Use of a Local Indicator Dilution Technique for the Measurement of Oscillatory Flow

By R. D. Lowe, M.D., M.R.C.P.

ABSTRACT
An indicator dilution method for measuring oscillatory flow in a vessel is analyzed in terms of a mixing chamber with a constant volume. For the correct measurement of mean flow, the time constant of detection of the indicator should be very much shorter than the shortest time constant of the mixing volume. The performance of such a system was examined with a thermal indicator. Although the apparent mixing volume was found not to be constant but to vary with flow, the method showed no significant error in the measurement of mean flow. There was no significant “distance distortion error” when the indicator was detected at two different points downstream from the site of infusion; this was attributed to the pattern of mixing, with detection within or close to the limits of the mixing volume. It is concluded that a properly designed indicator dilution system can measure mean blood flow without significant error, even when there is an oscillatory component.

ADDITIONAL KEY WORDS
distance distortion error
thermal dilution
mixing volume

When an indicator dilution system is used to measure blood flow, the following conditions must be fulfilled. (1) The indicator must be adequately mixed with the blood. (2) The precautions necessary to achieve mixing must not themselves alter the flow being measured.

A number of workers have used continuous infusions of indicator and have shown that such systems can accurately measure steady flow, but it is important to determine whether such flow-measuring systems accurately measure mean flow even when it is oscillatory.

A thermal indicator appears to offer the highest chance of success, although its use creates special problems because of its diffusibility. Throughout this article the terminology of thermal dilution has been used, although the principles involved can also be applied to other indicators.

An idealized model of a thermal dilution system is illustrated in Figure 1. Cold saline at a temperature $T_9$ is infused down a catheter, at a rate of 100 ml/min, into blood flowing at $Q$ ml/min, at a temperature of $T_b$. The temperature of the resulting mixture ($T_m$) is recorded downstream. The heat gained by the saline is equal to the heat lost by the blood and the rate of flow of blood is given by the formula:

$$Q = 100 \times \left( T_m - T_9 / T_b - T_m \right) \times K ( \text{or} \ 100 \times \frac{Y}{X} \times K; \text{see Fig. 1}),$$

where $K$ is a constant derived from the specific heats and relative densities of saline and blood. For simplicity, it will be regarded as unity. The lower graph in Figure 1 shows a hypothetical pattern of flow at 100 ml/min initially, followed by square-wave oscillations between 33.3 and 300 ml/min. The upper graph shows the oscillations of $T_m$ which would result from the illustrated oscillations of flow, if the thermal dilution system had an infinitely fast response time, i.e., if mixing was instantaneous, mixing volume infinitesimal, and $T_m$ recording infinitely fast. The ordinate is a linear temperature scale extending only from $T_b$ to $T_9$. As has been pointed out by Cropp and Burton (1), it is important to notice that the true mean flow integrated over one cycle ($\bar{Q}$) can be correctly calcu-
Top, an idealized model of a system for measuring steady blood flow by continuous infusion of saline at a temperature, $T_s$, into blood at a temperature, $T_b$. The flow can be calculated from $T_m$, the temperature of the mixture.

Bottom, the two graphs illustrate the application of a "perfect" thermal dilution system to the measurement of oscillatory flow. The lower graph shows square-wave oscillations of flow in milliliters per minute (continuous line); the upper curve shows the oscillations of $T_m$, which would result if the system had an infinitely fast response time. Notice that the true mean flow ($Q$, lower graph) differs from the flow calculated from the mean $T_m$. (See text.)

The simplest form of damping is that produced by lengthening the response time of the temperature recording. With increased damping of $T_m$, the oscillations of temperature disappear, leaving an almost straight line for $T_m$, which corresponds with the mean temperature, from which the mean flow cannot be correctly calculated.

The second form of damping is that introduced by the presence of a mixing volume between injection site and recording of $T_m$. As a first approximation, the mixing volume can be regarded as a discrete mixing chamber, with a definite volume independent of flow, and $T_m$ can be regarded as being registered as the mean of the instantaneous flow curve, i.e., $\frac{300 \times 33.3}{2} = 166.6$ ml/min, but that it cannot be calculated from the mean of the temperature (shown by the dotted line mean $T_m$).

A real thermal dilution curve system differs from the idealized one of Figure 1 in two important respects. First, the temperature of the mixture cannot be recorded instantaneously, but is detected by a device with a limited response time. Second, mixing is not instantaneous, with the result that there is a finite mixing volume between injection and recording of $T_m$. The system as a whole cannot, therefore, have an infinitely fast response time, but its response to changes of flow will be damped, and the effect of two different sorts of damping can be considered.

