ANALOG AND DIGITAL SIMULATION OF THE RADIOCARDIOGRAM

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ABSTRACT

A mathematical model of the radiocardiogram has been developed to deal with the pulsatile component of the tracing. It is applicable to the bedside radiocardiogram, radionuclide angiocardiographic studies with the scintillation camera, or description of other tracer studies in the central circulation. The model consists of four heart chambers, each ejecting a fixed fraction of its contained tracer with each systole, and a lung delay function.

Discrete-variable calculation of end-systolic and end-diastolic tracer content of the heart chambers and lung allowed development of simple, rapid programs for simulation by small digital computers. By this means, curve fitting and estimation of ejection fractions, end-diastolic volumes and mean lung delay may eventually be automated. A better understanding of the problems of extracting diagnostically useful information from such a multiparameter fit should result from study of these simulations.

Families of characteristic curves were generated for several disorders where pattern recognition as well as parameter estimation is important.

A small, light weight, portable electronic analog simulator has been developed to permit the same simulation and trial-and-error parameter estimation at the bedside. It puts a real-time tracing onto the chart recorder used for actual radiocardiograms. Its design features are described.

Some ideas unifying analog and digital modeling are expressed in differential equations. They provide a framework for future simulation of the radiocardiogram in the irregularly beating heart and an algorithm for potential extraction of detailed chamber-volume curves from the nonequilibrium portion of the radiocardiogram.
INTRODUCTION

Renewed interest in the radionuclide angiocardiogram has been stimulated by the recent availability of systems that combine short-lived gamma-emitting radionuclides, the scintillation camera, and fast relatively distortion-free digital recording and digital computing. More accurate and useful diagnostic information had been promised by this ability to rapidly record images externally and apparently to quantitate counting rates from individual heart chambers and other regions of the central circulation. In practice, however, it was soon found that even in the best of circumstances the counts recorded over the various selected areas of interest are weighted averages of several regions of the central circulation, leading to complications regarding the data that must be collected and in the mathematical analysis of the curves obtained. The great advantages of a simple, noninvasive technique are partly lost because of this complexity.

Application of the above techniques has brought out the diagnostic value of the high frequency or beat-by-beat information [1], which previously was largely ignored because it could not be recorded accurately. Interpretation of this information requires a mathematical treatment beyond that offered by classical compartment-system analysis.

In an effort to extend these radiocardiographic techniques learned with the camera to a simple, safe bedside method for serial evaluation of cardiac function and pulmonary blood volume, a single-probe dual-collimation system has been developed [2]. In this case as well, in contrast to the classical interpretation of the single-probe radiocardiogram, the beat-by-beat or pulsatile component of the newer tracing assumes importance in the analysis.

Our mathematical model [3] was developed to contribute to the understanding of both the single-probe and scintillation-camera radiocardiograms, unifying the treatment of the pulsatile component and the overall shape of such curves. This model is an extension of ideas about beat-by-beat ejection enunciated by such workers as Folsø & Braunwald [4] and Bianchi et al. [5], extended and made convenient by computer methods and combined with our own choice of an appropriate lung delay function.

An excellent study of the radiocardiogram from this beat-by-beat standpoint was published by Roux et al. in 1967 [6], employing an analog computer simulation. Although their pioneering effort had almost no influence on the studies reported here, it certainly would have if we had known of it earlier. Their model and ours share some features, but there are also certain key differences in approach, particularly in the handling of the atria, recirculation, and delayed injection. We have recently made their paper available in English translation.

There are two recent key papers in which classic compartment-system analysis is used as the basis for analog computer simulation and curve-fitting of the radiocardiogram [7,8]. These are mentioned as modern contributions that summarize much earlier work and go far in sophisticated handling of the gross features of the curves, but without explicit recognition of their pulsatile component.

