital instrument allows for processing of 1 to 96 samples or more, simultaneously, and can be easily integrated into existing lab workflows.

Features At a Glance

The EpiSonic™ 1100 incorporates an ultrasonic technology called Digitally Adaptive Sonocavitation™ (DAS) for efficiently and effectively processing biological samples, with the following key features:

Touch Screen Control - Simple, modern operation with intuitive menu navigation
High Degree of Precision - Adjust all settings digitally; no dials or knobs
Programmable Memory - Store successful protocols for future use
Chilled Environment - Included cooling system recirculates chilled water to maintain sample integrity and to prevent thermal degradation
High Throughput - Simultaneously process from 1 to 96 samples with standard 0.2 ml PCR single tubes or 96-well PCR plates
Cost-Saving - Capable of handling common 0.2 ml PCR tubes or semi-skirted PCR plates, as well as low-priced EpiSonic-provided consumables
Shallow Waterbath - Less liquid medium allows for faster and highly focused sonication on samples
Closed Vessel Processing - Non-contact sonication in sealed tubes/wells prevents contamination and sample loss

Specifications	
Input Voltage	100-120V or 220-240V
Power Rating	600 Watts
Program Memory	10 program slots
Operating Frequency	20 kHz
Timer Control	Digital
Single Throughput Capability	Yes
High Throughput Capability	Yes
Generator Dim. (L x W x H)	49.5 cm x 27.9 cm x 13.3 cm
Chiller Dim. (L x W x H)	19 cm x 12.7 cm x 17.6 cm
Sound Box Dim. (L x W x H)	25.5 cm x 25.5 cm x 42 cm)
Warranty Period	20 months

Scalability - Simple, removable, and interchangeable vessel rack allows for expansion to different vessel sizes
Fast Processing - Averages 2 minutes per sample at 100-600 bp (average 300 bp) fragments in a high throughput setup
Real-Time Energy Monitoring - Live screen output of amplitude, wattage, and joule readings
Real-Time Temperature Monitoring - Live screen output of temperature in sample reservoir (requires accessory)
Improved Bio-Safety - No aerosol formation; no tedious manipulation of probes
Workflow Integration - Streamlines into high-throughput or multi-sample chromatin immunoprecipitation (ChIP) and massively parallel sequencing workflows
Automatic Overload Prevention - Detects faults and shuts down to prevent damage to circuits
No Moving Parts - Eliminates any possibility of mechanical failure or breakdown
Extensive Warranty - Backed by a 20 month warranty to ensure quality and customer satisfaction

DESIGNED TO SHEAR DNA & CHROMATIN

Achieving The Right Fragment Sizes

High demand for massive parallel analysis of genetic and epigenetic alterations has driven the development of next generation ChIP and DNA sequencing technologies. In order to prepare the proper sample libraries for such technologies, an efficient, reliable device such as the EpiSonic™ is needed to generate the necessary DNA fragments. The EpiSonic™ provides optimal DNA and chromatin shearing at desired fragment sizes (e.g., 100-10,000 bp), with excellent sample yield, reproducibility, and consistency, and allows for rapid processing via 96-well PCR plates or standard laboratory tubes in a hands-free, pre-programmed manner. These advantages enable the device to be easily integrated into existing lab workflows and to fit the specifications from all commercial ChIP and sequencing vendors.

Compatible Sequencing Platforms

The EpiSonic™ 1100 can shear high quality DNA into any size under 2000 base pairs, which essentially covers all next-generation sequencing devices that require DNA library preparation. To be specific, some of the popular platforms that are compatible include the following: Illumina Genome Analyzer, Illumina HiSeq, Illumina MiSeq, Roche 454 Sequencing GS FLX, Roche 454 Sequencing GS Junior, Life Technologies SOLiD System, and Life Technologies Ion Torrent.

