A MATHEMATICAL REPRESENTATION OF THE THERMODILUTION CURVE

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Abstract:

The primary purpose of this study was to develop a mathematical representation of the thermodilution cardiac output curve. Further work focused on the development of an empirical model and a software implementation to measure cardiac output with improved patient diagnostic efficiency (speed) by area prediction. The empirical model is equivalent to a second-order over-damped system with a rectangular pulse as input. The output of the system represents the thermal response. The curve is constrained in that it follows the area criterion assumed by many cardiac output units. A software implementation of this model used to predict cardiac output takes in measured values of a thermal response up to the curve's peak and matches time constants with the model to derive a predicted curve. In matching the curve, the software also produces data that assesses the error between the two curves (measured and predicted).

Introduction

The Thermodilution waveform has been examined by Fegler [1] and is characterized by the following: a concave rise upwards, an inflection point, a peak, a concave down decay to an inflection point followed by an exponential decay. A 'recirculation artifact' appears towards the end of the exponential decay segment. Figure 1.

The area under the curve is used to determine flow rate, or more specifically, cardiac output from the Stewart-Hamilton equation. The recirculation artifact must be eliminated from the area calculation to achieve a more accurate result. This is normally done by algorithms that are derived from analysis of the curves. One common algorithm measures area up to the point on the curves downslope where the amplitude is 30% that of the peak amplitude [2]. This measured area is then multiplied by 1.22 to arrive at a total estimated area. The clinical procedure will take on the order of 10 to 15 seconds to produce a measurement from the time of injection.

For this algorithm to be accurate, some assumptions about the curves shape are implied. This investigation was primarily directed towards finding a mathematical model of the curve based on the aforementioned constraint and wave shape. The model could be useful in development of cardiac output simulations or for further research.

Method

Taylor [3] has proposed a model for the waveform based on a three-compartment system and solving three first order differential equations which results in a computational representation of the system. This will produce waveforms of the correct shape but they do not generally meet the criteria stated above for area estimation.

Common damped second order systems in engineering such as the series RLC circuit or spring, mass and dashpot will produce curves as in figure 1, when subjected to a square pulse input of voltage or force respectively. This model is appealing from its simplicity and a relationship to the thermodilution system can be postulated in that a bolus of chilled saline is injected and the temperature response is measured.

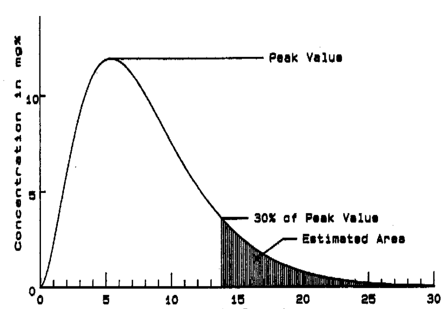

Figure 1 [3]: Thermodilution Curve

The analytical model of the thermodilution curve proposed here is based on a second-order differential system that has a rectangular pulse as the system input. The time domain response of this curve is shown below:

$$V(x) = \begin{cases} -\dfrac{ke^{(cx)}}{cd - c^2} + \dfrac{ke^{(dx)}}{d^2 - dc}, x < T_o \\ -\dfrac{k(e^{(cx)} - e^{(c(x-T_o))})}{cd - c^2} + \dfrac{k(e^{(dx)} - e^{(d(x-T_o))})}{d^2 - cd}, x \geq T_o \end{cases}$$

Equation 1: Second Order Response to Square Pulse Input

The output of the system, V(x), is a piecewise function containing the parameters c, d, x, k and To, c and d are the poles of the transfer function of the system on the s-plane. The response of the system is desired to be an over-damped response so values for c and d must be real valued (no imaginary components) unequal and negative. In the equation above x is the time in seconds, k is the height of the rectangular input (temperature in the case of thermodilution) and To is the width of the rectangular input (duration of injection of saline solution starting at 0 seconds). The value of k and To are then set to 1, allowing the values of the poles to totally characterize the shape of the output curve.

The area criteria (at 30% of peak amplitude on the down slope, the remaining area to infinity is equal to 22% of the measured area), which predicts the shape of a thermodilution curve, must then be imposed on the system. No analytical solution could be formed relating values of one pole to the other while maintaining the area requirement. This is due to a discontinuity at the endpoints of the function relating the poles to each other (Fig 2). A numerical bracketing method was used to determine pole values that would fit the area requirement.