Other groups have recently been making studies of the pulsatile component similar to ours [9-14] and developing models that share some features with it. Only two of these groups [9,12] model an entire four-chambered heart with lung delay. The particular virtues of the model and computer simulations that we present here appear to be the great simplicity of the digital computer programs, easily understood and able to run rapidly on a small computer in languages like FOCAL or BASIC, and the compactness and portability of the electronic analog simulator that we developed to carry this capability to the bedside. These systems are proving worthwhile as heuristic devices and teaching aids. We are beginning a study to extend their capability to automated curve-fitting and parameter estimation using the pulsatile model. From comparisons of this more realistic model with exponential-compartment modeling, the latter appears no longer to be an adequate way to estimate heart chamber volumes from the flow of tracer through the central circulation.
The model consists of four heart chambers, each ejecting a fixed fraction of its contained blood volume (and hence of its retained tracer) with each systole, and a function describing the lung delay (Fig. 1). By restricting the computation to points at end-systole and end-diastole, no integration is required in the program, and the calculation is simple and rapid.

Heart chambers

Each of the four heart chambers behaves as follows:

At end-diastole, \( q = q + I \)

At end-systole, \( r = q \cdot e \) and \( q = q \cdot (1 - e) \)

where \( q \) is total quantity of tracer in the heart chamber, \( I \) is the total quantity of tracer input to the chamber during its diastole, \( r \) is the quantity of tracer output from the chamber during systole, and \( e \) is the constant ejection fraction of the chamber.

The mechanism is written here in computer-language replacement statements instead of ordinary equations, because the recursion relations are very simple when so expressed and are unnecessarily complicated by subscripting to indicate the phase of each cycle and the chamber involved. The programming sequence shown in the sample programs below guarantees the required reciprocal behavior of the heart chambers and its relationship to the lung transit-time distribution.

Lung transit-time distribution

The transit-time distribution chosen to represent the delay of tracer in the lung is most simply represented for digital computation by its “residue function”:

\[
H^*_i = e^{-\lambda i} \sum_{k=0}^{n-1} \frac{(\lambda i)^k}{k!}
\]

and \( H^*_i = H^*_i \)

where \( i \) has values 0, 1, 2 \ldots. This generates a curve of the type shown in Fig. 2.

\( H^* \) is the residue function in the terminology of Bassingthwaighte [15], that is 1-\( H \), where \( H \) is the familiar cumulative frequency function, the integral of \( h \), the frequency function of tracer transit times. Here, however, we are dealing with a discrete or discontinuous frequency function in contrast to the continuous frequency function usually employed in circulatory dynamics. Justification for the use of the residue function—and of this particular one—is given in reference [5]. \( \lambda \) is the turnover constant of any single compartment in the series of equal size compartments that make up the lung delay. \( n \) is the number of such compartments. The mean time of tracer in the lung is given by \( n/\lambda \). Alternatively, the distribution may be regarded simply as a convenient and reasonable two parameter curve for the lung delay, with parameters \( \lambda \) and \( n \). \( i \) is the dummy index used to number each cardiac cycle. \( H^* \) is the value of the residue function at ventricular end-systole and \( H^* \) is used to indicate the corresponding value at ventricular end-diastole.
In the general case the lung transit-time distribution must be convoluted on the input from the RV. In our discrete-variable approximation this convolution is given by

\[ q_i = \frac{1}{k=1} (I_k \cdot H^*_{i-k}) \]

and \( q_i' = q_i \).

\( q_i \) is the quantity of tracer in the lung, where \( i \) indexes the cardiac cycles. \( I_k \) is the input from RV systole during any previous \( k \)th cycle. \( H^* \) is the lung residue-function described above. \( q' \) is used to indicate the value at ventricular end-diastole in contrast to \( q \) at ventricular end-systole.

The lung output to the LA is given by

\[ r_i = q_{i-1} - q_i + I_i, \]

where \( i = 1, 2, 3, \ldots \) and \( q_0 = 0 \).

For the case of a single one-beat injection direct into the lung, the above simplifies to

\[ q_i = H^*_{i-1}, \]

\[ q_i' = q_i, \]

and \( r_i = q_{i-1} - q_i \).

In this case the values of \( I_i \) and \( H^* \) need not be stored by the program at each cycle for later use, as is necessary for the convolution. In connection with one-beat injection direct into the RA, we have described a mathematical device that can take advantage of this simplification [3]. It consists of rearranging the order of lung and heart chambers for calculational purposes, putting the lung first for part of the calculation. It results in reduced computer time and core storage requirements that may be important in some small-computer applications. An example of this rearrangement can be found in the sample program, Fig. 3.

