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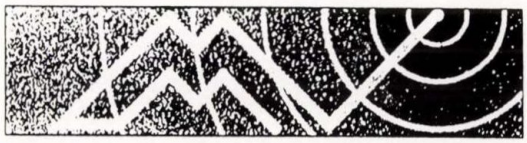

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Fax: (361) 135-5560

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EDITORIAL

From age to age every effort has been made to apply up-to-date knowledge in medicine for protection of human life. Medicinal herbs were used in the agricultural period, technology was used in the industrial society. In our days, when the information society is developing, information science is applied. Although the patient's history has been always used, functional capacities have been tested, developed changes have been examined, it has been done spontaneously. Since medicine has examined itself by means of informatics, it has been realized, that the three mentioned kinds of information represent time, function and structure.

Medicine changes from natural history into natural science by turning qualitative statements into quantitative ones. The rules of structural–functional connections, changing in time, can be included in a general formula. It could become individually valid by appropriate parameter estimation. In this way health care becomes scientifically established and individually optimized in large numbers. It is similar to the "custom designed method" used in the industry for production of individual products en masse.

Computarization is necessary for information processing because of the quantity and complexity of information even in individual cases. This is the reason why the computerization is expanding in medicine.

Computerization plays several roles in the text information handling:

- the computerization of administration relieves the medical personnel of the routine work,
- it makes possible the data base management by data collection and archivation,
- it can contribute to the diagnosis by processing the symptoms and their combinations by means of the theory of probability.

The analysis of the curves of the functional state amplitude/time function (ECG, EEG, impedance CG, flow, pressure, volumen, etc.) provides not only quantitative individual data, but also offers and automatic evaluation. It can be realized by means of the intelligence built in the measuring instruments or in the measuring system configuration, integrated into a computer.

Computerized handling of images, registrating structural changes (X-ray, ultrasound, nuclear, magnetic resonance, thermovision, near infrared, microscopic images) cover digitization, densitometry, density borderline detection and — besides of their analysis — 3-D reconstructions.

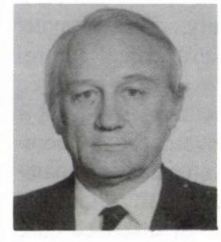
The combination of all these on a multimedia level makes an animated model-simulation possible. Beyond a simple, casual or epidemiological communication, the multidisciplinarity means a programmed communication in education and in extension training.

There are several technical problems (chanel capacity, transmission speed, noise, redundancy, transmission security, etc.) in comunication in the line "transmission – coding – transport – reception – decoding – interpretation". In addition to them there are some problems in medicine concerning ethics and privacy protection. One of the best solutions of these problems is the personalized chip card, which is the largest divided data base and the patient is the best data carrier. In this way a biological–technical combination of communication is taking shape.

It can be completed by metacommunicative elements of the personal doctor/patient meeting. These elements cover intuition, empathy, gesture, facial expression, intonation and the integration of all these, that is general impression.

Today these all together mean the available data that we use to avoid the danger that Sherlock Holmes has directed our attention to: There is nothing more dangerous than to draw conclusions before having data.

ATTILA NASZLADY
Cardiopulmonary Department,
National Institute of Pulmonology
Budapest, P.O.Box 124, H-1529



Attila Naszlady Author of scientific medical articles in domestic and foreign medical journals, Hungarian, Swiss, French, Polish and English, numbering more than 80. Attila Naszlady is also the author of more than 150 congress lectures and papers at home and abroad, Budapest, Gothenburg, Milan, Paris, Strasbourg (Invited by the Council of Europe, ECC in 1991) and Erfurt, and book chapters in "Progress in Respiratory Research", 1975, and "Diagnostics in Internal Medicine", 1982, etc. Born on 4 November 1931 in Budapest, Hungary, he earned his MD degree, Summa cum Laude, from Semmelweis Medical University, Budapest, 1958, qualified as a Specialist in Internal Medicine, Postgraduate Medical University, Budapest, 1962, took his ECFMG Examination, US standard, in Vienna, Austria, 1964, earned his Candidate of Sciences from Budapest, in 1968, took a Boearhaave Course in Leyden, the Netherlands, in 1971, became a Specialist in Cardiology, Budapest Postgraduate Medical University, 1979, earned his Academic Doctor of Medical Science degree, Hungary, in 1980, and became Professor, honoris causa, and Invited Lecturer, Semmelweis Medical University, Budapest, 1981, Resident Doctor in the Medical Department of Municipal Hospital, Esztergom City, 1958–60, he was a Research Fellow, and then Assitant Professor, National Institute of Cardiology, Budapest, 1960–70, and since 1970 has been Head of the Cardiopulmonary Department, Laboratory Clinic, National Institute of Pulmonology, and since 1992 he has been the General Director of that Institute. Dr. Naszlady is a member of the European Society for Clinical Respiratory Physiology, Editor in Chief of "Cardiologia Hungarica", Board of the Society of Hungarian Cardiologists, and Board of the Society of Hungarian Pulmonologists, and he is President of the Medical Section of J. v. Neumann Computer Society, Board member of the European Federation for Medical Informatics (EFMI) and National Representative in the Council of International Medical Informatics Association (IMIA), and in TC-13 of International Measserement Confederation (IMEKO). In 1968 he received an Award from the World Health Organization Followship, was Hungarian Academic Prize Winner in 1974 and again in 1978, and since 1980 has been World Health Organization Temporary Adviser. He has been elected active member of New York Academy of Sciences in 1992. In 1960 he married Éva Csürös, MD, Pediatrician, and Pediatric Cardiologist.

MODELLING IN PHYSIOLOGY AND MEDICINE: AN INFORMATION LINK BETWEEN REALITY AND THEORY

E.R. CARSON
CENTRE FOR MEASUREMENT AND INFORMATION IN MEDICINE
DEPARTMENT OF SYSTEMS SCIENCE, CITY UNIVERSITY
NORTHAMPTON SQUARE, LONDON, EC1V OHB
UNITED KINGDOM

This paper focuses on the modelling process as it is practised in physiology and medicine. It is shown that, by means of modelling activity, understanding, that is information gain, is achieved; and that in essence the modelling process can be regarded as the provision of an information link between reality and theory. The information requirements, in turn, define the most appropriate modelling approaches. It is then shown that integrated modelling methodologies exist which enable modelling activities to be undertaken in a manner conducive to the scientific or utilitarian objectives of the physiological or medical context being realised.

1. INTRODUCTION

From a systems perspective, the human organism is a classic illustration of organised complexity. For example, it exhibits structural complexity in its hierarchical control mechanisms; mechanisms which also reveal a high degree of autonomous decentralization. At a behavioural level it exhibits patterns of functionality that reveal all the complexities of non-linear, time-varying and stochastic dynamics. This is the complexity which in its healthy state the physiologist, and in its patho-physiological or diseased state the clinician, wishes to understand.

Understanding, which implies an information gain, can be achieved primarily through the use of models. Models are vehicles, whether at the conceptual or concrete level, whereby physiological or clinical theories can be expressed as a means of obtaining greater knowledge about the reality in question. The initial understanding of the physiological or medical systems of interest arises from data which provide a manifestation of that physiological or medical reality.

Models enable inferential measurement to be achieved (making estimates of quantities not directly measurable from the available data), patient state to be estimated and predictions to be made of response to therapy. These and other roles of modelling are described in the section that follows. The issues of available modelling modalities and the methodology for model building are then considered, identifying clearly the role of models within the clinical context. In its several and varied ways, it will be demonstrated that the modelling process provides an information link between reality and theory.

2. THE ROLE OF MODELS AS PROVIDERS OF INFORMATION

If the modelling process is to proceed successfully as an information link between reality and theory, it is necessary that the purpose of the model should be clearly and precisely defined; for only in this way can the validity of a model be assessed. The general types of purpose for which models are developed correspond to the three classical categories of descriptive, predictive and explanatory models.

Over and above the use of models as descriptions, where the purpose is essentially self-eivdent, the predictive use of models serves to determine how a system would respond to a stimulus or to a change in the system. A model may, for example, be used to predict the response of an organism to a drug or to loss of function in an organ.

The explanatory power of, for example, a mathematical model lies in the description it gives of the ways in which different features of system behaviour and structure depend on each other. This leads to a number of uses. First, of course, is for insight and understanding. Second, a model may be used as a hypothesis to be tested for the purpose of investigating a system. In this connection the model may indicate the critical tests that need to be carried out, thereby stimulating experimental research. Finally, a model may be used for the purpose of measuring in a system quantities inaccessible to measurement, from observations on accessible variables. Related to this is the use of models to diagnose, from observable behaviour, structural causes of an organism malfunction.

The principal purposes of model building in the physiological and clinical settings can thus be summarised as (adapted from Carson et al., [5]:

- Identification of physiological or biochemical structure.
- Estimation of parameters which are not amenable to direct measurement in physiology and in clinical medicine for diagnostic purposes.
- Dose–response relations in pharmacokinetics.
- Input/output predict for patient management.
- On-line control of intravenous drug administration.
- Design of experiments, using models such that the maximum infomation yield is obtained from a given experiment.
- Teaching.

A range of modelling modalities has been developed, with both qualitative and quantitative realizations being adopted where appropriate. The strength of qualitative approaches, particularly with regard to diagrammatic models has been highlighted by Puccia and Levins [12]. Their arguments include the fact that nature cannot be controlled in the sense of creating uniformity, and that there are real variables that are either non-quantificable or change in value with any attempt to measure them. They further argue that in biological (hence physiological) problems the search for quantification of links or establishment of accurately measured base lines ignores the fact that often the biological (physiological) reality resides in the rules of construction of the system and not in the absolute values.

Statistical modelling has progressed in a range of ways so that in relation to medicine it is no longer confined to applications such as time series analysis and modelling in terms of statistical transfer functions. A powerful recent development has been the adoption of causal probabilistic network modelling. Initially employed in diagnostic problems such as the interpretation of EMG signals (Andreassen et al., [1]), they are now being employed in relation to patient management. For instance physiologically-based models of this form are being used to predict the response of a diabetic patient to changes in insulin therapy (Andreassen et al., [2]). They have the merit of making predictions not in terms of single values, but rather as a probability distribution of the variable concerned (in this case blood glucose), incorporating the essential uncertainty of clinical reality.

Equally the term logical modelling embraces a range of approaches. These range from classical decision trees that can be used either for diagnosis or for treatment decisions, conceptual logical models derived from conceptual graphs (Sowa, [15]), through to rule-based implementations of classical knowledge-based systems.

The extent to which different modelling modalities, whether realised qualitatively or quantitatively, are effective in satisfying descriptive, predictive or explanatory purpose is shown in Figure 1. This again highlights the need to match the modelling approach to the problem under consideration if the maximum benefit, in terms of information gain, is to be achieved.

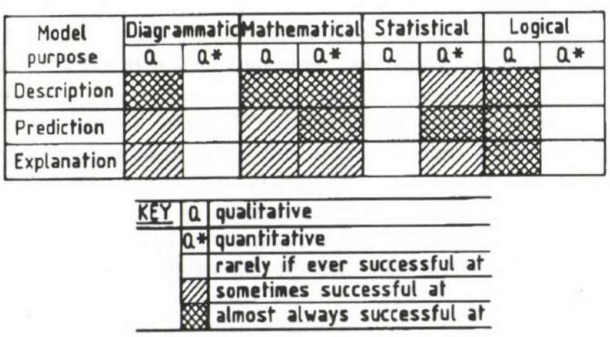


Figure 1. Relative success of modelling approaches in achieving qualitatively and quantitatively modelling purpose (adapted from Flood, [8])

An overriding feature of the modelling literature in physiology and medicine is its variety. Models may be complex and large scale, incorporating theories relating to enzyme dynamics (Garfinkel, [9]) or overall physiological regulation (Guyton et al., [10]); or they may be compact, incorporating just sufficient physiological theory as is required for the clinical problem, for instance quantifying features of abnormal carbohydrate metabolism (Bergman and Cobelli, [3]). Models may focus on practical problem solving or may seek to enhance understanding, from a systems science viewpoint, of the hierarchical complexity of physiological structure and process (Yates, [16]).

What is now apparent is that much challenging effort in modelling research involves seeking to combine and merge different modelling modalities as a means of enhancing the information yields; for instance exploiting the synergy of quantitative mathematical models as patient simulators, providing explanations or justification for advice offered by a rule-based logical model regarding therapy adjustment. Examples include application to insulin therapy in diabetes (Lehmann et al., [11]) and to fluid therapy in the critical care unit setting (Shamsolmaali et al., [13]). In other words it is at the interfaces between modelling approaches that future advance is likely to occur.

3. MODELLING METHODOLOGY

3.1. A General Framework

The problem settings, in physiology and medicine, which are perceived as being amenable to modelling activity as a means of increasing understanding, are essentially examples of structured situations. A methodology for the modeling of such structured situations is shown in Figure 2 which is adapted from Flood and Carson [7].

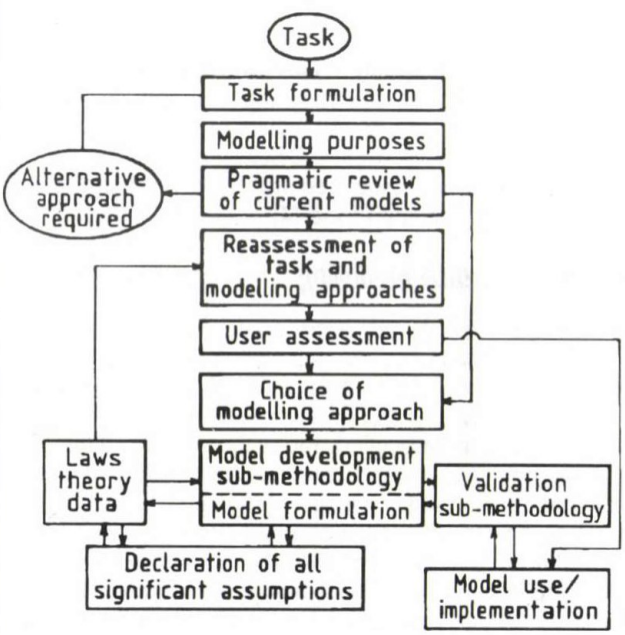


Figure 2. A methodology for modelling structured systems

Initially there is some task that focuses the attention of the physiological or clinical investigator, hence making the following activities purposeful. There is a need for task formulation. Structured approaches must not be considered a panacea for all task situations, and task formulation will help initially in deciding the appropriate route forward. An exit route from this methodology (to a non-structured approach) is therefore essential. Nevertheless, for the physiological or clinical investigator to have entered this methodology there will have been a strong sense (one usually arising out of experience) that the task is one for structured modelling.

As has been considered earlier, it is important to set the modelling pruposes in order to identify an appropriate approach. This can be substantially aided by undertaking a critical review of currently available models. The investigator is then able to incorporate a pragmatic element according to previous findings. The pragmatic review may suggest that structured approaches are not appropriate, hence exit may be required.