The time constant of the mixing volume is given by the formula:

$$T.C. (sec) = \frac{6.67}{Q + 100 (ml/min)} \times 60.$$  

This works out at 1 sec when $Q$ is 300 ml/min and 3.0 sec when $Q$ is 33.3 ml/min. From the resulting oscillatory curve of $T_m$, the mean flow can be correctly calculated. (See text.)
just at the exit from the mixing chamber. This
situation is illustrated in Figure 2 which shows
the same situation as Figure 1 modified by
the presence of a mixing volume of 6.67 ml.
After a square-wave change of flow, the
changes of \( T_m \) are damped by a time constant
equal to: mixing volume \((ml)\)/total flow rate
\((ml/sec)\) and therefore changes with flow. In
the example illustrated at a blood flow rate
of 300 ml/min the total flow of blood and
saline is 400 ml/min, and the time constant is
\[
\frac{6.67}{300 + 100} \times 60 = 1.0 \text{ sec.}
\]
At a blood flow ratio
of 33.3 ml/min the time constant is
\[
\frac{6.67}{33.3 + 100} \times 60 = 3.0 \text{ sec.}
\]
The original square-wave curve of \( T_m \) is therefore damped by a time constant
which varies inversely with the total flow rate.
It can be seen by inspection of Figure 2 that
this damped \( T_m \) curve oscillates about a value
of \( T_m \) which is different from the mean \( T_m \)
shown in Figure 1, and when the oscillatory
flow was calculated from this oscillatory \( T_m \)
curve, the calculated mean flow integrated
over a cycle length corresponded with the true
mean flow; whether the same is true for all
frequencies and for different waveforms re-
 mains to be determined.
In a real thermal dilution system, both types
of damping will be present, that introduced
by the time constant of temperature recording
and that introduced by the time constant of
the mixing volume, and it can be shown that
to avoid an error in the estimate of mean flow,
the former time constant must be substan-
tially shorter than the latter (e.g., an order
of magnitude smaller).
Two further complicating factors must be
considered; the first is the fact that the mixing
volume has no physical boundary and is dif-
cult to define or measure; it cannot there-
fore necessarily be regarded as constant at
different flow rates.

The second factor has been discussed in
some detail by Cropp and Burton (1) as a
"distance distortion error" and need only be
mentioned here. To enable the correct flow
to be calculated, the mixture must pass the
site of recording of \( T_m \) at the same velocity
as it entered the mixing volume. The site of
detection of \( T_m \) should therefore be within
the mixing volume or as close as possible to
its downstream limit. However, if the down-
stream limit of the mixing volume is not con-
stant but varies with flow, then the site of
detection of \( T_m \) may not be optimal for all
levels of flow.

The following experiments were carried out
in a model system in an attempt to clarify some of these problems.

**Methods**

Figure 3 illustrates the apparatus used, which consists of a section of Perspex tube 3 cm i.d. and 20 cm long, sealed at both ends with a rubber bung. Tap water at constant temperature ($T_b$) was pumped into the tube at the lower end, and overflowed from the upper end. There was provision for infusion of tap water at a different temperature ($T_s$) through a side hole. The mixture was stirred by an electrically driven stirrer whose speed could be varied, and the temperature of the mixture could be measured at either of two sites downstream by inserting a thermistor through side holes.

The main infusion of tap water ($Q_h$) was maintained by a Sigma-Motor pump, driven by a servo-controlled motor which simultaneously pumped water through two parallel circuits. The oscillations of flow due to the pump were damped out by air damping chambers to provide a constant flow through each of the two parallel channels. Approximately square-wave oscillations of flow could be produced by alternately diverting and restoring the flow from one of the channels, using artery forceps. Mean flow was measured by timed collection of the overflow in a measuring cylinder.

The thermal indicator was tap water at a different temperature ($T_s$) infused from a pressure-driven syringe whose rate of emptying was recorded from a potentiometer geared to the syringe plunger and whose flow could be abruptly diverted by turning a tap. This flow had the same value in all experiments (86 ml/min).

Temperature was recorded by thermistors (Standard Telephone & Cables U23, US/173) mounted in Wheatstone bridges, with linearizing shunts. The signals were amplified by d-c amplifiers and displayed on an ultraviolet recorder, using 100 cps galvanometers which were optimally damped. The current to the thermistors was not sufficient to make them sensitive to changes of flow. The frequency response of the thermistor-recorder system was tested by suddenly dipping the mounted thermistors from air into stirred water at a different temperature; in all experiments the time constants were less than 0.05 sec.