**Principal parameters**

The simplest set of parameters required as input to the model consists of the following six numbers: four ejection fractions, one for each heart chamber, plus the two parameters of the lung delay, often specified as its mean transit time and the factor \( n \) (number of compartments in series) for the shape of the delay.

Another useful set of parameters that specifies essentially the same information about the model, but which is often closer to the clinical interest of the user, is the following set of seven numbers: the stroke volume, four end-diastolic volumes, one for each heart chamber, plus two parameters for the lung delay, often specified as the lung blood volume and the shape factor, \( n \). From these the program easily calculates the primary set of parameters initially. We have not often found it useful to specify cardiac output and heart rate as input parameters, since only their ratio (stroke volume) is needed by the program, but this can of course be included if convenient.
If data are to be fitted by the model, if valvular regurgitation is included, or if a weighted average of chambers is simulated, one or more additional parameters must be specified.

**Sample programs and characteristic patterns**

Three short programs are shown as examples of computer applications of the model. They are all in the language FOCAL-12, although short FORTRAN and BASIC programs have also been written. The first program (Fig. 3) illustrates the basic sequence and the compact, storage-sparing program that can be written using the device of putting the lung first (described above). The second program (Fig. 4) illustrates a further elaboration: inclusion of the convolution required by the more general model that has the lung in its anatomic position. This version includes the capability of accepting an arbitrary input function to the RA, an example requiring the convolution method. The third program (Fig. 5), not described in detail in the text, is one that does not include the convolution, but that has been generalized to allow regurgitant behavior in each of the four valves, including combined defects. Up to four additional input parameters for the regurgitant fraction are required. When regurgitation is absent, this model reduces to the original one, but since the assumptions on which it is based are more complicated and more conjectural, and the program longer and slower, we prefer so far not to use this model for every case. The recursion relations on which it is based we have found to be the same as those used by Kirch et al. in their regurgitant valvular heart model [10,11] the assumptions behind it being a rather natural first approximation to the mixing behavior of the blood in the heart chambers in the regurgitant case.

Figures 6-10 are typical of the output of these programs.

**Discussion**

In addition to the curves shown here and in reference [3] for various abnormal values of ejection fraction and lung transit time, the model has been used to study an arbitrary input into the RA, injection directly into lung or LA, to simulate single and combined regurgitation through each of the four valves, and to simulate simple shunts. Preliminary studies have been made on recirculation of activity and on inclusion of the coronary circulation. The present model is capable of elaboration in a number of ways. In using it in these various forms, however, one quickly becomes aware that no single set of values obtained for the parameters is likely to characterize any given curve uniquely, an important thing for future curve-fitting with such a model.

In using the model to simulate the single-probe radiocardiogram, we have most often merely summed the tracer content of RV and LV. At present we lack the information to make a better weighted average. The model, however, calculates the tracer content of each chamber and can readily produce an appropriate weighted average if weights can be specified.

The lung delay can be generated by a set of equal-sized exponential compartments in series, where n is the number of compartments and H is the sum of the tracer content of all compartments. While it is useful to visualize it this way for some purposes, as seen in the analog model presented below, it should not be interpreted that we view the lung circulation as compartments in series, since there are other ways such curves—essentially lagged-normal curves—can be generated in circulatory beds. In all the simulations shown here, n = 10 was chosen rather arbitrarily. It gives much more realistic curves than n = 1 or n = 2.

There is no obstacle to multiparameter computer fitting with this mathematical formalism, but the theoretical significance of it, as well as the problem of providing meaningful data, requires more consideration. Recognizing some of the objections to fitting both multicompartment and deconvolution models to the data presently available [1,3], we have thus far used the model for
simulation only. Use of it for fitting at present might best be done by choosing the shape of the lung delay rather arbitrarily as we have done in our simulations, for lack of detailed knowledge on that point. The number of fitting parameters could be as many as 10 or 11 instead of the 6 of the basic model unless weights to be assigned in averaging chamber tracer content could be assumed or separately determined.

The continuous model of the same process recently presented by Castellana et al. [9] is similar to ours in many details, but allows greater flexibility in specifying the filling and emptying behavior of the heart chambers and other features. It seems important to recognize that in such models the derivatives are at best piecewise continuous and that the result at the discontinuities, end-systole and end-diastole, can be generated more simply and with a minimum of assumptions.