In many instances, the model will be incorporated into an existing situation and hence the modelling purposes will be utilitarian in nature particularly in the clinical setting. The proposed use has to be reflected in the model development and may influence the choice of modelling approach. A choice is then made. However, this can be altered at a later stage.

At this point, model construction begins by use of a model development sub-methodology. Incorporated into the thinking must be the availability of data (the problems of measurement), theories, and law. A set of assumptions concerning the model must be declared, adding a higher degree of transparency and falsifiability. These will be related to the quality of the data and the availability of laws. (Flood and Carson, [7]).

Validation (which is in fact an explicit part of the model development sub-methodology) then has to be considered more formally. This is achieved via a distinct validation sub-methodology. When some satisfactory correspondence between the situation, the model, and the modelling purposes has been attained, then model use and implementation are appropriate. This should reflect the needs of the user; however, validation will continue throughout this stage, particularly as the model may change the situation in which it is used. Discussion of some of the philosophical issues associated with model validation can be found in Carson and Flood [4].

3.2. Mathematical Modelling

The methodology, as appropriate for application to mathematical formalisms is depicted in Figure 3 (adapted from Carson et al, [4]). As is other fields, mathematical models in physiology and medicine are formulated on the basis of current knowledge about the system. This basis may be empirical, theoretical or a combination of empirical and theoretical knowledge. In general, as much theoretical a priori knowledge should be incorporated in the formulation as is consistent with the purpose of the model. Available theories (and data) reflect the stage of development of the particular area of research or application. As the field develops through increased availability of data, an increased theoretical basis for model formulation will normally result.

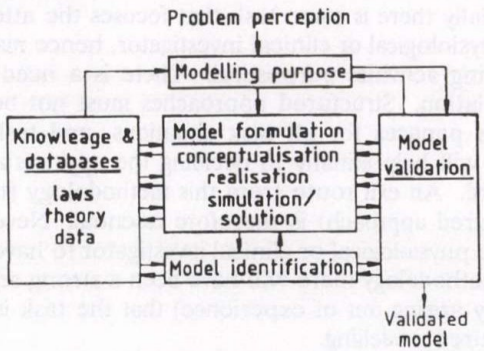


Figure 3. Mathematical modelling methodology (adapted from Carson et al., [5])

In terms of model formulation, the conceptual form represents the first stage, defining variables to be included and the nature of their inter-relationships.

In conceptual model formulation, assumptions of aggregation, abstraction and idealization are necessary, consistent with the purpose for which the model is intended in order that it should be tractable (any model is of course an approximation of reality).

Having produced the conceptual model, equations are constructed either describing the overall relations contained within the functional model or providing a detailed description of the physical processes involved. Such equations may then be solved to obtain the required explicit solutions and simulation used, for example to produce a prediction of patient response to a change in therapy. Direct solution may not be possible, however. In general there will be the need for model identification to be undertaken, designing input/output experiments to enable estimates to be made of unknown model parameters.

Once such estimates are in place then model solution and simulation may proceed. Of course there may be some instances where model parameters can be specified from a priori knowledge or by direct measurement. Formal estimation schemes are, however, required, where the model is to be used in the context of the individual patient; for example where a parameter value itself provides diagnostic information, or where a model is to be used to predict response to a given therapy regime.

Of prime importance is the need to ensure that in any modelling activity the model is valid, that is well founded, tractable and fulfilling the purpose for which it was formulated. The criteria in terms of which validity is assessed first involve judging conditions within the model without external reference to purpose, theory or data. The model should be consistent, containing no logical, mathematical or conceptual contradictions, and the algorithms used for solution or simulation should be appropriate and lead to accurate model solutions. Having satisfied these preliminary tests, the model should then be assessed in terms of its correspondence with available data and its consistency with accepted theories. If at any stage in developing and testing the model it fails to satisfy these criteria, it will be necessary to change the formulation of the model. The model should also be assessed in terms of the objectives of its intended use (e.g. are the clinical predictions of the model sufficiently accurate to be useful).

Validation is carried out both during the development of the model as well as upon the completed model. Focusing upon the final stages of validation, dependent upon the model's testability, this involves performing tests and evaluating results obtained in terms of a number of criteria of empirical validity. For models in which the parameters are estimated using input/output data obtained from dynamic identification experiments, assessment of validity involves the following quantitative measures:

- Examination of whether the parameter estimates actually achieved are sufficiently accurate and precise, e.g. for them to lead to useful predictive capability in the model.
- Examination of the goodness of fit of the model to the data.
- Testing the statistics of the residual fitting errors to enhance freedom from bias.

After examining the fit of the model, its plausibility is tested in terms of the plausibility of the estimated parameters and of other features of structure, parameters and behaviour. It is then important to consider the extent to which the model is compatible with current physiological knowledge.

4. MODELS IN HEALTH CARE DELIVERY: FEEDBACK AND FEEDFORWARD

In the clinical context, models offer potential of assisting in clinical decision making. In order for models to be used to best effect in terms of information gain by the clinician, there is the need to understand clearly the nature of the health care delivery process. This in turn can be achieved using the meta-level models described below.

The fundamental feature of the cybernetic model depicted in Figure 4 is that of feedback, and this model is capable of describing and explaining a substantial proportion of the activity associated with the delivery of health care. This implies that decisions are made, based on available information, resulting in action being taken, the effectiveness of which is subsequently assessed in relation to its having brought about the desired change in patient condition.

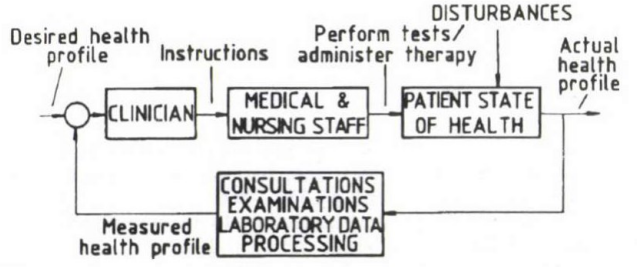


Figure 4. A cybernetic, feedback model for the delivery of patient care

However, feedback does not provide a complete model of clinical action. The feedback model must be complemented by one of feedforward. Indeed, the action of the clinician in relation to patient management provides a very good example of feedforward control. One of the principal features of clinical control (in addition to the feedback control action described above in the cybernetic model) is the taking of action at the current time in order to predicted, desired state. Equally, there is the need to prevent a predicted, undesired state. This is the principle of feedforward control action, as depicted in Figure 5.

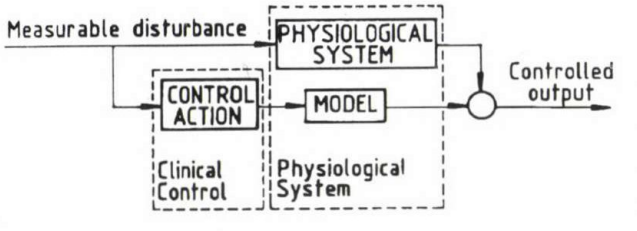


Figure 5. Feedforward control within the clinical process

In response to a measurable disturbance, as an indication of a disease process, the clinician acting as a controller responds in such a way as to eliminate the effect of that disturbance on the particular physiological process which has been deranged by the disease process. In doing this the clinician makes use of a conceptual model (or looking towards the future a computer-based model) of the specific physiological system in order to predict the result of implementing a proposed control action (treatment). The control action is chosen so that its effect on the controlled output of the assumed model would tend to cancel out the effect of the measurable disturbance on the corresponding output of the real physiological system.

This control action taken by the clinician is essentially anticipatory, predicting the likely effect of the control action, in other words feedforward control. In effect this is a process which is engaged in by the clinician when either feedback is not available from the information system of the cybernetic model or else a rapid clinical decision is required on first consultation before the full cybernetic process has had time to be brought into action. A general model of clinical control can thus be seen to be one of feedforward actions embedded within an overall feedback, cybernetic model.

Having defined the meta-level modelling framework in terms of these cybernetic feedback and feedforward representations, the role and scope of the lower level model as the information provider can be clearly defined. In the case of the feedback loop depicted in Figure 4, the term "clinician" is short-hand for model-based clinical decision making.

The model here may be the conventional mental constructs of a conceptual model of issues impinging upon the clinical decision at one end of the spectrum, to a computer implementation of a knowledge-based model, quantitative or qualitative at the other. The 'model' component embedded with the feedforward meta-level model has already been discussed.

5. AN INFORMATION PERSPECTIVE

Whether the overall purpose of modelling is descriptive, predictive or explanatory, the information gain which results from successful modelling activity can be regarded as the output of a transformation process as depicted in Figure 6.

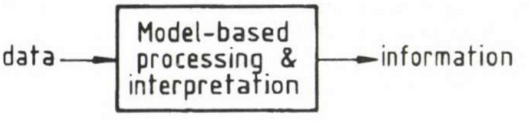


Figure 6. The role of models in transforming data into information

As described earlier, the initial manifestation of clinical reality is data. In high dependency medicine such data would typically comprise on-line physiological measurements, bedside clinical observations and the results of laboratory analysis of blood and urine samples. In order to move towards an assessment of patient state and clinical decision making regarding either the requirement for further tests or the administration of a particular therapy regime, there is a need for the data to be processed, and interpreted in context in order to yield information. Data are not synonymous with information. In a typical critical care unit it is possible for the data rate to reach over 4000 data items per patient per day (Carson et al., [6]). This data overload must be resolved by model-based transformation, reducing a potentially chaotic situation to one which maximizes information gain.

As an aside, it is worth clarifying the distinction between the terms data, knowledge and information; terms which are often quite eroneously used interchangeably

(Shortliffe and Barnett, [14]). A datum, a single observational point characterizing a relationship, can be regarded as a value of a specific variable or parameter for a particular object (for instance, a patient) at a given time. A datum may be quantitative or qualitative. Knowledge is derived through the formal or informal analysis (processing and interpretation) of data. As such it includes the results of formal studies and also common sense facts, assumptions, heuristics and models. It should be noted that any of these may reflect the experience of bias of those involved in the interpretation of the original data. The term information is more generic in that it includes both organised (that is, at least, processed) data and knowledge.

Models can thus be seen as a means of moving from a lower level perception of reality, one limited largely to data, to a higher level one which is richer in knowledge and information. It is the degree and extent of this transformation wich can be regarded as providing another overarching measure of model validity.

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Ewart Carson was educated at Liverpool College, the University of St Andrews where he graudated with a BSc in Electrical Engineering and City University where he was awarded an Msc in 1968, a PhD in 1975 and a DSc in 1990. From 1965 to 1967 he was employed by Philips, and from 1968 to 1984 at City University as Lecturer, Senior Lecturer and Reader in Systems Science. He is Director of the Research Centre for Measuremet and Information inMedicine, Professor of Systems Science at the University, and Visiting Professor in Medical Informatics at UMDS. His research interests are in the development of computer support systems for medical decision making, including dynamic modelling and knowledge based systems. His publications include 10 authored and edited books and over 200 papers. He is a Member of the Science and Engineering Reserach Council Committee on Medical Engineering and Sensors and Chairman of International Measurement Confederation (IMEKO) Technical Committee on Measurement in Medicine.

6. SUMMARY

This paper has focused upon issues associated with modelling as applied in physiology and medicine. The initial manifestation of the physiological or medical reality for the modeller is usually data. Theories in terms of which to describe, predict or explain the behaviour of the physiological or medical system can then be realised in terms of an appropriate model. The appropriate choice of model in relation to purpose then enables a transformation to take place such that the original 'poor' manifestation of reality as data is converted to a 'richer' one yielding information and knowledge concerning the reality which is being modelled.

Some of the richness and variety of modelling approaches, and underpinning methodologies, have been explored. This has illustrated the range of ways in which an appropriate increase in information can be the successful conclusion to modelling activity in physiology or clinical medicine.

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ENGINEERING CONTRIBUTIONS TO THE MODERN ELECTROCARDIOLOGY

GY. KOZMANN
RESEARCH LABORATORY FOR BIOMEDICAL ENGINEERING
HUNGARIAN ACADEMY OF SCIENCES
P.O.B. 49, H-1525
BUDAPEST, HUNGARY

Selected chapters of engineering contributions to the modern electrocardiology are reviewed, like infrared ECG telemetry, computer-aided measurement and interpretation of conventional ECG, body surface distribution maps, and late diagnostic capabilities of the standard ECG procedures due to the improved spatial, amplitude and frequency domain resolution, and due to the sophisticated deterministic or statistical interpretation methods realized. Beyond the general survey recent results on the multipolar content of cardiac electric sources and on the temporal and spatial sampling rate requirements are given. Two nonparametric feature extraction methods of statistical body surface map analysis and the adequate group representation accuracy vs. sample size relationship is discussed in details.

1. INTRODUCTION

Engineering contributions to the modern electrocardiology are mainly due to the recent progress in measurement and computation techniques. According to a recent report at the end of the eighties in the United States more than 50 million ECGs per year were processed by computerized ECG systems. At the end of the seventies this figure was still in the range of 4 millions per year.

The success of computer applications are partly due to the valuable support in diagnosis making, but there are clear cut advantages due to the ease of accurate and safe measurements, the increased possibilities of sophisticated signal processing, storing and retrieval of data on a large scale in addition to the convenience in computer supported report generation or billing.

The progress in different new branches of electrocardiographic techniques promise even more clinically usable information. The computer aided processing and interpreting methods demand new attitude from the side of medical doctors as well. It is obvious that large data bases are required consisting from the combination of invasive and noninvasive diagnostic tests to correlate the eletrocardiographic changes with certain normal or abnormal states. The data acquisition needs new technology, with increased requirements on the accuracy and especially on the patient safety aspects. The increased computation power facilitates the deeper understanding of the electric phenomena in the heart.

In this review a few selected problems of the modern electrocardiology are outlined. A short review on infrared telemetry offering a new way for safe and high-fidelity ECG measurements is given, subsequently the emphasis is put on two recent electrocardiographic methods extending the diagnostic capabilities of the standard 12 lead ECG measurements. This part of the paper summarizes the rational of the extensions studied, some selected problems of sampling rate requirements, biophysical and statistical interpretation are discussed, including the frequently overlooked problem of the sample size requirements of reliable group representations in statistical classification schemes.

2. MEASUREMENTS: INFRARED TRANSMISSION OF ECG SIGNALS

Protection of patients from all kinds of electrical shocks which are potentially possible when an individual is connected to an electrical medical equipment is of paramount importance. The risk results from electrical current flowing through the body. Medical devices are designed to minimize the exposure of patients to hazardous voltages.

Safety requirements can be easily fulfilled by the use of battery operated input units with ECG amplifiers, A/D converters and transmitter for telemetry.