Compatible ChIP Analysis Platforms

The EpiSonic™ 1100 is ideal for generating the most optimal fragment size of 200-600 base pairs for use in any chromatin immunoprecipitation (ChIP) procedure. Digitally controllable shearing with the EpiSonic™ 1100 along with a temperature control system prevents heat damage to epitopes of precious samples and eliminates shearing biases, thereby increasing efficiency of ChIP and providing reproducible results. The EpiSonic™ is also compatible with Epigentek's ChromaFlash™ Chromatin Isolation & Shearing Kit to prepare ideal chromatin samples from cells or tissues, which can be used in any ChIP protocol and downstream ChIP analysis application including ChIP-PCR/qPCR, ChIP-chip, and ChIP-Seq.

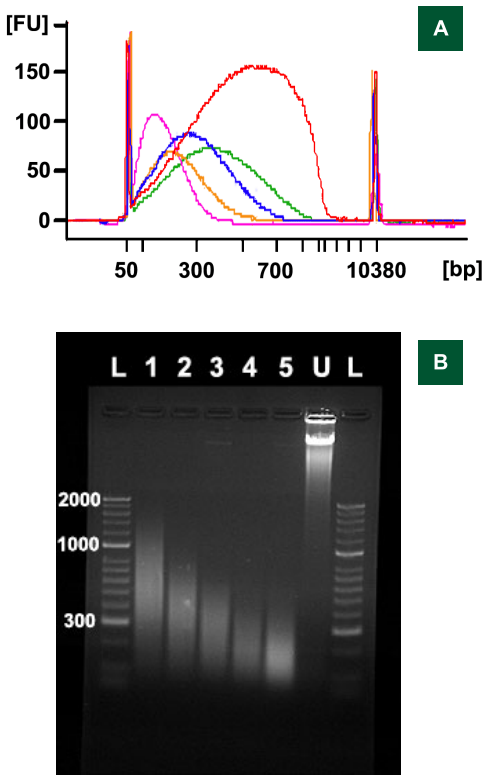


Fig. 1 | *Demonstration of precise DNA shearing of different sizes*. 3 µg of placental DNA in 0.2 ml tubes were sheared with the EpiSonic™ 1100 at different sonication durations (10, 15, 20, 45, and 62.5 min). The resulting lengths of the sheared DNA were analyzed with an Agilent Bioanalyzer 2100 [A] and an agarose gel [B].

DELIVERING RESULTS THAT MATTER

Precise, Consistent, & Reproducible

The EpiSonic™ 1100 has been extensively tested and optimized for shearing samples in a precise, consistent, and reproducible manner with a high dsDNA yield (>75%). Desired sample sizes are able to be achieved due to the digital precision of the amplitude controls by allowing for user adjustment in intensity intervals of 1% at a time. Furthermore, samples placed in different positions in the interchangeable vessel holder are able to maintain consistency and equal sizes between each other. Most importantly, samples are sheared in reproducible lengths between the first run and the next run, creating predictable results and eliminating optimization time and labor.

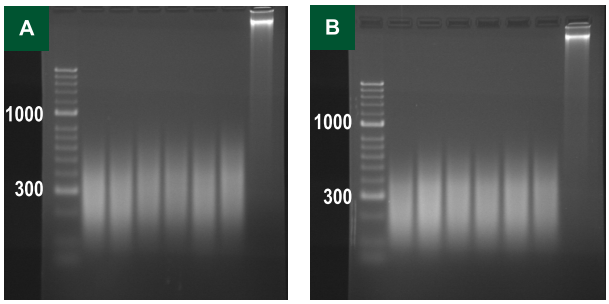


Fig. 2 | *Demonstration of Sample-to-Sample Consistency*. 2 µg of placental DNA in 30 µl buffer were placed in well positions B2, B6, D6, E7, F9, and G11 of a 96-well PCR plate and sheared with the EpiSonic™ 1100 for 40 cycles [A] and then repeated in a subsequent run with the exact same conditions [B].