A PORTABLE ELECTRONIC ANALOG SIMULATOR BASED ON THE ABOVE MODEL

The simple digital simulation led us to realize that an electronic analog of such a model could be small and portable. In this form it should help introduce people to the mathematical model, its assumptions and capabilities, and make it possible to demonstrate the principles in the ward and clinic. One can also do limited curve-fitting with it in such circumstances and use the obtained information to assist in designing an automated method of quantitation of ejection fractions and mean lung delay. Although the calculation can easily be handled by a number of small programmable calculators, and that method undoubtedly deserves further development, the need for analog input and output in a compact, portable system led us to develop this all-analog simulator.

In the electronic analog, the major properties of heart chambers and lung described earlier are retained. Operational amplifiers serve as the basic analog building blocks, and the analogy of filling and emptying of heart chambers is done with integrals of square waves. The mathematical correspondence of this approach with that of the digital model is covered in more detail in the discussion below.

The simulator is small and light weight. Dimensions of the metal container are 23 X 15 X 13 cm and total weight 2.2 kg. Output is a 0 to +10 volt signal simulating a radiocardiogram in real time. The output can be recorded on the chart recorder used for actual radiocardiograms. Ejection fractions are set by four direct-reading dials. The mean lung delay dial has continuous control from 1.5 to 30 sec. A dial is provided for heart rate, and another for ratio of systolic to diastolic time intervals. On the front panel one also chooses injection into RA, RV, lung, LA or LV, and sampling either at one of these same sites or else at a combined RV-LV site for the standard radiocardiogram. When the latter output is chosen, another dial varies the relative contribution of RV and LV from zero to 100%.

Figures 11-13 show the principal circuit design features of the simulator. It has 34 integrated-circuit operational amplifiers and 4 analog multipliers. All components except the power supply are located on three printed circuit cards. The heart rate adjustment does not interact with any of the other adjustments. The four analog multipliers are required in order to keep injection quantity constant when heart rate is varied. The lung delay is formed by ten stages of variable exponentials, each stage consisting of a voltage follower operational amplifier and CdS-LED pair.

Figure 14 shows a typical series of tracings made by the simulator. The variable injection and sampling sites permit simulation of central-circulatory tracer curves other than the radiocardiogram. The value n for the lung delay was fixed at 10, but could easily be given variable integral values instead.

Inclusion of variable heart rate and systolic/diastolic ratio permits better simulation in real time and easier matching with actual radiocardiograms. It should facilitate trial-and-error curve
fitting. The interaction of systolic/diastolic ratio with mean lung time does, however, create problems in calibrating the lung delay.

PRESENT AND FUTURE MODELING—GENERAL DISCUSSION

One way to unify the above subject matter is to state it in differential equation form. Rather than attempt a very general presentation that can include shunts, regurgitation, etc., we have chosen a level of abstraction and complication that can 1) encompass our discrete and analog models as special cases, 2) model the radiocardiogram in the irregularly contracting heart in real time, and 3) provide a basis for either simulation or analysis of detailed curves between the end-systolic and end-diastolic points. The other complications, which we have considered separately, could be added to it. This approach has also clarified the relationship of our models to the broader differential equation description of Castellana et al. [9] and to the analog model of Roux et al. [6].

If, after stating the problem in differential equation form, one simply makes some assumptions about a reasonable functional form for the cyclic curves of chamber volumes as a function of time and uses approximate integration in a digital system, one has essentially the method of Castellana et al. It yields the same result as an analog system except for a problem of speed versus accuracy of integration that is negligible in the analog system.

One may consider the method of solution of the differential equations, once they are formulated, as trivial, but our own interest was to explore simplifications and to avoid any unnecessary assumptions. In order to shorten programs and speed them, particularly using discrete variable, we looked for simple solutions in closed form. However, in order to handle all cases of interest and the continuous aspects of the problem between end-systolic and end-diastolic points, we must return to a more general statement of the problem in differential equation form.