Recently substantial interest in infrared (IR) telemetry has developed because of the entirely different propagation and reflection properties of IR light as compared to radio waves [1], [2]. IR light hardly penetrates most materials except for glass, and is reflected from obstacles. As a practical consequence IR radiation can easily be kept within a room. That is, the same IR frequency can be used in adjacent rooms.

In the field of ECG applications, the Swiss company MEDESE AG has introduced a kit consisting of a battery operated 12 lead ECG amplifier, an IR transmitting unit and finally an IBM PC interface. The transmission has a unidirectional data link between the sensor and the receiver. The converted samples (12 bit) are transformed into a series of pulses which modulate the infrared carrier (code modulation). In addition to the bits of the converted signals the system use error detecting bits, as well. The codes of the different channels are separated and the beginning of a new sample package is also identified [3].

This set up easily and completely is able to fulfill all the safety requirements (AHA, IEC), offers a freedom in body movements, and significantly reduces the disturbances originating from ground loops, etc.

3. INCREASING THE LIMITS OF THE CONVENTIONAL ECG BY COMPUTERIZED PROCESSING AND INTERPRETING

Two major categories of ECG interpreting programs has been developed in the last few decades. In the first category belong the decision-tree-type (deterministic) programs, while the second category use multivariate statistical analysis [4], [5].

Obviously a large variety of criteria are needed to evaluate computer programs. From clinical point of view diagnostic accuracy is the most important issue. The objective evaluation of the programs is a key factor from the point of view of future acceptance. By 1978, it was already clear that without properly validated common reference data set this type of evaluation can not be carried out. The collection of an independent, representative test library of validated ECG recordings were highly recommended. However, this goal has been accomplished only recently by a common effort of several European centers (in the framework of the Common Standards for Electrocardiology, CSE, project).

According to a study published recently the statistically based programs performed better than the deterministic (decision-tree-type) programs [6]. Between the 9 programs compared the Hannover program (installed e.g. in MEDESE LIBERO ECG systems) seems to be the best [7]. The performance of the average computer program remains slightly below the diagnostic accuracy of the average performance of 8 well trained cardiologists. However, there are evidences, that the performance of a cardiologist supported by computer is significantly better than that one without computer support.

3.1. Sample size vs. dimensionality considerations in statistical evaluations

In the development of statistical classification schemes the proper selection of the number of parameters relative to class sample sizes is a crucial issue. Use of too many variables will likely yield overly optimistic estimates of classifier performance and will prove unacceptable when prospectively tested on data with large class size [8], [9].

A recent study determined the number of uncorrelated features appropriate for given sample sizes [10]. Sample size was considered adequate if the mean distance between two sample sets taken from the same continuous multivariate distribution and projected on the best separating direction remained below a prescribed level. Consider two mutually independent sets of N random vectors, A and B, with samples rearranged in increasing order of magnitude. If the ordered set of samples in the best separating projection has the elements of $a_1 < a_2 < \ldots < a_N$ and $b_1 < b_2 < \ldots < b_N$, then the corresponding empirical cumulative probability distributions (ECPDs) are:

$$F_A(y) = \begin{cases} 0 & \text{for } y \le a_1 \\ n/N & \text{for } a_n \le y \le a_{n+1} \\ 1 & \text{for } y \ge a_N \end{cases}$$

$$F_B(y) = \begin{cases} 0 & \text{for } y \le b_1 \\ n/N & \text{for } b_n \le y \le b_{n+1} \\ 1 & \text{for } y \ge b_N \end{cases}$$

The distance $D_{\max}$, between $F_A(y)$ and $F_B(y)$ is defined as:

$$D_{\max} = \max |F_A(y) - F_B(y)|$$

For a sample size N, the maximum possible value of $D_{\max}$ is 1, indicating a complete separation between the two sample sets in the best separating direction. By increasing N, $D_{\max}$ will converge to zero. Statistically the D distribution as a function of sample size N, and dimensionality M, can be characterized by the distribution

$$P(D)_{M,N} = P\{D_{\max} < D\}$$

The detailed nature of $P_{M,N}(D)$ distributions are discussed in [10]. In Fig. 1 the mean values, $< D >$, are plotted against the sample size with different parameters of dimensionality, M. If we arbitrarily set $< D >= 0.2$ as a reasonable criterion of adequate group representation accuracy for each dimensionality, then based on Fig. 1, the corresponding minimal sample sizes are: $N = 20, 70, 110$, and 140, respectively.

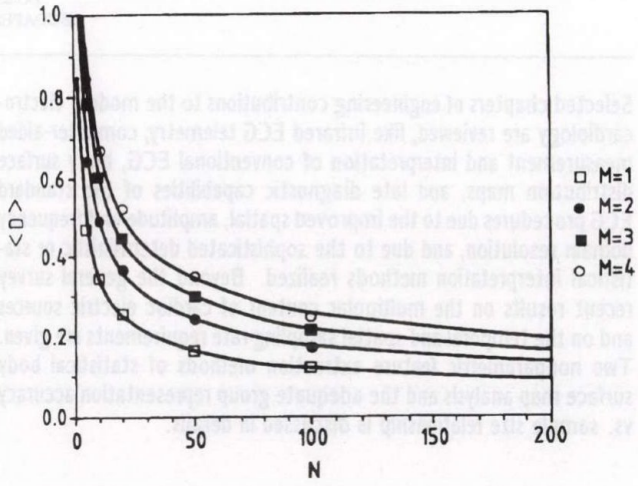

Figure 1. Mean values, $< D >$, of the $P(D)_{M,N}$ distributions vs. sample size, N, parametrized by dimensionality, M

4. ENHANCED SPATIAL RESOLUTION: BODY SURFACE POTENTIAL MAPPING

Body surface potential mapping (BSPM) is an extension of conventional electrocardiography aimed at refining the noninvasive characterization and use of heart generated potentials [11]. Though even a single electrocardiographic lead may be enough for detecting significant cardiac pathologies, but it does not permit a detailed determination of cardiac electric events on a regional basis. BSPM provides the necessary spatial information and offers a theoretical and even a practical possibility for the identification of local electrical activity, i.e. to establish an electrical imaging technique for detailed heart studies.

4.1. Background, techniques

4.1.1. Rational of BSPM

Multipolar expension (ME) is a method for characterizing the potential field of the real cardiac bioelectric sources with an infinite set of equivalent multipolar sources placed in the origin of a suitably chosen coordinate system [12]. The potential value in an arbitrary field point, $U(P)$, can be described as:

$$U(P) = \sum_{n=1}^{\infty} \sum_{m=0}^{n} [A_{nm} Y^e_{nm}(\alpha,\beta) + B_{nm} Y^o_{nm}(\alpha,\beta)] 1/r^{n+1}$$

where

A_{nm} and B_{nm} multipolar expansion coefficients
Y^e_{nm} and Y^o_{nm} even and odd tesseral harmonics

r	distance of the field point considered from the origin of the multipolar expansion
α, β	azimuth and elevation angles of the field point considered in polar coordinates

The field of the equivalent sources is convergent everywhere around the heart outside of a sphere enclosing all the bioelectric sources. Due to the $(1/r)^{n+1}$ type dependence of multipolar term contributions to the total BSPM, it is obvious, that at a distance large compared to the heart size, the dipolar component remains the only dominant source. This is the theoretical explanation for the use of simple heart models as the dipolar one, which completely ignores the complex nature of cardiac source distributions. However, at the precordial chest surface still some of the ME components may contribute significantly to the total signal energy.

In a case study the convergency of truncated ME was assessed by systematically increased number of terms. The field of truncated ME expansion was compared with experimental data to assess the required heart representation complexity in different problems of clinical importance. In our examples tank-wall potential distribution (TWPD), tank-wall isochrone map (TWIM) and epicardial activation map (EAM) simulations were considered [13]. Experimental data were collected in an isolated dog heart experiment performed at the University of Parma. In the analysis 72 electrodes close to the heart supplied reference data on the epicardial signals, while 108 tank-wall ECGs were used for estimating equivalent multipolar sources throughout the cardiac cycle in each 2 msec. ME was carried out up to 4 terms, i.e. up to 24 components (dipolar, D:3, quadrupolar, Q:5, octupolar, O:7, hexadecapolar, H:9) by the least-squares truncation method suggested by Geselowitz [14]. The origin of ME was placed in the approximate center of gravity of the heart. The sphere which encompassed all the cardiac sources had a radius of 5.5 cm. EAM was estimated on a heart-shape like surface 3 cm apart from the epicardium. The time of activation in an arbitrary electrode location was determined as the instant of the maximal negative time derviative. The same definition was used when computing TWIM. Correlation coefficients (CC) and RMS errors characterized the quality of simulations.

In TWPD simulations a high average CC of 0.95 could be achieved using only one ME term (Fig. 2). However, the CC in the time instant with the lowest correlation remained below 0.9 until all the four terms were considered. Likewise at TWIM simulations the CC surpassed the threshold 0.9 only with four terms. By this heart representation complexity not only the general TWIM pattern, but also the time and spatial location parameters of the earliest and last isochrone lines matched properly with the experimentally derived parameters. The EAM computed directly from the epicardial ECG signals and that of estimated is on the "quasi-epicardial" surface had a rather low correlation (CC=0.71) even when all the 4 terms were considered. However, the general pattern of the activation sequence was preserved. Considerable differences were found in the details of activation time estimates. The RMS value of the activation time estimation errors was 3.65 ms, with a maximal error of 24 ms. The average mismatch in epicardial breakthrough sites was in the range of a few cm. The percentage of the cumulative tank-wall signal energies of the subsequent ME components are 84 % (D), 88 % (D+Q), 91 % (D+Q+O), the rest of the energy comes from the infinite number of higher order multipolar sources.

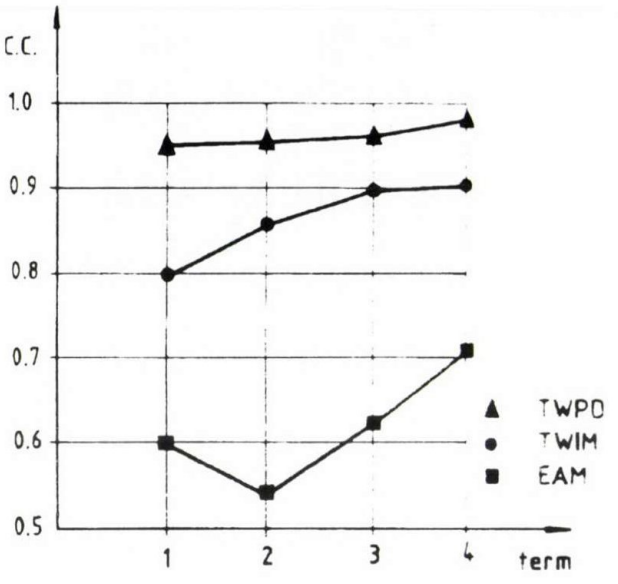

Figure 2. Correlation coefficients (CC) of the measured and estimated TWPD, TWIM, and EAM vs. the multipolar terms considered by the simulations

Based on the findings above the recovery of the details of the cardiac source distributions requires an experimental technique which is able to measure even the low amplitude details of the body surface distribution in order to provide data to the determination of higher order ME components, or other descriptors of the spatial source distribution.

4.2.2. Sampling requirements of BSPM, principle of limited lead systems

Because the electrical events of the heart are both space and time dependent, in BSPM the potential distributions are characterized by a series of instantaneous potential maps taken in subsequent time instants. The experimental data of map computations are collected by an extensive spatial and time domain sampling of body surface potential field. In the last decade several papers have been published on the spectral content and on the sampling rate requirements of ECG signals. From the viewpoint of BSPM the most important paper was published by Barr and Spach [15]. In their study the expected interpolation error as a function of sampling rate was approximated in graphic form, parametrized by the interpolation strategy used. For adults a sampling rate of 500 samples per sec ensures a time domain reconstruction of ECG curves with less than 1 % mean error (defined as the squared difference between the original waveform and the reconstructed wave, divided by the mean square value of the original waveform). Based on similar criteria a relationship between the spatial sampling rate and the mean error of field reconstruction was estimated by Kozmann et al [16]. By comparing the time and the space domain sampling requirements,

it seems reasonable to expect that for a spatial sampling comparable in error with that of a 500 Hz per sec time domain sampling, an equidistant electrode matrix with a spacing of 3 cm is needed (Fig. 3).

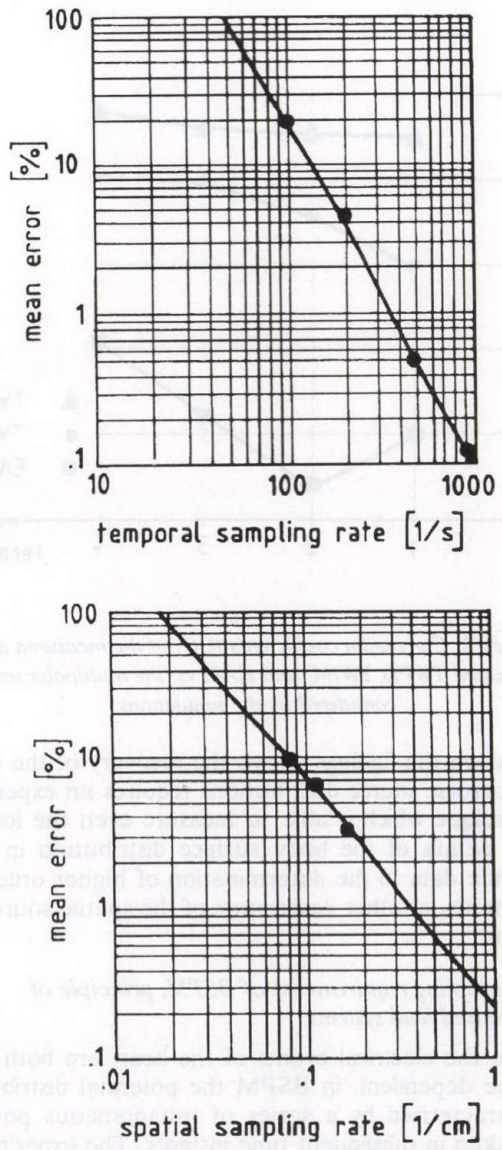

Figure 3. Approximate time domain and space-domain mean error of ECG and body surface potential field reconstruction by linear interpolation vs. sampling frequency/interval

A significant reduction of the number of recording sites can be achieved by taking into consideration the redundant nature of "complete" lead systems. Based on a large number of maps recorded by a 16×12 electrode lead system, using a Gram–Schmidt ortogonalization procedure R.L. Lux has introduced a 32 lead "limited lead system" [17]. In his approach those electrode locations were kept from the original array where the maximum of the uncorrelated signal energy was found. The rest of the ECG signals, U_U, were estimated from the measured signals, U_M, by a linear transformation T_{UM} such that:

$$U_U = T_{UM} U_M.$$

The transformation T_{UM} was determined as:

$$T_{UM} = K_{UM} K_{MM}^{-1}$$

where

K_{MM} covariance matrix of the measured potentials
K_{UM} cross covariance matrix between the measured and unmeasured potentials.