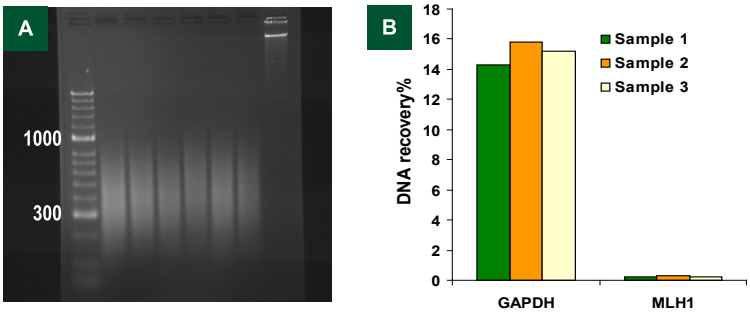


Fig. 3 | *Demonstration of chromatin shearing followed by ChIP*. 8 µg of chromatin (in 40 µl of buffer) were extracted from 6 different samples of MDA-231 cells and sheared in a 0.2 ml tube with the EpiSonic™ 1100 for 20 cycles [A]. The sheared chromatin was used for ChIP-qPCR analysis [B] of RNA polymerase II enrichment in GAPDH and MLH1 promoters by using Epigentek's ChromaFlash™ One-Step ChIP Kit and Methylamp™ MS-qPCR Fast Kit.

Unbiased, High Throughput Shearing

Processing one sample at a time increases the risk of size variation of sheared DNA and chromatin fragments. Furthermore, a lack of a cooling unit may lead to overheating, subsequently causing biased shearing at AT-rich regions due to the lower annealing temperature of AT base pairing for chromatin shearing. Through parallel processing of multiple samples and a temperature control system, the EpiSonic™ 1100 is able to overcome biases caused by excessive heat in the sample during the mechanical shearing process while also eliminating sample-to-sample variation caused by shearing one sample at a time.

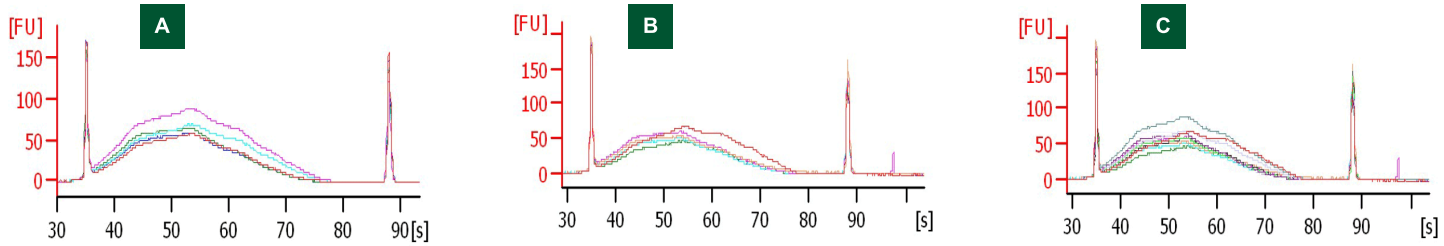


Fig. 4 | *Demonstration of high reproducibility.* 3 µg sample of placental DNA (30 ul) in the different wells of a 96-well plate was sheared with the EpiSonic™ 1100 for 40 cycles. The resulting lengths of the sheared DNA were analyzed with an Agilent Bioanalyzer 2100. Average sheared DNA size is 380.4 bps for the first run [A] and is 379.2 bps for the next run [B]. The two Bioanalyzer images were then overlapped to visualize the high reproducibility [C]. The CV% of sample to sample in the same run is 1.1 to 4.7% and is 0.3% between the different runs. Average percentage of dsDNA recovered from 10 samples is 75.2%.

MADE WITH SMARTER SCIENCE

The Working Principle

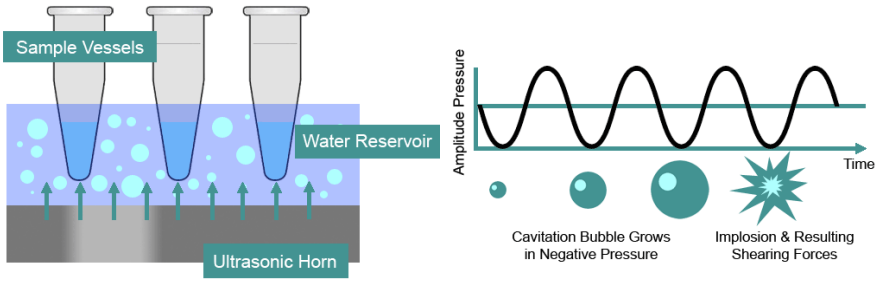


Fig. 5 | DAS™ technology allows sonication energy to form a high pressure field throughout the entire liquid medium (water) within the shallow waterbath so that an uniform level of acoustic energy and shearing power is evenly distributed to all samples.

