A Flow Measurement Guide
for Industry Bioengineers

FLOW MEASUREMENT TECHNOLOGIES

transonic
THE MEASURE OF BETTER RESULTS.
www.transonic.com

Transit-time Ultrasound Flow Measurement (TTFM)

At Cornell University's NYS Veterinary College in Ithaca, NY 35 years ago, Transonic's founder and president Cornelis Drost devised a method to measure the amount of blood flowing through blood vessels, ducts or tubing in a way that would not interfere with the flow inside the conduit itself. In 1978, the Cornell group presented this theoretical breakthrough (transit-time ultrasound technology) to the world.[1]

The technology uses non-invasive ultrasound. Its revolutionary aspect is that it measures the actual amount of blood flowing through the vessel, duct or flexible plastic tube directly with high accuracy, without manipulating the conduit in a way that would alter the very flow that is being measured. Measurements can be made in *vitro* bench-top models and *in vivo* animal models from an array of animal models ranging from a mouse to humans.

The technology was soon cited as the gold standard technique for measuring volume flow. Based on this transit-time ultrasound measurement technology, Transonic was founded in 1983. Now its highly accurate measurement devices are sold throughout the world. More than 4,000 publications cite the use of transit-time ultrasound measurement (TTFM) technology in their studies.

Ultrasound Dilution Technology (UDT)

Transonic's product scope expanded when Russian Biomedical Engineer, Nikolai Krivitski PhD, DSc joined Transonic in 1992. Well versed in classic dilution technology, he soon had an "Aha!" insight that existing transit-time ultrasound technology could be married to classic indicator dilution technology to create a superior "ultrasound dilution technology." This ushered in a whole new world of technology and application innovations for biomedicine.

When nephrologists presented Transonic with a basic clinical blood flow measurement problem, Nikolai had another "Aha!" insight: Transonic's standard transit-time ultrasound hardware combined with the dialysis machine would make it possible to identify life threatening blood flow problems in dialysis patients. His innovation took off like a storm. Only four years after its first patent was filed in 1994, ultrasound dilution technology was recognized in the new Guidelines of the American Kidney Foundation as gold standard technology – the technology by which all other measurements should be compared.

Now, ultrasound dilution technology constitutes the basis for other critical care devices including the Transonic® Extracorporeal Life Support Assurance (ELSA) Monitor and the Transonic COstatus Monitor, both which provide vital hemodynamic information to intensive care clinicians.

TTFM & UDT Capabilities Summary

TECHNOLOGY	TTFM	UDT
MEASUREMENT CAPABILITIES	Liquid flow through a vessel/tube	Vascular access flow/patency
	Ultra filtration rate	Recirculation
	Liquid properties	Cardiac Output
	Zero flow & low flow resolution	Central Blood Volume
	Total liquid volume	Filter volume and clotting
	Bubble detection	

PV Cardiac Function Technologies for Pre-clinical Testing

In addition to Transonic's transit-time flow measurement and ultrasound dilution technologies, Transonic also offers Pressure Volume Loop technology from Transonic Scisense (London, Ontario, Canada) that is used in development and pre-clinical testing of biomedical devices. Their ADVantageTM Pressure-Volume system, using admittance technology, is state of the art and addresses some the shortcomings of the classical conductance technology. It offers these advancements:

- Parallel conductance is calculated as a dynamic value in real-time
- The signal coming out of the control unit is a TRUE ventricular volume signal and requires no post-processing
- Phase angle (an index of myocardial capacitance) is reported, which provides feedback as to catheter position within the ventricle
- An improved conductance-to-volume conversion equation (Wei's Equation)

This technology along, with the complementary hemodynamic parameters such as cardiac output and blood volumes measured by the ultrasound dilution COstatus® device, can provide crucial information to both researchers and, in the case of COstatus, pediatric cardiac clinicians.

This section of the handbook will present the theory behind TTFM, UDT and PV Loop measurements.