This estimator minimizes the mean squared error. The transformation matrix, T_{UM}, is the same for all subjects. The method outlined was adapted in the BSPM instrumentation developed at the Central Research Institute for Physics, Budapest.

3.1.3. Data processing and visualization in BSPM

The collected raw data are processed to remove low and high frequency noises and finally visualized in the form of potential distribution maps. The most frequently used method of visualization relies on contour line maps, where the contour lines connect all the sites which have the same potential. Each map is labelled by the time instant when it was measured. Fig. 4 shows an example on the map representation used at the University of Utah, Salt Lake City.

4.2. Computer-aided interpretation of body surface potential distribution

4.2.1. Understanding of heart-to-body surface transfer properties: The forward problem of electrocardiology

The forward problem in electrocardiography considers the generatio of poitential fields within and on the torso resulting from a specified source or source arrangement. The heart source models include: dipoles, multipoles and epicardial potentials. The forward problem is concerned with the determination of the fields taking into account body or heart shape, and eventually the distribution of inhomogenities and anisotropies.

Real body, heart, lung, blood cavity geometries can not be represented by quadratics of revolution therefore the whole problem solution needs the utilization of numeric techniques. The basic relationship between the heart surface potential and the body surface potential distribution can be charaterized by a linear equation system:

$$U_B(t_i) = T_{HB} S_H(t_i)$$

where

$U_B(t)i)$ vector of body surface potentials at the time instant of t_i,
T_{HB} transfer matrix relating source distribution and body surface potentials,
$S_H(t_i)$ vector of sources at the time instant of t_i.

The elements of the transfer matrix, T_{HB}, can be computed exclusively from the heart and chest geometry data and in the case of inhomogeneous volume conductor models from the conductivities of the homogenerous subregions (lung, blood, fat, etc.) [18], [19]. Transfer matrix T_{HB}, acts as a spatial filter, smearing the body surface reflection of cardiac electric events, well separated in the myocardium..

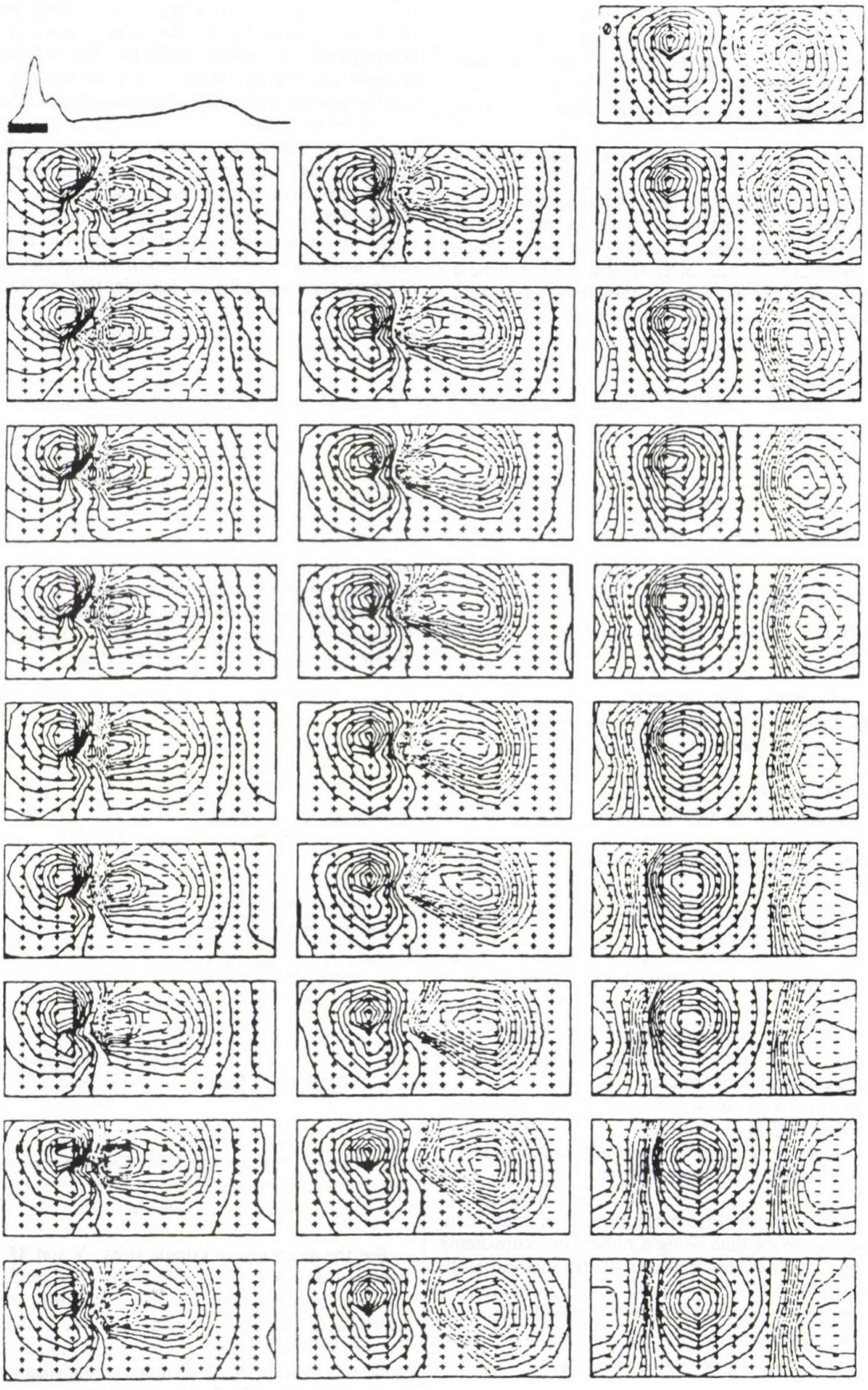

Figure 4. Sequence of body surface potential maps of a normal subject. In each panel the anterior and posterior surfaces of the chest are on the left and right halves of the frame, the upper and lower edges of the frame correspond to levels on the thorax at the sternal notch and umbilicus, respectively. Plus and minus signs show each of the 192 electrode locations as well as potential polarities.

4.2.2. The inverse problem of electrocardiology

The basic aim of the deterministic approach of BSPM is to compute cardiac electrical source distribution from the potential distribution measured on the thoracic surface. Usually two types of sources are considered in the inverse computations. The first one is the set of constrained multiple equivalent dipoles, the second one is the epicardial potentials.

The computation itself can be separated into two independent steps. The first one is basically the solution of the forward problem, that is relating the body surface potential distribution to the body surface potential field. The second step is the inversion of the above expression, that is to relate the epicardial potentials (multiple dipole sources) to the measured body surface potentials. Because of the ill-posed nature of the inverse procedure (i.e. small perturbation on the measured potential and/or geometrical data yield "amplified" oscillations in the estimated source distributions), the solution must incorporate a method of regularization which stabilizes the inversion [20], [21].
Mathematically the inverse problem can be formulated in the following way (Cauchy problem):

Find $U(x)$ on G_H where U satisfies:

$$\begin{aligned} \Delta U(x) &= 0 && \text{in } V \\ \partial U(x)/\partial n &= 0 && \text{on } G_B \\ U(x) &= U_T(x) && \text{on } G_T \end{aligned}$$

where:

G_H a surface enclosing the heart
G_B geometry of the external body surface
G_T geometry of the thorax where the potential values are measured
V volume between G_H and G_B
$U(x)$ potential value at location $x \in V$, at time t
$U_T(x)$ measured potential distribution on G_T at time t.

Using the regularization method finally the following expression, F, has to be minimized:

$$F = \|U_T - T_{HT}U_H\|^2 + pF(U_H)$$

where $F(U_H)$ is one of the following: $F = \|U_H\|^2$ (Tikhonov zero order regularization), $F = \|R\, U_h\|^2$ with R as a Laplacian or gradient operator. The parameter p is termed regularization parameter.

From practical point of view the solution of the inverse problem needs the BSPM, chest and heart geometry, eventually the geometry of the most important inhomogenities, like major blood cavities, lungs, fat, muscle layers. Furthermore, the conductivities of these regions should be known as well. An accurate measurement of these data is possible, but for the time being is rather time consuming and the most sophisticated methods of the medical technology is required [22]. Reasonable assumptions can be achieved by transfer matrices "tailored" to the subject measured. The inaccuracies in the heart position and heart size seem to be the most disturbing factors [23].

4.2.3. Statistical approach of body surface map interpretations

Statistical analysis of body surface potential maps is a vehicle for quantitative interpretation and may be the only robust approach when information about the physical and geometrical properties of the body volume conductor is not available. However, clinically classified maps can be collected and the potentials of features derived from them used to represent the clinical entities studied. Pairwise separation of map classes can be considered as an elementary tactic of the statistical approach of map classification. To make this task statistically robust and efficient, the number of map features required to discriminate between map classes should be kept small. The methods to be outlined below are nonparametric and identify the most discriminant spatio-temporal information in map dichotomies and the best separating linear combination of leads, respectively. The nonparametric nature of these methods seems to be important, as the assumption of normality widely used in other methods is not valid in general [24].

For the determination of the most discriminative lead corresponding to a given dichotomy, let us assume two clinically classified, homogeneours groups A and B, with sample sizes N and M, respectively (Fig. 5). Potentials at sites (l) and times (t) are selected for comparison [25]. Measured sample sets in groups, A and B, were considered to be comparable if the location, l, and normalized time parameters, t, were the same. For each pair of comparable sample sets, empirical cumulative distribution functions, F_A and F_B, were computed. Statistical comparison of these ECDF's was performed by the Kolmogorov–Smirnov (K–S) test of homogenity. The distance of the ECDF's was defined as:

$$D = \max |F_A(x) - F_B(x)| .$$

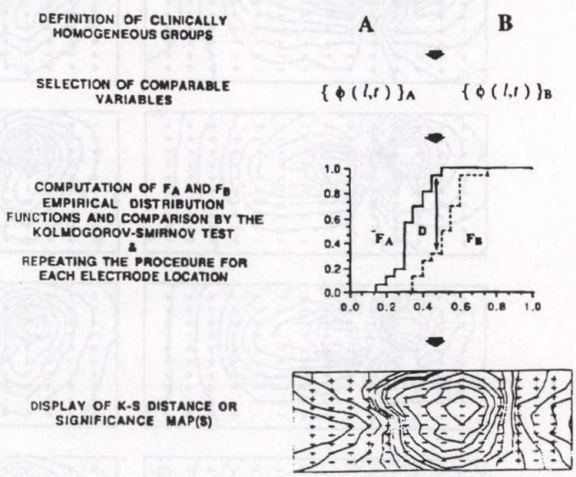

Figure 5. Principle steps of the Kolomogorov–Smirnov nonparametric comparison between surface potential maps of two classes

For the given group sample sizes, N and M, the significance of distance, D, is tabulated. The outlined method characterizes the between group distance and its significance at a particular normalized time t and location l. By systematically applying the method to each lead at the same time instant K–S distance or significance maps can be created. In a K–S map the location and the value of the maximal absolute distance identifies the location and the expected diagnostic performance of the best discriminating lead at the given time instant. Subsequently systematically repeating the procedure for each time instant or

interval, the best separating spatio-temporal sample can be identified. The method discussed actually selects the best dicriminating spatio-temporal sample at a given dichotomy, but obviously ignores a certain part of the diagnostic information available in the whole map of potential distribution. This shortcoming can be diminished by the use of the approach summarized below.

Let us suppose again that classes, A and B, are represented by N and M samples, the aim is to find a vector, γ, which when multiplied by the vector of the potential values in a map, U_T, results in the least overlapping one dimensional distribution of the scalar variables:

$$x = \gamma^T U_T$$

To achieve this goal suitable between and within group measures has to be defined. As an example, with the definitions of ν_b^2 and ν_{bw}^2 distances the Sebestyen type linear transformation wish to maximize the between group distance ν_b^2 while keeping constant the average of the between and within group distances, ν_{bw}^2. This transformation satisfies a generalized eigenequation, and geometrically defines that direction (direction of the normal vector of the best separating hyperplane in Sebestyen sense) along which the separation is maximal. The γ vector can also be represented in the form of a "weighting coefficient map" [25].

The application of the above methods consistently proved that:

$$P_{\mathrm{BSL}} < P_{\mathrm{BUL}} < P_{\mathrm{BLC}}$$

where:

- P_{BSL} diagnostic performance of the best separating standard lead
- P_{BUL} diagnostic performance of the best separating BSPM unipolar lead
- P_{BLC} diagnostic performance of the best separating linear combination (SLT).

The superiority of BUL supports, that the significant diagnostic information very often is not projected on body surface areas explored by the standard 12 lead ECG system. The superiority of the BLC over the BUL probably comes from the fact that the BLC has a more "selective" spatial filter characteristics than the BUL, consequently, it is less influenced by the random variations in cardiac sources irrelevant from the point of view of the basic difference of the groups in the dichotomy considered [26].

5. LATE POTENTIAL MEASUREMENTS

Recording of high-resolution ECGs is an other extension of conventional ECG. There are strong evidences, that the information content hidden in the ECGs is nor necessarily proportional with the amplitude (energy) of the signals recorded. As an example the quantitative stratification of patients from the point of view of elevated risk for sudden cardiac death needs the detection of μV level details of the QRS complex especially at the end of cardiac depolarization. These potentials are called late potentials (LP).

Because LPs are small in amplitude, conventional ECG is unable to detect these signals. In addition, a simple amplification is usually not enough, because the useful signals are masked by different types of noises. Sophisticated measuring and/or data processing techniques are required for a reliable detection of LPs.

Signal averaging is a technique used to reduce ambient noise. There are currently two methods of averaging that have been applied to the recording of LPs: temporal averaging (averaging the ECGs of successive cardiac cycles), or spatial averaging (instantaneous averaging of the ECGs taken parallel from closely spaced electrodes).

Temporal signal averaging is the most frequently used method of noise reduction (in addition to the use of electrical cable shielding, appropriate grounding of instruments, the use of preamplifiers with a high signal-to-noise ratio and the incorporation of appropriate bandpass filters to reduce signal components without clinical importance). The basic assumption at this approach is that the cycles involved in the averaging have identical useful signal components, while the additional noise component is random, consequently during the averaging the degree of noise reduction is proportional with the square root of the number of complexes sampled. From practical point of view the proper clustering of complexes (i.e. the selection of complexes with the same pattern) and the careful selection of the reference or fiducial points in the cycles to be averaged has a paramount importance. By the LP measuring set up of the MEDIAS Ltd, Budapest, using 130 sec of ECG records, typically $0.3-0.5\ \mu V$ residual noise can be achieved, significantly lower than the value formulated in the recommendations of the European Society of Cardiology, the American Heart Association and the American College of Cardiology [27].