The technology that drives the EpiSonic™ 1100 so well is Digitally Adaptive Sonocavitation™ (DAS), a principle that is ideal for shearing DNA or chromatin as well as for lysing cells and tissues. During the DAS™ process, the electronic signal produced by a digitally-controlled generator is converted into acoustic/mechanical energy through a piezoelectric converter (also known as a transducer). When the acoustic energy is produced in water, negative pressure is generated and causes the distance between the water molecules to exceed the maximum molecular distance necessary to hold liquid intact. Consequently, the liquid breaks down to create millions of cavitation bubbles.

These cavitation bubbles expand in size through several acoustic cycles as more acoustic energy is introduced. The size of the cavitation bubbles and the corresponding cavitation energy can be manipulated and digitally controlled by adjusting fully scaled amplitude levels (1-100% in intervals of 1%) with a DAS™-based device such as the EpiSonic™ 1100. When the acoustic energy is suddenly removed, these cavitation bubbles collapse, creating intense shock waves in an extremely short period of time (microseconds), which transmit into vessels containing samples. This in turn forms highly targeted shearing forces to break up or disperse biomolecular samples including DNA, chromatin, and tissues in a non-contact, non-invasive manner. In a nutshell, a DAS™-based device such as the EpiSonic™ 1100 is able to shear samples with more precision and reproducibility than non-DAS™ instruments.

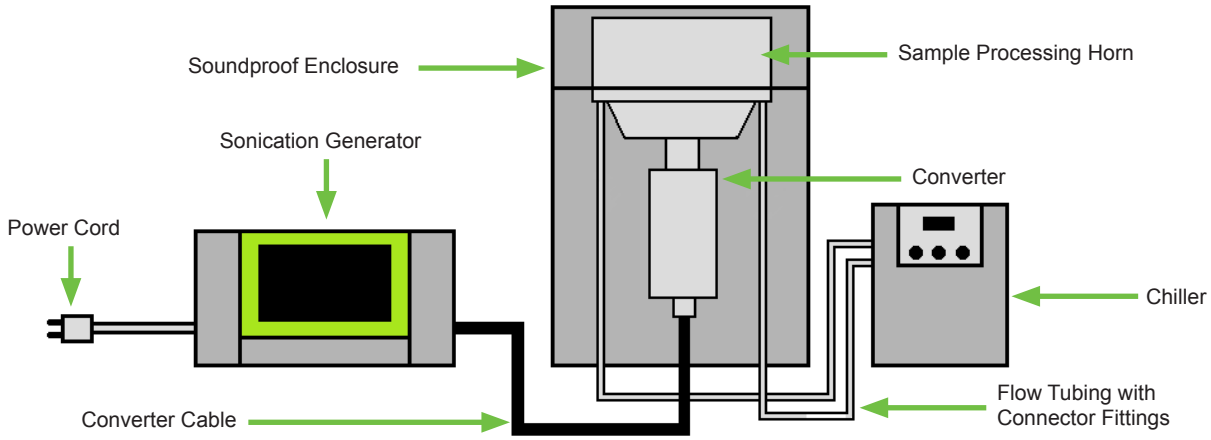


Fig. 6 | Setup diagram of the EpiSonic™ Multi-Functional Bioprocessor 1100.