TTFM Theory of Operation

TTFM MEASUREMENT CONCEPTS

Ultrasound

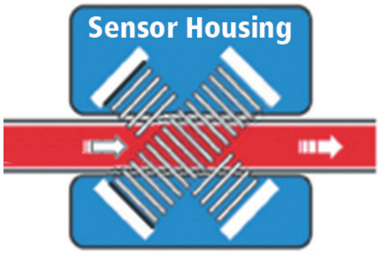
Ultrasound refers to high frequency sound waves that are outside of auditory range. Ultrasound velocity depends on the acoustic properties of the liquid being measured and its temperature. Transonic Flowsensors are calibrated based on known liquid properties and temperature conditions.

Transit Time

Transit time is the length of time it takes for ultrasound waves to pass through the material being measured.

Transit Time = Distance/Velocity

Knowing the time of travel over a given distance allows for the velocity to be calculated.



With X-style configuration of a Flowsensor, four transducers pass ultrasonic signals, alternately intersecting the vessel/ tube in upstream and downstream directions.

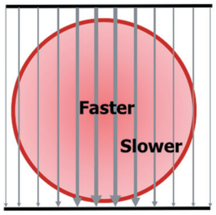
Upstream / Downstream

All ultrasound waves begin at the same frequency and velocity. As the ultrasound waves travel downstream or with the flow within the vessel or tube, its velocity increases. As ultrasound waves travel upstream or against the flow, its velocity decreases. Faster flow produces a greater change in ultrasound wave speed. One ray of the ultrasonic beam undergoes a phase shift in transit time proportional to the average velocity of the liquid times the known path length over which this velocity is encountered. The Flowmeter subtracts the average downstream transit times from the average upstream transit times. This difference is directly proportional to Volume Flow.

Calibration supplies the flow Gain constant (k) which transforms the proportional signal to true volume flow.

Differential TT x k_{gain} = Volume Flow

Wide Beam Integration



Since wtime is sampled at all points across the diameter of a vessel or tube, volume flow is independent of the flow velocity profile. Ultrasonic beams which cross the acoustic window without intersecting the tubing or vessel do not contribute to the volume flow integral.

With wide-beam ultrasonic illumination, the receiving transducer integrates these velocity-chord products over the vessel's full width to yield volume flow.

When measuring flow in vessels with perivascular flowprobes, wide beam illumination allows volume flow measurement even when the vessel is smaller than the flowprobe acoustic window. No assumptions of vessel diameter need to be made to measure volume flow.

Transit Time measures through the cross section of a vessel- or tube and measures Average Displacement of liquid through the sensor, and is calculated:

Volume Flow =
Integrated Differential Transit Time X K_{gain}

TTFM Advantages

Ultrasound TTFM Measures Volume Flow

Transit-time Flowsensors measure the velocity of liquid across the entire vessel lumen to derive VOLUME FLOW in mL/min or L/min. Doppler derives flow from separate estimates of average VELOCITY in cm/sec of sound particles reflected from the field.

TTFM Measures Flow in Most Liquids

Transit-time ultrasound measurements are not dependent on particulate matter in the liquid in order to measure flow. Liquids such as saline, water and physiological buffers can be measured with transit-time ultrasound, unlike Doppler technology which requires signals to bounce off moving particles such as red blood cells within a liquid in order to measure flow. Even lymph can be measured with TTFM.

Unmatched Zero Flow Stability

The Flowmeter’s oscillator drives its transmitting circuitry and functions as the phase reference signal for its sensitive receiver amplifiers and detectors. Direct pickup of the (loud) oscillator signal onto the (far weaker) received signals (via power lines or capacitive or over the air) can manifest as a zero-flow offset, as it will alter the phase and zero crossings of the upstream/downstream received signals.

If the phase relationship between the transmit and received signal fluctuates due to variations in acoustic transit-times as a result of temperature or other liquid property changes, this pick-up signal will exhibit itself in a varying zero flow offset. This effect is indistinguishable from a change in true flow unless the flow is stopped and the flowmeter is re-zero’ed.