Temporal signal averaging is unable to enhance signals that do not occur in a fixed relationship to the fiducial point. A typical example of this occurrence is the Wenkebach like movement of LPs relative to the fiducial point. In these situations the spatial averaging of the signals offer a solution. This technique involves the summation of potentials simultaneously recorded from multiple pairs of closely spaced electrodes. The rationale of this approach is based on the assumption that the CGs measured between any pairs of electrodes are almost identical, whereas the noise components (from electrode-skin interface, amplifier, electromyographic) are independent (uncorrelated) from each other. The above assumption seems to be valid for the electrode and amplifier noise, but rough approximation for myographic components, unless the distance between the electrodes is large enough, but in this case the "almost identity" of the ECGs can be questioned. A study carried out in our laboratory suggested, that from the point of view of myographic components an interelectrode-pair distance of 5 cm or more is necessary to meet the independence of noise components [28].

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György Kozmann received the M.S. degree in electrical engineering from the Technical University of Budapest, Hungary, in 1964 and the C.Sc. degree in engineering science in 1981. Since 1964 he has been working at the Central Reserach Institute for Physics, and in the meantime in 1972-73 he was with the Institute Laue-Langevin, Grenoble, and in 1986–89 with the Nora Eccles Harrison Cardiovascular Research and Training Institute, University of Utah, Salt Lake City. Currently he is the head of the Research Laboratory for Biomedical Engineering. His main reserach interest is in the field of noninvasive measurement techniques in cardiology, statistical and deterministic interpretation of biological data.

SOME NEW ASPECTS OF MEDICAL IMAGERY

I. LOVÁNYI and Á. NAGY

DEPARTMENT OF PROCESS CONTROL
TECHNICAL UNIVERSITY OF BUDAPEST
H-1111 BUDAPEST, Műegyetem rkp. 9.

Prior to nowadays the evaluation of visual information was not feasible in many medical applications due to inadequate performance of available systems in spatial resolution, number of grayscale levels, processing speed or storing capacity. Until now image acquisition, transmission and processing at an acceptable rate have not been possible or investigations resulted in too expensive experimental systems. This paper describes some recent results of medical imagery: as the integration of multisource medical pictures with other clinical data using new powerful multimedia systems or the creation of medical imaging centers with inter-hospital tele-imagery. Up-to-date imaging techniques are also mentioned. In the second part of this article a high performance multi-purpose imaging workstation and a radiographic expert system are presented as potential elements of a future medical imaging center.

1. INTRODUCTION

Digital image handling capability within a medical information system facilitates the clinician's work of making patient care decisions in a fast and accurate way. The integration of image and text provides a more complete view of patient data and supports consultation between clinicians. Specific benefits in the educational and research area can be found too. Integration of imaging with hospital information system occurs at different levels: at the image workstation level, at the network level and at the medical information system application level.

2. INTEGRATION OF MULTISOURCE IMAGES

One of the goals of an integrated imaging system is to provide high quality image data from cardiology, pulmonary and gastrointestinal endoscopy, pathology, radiology, hematology, and nuclear medicine. Different kinds of biomedical images often contain complementary information. For instance the integration of the anatomical–structural information from CT or MR with functional data from PET and SPECT represents a useful tool for the enhancement of new information for clinical diagnosis.

However it is necessary to use a standard image format in order to allow common data processing and archivating. To achieve device independence, at the medical information system level only logical devices appear as ports for imaging I/O. In this case all application programmes may refer to different image sources and image processing, displaying functions — no matter of the actual hardware setup.

3. INTEGRATION OF IMAGES WITH OTHER CLINICAL DATA

In medical information systems images of different sources have to be completed with graphics and text containing informations related to image studies or other clinical data from the patient. Captured images might be improved by zooming or grayscale operations. The mixture of still and motion pictures or composite displays of multiple image abstracts on a single screen is also very important. The image storage and processing capability attracts also those clinicians who were not using conventional medical information systems. It is believed by experts that throught processes related to medical images tend to be visually based. Decision making is much more convenient, communication between colleagues is very rapid when the selected images are available. It is always easier to input and interpret an image than to create a descriptive text.

Medical multimedia, a new era in personal computing is offering desktop solutions. Multimedia softwares and special real-time processors to handle multimedia's incredible demands for computing are just appearing on the market.

4. MEDICAL TELE-IMAGERY

Existing telephone networks can provide inter-hospital or clinic-to-hospital data communications. Distributed image processing is also possible implementing efficient real-time image compression/decompression techniques.

There is an idea to realize well equipped but expensive medical imaging centers meeting all demands of a region. Different kinds of medical images might be captured and stored in this center. Easy access to this data base can be provided from low-cost remote terminals.

For example utilizing existing connectivities and PC facilities a low-cost ISDN/LAN Inter-Hospital Tele-Radiology center was implemented [1]. Within the hospital, different medical image sources, displays, mass storages, mainframes and workstations were connected to an Ethernet achieving 10 Mbps image transmission rate. External connectivity was realized by PC based ISDN workstations with a 128 Kbps capacity. All workstations were directly connected to the Central Office providing parallel data and voice communications, as it is shown in Figure 1. Using multiple ISDN channels for image transmission up to 6 Mbps bandwidth was achieved. The low-cost ISDN workstation can be installed in a Physician Office too. For image transmission efficient (1:40) compression was implemented without significant distortion. Using a 64 Kbps transmission rate, the delivery time of a 1K×1K radiographic image was reduced to 6 seconds. Image compression can be made by real-time chips working under the CCITT/ISO FAX/Image compression standards. Images are archivated on optical Mass Storage. At first step a relatively low quality lossy image is recalled. Then a correction information aiming to reconstruct the lossless information of an interactively selected region of interest is transmitted. Therefore the images have to be archivated in several sub-bands and error bands. These sub-bands might be parallelly accessed over the parallel ISDN system.

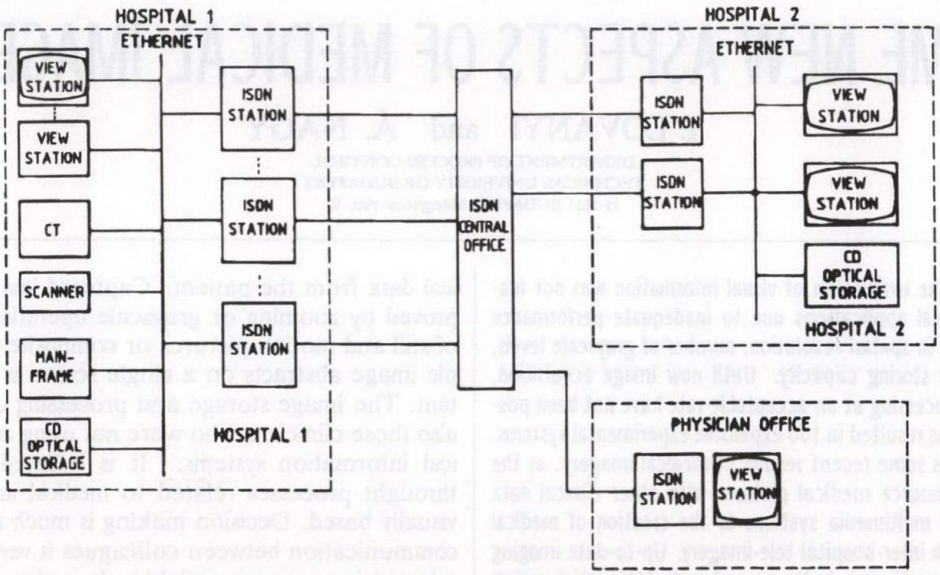

Figure 1. Inter-hospital Tele-Radiology Center

5. NEW MASS ARCHIVATION TECHNIQUES

Clinical data, especially images need huge mass storage capacities. As there are different types of information a variety of available techniques is proposed:

- Rewritable Magneto-Optical Disk (RMOD) archivating information generated within the imaging center and/or often altered.
- CD-ROM containing centrally generated and generally used data-bases as pharmaceutical product list, medical treatment information, educational material, etc.
- PHOTO-CD, a quite new WORM (Write Once Read Many) device which seems to be a good compromise compared to RMOD or CD-ROM.

  - A RMOD is a long life storage capacity for texts, graphics and images. A cartridge has about 650 MB recording capacity. Average transfer rate: 150 Kbps (write), 450 Kbps (read). The rewritable option makes the use of RMOD very flexible, but the price of the drive and the cartridge is relatively high. The production of a 35 GB RMOD jukebox is planned for long term archives.
  - With desktop multimedia applications low-cost, high performance CD-ROM drives appeared on the market providing animation, mixture of text, graphics, image and sound. The capacity of a disk is around 600 MB, average reading rate is over 160 Kbps. The main concern is to produce disks archivating up-to-date medical informations.
  - For 1992 KODAK announced the PHOTO-CD system. The player and the disk itself are even cheaper compared to the CD-ROM system. Manipulations (search, copy, mixture, zoom, altering colors, etc.) on still images are supported. As the price of a Diskwriter device seems to be affordable for medical imaging centers cheap data bases can be created within hospital.

At the moment we use RMOD and CD-ROM for archivation purposes, but we intend to integrate PHOTO-CD in our imaging applications as soon as possible.

6. DISPLAYING MEDICAL IMAGES

Computer aided evaluation of medical images is an interactive procedure, as clinician can be helped but not replaced by computer vision in decision making. Therefore displayed image quality preserves its importance in medical imagery. Using a high resolution analog RGB color monitor equipped with a 20 inches diagonal color raster scan CRT, a 1280×1024 pixel non-interlaced digital image can be visualized in our imaging workstations.

7. STATE OF THE ART IN SILICON BASED FAST IMAGE COMPRESSION

Due to the increasing number of digital images the necessity to compress data in order to improve archivating and transmission of image sequences is a widely held opinion in the medical imaging field. The data rates and storage requirements are much greater than can be supported by the recent data transmission networks, or stored on current backup media, so the development of real-time compressing methods is one of the most important field concerning Medical Imagery Systems (medical image management, archivating, communication, multimedia).

Several methods have been studied to compress medical images. Some of the classical software based techniques are very powerful in terms of compression ratio, but cannot be used in practice due to the time-cost of the implementation. Only the development of highly sophisticated VLSI devices in the last few years made it possible to establish dedicated compression subsystems, which combine significant compression ratio and appropriate image quality with reasonable amount of coding/decoding time-cost.

To speed up the growth of image compression technology three different video compression standards have been proposed [2]:

- JPEG (Joint Photographic Experts Group) standard for still picture compression
- MPEG (Moving Pictures Experts Group) standard for full motion compression on digital storage media (DSM)

- CCITT Recommendation H.261 for video teleconferencing (Figure 2.)

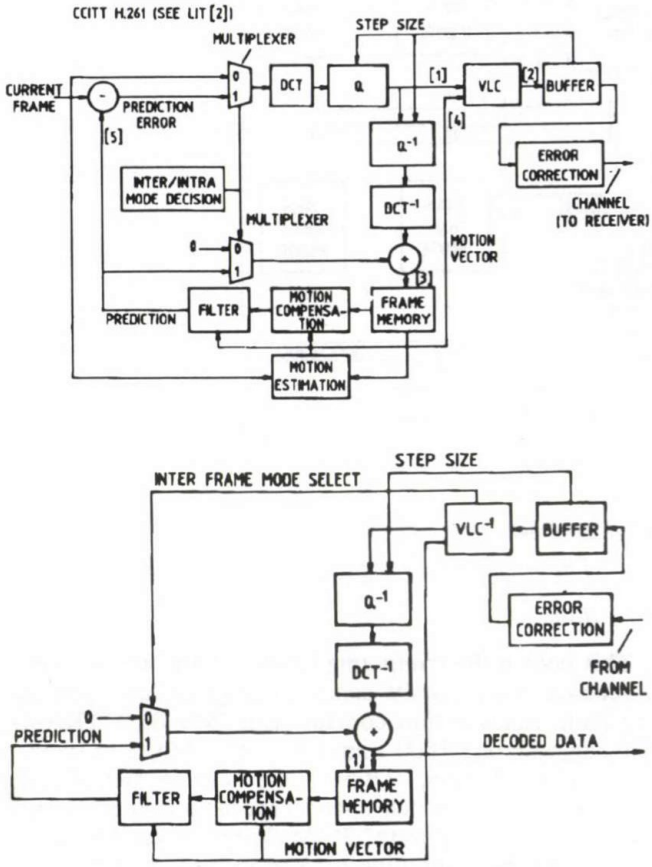

Figure 2. CCITT H.261 Encoder/Decoder

The JPEG baseline algorithm is one of the transform-based image coding techniques. Since this system is for still images, no predictive coding or motion compensation is needed. A color image can be represented in different color systems (e.g. RGB, Y-U-V, C-M-Y-K, etc.). Each component of the original image is divided into adjacent blocks of size 8-by-8 pixel, and then transformed using the two dimensional discrete cosine transform (DCT). The resulting coefficient values represent the frequency contents of the given block. The lowest frequency or DC coefficient contains the average value of the block, while the high frequency coefficients indicate the fine details of the picture. The next step is the frequency and commponent dependent quantization of the coefficients (the high frequency coefficients can be quantized with a greater stepsize — that is more coarsely, as they are subjectively less important). The quantization is followed by zig-zag scanning, run length coding and Huffmann coding.

Developing a medical imagery workstation for managing temporal or spatial image sequences the new MPEG-2 standard using also the advantages of the predictive coding seems to be more appropriate. In addition to the JPEG the MPEG proposed standard is full-motion compression algorithm with both intra- and inter-frame modes, and was originally introduced for digital storage media like CD-ROM drives, digital audio tape drives and magnetic hard disks. Because of the limited data rate — which may not exceed the 1.5 Mbit/sec — a second phase of the standardization has begun to satisfy the demands of next-generation media with the goal to produce a compression speed of 10 Mbit/sec.

Because of the possibility of handling temporal image frames this standard is also capable of compressing medical image sequences, where the spatial slices (e.g. CT) or the dynamic scenes can be considered as subsequent frames of an ordinary video. This technique is a real challenge which has not yet received much attention even if the 3D orthogonal transforms to perform interframe compression were widely used.

Since the end of 1989 dedicated image compression chips were announced, which integrate the above mentioned standards and techniques into silicon. Some of the importants are:

- CL-550 from C-Cube Microsystems Inc. which conforms to an early revision of the JPEG
- The semi custom L64735 DCT processor, L64745 quantizer from LSI Logic
- the LSI Logica H/261 line, which contains four processors and three codec chips (L64720 motion estimation processor, L64730 DCT processor, L64740 quantizer, L64760 intra/interframe decision processor, L64715 BCH error correcting codec, L64750 variable-length encoder, L64751 variable-length decoder). The MPEG video coding loop can be also developed with these elements.
- The SGS-Thomson (Inmos) DCT processors (STV3200, STV3208, A121) and the STV3220 motion estimation processor.