STANDING OUT FROM THE CROWD

DAS™ vs. Other Sonication Technologies

The shallow waterbath design of the EpiSonic™ 1100 provides an optimal ratio of power intensity to liquid volume and creates a highly homogeneous energy distribution. This forms a high pressure field throughout the entire liquid medium (water) within the shallow bath with a uniform level of energy, allowing for all samples in the field to receive the same shearing energy (>1 MPa per sample), while the heating side-effect can be eliminated by the included cooling system. Thus it is equivalent to providing an even acoustic environment to each sample accordingly and is very suitable for shearing many different samples simultaneously and consistently.

On the contrary, a tank-based deep waterbath design using an adaptive cavitation method provides too much room for ultrasound waves to travel through, which are subsequently reflected by the walls of the tank. As the ratio of power intensity to liquid volume is significantly less optimized, the random, uneven, and indirect energy caused by this results in only a very small fraction of the acoustic energy being received by the samples. The necessary shearing intensity targeted to the samples could be 5 to 10 times lower than that with EpiSonic™ DAS™ technology, making it inconsistent and not ideal for shearing multiple samples simultaneously.

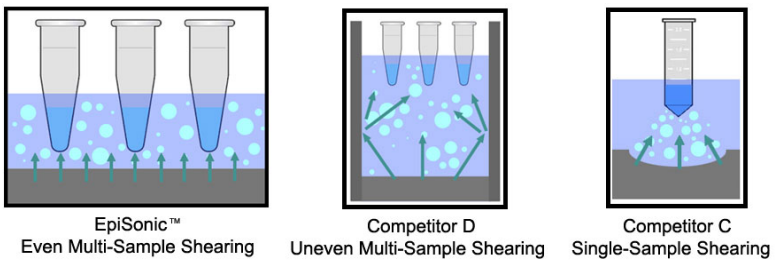


Fig. 7 | *Left Image:* EpiSonic's shallow waterbath method with DAS™ technology evenly distributes ultrasonic waves and can directly target multiple samples in a consistent and predictable manner; *Center Image:* Tank-based deep waterbath method with adaptive cavitation and unfocused transducer unevenly processes samples due to extraneous room for ultrasonic waves to travel and be reflected by the walls of the tank; *Right Image:* High frequency focused acoustic method with a local point transducer can only process one sample at a time as multiple local point transducers would be highly expensive.

Other high frequency focused acoustic methods form a localized high pressure region located in the target vessel and create 1MPa in the sample with 0.8 Watts of power. Because the high frequency focused acoustic method requires use of a localized shearing pressure generated by a focused acoustic beam, only a single sample can be sheared at a time, therefore rendering it unsuitable or uneconomical for processing multiple samples simultaneously.

Comparative Features	EpiSonic 1100	Supplier D*	Supplier C*	Probe-based
Precise DNA Shearing Control	Yes	No	No	No
High Yields of Unbiased dsDNA	Yes	Yes	N/A	No
Max No. of Optimal Samples Per Run	96	12	1	1
Prevents Risk of Contamination	Yes	Yes	Yes	No
Digital Readouts & Touchscreen Display	Yes	No	No	No
Small Sample Volume Permitted (<20 µl)	Yes	No	No	No
Microplate Vessel Capability	Yes	No	No	Yes
Fits Into Existing Lab Workflows	Yes	Yes	No	Yes
Protocols Programmable Into Internal Memory	Yes	No	No	No
Reproducible	Yes	N/A	Yes	No
Device Warranty	20 Months	12 Months	12 Months	N/A
Cost Per Sample Processed	Low	Medium (~5X more)	Very High (~100X more)	High (~40X more)

* Based on most common models on the market.

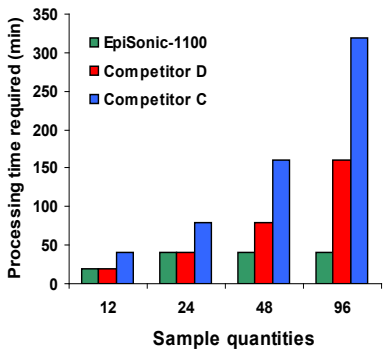


Fig. 8 | Time required for parallel processing of multiple DNA samples (target peak fragment size is 300 to 400 base pairs).