Time tested and honed over more than thirty-five years, the sophisticated engineering of Transonic Flowmeters is demonstrated by their hallmark high stability and low, stable zero offset. This same gold-standard performance in now available in ASIC Flowmeter designs!

Mimimally and Noninvasive Technology:

The transit-time method requires minimal intervention with the liquid flow stream to provide its flow measurement. For intraoperative measurement on arteries and veins, Transonic Perivascular Flowprobes do not require an exact nor constricting fit on the vessel to provide accurate results, thus making them the method of choice for adequate flow confirmation in CABG bypass and transplant surgeries. Transonic Tubing Flowsensors have no contact with the liquid media to derive volume flow measurements, making the technology perfectly suited for blood pumps or delivery of sterile therapies and high purity conditions.

Sensitivity Scaled to Sensor Size

By using a range of ultrasound frequencies scaled to vessel or tubing size, Transonic Flowprobes and Flowsensors are able to match high resolution measurements proportional to the vessel or tubing size. This allows the instrument to realize super low flows of tenths of a milliliter in the smallest Flowsensors and Flowprobes, while scaling up to 100 L/min using the largest Flowsensors. Pulsatile flows are resolved with picosecond sampling and filtered to present accurate waveforms in real time.

References:

Drost CJ, “Vessel Diameter Independent Volume Flow Measurements Using Ultrasound,” Proceedings San Diego Biomedical Symposium 1978; 17: 299-302. US Patent 4,227,407, 1980.

Precision Flow Sensors for Tubing Applications

Clamp-on or Inline Tubing Sensors measure volume flow in most non-aerated liquids including saline, buffer solutions, blood, water, blood analogs including concentrations of glycerine and water and even diesel fuel with high resolution and low zero offset. Flow sensors that match the flow circuit requirements are available.

Clamp-on Flowsensors

- Non-contact Clamp-on Sensors do not break circuit sterility
- Small diameter Sensors for industrial use
- Used in pre-clinical and medical flow apparatus design

Closed clamp-on sensor with tubing inserted.

Innovative transit-time technology revolutionized blood flow measurement in medical tubing applications with these Clamp-on Flowsensors that clip onto the outside of flexible tubing to measure the flow within. They have become the standard for medical design and pre-clinical extracorporeal use by providing non-invasive measurement with high accuracy and stability. Measurements are reliable even in challenging electromagnetic environments.

The easy clip-on operation of the PXL Flowsensors also make these Sensors ideal for industrial flow measurement applications when process testing needs to be quick, repeatable and applied to multiple circuits without flow interruption. Unlike large diameter industrial flow measurement devices, Transonic® provides high resolution Clamp-on Sensors for small diameter tubings down to 1/8” OD.

Inline Flowsensors

- Measure flow over a wide dynamic range
- Flexibility for tubing circuits that may vary or are still in the design phase
- Highest sensitivity Flowsensors for low flow applications

19 PXN Inline Flowsensor

PXN Inline Flowsensors are flow-through Sensors with a smooth, cylindrical interior with high measurement accuracy. These Flowsensors offer more flexibility than Clamp-on Sensors as measurement calibration doesn’t depend on the type and exact size of tubing on which they are used. Small diameter PXN Inlines are ideal for low flow isolated heart or perfused organ studies.

Maximizing Performance in Tubing Applications

Uniform Conditions

Acoustic principles govern the design, manufacture and proper use of Transonic clamp-on Tubing Flowsensors. Because acoustic properties of the tubing material affect Sensor accuracy, Transonic calibrates the Sensor for the specific tubing material.