8. THE ARCHITECTURE OF THE QUALIMED GENERAL PURPOSE MEDICAL IMAGERY WORKSTATION

Because of the demand of acquiring, transmitting and processing the huge amount of picture data we decided to establish the imagery workstation on a decentralized transputer link based modular architecture. This architecture takes the form of a network of dedicated sensing (communication) processing nodes. This architecture has many desirable properties including flexible data acquisition, reduction and processing, and enables topological reconfiguration under program control for dynamic load balancing. Integrating the considerable computing power and the flexible transparent communication facility the industry standard TRAM concept and the transputer itself is an ideal way to construct such a structure [3]. Building up the bus system we also took into account the new possibilities provided by the T9000 family — the full technical disclosure was given in April 1991 by Inmos —, which will dramatically increase the performance of transputer networks (200 MIPS and 25 MFLOPS peak processing performance, 80 Mbytes/sec peak bidirectional bandwidth) [4].

The nodes of the basic configuration are as follows (Figure 3.):

- image acquiring and preprocessing node for interfacing CCD matrix and high resolution CCD line-scan cameras
- TRAM based expandable image procesing/general purpose computing node
- real-time compression/decompression node with SCSI and Ethernet interface
- transputer link/IBM-AT host interface with dual-port RAM based bus converter

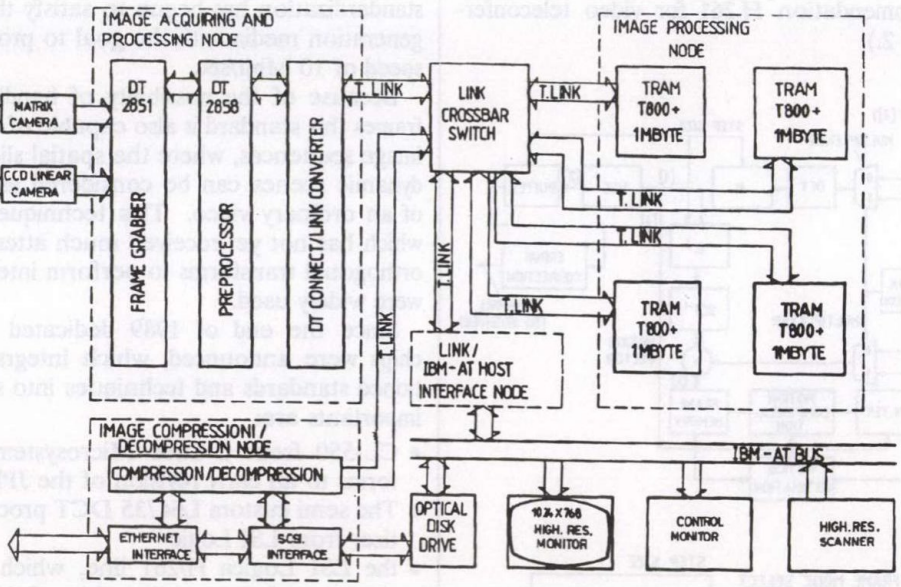

Figure 3. Architecture of Qualimed

8.1. The image acquiring and preprocessing node

The unit contains the Data Translation DT-2851 frame grabber, the DT-2858 preprocessor board and the DT-Connect/transputer link converter [5].

The DT-2851 is a 512×512×8 bit real-time frame grabber on an IBM-AT basis. The board digitizes a video signal, stores the image in one of two on-board memory buffer, and displays the image at a rate of 20 frames per second. It accepts color (NTSC, PAL) or monochrome (RS-170, RS-330, CCIR) video input from ordinary video cameras or VCRs and is also capable of receiving non-standard slow-scan input from devices like high-resolution scanners — e.g. for pick up radiographic images — or electron microscopes.

The DT-2858 is a pipelined frame processor board connected with the DT-2851 frame grabber via a video speed bus (DT-Connect). The board greatly reduces the time required to accomplish arithmetic-intensive operations like convolution, histogram evaluation, frame averaging, normalization, arithmetic and logic operations, zoom, etc.

The goal of the widely used DT-Connect interface is to circumvent the bottleneck in transmitting picture data between the frame grabber and the preprocessing board. It consists of two independent interconnect paths of 16 bit, which transfer data parallelly at a 10 MHz rate. Via the DT-Connect the picture data of the frame grabber (DT-2851) can be transferred to the memory of the preprocessor board (DT-2858). Simultaneously, the preprocessor can manage the high-speed processing of the input data, and at the same time send back the results to the display section of the frame grabber.

For more sophisticated high-speed software evaluation it is necessary to pass on the preprocessed image data to the TRAM based image processing node. For this purpose we developed a video speed bus transformer, which converts the DT-Connect interface into transputer links and vice versa.

In this way we have a bidirectional picture processing pipeline with the capability of managing general image processing operations with the desirable speed.

8.2. The image processing/general purpose computing node

This node is the computing harness of the workstation. It receives and transmits data via transputer links, and in the basic configuration contains four IMS B411 TRAM modules with one T800 transputer and 1 Mbyte of memory in each of them. Utilizing the network facilities of the C004 crossbar switch optional special purpose TRAM modules — even separate TRAM clusters — can be added to increase the computing performance to meet specific demands.

8.3. The transputer link/IBM-AT host interface

There is a dedicated chip (C011) in the transputer family for this purpose, but its data bandwidth is limited. To avoid this problem our solution is a prototype TRAM based host interface which communicates with the IBM host bus via a 8K dual port SRAM. The maximal data transfer capacity of the IBM DMA controller can be utilized with this technique.

8.4. The real-time compression node

Developing our transputer module based modular medical imagery workstation, our purpose was to create a real-time compression module which can be cascaded and connected directly to the high-speed video bus of the image acquisition and evaluation unit. Because of this flexible structure our medical imagery workstation can be used in a variety of different application areas.

Planning the real-time compression unit we focused our attention first of all on dynamic medical image sequences (nuclear medicine, CT, MRI), where the demand of taking into account the third dimension (time or space) of sequences offers the possibility of using dedicated hadware DCT (Discrete Cosine Transform)/motion compensation devices. Choosing this way the system will be also capable of following the today's JPEG/MPEG/CCITT standards.

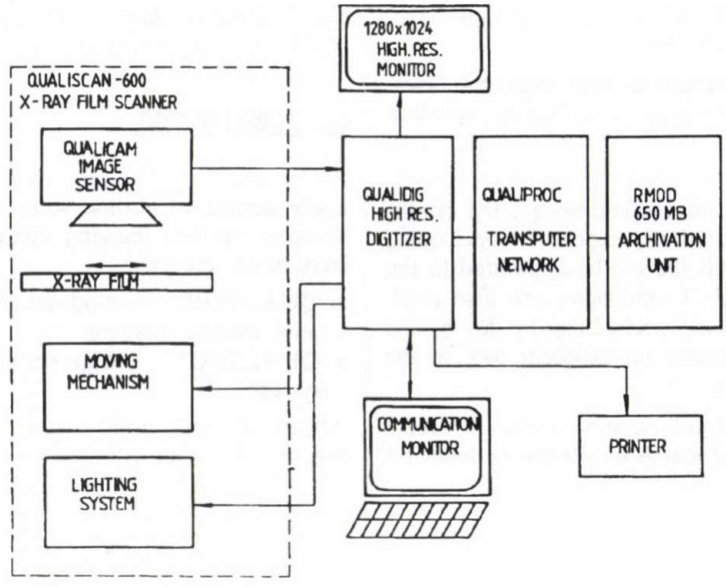

Figure 4. QUALIRAD Radiographic Imagery Workstation

Using the above dedicated function-specific elements we are in the situation to create a cascadable image compression building block for our modular imagery workstation.

The image compression building block (Figure 3.) of our workstation can be characterised by the following key features:

- dedicated LSI chip set for real-time hardware compression/decompression (raster-to-block converter, DCT transformer, quantizer, motion estimation processor)
- implementation in an industry standard package, the TRAnsputer Module (TRAM), to allow a flexible, reconfigurable compression subsystem
- communication and image data feed via the standard TRAM links for fastest possible data transfer
- SCSI bus interface, which allows the compression subsystem to connect directly to Winchester disks, optical disks, CD-ROMs and other peripherals via the SCSI bus
- Ethernet interface to connect the compression subsystem to computer networks via IEEE802.3 LANs, driven by TCPIP/UDP software.

Scanning medical imagers with extremely high resolution

As we mentioned our general purpose imaging workstation is capable to accept color (NTSC, PAL) or monochrome (RS-170, RS-330, CCIR) standard video inputs. On the other hand medical radiology has to deal with extremely high resolution digital images — not to loose relevant information. Therefore a special (non-standard) scanner and preprocessor unit was developed containing special sensors mechanics and lighting systems.

9.QUALIRAD-RADIOGRAPHIC IMAGERY WORKSTATION

QUALIRAD is a system for computer aided evaluation of X-ray films. The system consists of the following components (see Figure 4.).

9.1. QUALISCAN-600 X-ray film scanner

- line resolution: max. 200 dpi (programmable) for a film of 300 mm in width
- moving mechanism, resolution: min. 25 micrometer (programmable)
- film length up to 800 mm (programmable)
- sensing: antiblooming, automatic light and integration time control, real-time shading correction, analogue dynamic range 5000:1 RMS, A/D conversion 8 bit/pixel
- scanning speed up to 100 lines/sec (it means 1 minute scanning time for a 500 mm film of average density and maximal resolution).

9.2. IBM-AT compatible computer configuration

- i80386/8 Mbyte RAM/80 Mbyte hard disk/1.2 Mbyte floppy/S-P port
- visualisation window 1280×1024×256 gray-scaled levels (or 256 pseudo color from a palette of 256K), hardware roll, pan and zoom look-up table manipulation
- 650 Mbyte optical disk image archivation unit
- QUALIDIG special interface for QUALISCAN-600 scanner
- QUALIPROC-T800 high-speed transputer network for fast image compression and preprocessing

9.3. Archivation and interactive evaluation software, main functions

- image acquisition: optimal parameter selfsetting of scanning depending on density of actual film
- evaluation: in the interactive evaluation mode the clinician labels on the screen the regions of interest, from that point the system automatically measures with high precision some parameters of labelled object (e.g. size, thickness estimation based on density measurement, position, etc.). The evaluation is supported by efficient manipulations on images too:
- composite display of films belonging to the same patient with automatical scale assignment

- roll, pan, zoom, contrast enhancement, pseudocolor, creation of alfanumerical overlay
- display of additional informations like diagrams, "classifying rules" of different scenes described by standard tutorial film
- archivation: after evaluation the system automatically creates a file containing the original image, the results and parameters of evaluations, exposure, developing and digitizing of film. This file will be appended to the database. Different kind of hardcopies are also available. The knowledge base enriched day by day by the decision of experts is besides an excellent tool in the training of new specialists.

The database mentioned above is very useful to create more complex statistics, and makes it possible to develope a radiographic expert system, which is a key element to realize more automatical evaluation in the near future.

10. CONCLUSIONS

The paper tried to give a survey of desktop medical imagery aiming to outline some new elements of a future low-cost medical imaging center. Two implementations have been detailed:

- QUALIMED – a modular architecture for general purpose medical imaging
- QUALIRAD – a high resolution radiographic imaging system

Affordable medical imaging centers seem to be feasible in this decade in Hungary too.

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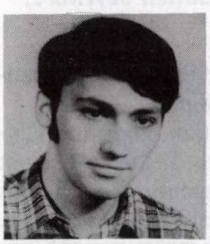

István Loványi received the M.S. degree in electrical engineering from the Technical University of Budapest, Hungary in 1975. He wrote his doctoral dissertation in the field of digital image processing 1981. Dr. Lóványi is currently an assitant professor at the Department of Process Control at the TU budapest. His research activities include digital image processing applications, computer-aided quality control, robotics and industrial measurement techniques. He is responsible for the "Filiere Francophone" at the Faculty of Electrical Engineering and at the same time he animates reserach cooperations with several French universities in the disciplines mentioned above.

Ákos Nagy received the M.S. degree in electrical engineering from the Technical University of Budapest in 1986. Currently, he is a cnadidate for the Ph.D. degree in the INSA de Rennes, France. His primary research interests include transputer networks, industrial and medical image processing and NDT diagnostics. Ákos Nagy is in the executive committee of the Hungarian Transputer User Group.

COMPUTER ANALYSIS OF THE PHYSIOLOGICAL PROCESSES

Z. BENYÓ
DEPARTMENT OF PROCESS CONTROL
TECHNICAL UNIVERSITY OF BUDAPEST
H-1111 BUDAPEST, Műegyetem rkp. 9.

In physiological research the need for an exact mathematical method is felt more and more. The computer aided analysis includes all the theoretical processes allowing us to describe the behaviour of a biological system by means of a mathematical model.

1. INTRODUCTION

In medical–biological research the need for an exact mathematical method is felt more and more. The compartmentalized analysis includes all the theoretical processes allowing us to describe the behaviour of a biological system by means of a mathematical model. This model has the same importance as state equations in modern control theory or frequency methods applied in the classical control techniques. The first part of the article is to deal with — proceeding from simpler cases towards more complicated systems — the application techniques of one compartment systems to that of multi compartment systems. In case of a concrete application, the mathematical model and its solution, as well as computerized simulation and identification will be introduced.

An event recognition method has been used for the nature of illnesses. Different illnesses (defined as outer variables) are simulated after the symptom signals have been recorded as the function of the time (as state variables). Based on these functions the multivariable linear state equation system is determined as follows. After that, on the basis of continuous measurement of the real symptom signals and the outer variables, the type of illnesses can be recalculated by the state equations.

By this the physiological system can be determined.

Modern computerized statistical analysis of great significance in preventive medicine and in the increased effectiveness of daily therapeutic work. The authors [14] are aiming at the processing of data collected from a high number of patients by a computer including the analysis of laboratory findings, complaints, symptoms, and examinations. The connections between diagnosed illnesses the discovery of relationships are on the basis of documents of the Department of Surgery of the "Jáhn Ferenc" Hospital, Budapest. New methods of multivariable statistical analysis were needed to solve the problem appropriately. The relationships explored can be the basis for an expert system of surgical knowledge.

2. COMPARTMENT ANALYSIS

The compartmental analysis is a set of theoretical processes, allowing us to describe the haviour of a biological system in terms of a mathematical model [1]. Therefore in medical–biological research the compartmental analysis is of the same importance as the state equations in modern control tyheory or frequency methods previously applied in process control. Compartmental analysis is dealt with in literature in many cases [2], [3], [4], [5], etc. This article performes the description of biological systems, which are often found in practice. We will introduce the application techniques of compartmental analysis and the main features of a computerized simulation programing system.