The equations can be written as a single set covering all time of interest. They are then simultaneous linear differential equations with time-variant coefficients [16]. The coefficients, however, usually have a value that is either zero or nonzero and constant throughout any particular half cardiac cycle. Alternatively, the same information can be given as part of a table of functional relations [9]. The end result however can be viewed as switching coefficients alternately on and off at the end of each half cycle (actual physical switching in the case of the analog simulator). We have used the equivalent means of simply writing separate sets of equations for systole and diastole. Throughout the whole sequence of simulated cycles, continuity of chamber volumes and quantity of tracer are obvious boundary conditions on the solutions, so that the end of each half cycle is the appropriate starting point for the next.

Our problem can be stated in the sets of differential equations given below. The following notation is used.

i is a subscript indexing the heart chambers, 1 through 4.

j is a subscript indexing the series of exponentially washed out compartments used to generate the lung delay.

q is the fraction of the injected dose of tracer in a region of interest, a heart chamber or portion of the lung circulation.

V is the volume of blood contained in a given heart chamber.
c is a concentration of tracer, either flowing into or out of one of the regions of interest, or present in it, as indicated by subscripts.

r is a rate of tracer transfer (dq/dt) from one chamber or region of interest to another.

e is the ejection fraction of a given heart chamber, such that \( e_i \) is defined as \( (V_{ED,i} - V_{ES,i})/V_{ED,i} \). Although it can be defined retrospectively for any given systolic half-cycle, \( e \) is used below only in the context of constant ejection fraction throughout the whole period of interest.

In the equations given, not every continuous function of time is explicitly indicated as such by the notation \( f(t) \), but from subscripting or lack of it, it should be clear which quantities are treated as constant for the half cardiac cycle in question and which as functions of time.

Heart chambers

During systole: \( dq_j/dt = c_{S,i}dV_j/dt \)

where the constant systolic concentration \( c_{S,i} \) is defined as \( q_{ED,i}/V_{ED,i} \), two values held from the preceding end-diastole. The solution of this differential equation is the very simple relation \( q_i = c_{S,i}V_i \). However, in the analog system the hardware solves it by integration.

During diastole: \( dq_i/dt = c_{IN,i}dV_i/dt \)

where \( c_{IN} \) refers to the input concentration to the chamber during diastole. It is important whether \( c_{IN} \) is a function of time, is zero, or is constant throughout the diastolic half cycle. If \( c_{IN,i} = 0 \), then \( q_i = \text{const.} \) for that half cycle. If \( c_{IN,i} \) is constant for the half cycle because it is the inflow from a well mixed preceding chamber, then the simple solution \( q_i = q_{ES,i} + c_{IN,i}(V_i(t) - V_{ES,i}) \) applies. However, when \( c_{IN,i} \) is a function of time during the half cycle, a more complicated integral equation must be solved by one or another means. In the analog system, the integration presents no particular difficulties in any of these three cases.

Lung delay

During systole: \( dq_j/dt = r_j(t) - kq_j \)

a series of simple linear first order differential equations, where

\[ r_1(t) = \text{output from RV} \]

and \( r_j(t) = kq_{j-1} \) for \( j \neq 1 \).

During diastole: \( dq_j/dt = 0 \).

For the lung, \( j \) indexes the order of the series of exponentially washed-out compartments used to generate the lung delay, so that \( q_j \) refers to the quantity in only one of these compartments, and the quantity of tracer in the entire lung is given by \( \sum_{j=1}^{n} q_j \). The solution for this system is available in closed form as shown in a preceding section, but in the analog system its solution is obtained by integrating these differential equations.
It can readily be shown that our discrete-variable solution for end-systolic and end-diastolic points can be derived as a degenerate case of this model. The only additional assumption required is that end-systolic and end-diastolic chamber volumes have constant values (constitute a periodic series) so that ejection fractions are well-defined constants.

Our analog version of the model computes the points by integration but essentially ignores the true shape of the intervening curves. It can be represented by the sets of differential equations given below. They are simple algebraic manipulations of those just given, with the additional assumption that the volume curves of the heart chambers are periodic functions. This assumption not only results in well-defined values of the e; but makes possible the representation of the volume curves by any of a variety of simple periodic functions (merely straight lines in the present analog) scaled so as to sawtooth from zero to some fixed voltage with each half cardiac cycle.