KEEPING OUR COOL

DAS™-based Temperature Control Mechanism

Because sonication generates heat, controlling the sample temperature during shearing is critical to obtaining reproducible and predictable results by preventing thermal damage to the sample. The EpiSonic™ DAS™ technology can tightly control the sample temperature in the vessel through four featured approaches: (1) the targeted acoustic dose per sample volume is low (<0.1 Watts per sample) and optimized for efficient shearing; (2) the highly-efficient cooling system rapidly re-circulates chilled water; (3) an optimized ratio of sample liquid volume to the surface area of the vessel enables rapid heat transfer away from the sample and to the vessel; and (4) DAS™ enables the formation of extreme turbulence in the sample liquid to further enhance heat transfer which isothermally removes heat from the sample into the vessel walls and the surrounding water.

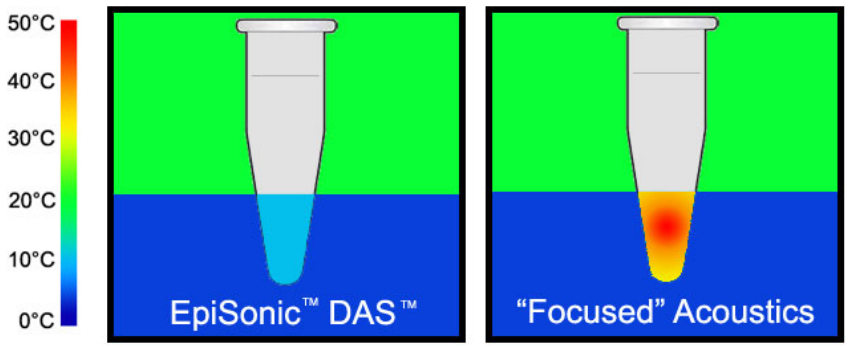


Fig. 9 | Sonication temperatures during 120 seconds of ultrasonic processing with either the EpiSonic™ 1100 (left), or with a high frequency focused acoustic sonicator (right). Green regions represent 20ºC air, deep blue regions represent a water bath with temperatures of 6ºC to 9ºC during the sample processing, sky blue regions represent 10ºC to 13ºC in the sample, and red regions represent > 40ºC in the sample. The EpiSonic™ DAS™ technology (left) keeps the temperature at 10-13ºC during the entire sonication process while high frequency focused acoustic sonication (right) quickly elevates the temperature of the sample inside of the vessel to higher than 40ºC for a moment before it can actually be cooled.

A continuous measurement of actual temperature inside of the sample with a real-time temperature-sensing probe during a test run of continuous sonication for 2 minutes with a 0.2 ml PCR tube demonstrated that the temperature of the sample in the vessel is only slightly higher (3-4ºC) than that of the surrounding water in the shallow waterbath. When the temperature of water in the shallow waterbath was 20ºC, the temperature of the sample in the vessel was only 24ºC at an acoustic dose level necessary for efficient shearing with this method. Thus, the EpiSonic™ 1100 is able to shear samples in a controlled temperature range without causing thermal damage to the sample.

Non-DAS™ methods may be problematic in maintaining a true isothermal environment. Unlike the smooth and gradual delivery of energy to the sample with the EpiSonic™ DAS™ method, a high frequency focused acoustic method directly sends a disproportionate burst of energy into the liquid phase of the sample with a high acoustic dose (>0.8 Watts per sample) while neglecting much-needed "off", or cool-down, cycles. This initial burst of acoustic energy could dramatically elevate the temperature of the sample in the vessel for a moment, causing severe degradation to the sample quality in a short period of time. For example, a 1.5 ml vessel containing 1.0 ml of sample in 500 kHz focused acoustic region will result in a sudden sample temperature increase from 20ºC (external waterbath temperature) to up to 90ºC in two minutes at an acoustic dose level necessary for efficient shearing with this method. Although this rise in temperature can be quickly reduced through heat transfer into the surrounding water, the thermal damage has already impacted the sample quality in an adverse manner with a "focused", non-DAS™ method.

EPISONIC™

multi-functional bioprocessor