This investigation is interdisciplinary in nature and among the authors of literature about compartmental analysis include doctors, engineers, biologists and mathematicians. For this reason the uniform interpretation of definitions and terminology and a consistent notation system are of particular importance. A uniform notation system is applied throughout the article.

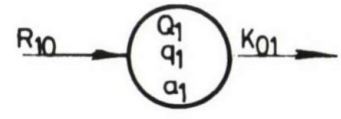

Figure 1. One Compartment System

The theoretical model can be seen in Figure 1. The behaviour of the system is represented by equation (1):

$$\frac{dQ_1}{dt} = R_{10} - k_{01}Q_1 \tag{1}$$

The system is in steady state, therefore

$$\frac{dQ_1}{dt} = 0, \quad R_{10} = k_{01}Q_1 \tag{2}$$

The behaviour of the tracer injected into the system at $t = 0$ is represented by the following equations:

$$\begin{aligned} \frac{dq_1}{dt} &= -k_{01}q_1 \\ Q_1\frac{da_1}{dt} &= -k_{01}a_1Q_1 \end{aligned} \tag{3}$$

Rearranging and integrating:

$$-k_{01}\int_0^t dt = \int_{a_1(0)}^{a_1}\frac{da_1}{a_1}$$

$$-k_{01}t = \ln a_1 - \ln a_1(0) = \ln\frac{a_1}{a_1(0)}$$

* Research supported by the Hungarian National Foundation for Scientific Research, Grant 407.

The solution:

$$a_1 = a_1(0)e^{-k_{01}t} \tag{4}$$

Amount of subtance in Q_1 compartment:

$$Q_1 = \frac{a_T q_T}{a_1(0)} \tag{5}$$

where q_T is the tracer amount and a_T is the specific activity of the tracer before injection.

2.2. Simple two Compartment System

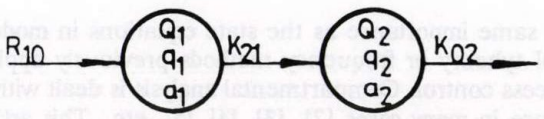

Figure 2. Simple two Compartment System

Differential equations discribing the system in Figure 2:

$$\frac{dq_1}{dt} = -k_{21}q_1$$
$$\frac{dq_2}{dt} = k_{21}q_1 - k_{02}q_2 \tag{6}$$

or:

$$\frac{da_1}{dt} = -k_{21}a_1$$
$$\frac{da_2}{dt} = k_{21}\frac{Q_1}{Q_2}a_1 - k_{02}a_2 \tag{7}$$

The solutions:

$$a_1 = a_1(0)e^{k_{21}t}$$
$$a_2 = \frac{k_{21}a_1(0)Q_1}{(k_{21}-k_{02})Q_2}\left(e^{-k_{02}t} - e^{-k_{21}t}\right) \tag{8}$$

$a_1(0)$, Q_1 and k_{21} can be calculated in the manner of the previous section.

2.3. Multiple Dosage

First multiple dosage was applied by Atkins [3]. The tracer was added in n equal dosages, at equal time intervals to a compartment system. With a great amount of ^{13}C-ascorbic and ^{13}C-oxalic acid Atkins signed the ascorbic acid of the patient. The excretion was monitored for many weeks. A single dose can not disturb the steady state, therefore the tracer was given 32 times every six hours.

For the system the differential equation given for one compartment system is valid, in the interval between tracer injection:

$$\frac{dq_1}{dt} = -k_{01}q_1 \tag{9}$$

At $t = 0$, $a(0)$ tracer of specific activity is added into the system.

The specific activity at the moment t_1:

$$a_1(t_1) = a_1(0)e^{-k_{01}t} \tag{10}$$

Then another dosage is added. The specific activity after a little while (σ_t):

$$a_1(t_1 + \sigma_1) = a_1(0)\ \ (1 + e^{-k_{01}t}) \tag{11}$$

After another time interval:

$$a_1(t_2) = a_1(0)\ (1 + e^{-k_{01}t})e^{k_{01}t} \tag{12}$$

After the third injection:

$$a_{1(t_2+\sigma_t)} = a_1(0)\ (1 + e^{-k_{01}t}/e^{-k_{01}t} + a_1) =$$
$$= a_1(0)\ (1 + e^{-k_{01}t} + e^{-2k_{01}t}) \tag{13}$$

After n injections:

$$a_{1(t_2+\sigma_t)} = a_1(0)\ (1 + e^{-k_{01}t}/e^{-2k_{01}t} + \ldots$$
$$= \ldots + e^{-(n-1)k_{01}t}) = \tag{14}$$
$$= \frac{a_1(0)\ (1 - e^{-nk_{01}t})}{(1 - e^{-k_{01}t})}$$

After $n \to \infty$ injections:

$$\lim_{t\to\infty} a_1(t_n) = \frac{a_1(0)}{(1 - e^{-k_{01}t})} \tag{15}$$

The effect mechanism can be followed in Figure 3.

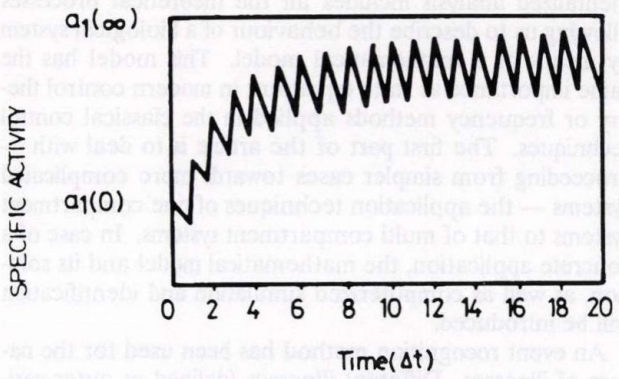

Figure 3. Multiple dosage

2.4. Two Compartment Closed System

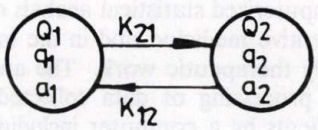

Figure 4. Two Compartment Closed System

The theoretical model is shown in Figure 4.

The mathematical model:

$$\frac{dQ_1}{dt} = k_{12}Q_2 - k_{21}Q_1 = 0$$
$$\frac{dQ_2}{dt} = k_{21}Q_1 - k_{12}Q_2 = 0 \tag{16}$$

For the tracers ($q_1 + q_2$ =constant):

$$\frac{dq_1}{dt} = k_{12}q_2 - k_{21}q_1$$
$$\frac{dq_2}{dt} = k_{21}q_1 - k_{12}q_2 \tag{17}$$

For the specific activities:

$$\frac{da_1}{dt} = k_{12}a_2\frac{Q_2}{Q_1} - k_{21}a_1$$
$$\frac{da_2}{dt} = k_{21}a_1\frac{Q_1}{Q_2} - k_{12}a_2 \qquad (18)$$

The solution can be achieved, for example, by Laplace-transformation: if a tracer is injected into Q_1 at $t = 0$, the solution of equation (18) is as follows:

$$a_1 = \frac{k_{12}a_1(0)}{(k_{21}+k_{12})} + \frac{k_{21}a_1(0)}{(k_{21}+k_{12})}e^{-(k_{12}+k_{21})t} =$$
$$= X_0 + X_1e^{-\lambda t} \qquad (19)$$
$$a_2 = \frac{k_{21}a_1(0)}{(k_{21}+k_{12})}(1 - e^{-(k_{12}+k_{21})t}) =$$
$$= X_0\,(1 - e^{-\lambda t})$$

The parameters a_1 and a_2 are shown in Figure 5.

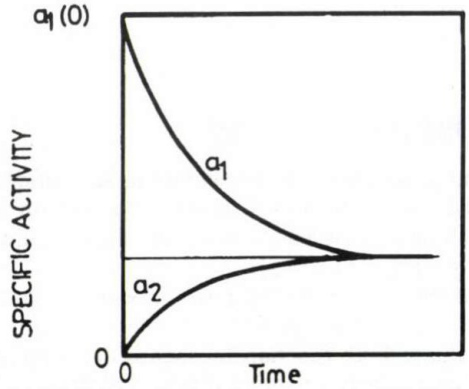

Figure 5. Time-functions of a_1 and a_2

Q_1, Q_2, k_{12} and k_{21} can be obtained in different ways. Either by the Bleehan–Fischer procedure or by means of curve analysis we give the equations of isotopic dilution for Q_1.

A third method is known as well:

$$\lim_{t\to\infty} a_1(t) = X_0$$

Rearranging (19):

$$\frac{a_1}{a_1(\infty)} - 1 = \frac{X_1}{X_0}e^{-\lambda t} \qquad (20)$$

If equation (20) is plotted on semilogarithmic graph paper, then parameters can be calculated on base of the straight line.

2.5. Two Compartment Open System

First of all, we have to look at the theoretical model in Figure 6. and at the differential equations representing the system:

$$\frac{dq_1}{dt} = k_{12}q_2 - k_{21}q_1 - k_{01}q_1$$
$$\frac{dq_2}{dt} = k_{21}q_1 - k_{12}q_2 \qquad (21)$$

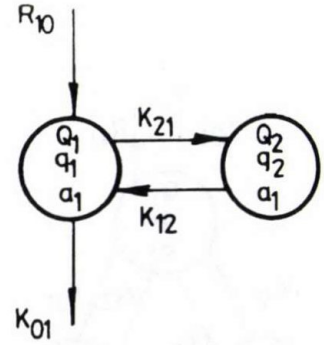

Figure 6. Two Compartment open System

Representation with the specific activities

$$\frac{da_1}{dt} = k_{12}a_2\frac{Q_2}{Q_1} - k_{21}a_1 - k_{01}a_1,$$
$$\frac{da_2}{dt} = k_{21}a_1\frac{Q_1}{Q_2} - k_{21}a_2 \qquad (22)$$

If we add the tracer into the first compartment, the solution of the above equation is as follows:

$$a_1 = \frac{a_1(0)}{\lambda_1 - \lambda_2}(\lambda_1 - k_{12})e^{-\lambda_1 t} + (k_{12} - \lambda_2)e^{-\lambda_2 t}$$

$$a_2 = \frac{a_1(0)k_{21}Q_1}{(\lambda_1 - \lambda_2)Q_2}(e^{\lambda_1 t} - e^{-\lambda_2 t}) \qquad (23)$$

$$-\lambda_{1,2} = \frac{-(k_{12}+k_{21}+k_{01})}{2} \pm$$
$$\pm \frac{\sqrt{(k_{12}+k_{21}+k_{01})^2 - 4k_{01}k_{12}}}{2}$$

The equations can be given in the following way as well:

$$a_1 = X_1e^{-\lambda_1 t} + X_2e^{-\lambda_2 t}$$
$$a_2 = X_3e^{-\lambda_1 t} + X_3e^{-\lambda_2 t} \qquad (24)$$

The specific activity-time curves can be followed in Figure 7. The parameters are determined by means of curve analysis.

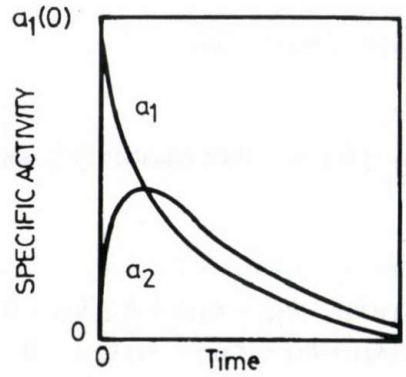

Figure 7. Time curves of the specific activity

2.6. Three Compartment System

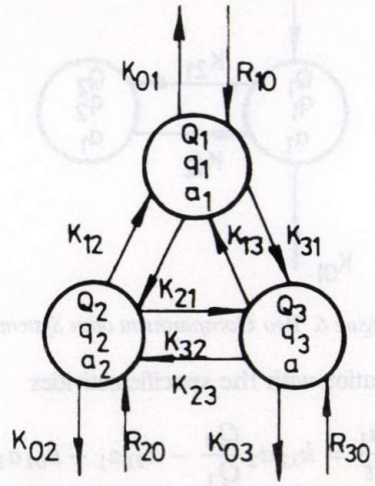

Figure 8. Three Compartment System

We examine the three compartment systems represented in Figure 8. The mathematical model:

$$\begin{aligned}\frac{dq_1}{dt} &= -(k_{01}+k_{21}+k_{31})q_1 + k_{12}q_2 + k_{13}q_3\\ \frac{dq_2}{dt} &= k_{21}q_1 - (k_{02}+k_{12}+k_{32})q_2 + k_{23}q_3\\ \frac{dq_3}{dt} &= k_{31}q_1 + k_{32}q_2 - (k_{03}+k_{13}+k_{23})q_3\end{aligned} \tag{25}$$

Or:

$$\begin{aligned}\frac{da_1}{dt} &= -(k_{01}+k_{21}+k_{31})a_1 + k_{12}\frac{Q_2}{Q_1}a_2 + k_{13}\frac{Q_3}{Q_1}a_3\\ \frac{da_2}{dt} &= k_{21}\frac{Q_1}{Q_2}a_1 - (k_{02}+k_{12}+k_{32})a_2 + k_{23}\frac{Q_3}{Q_2}\\ \frac{da_3}{dt} &= k_{31}\frac{Q_1}{Q_3}a_1 + k_{32}\frac{Q_2}{Q_3}a_2 - (k_{03}+k_{13}+k_{23})a_3\end{aligned} \tag{26}$$

The characteristic polynomial is:

$$0=\begin{bmatrix}(k_{01}+k_{21}+k_{31}+s) & -k_{12} & -k_{13}\\ -k_{21} & (k_{02}+k_{12}+k_{32}+s) & -k_{23}\\ -k_{31} & -k_{32} & (k_{03}+k_{13}+k_{23}+s)\end{bmatrix} \tag{27}$$

The roots are the system's eigenvalues. We will examine the most important special cases.

Closed System

If $k_{01} = k_{02} = k_{03} = 0$, then equation (27) simplifies to equation (28)

$$\begin{aligned}&s^3 + s^2(k_{12}+k_{13}+k_{21}+k_{23}+k_{31}+k_{32})+\\ &+ s[k_{13}(k_{21}+k_{12}+k_{32}) + k_{21}(k_{23}+k_{32})+\\ &+ k_{31}(k_{23}+k_{12}+k_{32}) + k_{12}k_{23}] = 0\end{aligned} \tag{28}$$

The system's eigenvalues are: zero and the roots of the second order expression of (28).

Open System

Supposing in (27) each $k_{ij} = 1$ the characteristic polynomial is:

$$s^3 + 9s^2 + 24s + 16 = 0 \tag{29}$$

The system's eigenvalues are: $-\lambda_1 = -1$, $-\lambda_2 = -4$ and $-\lambda_3 = -4$. That means the root multiplicity of $-\lambda = -4$ is two. Though it is a three compartment system, there are only two different integration constants.

