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Kent S. Kapitan
Southern Illinois University Carbondale

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Kent S. Kapitan

Department of Medicine
University of California, San Diego
San Diego, California 92093

Monte-Carlo simulation allows a theoretical evaluation of the Va/Q distributions recovered from inert gas elimination data. However, when the underlying distribution is narrow, or when significant experimental error is present in the data, Monte-Carlo simulation becomes computationally impossible. A new algorithm is presented which avoids these limitations by directly producing randomly distributed data points lying within the column space of the defining inert gas model.

Monte-Carlo simulation is an important numerical tool which has a critical role in the multiple inert gas elimination technique because it allows a theoretical evaluation of the effects of random error on the Va/Q distributions recovered from inert gas elimination data [1]. In combination with Monte-Carlo simulation, one may determine the upper perfusion bound of the Va/Q distribution, assess its modality, formulate confidence limits for its central moments, and assess the significance of small changes in the Va/Q distribution by applying linear programming techniques [2,3]. However, when the underlying Va/Q distribution is very narrow, or when significant experimental error is present in the data, Monte-Carlo simulation becomes computationally impractical or impossible. The objective of this paper is to present a simple algorithm for improving the efficiency of this process.

The basic equation of inert gas retention [4] relates the retention of an inert gas to the underlying Va/Q distribution:

$$R = \int \lambda / (\lambda + VQ)\ Q\ dVQ \qquad (1)$$

Here, R is the retention of the inert gas, λ is the corresponding blood:gas partition coefficient, VQ is the Va/Q ratio, and Q is the fractional perfusion, which is constrained to be nonnegative and less than or equal to 1. The range of Eqn 1 defines a convex region in space, which has been called the 'region of possible outputs' [1]. Importantly, it is composed of all the retention sets which are compatible with some Va/Q distribution, and points outside of the region are not compatible with a parallel model of steady-state gas exchange.

Because the region of possible outputs is quite small and because experimental error is always present in retention measurements, a measured retention set almost always lies outside of this region. Since no Va/Q distribution is compatible with such a measurement, one must estimate the true retention set from the data by asking which point within the range of Eqn 1 will produce the measured set when it is perturbed by experimental error. Traditional Monte-Carlo simulation answers this question by estimating the resposible retention set as follows [1].

Random errors of the magnitude encountered in practice are repeatedly subtracted from the measured retention set and each perturbed set so produced is then tested to determine whether it lies within the range of Eqn 1 and is thereby compatible with a parallel model of gas exchange. If it does not, it is discarded and the process is restarted. This process is repeated until a library of fifty interior points has been identified. These fifty sets are then used as a statistical sample of the probable location of the real retention set which gave rise by addition of experimental error to the measured retentions.

The efficiency of the Monte-Carlo method, and thus the time it takes to generate the fifty interior retention sets, depends critically upon the fraction of generated points which fall within the region of possible outputs. In practice the efficiency is typically less than 0.5%, and measured retention sets which are associated with narrow Va/Q distributions or those containing more than average experimental error, have an even smaller fraction of the perturbed points falling within the region. This leads to very long computer runs, and for some data sets the Monte-Carlo technique may never identify even a single interior set.

The Monte-Carlo method can be greatly accelerated by modifying it to randomly generate only interior points. The algorithm for accomplishing this is quite simple and relies upon the observation that the range of Eqn 1 is convex and is bounded by the columns of the inert gas matrix. It is most easily understood step by step: (1) Perturb the measured retention of one gas with random error of an appropriate magnitude. (2) Using linear programming with Eqn 1 applied to the

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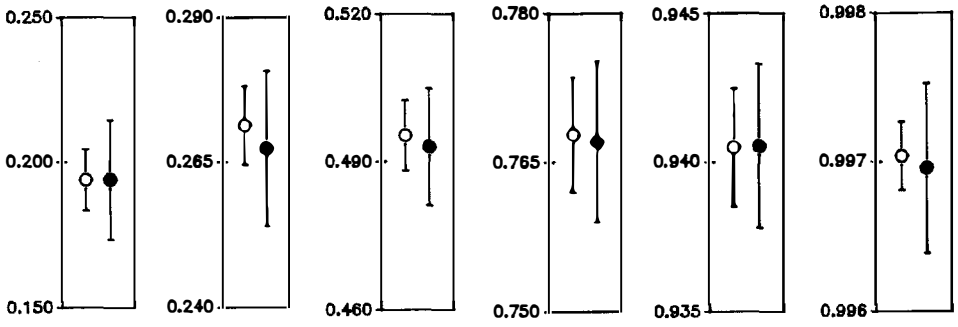

Figure 1. Comparison of feasible retention populations computed using conventional Monte-Carlo (O) and modified (●) algorithms. Means and standard deviations are shown. Gases studied are from left to right: sulfur hexafluoride, ethane, cyclopropane, enflurane, diethyl ether, and acetone.

perturbed datum as a constraint, compute the maximum and minimum retentions a second gas could have. (3) Randomly choose the retention of Gas #2 from within this range, using a Gaussian distribution. (4) Repeat steps 2 & 3 for each remaining gas, using the perturbed retentions of the preceeding gases as constraints.

The above algorithm was programmed in FORTRAN and run on a Perkin-Elmer laboratory computer. Data sets were constructed from typical Va/Q distributions and were perturbed with known amounts of experimental error. Runtimes and results for these data sets and for experimentally measured data sets were compared with those obtained using the traditional algorithm. The modified algorithm had a fixed runtime of ten minutes, while the traditional algorithm runtime varied widely with the data set, and failed when faced with data sets associated with narrow Va/Q distributions or with those having greater than expected amounts of error. A typical comparison is shown in Fig 1. The estimated retention sets resulting from the two algorithms were not statistically different.

Finally, it is worthwhile to note that the range of Eqn 1 becomes smaller as the number of dimensions increases, and this limits the traditional Monte-Carlo algorithm to problems having relatively few dimensions. The modified algorithm is free of this limitation and therefore can also be applied to higher dimensional physiological problems, such as the interpretation of the multiple-breath nitrogen washout [5].

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mailing address: Department of Medicine
UCSD Medical Center V-111J
San Diego, Calif. 92103
619-453-7500 Ext. 3541