**Results**

Completeness of mixing.—Under constant flow conditions it was relatively easy to define whether at any given point downstream, adequate mixing had occurred. When the stirrer was not rotating, the temperature of the mixture ($T_m$) varied with the position of the detector. As the speed of the stirrer was increased, $T_m$ showed rapid and large oscillations at a frequency of 5 to 20 cps (due to local turbulence of fluid at different temperatures) which then reduced in amplitude as the speed of the stirrer was further increased. Even when the oscillations were still fairly large (with an amplitude of up to 10% of the temperature difference $T_b - T_m$), the observed mean $T_m$ did not differ from the expected mean $T_m$ calculated from the known rates of flow, and there was no significant gradient of mean $T_m$ either across the stream or down the stream. Further increase in speed of the stirrer virtually abolished the oscillations of temperature, and $T_m$ remained uniform at all other points across or downstream; mixing was therefore regarded as being complete.

**Figure 4**

Effect of a square-wave change of flow. The infusion of thermal indicator was abruptly stopped at time 0. The upper graph shows a tracing of the original records of $T_m$ prox and $T_m$ dist as the temperature falls toward that of the tap water ($T_b$). The lower graph shows a semilogarithmic plot of the upper curves, with the ordinates in millimeters of deflection from baseline. Note that $T_m$ prox initially falls more steeply than $T_m$ dist and never forms a straight line, whereas $T_m$ dist generates a straight line after the first few seconds.
Under conditions of oscillatory flow, completeness of mixing became very much more difficult to define because the slow oscillations of T_m due to changes of flow did not occur at the same time throughout the chamber, resulting in gradients of T_m both across and downstream. However, as the speed of the stirrer was increased, the rapid oscillations of flow (due to local turbulence of incompletely mixed streams) went through the same sequence as with constant flow. The "completeness of mixing" could therefore be defined in terms of the magnitude of those oscillations; in all experiments the stirring speed was maintained sufficiently high to keep the amplitude of such rapid oscillations below 3% of T_m — T_m, and was in excess of that rate which had produced adequate mixing during steady flow at a rate equal to the peak oscillatory flow.

Measurement of apparent mixing volume.—Attempts were made to estimate the "mixing volume" by watching the distribution of injected dye, without success. An alternative approach is to analyze the behavior of the system to see if in any respect resembles a true mixing chamber with physical limits to the mixing volume. If the zone of mixing behaves as a mixing chamber, then when the rate or the temperature of the inflow is suddenly changed from one constant level to another (a step function) T_m will follow in an exponential curve, with a time constant such that 

\[ T.C. = \frac{\text{mixing volume (ml)}}{\text{flow rate (ml/sec)}} \]

that T.C. = mixing volume (ml), if the flow rate and the time constant are known, the apparent mixing volume can be calculated.

The response of the system to a step function was studied by infusing Q_b and Q_a until a steady T_m had been achieved. Q_a was then suddenly reduced to zero by turning a tap, and the resulting change of T_m was recorded at two different sites downstream—T_m,CONT and T_m,DIS (Fig. 3). Figure 4 illustrates the results of such an experiment. After the first second or two, T_b — T_m,DIS follows a single exponential decay curve. T_b — T_m,CONT changes in a different way, more steeply at first, and some time later it approximates to an exponential curve with a time constant similar to that of T_m,DIS. This difference between the two curves was consistent in all experiments, with T_m,DIS following a single exponential and T_m,CONT showing a steeper initial slope. The concept of an apparent mixing volume therefore can be applied to the system but only when T_m is recorded distally.

Variation of apparent mixing volume with flow.—The apparent mixing volume was determined at several different rates of steady flow and the results are summarized in Figure 5; as the rate of flow increased, the apparent mixing volume fell. The apparent mixing volume was also found to vary with the stirrer speed, from which it is concluded that the precise design of the mixing device will affect the frequency response of such a system.

Measurement of oscillatory flow.—The foregoing results identified the precise experimental conditions in which the method would be most likely to be in error—when the apparent mixing volume varied with flow. The method was therefore used to measure os-

![Figure 5](http://circres.ahajournals.org/content/22/1/53.full)

**Figure 5** Variation of apparent mixing volume with flow. The ordinate shows the apparent mixing volume (M.V.) calculated from the time constant of decline of T_m,DIS following a sudden cessation of the infusion of thermal indicator (M.V. = T.C. X flow). The apparent mixing volume varies with flow (Q_b) and also with the speed of the stirrer (fast = 2400 rpm and slow = 1200 rpm).
Effect of oscillations of flow. The upper curve shows the approximate pattern of flow oscillating at 0.1 cps. The lower two curves show tracings of the corresponding oscillatory curves of \( T_m \) recorded both distally and proximally. The two curves differ in shape, amplitude, and phase.

Circuitry flow at the flow rates and stirrer speeds illustrated in Figure 5.