"Squaring Off"

Tubing can attenuate, reflect, focus or delay ultrasound timing dependent upon tubing material, density, wall thickness and temperature. Since the most accurate transit-time measurements are achieved under uniform acoustic conditions, the challenge in Flowsensor design is to ensure conditions where the tubing affects ultrasound transmission in a uniform predictable way. Thus, Transonic Tubing Flowsensors "square off" the tubing circumference to minimize focusing of the ultrasound and variable path lengths of the acoustic beam. The ultrasound transmit level and received signal timing window, and calibration factor are determined and set specifically for the tubing to be used. Even so, there are conditions of acoustic mismatch which affect accuracy. If anticipated, these can be minimized.

Temperature

The most significant changes in uniformity of the acoustic beam occur at the Sensor/ tube border and the tube/liquid border. Fluctuations in temperature can affect the acoustic properties of these interfaces. To minimize these effects, we recommend that the Sensor be allowed to equilibrate on the tube before measurement. Zero stability can be improved for measurement of circulating cold liquids by cooling the Flowsensor as well. This can be as simple as insulating around the Sensor and tube with foam or maintaining the tubing circuit and Sensor in a controlled environmental chamber.

Acoustic Seal

Tubing (especially stiff pvc types) is best seated into the sensor slot with an acoustic coupling media. A wipe of alcohol is hygienic and works very well. Vaseline has been used traditionally. Water-based acoustic gels should not be used with tubing sensors. General ultrasound gels can dry out and build up on the sensor as a dirty layer that can contribute offset error.

Calibration

A discussion of accuracy in tubing flow measurement would not be complete without consideration of the acoustic properties of the liquid to be measured. Transonic will custom calibrate the Sensor for the specific liquid if a sample is provided. Changing the liquid (or temperature) will affect the calibration. Some Transonic Flowmeters allow the user to adjust the calibration gain on site.

Flow Profiles

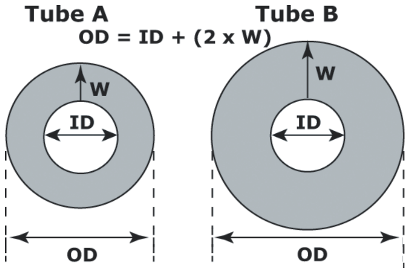
While it is technically possible for the Flowsensor to be used on liquid with turbulent or undeveloped flow, there is an increased chance for inaccuracies, making it inadvisable. Since the ultrasonic field of the Flowsensor is not 100% uniform, one portion of the flow may be sensed in an area that is more sensitive and another portion in an area that is less sensitive. With laminar flow, these areas are appropriately integrated across the entire Flowsensor. However with turbulent flow there is no control over which areas of

Maximizing Performance in Tubing Applications

high, low, average or reverse flow fall within the sensitivity window of the ultrasonic field, this could lead to widely varying flow rates or highly inaccurate values.

To ensure the flow profile will be uniform and developed before entering the Flowsensor have a straight segment of tubing 10 x ID of the tubing before the Flowsensor and just about the same after. Even tubing connectors can cause turbulence.

Note: Laminar flow can develop over a shorter distance than 10 x tubing ID depending on flow conditions and liquid properties.



Tubing outer diameter (OD) is calculated by adding the inner diameter (ID) and twice the tubing wall thickness (W). OD= ID + (2 x W). These two tube cross sections have the same ID, but very different OD. Tubing size must be specified by at least 2 dimension parameters.

Flow Straighteners

When it is not reasonable to have the necessary length of straight tubing for fully developed flow (10xID), flow straighteners may be used to reduce turbulence. Flow straighteners often resemble a sieve or a bundle of small tubes and act as a physical interruption to turbulent effects such as swirl and allow for faster development of laminar flow profiles by reducing the Reynolds number. The Reynold’s number is directly proportional to the diameter of a tube. Reducing the tube diameter by turning one big tube into many small tubes reduces the Reynold’s number which corresponds with more laminar flow behavior which is perpetuated when the flow is recombined into a single stream. The diameter and length of the small tubes needed to create laminar flow depends on the liquid viscosity, flow rate and the amount of turbulence to be corrected.