The modified equations solved by the present analog model are as follows:

Heart chambers for constant $e$

**During systole:**

$$\frac{dq_j}{dt} = -q_{ED,j} \cdot \frac{dF_j}{dt}$$

where $\frac{dF_j}{dt}$ is a simple square wave in the present electronic analog simulator. The solution of this differential equation is $q_j = -q_{ED,j} \cdot F_j(t)$ but in the electronic analog system the differential equation is instead solved by integration done by the hardware.

**During diastole:**

$$\frac{dq_j}{dt} = c_{IN,j} \cdot (V_{ED,j} - V_{ES,j}) \cdot \frac{dG_j}{dt}$$

where $\frac{dG_j}{dt}$ is merely the same square wave in the present analog simulator. If $c_{IN,j} = 0$, then $q_j = \text{const.}$ for that half cycle. If $c_{IN,j}$ is constant for the half cycle because it is the inflow from a well mixed preceding chamber, then $\frac{dq_j}{dt} = q_{IN,j} \cdot \frac{dG_j}{dt}$ and the solution is $q_j = q_{ES,j} + q_{IN,j} \cdot G_j(t)$. When $c_{IN,j}$ is a function of time during the half cycle, a more complicated integral equation must be solved by one or another means—no particular problem for the analog system.

Lung delay for constant $e$

The lung delay is handled in identical fashion to that given above for the more general model.

Discussion

Solution of these equations requires track-and-hold and switching circuitry that is not necessary in classical nonpulsatile modeling.

The more general model described by the previous set of equations would be capable of simulating the radiocardiogram of the irregularly contracting heart in real time given the volume curves of the chambers, and also provides the algorithm one would need for obtaining detailed volume curves from an average of several beats in the nonequilibrium portion of the radiocardiogram, if that proved desirable.

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REFERENCES


FIG. 1. Schema for mathematical model of the radiocardiogram. Circles indicate that the transfer function for each heart chamber is a departure from compartment-system theory. Lung delay of tracer is a simple mathematical function that is neither a fixed delay time nor a single exponential (see text).
FIG. 2. Lung transit-time distribution. Abscissa: cardiac contractions, indicated by discontinuities in curve. Ordinate: fraction of tracer remaining that entered lung on first beat. Upper curve is $H^*$, the residue function; lower curve is tracer transit-time distribution generated from changes in $H^*$ per beat. Curves simulate lung tracer content and rate at which tracer leaves lung following rapid single injection into pulmonary artery.
FIG. 3. Sample computer program in FOCAL-12 language, illustrating basic features of the mathematical model. Uses calculational device of putting lung first to avoid convolution (see text).
FIG. 4. Sample computer program in FOCAL-12 language illustrating more general convolution method of calculation, with lung in its anatomic position. Includes arbitrary beat-by-beat input into RA. Requires more storage of intermediate values than previous program.
FIG. 5. Sample computer program in FOCAL-12 language illustrating elaboration of the model of Fig. 3 to include valvular regurgitation.
FIG. 6.  Theoretical normal radiocardiogram, using values given in Ref. [3].  (A)  Tracer content of RV + LV.  (B)  Tracer content of lung.
FIG. 7. Theoretical radiocardiograms following RA injection. (A) Tracer content of RV, with RV volume 1, 2, 3 and 4 times normal. (B) Tracer content of LV with LV volume 1, 2, 3 and 4 times normal.
FIG. 8. Theoretical radiocardiograms of progressive RV dilatation. Top curve normal. In descending order, RV volume 1, 2, 3 and 4 times normal.
FIG. 9. Theoretical radiocardiograms of progressive decrease in pulmonary blood vol. Top curve normal. In descending order, PBV 1, 1/2, 1/4 and 1/8 times normal.
FIG. 10. Theoretical radiocardiograms of progressive decrease in PBV combined with decrease
RV dilatation. Top curve normal. Second curve: RV volume twice normal, PBV one-half normal.
Third curve: RV volume three times normal, PBV one-third normal.
FIG. 11. Overall block diagram of electronic analog simulator.
FIG. 12. Block diagram of one of the four identical heart chamber analogs of the simulator.
FIG. 13. Diagram of one of the two atrioventricular pairs employed in the analog, showing detail of circuitry and components.
FIG. 14. A series of radiocardiograms drawn on a chart recorder in real time by the electronic analog simulator.