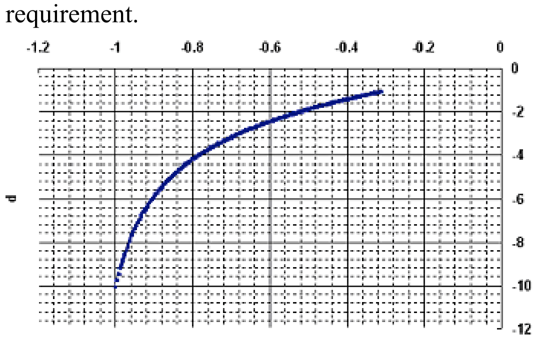

Figure 2: Pole Values (c vs d)

The numerical bracketing method fixed one pole value while varying the other. The area was then checked iteratively (allowable error was set to 0.1%) until the variable pole value was found. If the algorithm didn't converge, the "pole pair" was not added to the plot.

Area Prediction

Having obtained a mathematical representation of a thermal dilution curve, some investigation was carried out to see if the derived curves matched actual clinical curves and if the characteristics of a measured curve up to its' peak could be sufficient to estimate the remainder of the curve from comparing to the model. To find the values of poles that will match the modeled curve to a measured curve one has to measure the time to which the thermodilution curve peaks, subtract the measured time at which the injection of indicator stopped and normalize this to the measured peak time ($(Tpeak_{measured} - To_{measured}) / Tpeak_{measured}$). One can then look to the table and calculate $(Tpeak_{modeled}-1) / Tpeak_{modeled}$ and choose the pole values that most closely match the measured parameter. The modeled curve must then be scaled linearly in time and temperature to match the measured curves peak. The area from peak time to infinity can then be calculated based on the analytical model's governing equation. A software application was then developed to implement this modeling process.

Results

To test the above analytical model, some sources were found that illustrated cardiac output curves from patient clinical data. This section will address the results of a 3L/minute and a 5L/min cardiac output curves obtained by the process of thermodilution [4].

Two statistical measures were looked at to help to determine goodness of match. The differences between y-values of the measured data and modeled curve were found ($y_{measured} - V(x_{measured})$) and saved as a list. Using MAPLE the average difference was found in the list (this is a measure of how close the modeled curve actually is to the measured curve) and the standard deviation was found as well (used as a measure of how similar the shapes of the curves are). Table 1 contains the results of matching the curves.

Parameter	3L/min Curve	5L/min Curve
C pole	-0.466	-1
D pole	-1.756	-10.1
STD Deviation	0.0153053	0.0590746
Ave Difference	-.0074283	.002809

Table 1: Matching results

From the above results we can see that the 3L/min curve was matched better than the 5L/min curve this is due to the fact that there was no "pair of poles" from the look-up table that could match the normalized difference between $Tpeak_{measured}$ - $To_{measured}$, so the closest extreme value in the table was selected. Overall the curve matching procedure provides accurate results.

A Java based software application was designed and implemented to encapsulate and carry out the matching of measured data to an analytical model. The implementation extracts parameters from the curve, Tpeak, To and T_{30} and looks up corresponding pole values from a look-up table.

Overall the implementation of the analytical model in software works well. The fact that the software uses linear interpolation between pole values in the look-up table, allows it to make a somewhat more accurate match if possible.

Conclusion

Both segments of this project, the analytical model and software implementation, have given good preliminary results with actual curves. There have been some issues with the analytical model not matching the digitized curve. This can be attributed to the fact that there is no second-order differential system that can both meet the required curve shape and also maintain the 22% area criteria discussed earlier. When a match is exhibited area estimation speed can be improved over the conventional approach. This increase in speed is due to the fact that the area can be calculated by the model from the peak of the curve, instead of waiting for the curve to decay to 30% of it's peak amplitude.

Recommendations and Future Development

There are some issues that could provide more possible development of this project, they are:

- Analytical modeling of the relationship between the poles of the second-order system's transfer function.
- Further testing of the model to determine modifications to the model's governing equation to accommodate more type of curves.
- Further software development once an improved model is developed.

References:

[1] "Measurement of cardiac output in anesthetized animals by a thermo-dilution method." Fegler G., *Q J Exp Physiol Cognate Med Sci*. 1954;39:154-64

[2] "Cardiac Output", Biomedical Measurement Series – *Space Labs Inc.*, Redmond, Washington, 1991.

[3] "Understanding Techniques For Measuring Cardiac Output" Bruce C. Taylor, Daniel B. Sheffer, *Biomedical instrumentation & Technology*, May/June 1990.

[4] "Cardiac output detection by multiple frequency thermodilution", Newbower Ronald S.; Philip, James H.; *Patent: US4236527*