Approximately square-wave oscillations of flow \( Q_b \) were produced at a frequency of 6 cycles/min and an amplitude of 66% of the mean flow, which ranged from 18 to 35 ml/sec. Temperature was recorded at two points downstream, \( T_{m\text{dist}} \) and \( T_{m\text{prox}} \). \( T_{m\text{prox}} \) was within the limits of the apparent mixing volume at all levels of flow. \( T_{m\text{dist}} \) would be inside the apparent mixing volume at low rates of flow and outside it at high rates of flow. Mean \( Q_b \) was measured by 30-sec collection of the overflow just before and just after the estimate of flow by thermal dilution.

Twelve experiments were carried out. Each experiment yielded five cycles of oscillations of temperature, of which the last two or three cycles were almost identical in amplitude and shape; these were selected for analysis. The ordinates of the temperature curve were measured at 1-sec intervals, and a corresponding flow curve was calculated. The mean flow was calculated by planimetry from each of the oscillatory cycles of flow.

Figure 6 illustrates the results of a typical experiment. The \( T_{m\text{dist}} \) curve differs in shape and amplitude from the \( T_{m\text{prox}} \) curve as well as showing a phase lag. However, when the mean flow for each cycle was calculated, there was no significant difference between results from the two sites of recording; the mean difference over 26 cycles of flow was 0.06% (standard deviation 1.1%) (Fig. 7).

To define the accuracy of the thermal dilution method, the calculated oscillatory flow curve was averaged over 2 or 3 cycles and compared with the mean of two timed collections in a measuring cylinder. (Fig. 8). The mean difference between the two was very small.

\[ \text{FIGURE 6} \]

\[ \text{FIGURE 7} \]
Comparison of calculated and measured flow. The experiment was as illustrated in Fig. 6, with square-wave oscillations of flow at 0.1 cps. The mean flow ($Q$) was calculated from either two or three cycles of oscillation of $T_m$ and is plotted against the mean of two measurements of flow by timed collection in a measuring cylinder before and after the calculated flow. The correlation coefficient is 0.996.

Discussion

These results show that a correctly designed thermal dilution system can accurately measure mean flow even when it is oscillatory. The two important features of the system are: first, the time constant of temperature recording should be fast compared with the time constant of the apparent mixing volume; second, mixing must be effective.

Some aspects of these results are somewhat puzzling. Although it is likely to be relatively easy to prove mathematically that an indicator dilution system should give the correct estimate of mean flow when the indicator is sampled at the exit from a constant mixing volume, it is not clear that the same will be true when the apparent mixing volume varies, as in the present experiments. Nor is it clear why the mean flows calculated from $T_{m \text{ prox}}$ and $T_{m \text{ dist}}$ do not differ significantly.

The effect of the mixing device used in these experiments is very complex. There would be effective mixing in a horizontal slice of the fluid, by virtue of the horizontal plane of the stirrer. There would also be considerable axial mixing because the centrifugal force of the stirrer would create a central zone of low pressure, and there would be reverse flow against the stream along the center of the chamber. (This was, in fact, observed with dye injections.) The phase lag between $T_{m \text{ prox}}$ and $T_{m \text{ dist}}$ was therefore much shorter than would be expected from the flow rate and the known volume of fluid separating them. It seems likely that the complex nature of mixing was responsible for the fact that there was no detectable “distance distortion error” (1).

Of the thermal dilution systems so far described, several use mixing devices which would have effects similar to the one used in these experiments. Afonso (2) used an electrically driven rotary stirrer; Lowe and Dowsett (3), and Clark and Cotton (4) used radial jets which would also cause some axial mixing. If there were sufficient axial mixing, then these systems too would be free of “distance distortion error,” and the siting of the downstream recording of $T_m$ would not be very critical, provided it was within the apparent mixing volume. All three of these systems described fail to meet the specifications for correct measurement of oscillatory flow in that the time constant of temperature recording is unsuitably long compared with the time constant of the mixing volume. Fortunately, the errors involved are likely to have been small.

The ideal local indicator system has yet to be developed. All such systems have the limitation that flow must be unidirectional. The special problems and difficulties caused by the diffusibility of a thermal indicator lead one to seek an alternative nondiffusible indicator which can be detected intravascularly with a detector having a very fast response time and a linear output. Even when such an indicator is developed there remains the other major difficulty of obtaining consistently ade-
quate mixing of indicator and blood in a short segment of vessel; the method of Afonso so far seems to be the most effective solution to this problem. The more common alternative has been the use of multiple jets, but there has been no systematic study of various configurations and directions of spray injection to determine what gives the most effective mixing in the smallest and least variable mixing volume. If the frequency response of indicator dilution systems is to be improved further, work is still needed on this topic.

References
Use of a Local Indicator Dilution Technique for the Measurement of Oscillatory Flow
R. D. LOWE

Circ Res. 1968;22:49-56
doi: 10.1161/01.RES.22.1.49

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1968 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/22/1/49

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/