Additive Errors

When using multiple Flowsensors on a single flow system such as input/output measurements, it is important to remember that absolute accuracy of the Sensors is ±10% and that error is additive. In a worst case scenario, two Sensors with error in the opposite direction could give a total system error 20%. However, it is possible to mitigate such total system error by calibrating the Sensors together against a known flow, determining a correction factor for each and adjusting the gains of the Sensor through the program on the TS410 Flow Module. This gives the tightest overall accuracy for the whole system.

Sensor Sizes Correlate to Outer Tubing Diameters

Transonic Clamp-on Sensors are sized to the outer diameter (OD) of the tube so that the tubing fits properly in the tubing slot of the Sensor. Sensor sizes vary in 1/16” increments. The number within a Flowsensor name refers to this OD size in 1/16 inch steps. Sizes for metric OD sizes (4mm to 25mm) are available on special order.

Sensors Can Be Custom Matched

Some tubing types do not conform to the standard OD dimensions that are listed on the Transonic Clamp-on Sensor specifications list, but may be suitable for use with Transonic Sensors (such as tubing sized in mm). A sample of the tubing may be sent to Transonic Systems for evaluation, and Transonic® will match the tube outer diameter to the nearest standard Sensor size to see if it gives acceptable signal.

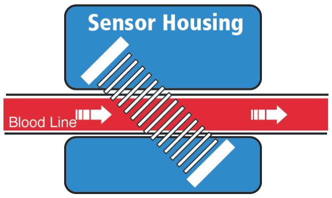
UDT Principle of Operation

Indicator dilution (UDT) combines two technological principles:

1. Differential Transit-time Ultrasound
2. Indicator Dilution

Each are described succinctly below.

Principle I: Differential Transit-Time Ultrasound



The blood line is inserted into the groove of the flow/dilution sensor body. Direction of flow is indicated by arrows. Ultrasonic beam is shown emanating from the two transducers in the sensor body.

Paired clip-on sensors transmit beams of ultrasound through the blood line many times per second. Transducers pass ultrasonic signals back and forth, alternately intersecting the flowing blood in upstream and downstream directions as described on page 17. The Flowmeter/Monitor derives an accurate measure of the changes in the time it takes for the wave of ultrasound to travel from one transducer to the other ("transit time") resulting from the flow of blood in the vessel/tube. The integrated differences between the upstream and downstream transit times over the distance of the tubing/vessel provide a measure of volume flow.

During hemodialysis, extracorporeal membrane oxygenation (ECMO) or cardiopulmonary bypass (CPB), two matched flow/dilution sensors are clipped onto the arterial and venous lines, respectively. The Monitors continuously display both delivered blood flows (one from the arterial sensor and one from the venous sensor). Comparison of the readings with the pump flow setting (i.e., the flow the pump is assumed to deliver) provides an opportunity to identify and correct flow delivery problems.

Principle II: Indicator Dilution

Flowmeters/Monitors coupled with Flow/dilution Sensors measure ultrasound velocity. A bolus of isotonic saline (ultrasound velocity: 1533 m/sec) introduced into the blood stream dilutes the blood and thereby reduces the ultrasound velocity of the liquid. Paired flow dilution Sensors, attached to an extracorporeal circuit and connected to the Flowmeter/Monitor, sense this decrease in the ultrasound velocity of blood dependent on its protein concentration.

UDT Principle of Operation

Principle II: Indicator Dilution cont.

Flow/dilution Sensors record this saline bolus as a conventional indicator dilution curve. First, the Flowmeter/Monitor displays a curve sensed by the arterial sensor and then a second curve sensed by the venous sensor. The areas under the curves are calculated by the Flowmeter/Monitor using classical dilution equations to produce results for recirculation, vascular access flow and cardiac output during hemodialysis, recirculation and oxygenator blood volumes during ECMO and a host of cardiac function parameters during critical care therapy. These results are then displayed on the Monitor’s screen.

Ultrasound Velocity

0.9% NaCl: 1533 m/sec
Blood: 1580 m/sec