Catenary System

In case of a catenary system $k_{13} = k_{31} = k_{01} = k_{02} = 0$. We examine the special case when $k_{12} = k_{21} = k_{23} = k_{32} = k_{03} = 1$. Then eigenvalues are given by the roots of (30):

$$s^3 + 4s^2 + 3s - 1 = 0 \tag{30}$$

This equation has three different negative real roots.

Mammilary System

In three compartment mammilary system:

$$k_{23} = k_{32} = k_{02} = k_{03} = 0$$

If $k_{12} = k_{21} = k_{13} = k_{31} = k_{01} = 1$, the eigenvalues are the roots of (31):

$$s^3 + 6s^2 + 9s + 3 = 0 \tag{31}$$

2.7. Computarized Simulation

The introduction of computers into all scientific branches during the last years made it possible to develop the theories published in the past and to find their application in practice [6], [8], [15], [16], [17].

For example it opened the possibilities of examining the mechanism of certain medicines exactly (pharmokinetics) or to evaluate liver function by means of computers. In fact, without computer the mathematical model of a system with more than three compartments is so complicated, that its analytical solution is almost impossible. Even if we could determine the analytical solution in some way, it would be too complicated to apply it in every day practice (in medical treatment for example).

Taking the above ideas into consideration, the Technical University of Budapest, its Department of Process Control has developed a computer program available for the analysis of physiological processes. In this simulation program the possible number of compartments is arbitrary. The system can be closed or open. With given input parameters the program decides automatically whether it is a catenary or a mammilary system. The program is menu oriented and is written for the IBM PC. The application is supported by appropriate graphs. It has often been applied successfully in practice (for example for evaluation of liver function examination, in case of different tracers, for examinations of enterohepatic circulation, etc.).

3. IDENTIFICATION OF PHYSIOLOGICAL SYSTEMS

Dynamic characteristics of a physiological system in the time domain are described by means of a differential equation, or a system of differential equations. The procedure of writing the differential equation, or system of differential equations describing the system is termed identification. According to preliminary information on the

system, two extreme cases of identification may be distinguished. If the structure of the mathematical model is known, namely, how many compartments are needed to model the physiological system, and how they are related, it is a case of parameter assessment. For a tested system of unknown structure, the problem is termed system identification. Most problems are somewhere in between these two extreme cases.

In the case of diagnostic tests, preliminary medical tests define the model structure, hence evaluation of measurement results simplifies to parameter assessment. Of course, this is not to say that development of measurement and evaluation methods would not entail refining of the model structure.

There are several mathematical models to solve identification problems. The most convenient of these has to be chosen for the given problem [2], [3], [5], [6], [15], [16].

3.1. Computer evaluation of measurement data from clearance tests

The compartment model of clearance test is described generally by a linear differential equation system of the first order. Evaluation of the test consists essentially of determining parameters X_i and λ_i in Eq. (32). And then solving this sytem of differential equations.

$$y = \sum_{i=1}^{m} X_i e^{\lambda_i t}, \quad \text{where} \quad \lambda_1 = 0 \qquad (32)$$

Thereafter, a curve of the sum of exponential terms has to be fitted to the set of measurement points bearing test results, and after having achieved an appropriate accuracy of a given degree, values of coefficients X_i and of exponents λ_i have to be printed out.

For the computer evaluation of clearance-type tests, the algorithm relying on the least squares principle, developed by D.W. Marquardt, proved excellent [7], [8].

3.2. Short description of the algorithm

Let

n	number of measurement data;
k	number of assessed parameters;
$t_1, t_2 \ldots t_n$	sampling times (independent variables);
$y_1, y_2, \ldots y_n$	measurement data at the time instants above;
$b_{10}, b_{20}, \ldots b_{k0}$	initial values of the parameters to be assessed be given.

3.3. Problem

Let us determine parameter values $b_1, \ldots b_k$ for which the sum of the square of differences between measured data y_i and computed assessments $\hat{y}_i$ is minimum, that is, minimize

$$\phi = \sum_{i=1}^{n} (y_i - \hat{y}_i)^2 \qquad (33)$$

To determine assessment $\hat{y}_i$, let us rewrite (32):

$$\hat{y}_i = b_1 + \sum_{l=2,4,\ldots}^{k-1} b_l \exp(b_{l+1} \cdot t_1) \qquad (34)$$

To minimize (33) parameter vector $\overline{b}$ has to be changed stepwise, according to some convenient strategy. After some experimentation we used an iterative computing method [7].

In conformity with this strategy, repeating iteration steps yields the minimum for Φ. Condition of stopping the iterative computation may be defined either by specifying a given value for Φ minimum, to stop after its achievement, or by observing the rate of convergence, and to accept the result after a certain slowing down in the rate of convergence.

Namely, the rate of convergence abruptly drops after starting with very high value.

If the rate of convergence drops below a given value, the increase in the accuracy is not proportional to the runtime. Since measurement results from diagnostic tests comprise many with significant errors (convergence rate abruptly drops at a relatively high sum of squares of the number of errors), iteration is best stopped at a given value of the rate of convergence.

3.4. Evaluation of liver flow tests by colloid 198 Au

The program which was written in Turbo Pascal for an IBM PC personal computer and based on the algorithm under (32) has been applied, among others, to evaluate liver flow tests made with colloid 198 Au. The test relies on colloids of a given particle size being screened out from the plasma by RES (reticulo-endothelial system) cells of the organism. Most of these cells are found in the liver, but there are some in the spleen and the medulla.

The test procedure: Colloid 198 Au is administered to the patient. After the tracer has been assimilated, plasma activity over the brain (counts per minute) is determined. Theoretically, measurement points lie on an exponentially decreasing curve. Structure of the mathematical model of the test is a so-called mammilary system of four compartments (Fig. 9.)

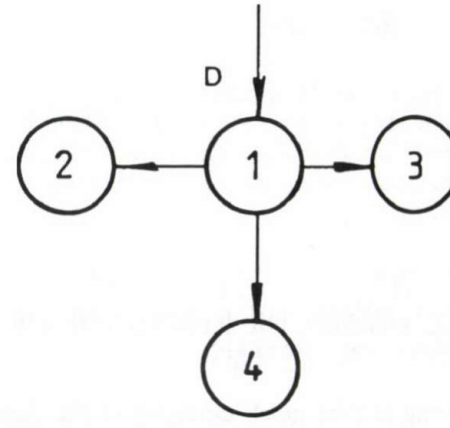

Figure 9. Mammilary model of the liver flow-test

After input of measurement data, the program computes the parameters of the mathematical model, then physiological data much more informative for the doctors (biological halving times for liver, spleen, medulla, and blood flow in the liver as a percentage of the volume per minute of circulation). An example for measurement evaluation is seen in Fig. 10.

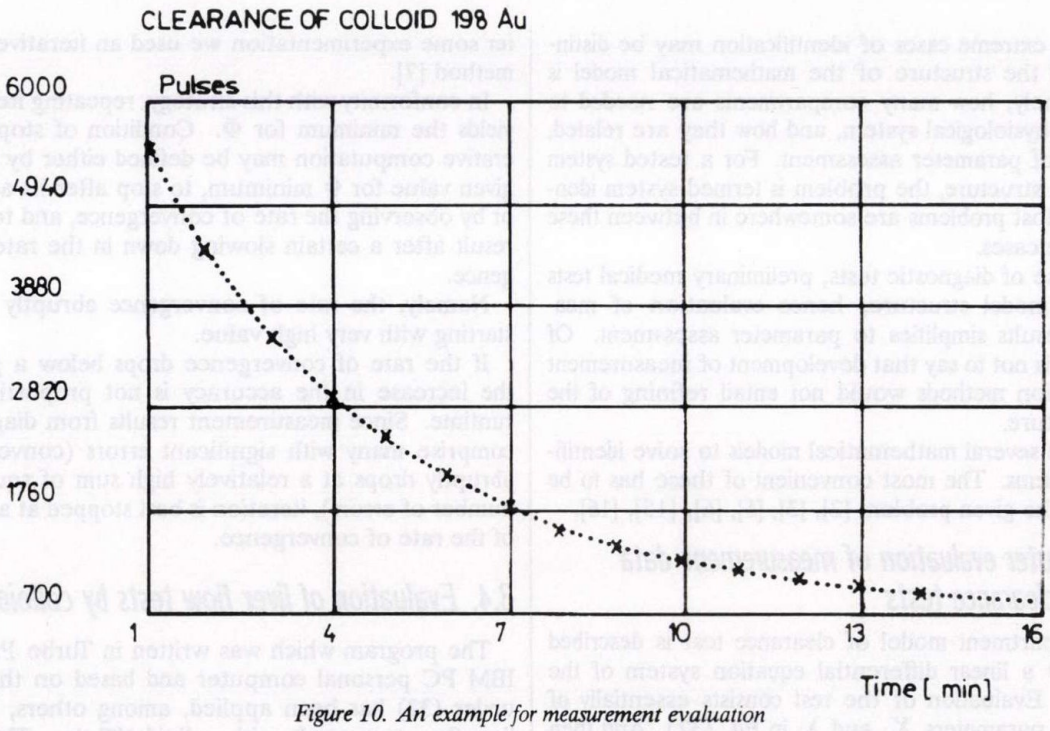

Figure 10. An example for measurement evaluation

Exponential regression outputs:

$$Y = B(1) + B(I)EXP(B)I + 1(X)$$

where $I = 2, 4, 6 \ldots$

$B(1) = 223$

$B(2) = 4729$

$B(3) = -.32$

$B(4) = 1243$

$B(5) = -.142$

$B(6) = 784$

$B(7) = .036$

Halving time for liver RES cells: 2.16 (min)
Halving time for the spleen RES cells: 4.9 (min)
Halving time for the medulla RES cells: 19.36 (min)
Blood percentage flowing through the liver
$V = 32.03\ \%$.

4. USE OF AN EVENT RECOGNITION METHOD FOR DETERMINING THE ILLNESSES OF THE PHYSIOLOGICAL SYSTEMS

Monitoring and the quick detection of the illnesses of the physiological systems are of great importance. An inverse event recognition method [9] has been used for the quick detection of the illnesses of the physiological systems.

As a first step the parameters of a linear process model should be identified in the case of different system illnesses (as outer variables). After that the monitoring of state variables and using a proper event recognition method, the outer variables (nature of illnesses) can be recalculated by an identified linear model. In this way the possible illnesses of the system can be located.

4.1. Linear Model

Let us consider the following linear multivariable dynamic model:

$$\dot{x}(t) = Ax(t) + Bu(t) \tag{35}$$

where $x(t)$ is measurable state deviation vector characterizing the deviation from the normal steady state, $u(t)$ is so-called event indicator vector. Whenever the j-th event takes place $u_j = 1$, otherwise $u_j = 0$. The elements of the A and B matrices can be identified by the "teaching" process.

4.2. Teaching Process

The "teaching" of the linear model, the identification of its matrix coefficients can be carried out by direct measurements. During this identification process the events to be recognized are numerically simulated one by one and the matrix elements a_{ij} and b_{ij} can be computed on the basis of the $x(t)$ trajectories provided by the physiological hybrid model by minimizing the following multivariable nonlinear function:

$$I(a_{ij}, b_{ij}) = \sum_{n=1}^{N} \int_0^T (\dot{x}_m^n - Ax_m^n - Bu_m^n)^2 dt \tag{36}$$

Where $x_m^n(t)$ is the measured trajectory (in our case computed by the nonlinear model) in the n-th experiment, when only the n-th element of the u vector differs from zero.

4.3. Event Recognition

The event recognition is based on the measurement of the state variables and the inverse solution of (35). The solution of the linear system (35) for discrete time step ΔT in recursive form is [10]:

$$x^{k+1} = \Phi(\Delta T)x^k + \frac{\Delta T}{2}Bu^{k+1} + \frac{\Delta T}{2}\Phi(\Delta T)Bu^k \tag{37}$$

Where the trapezoidal rule was used and

$$\Phi(\Delta T) = e^{A\Delta T}, \quad x^k = x(t), \quad t = k\Delta T \qquad (38)$$

Reordering equation (37) for the event indicator-vector, we get

$$u^{k+1} = \frac{2}{\Delta T} B^{-1} x^{k+1} - \frac{2}{\Delta T} B^{-1} \Phi T x^k - \\ - B^{-1} \Phi(\Delta T) B u^k \qquad (39)$$

In the case where disturbance of j-th type has occured, the $x(t)$ state deviation vector will change accordingly and the value of the event indicator computed by the recursive algorithm (39) will approach (35).
As the linear model estimates the states of the nonlinear process in integral or global way (see Eq. (36)), therefore using an integral (global) $U(t)$ indicator vector is more efficient [17].

4.4. Case Study

The method described in the previous section was applied, to the analysis of a multivariable physiological model, published in [18]. The goal of our investigation was to recognise the following illnesses: hepatitis, tumor, etc. (as events U_i). At the same time the measured physiological parameters are: different blood flows in liver spleen and medulla and blood preasure, etc. (as state variables x_i).

The computed event indicators versus time are shown in Fig. 11. An event is considered as "recognized" when its related event indicator is about 1.

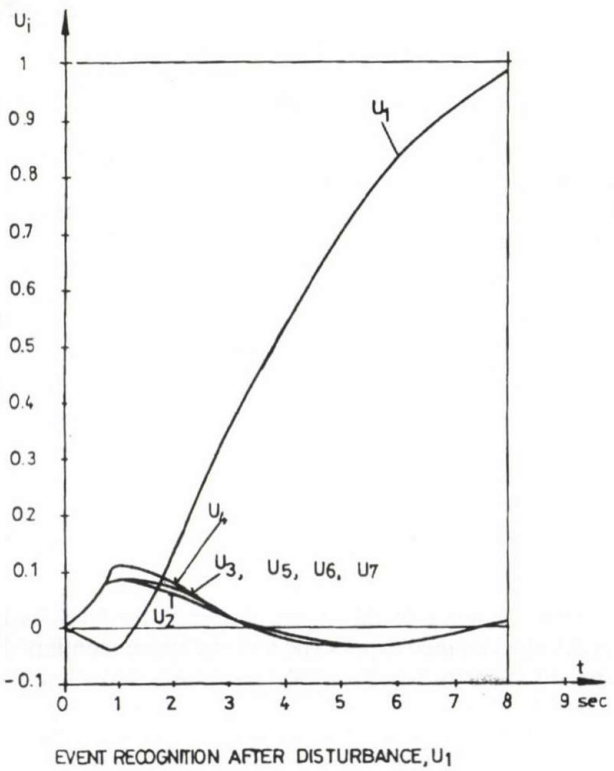

Figure 11. Event Recognition after disturbance: $u_1 = 1$

The method also works when different events (illnesses) occur in the time. Fig. 12. shows clearly this method has recognized the events, although the teaching process has not been carried out for this mixed event case.

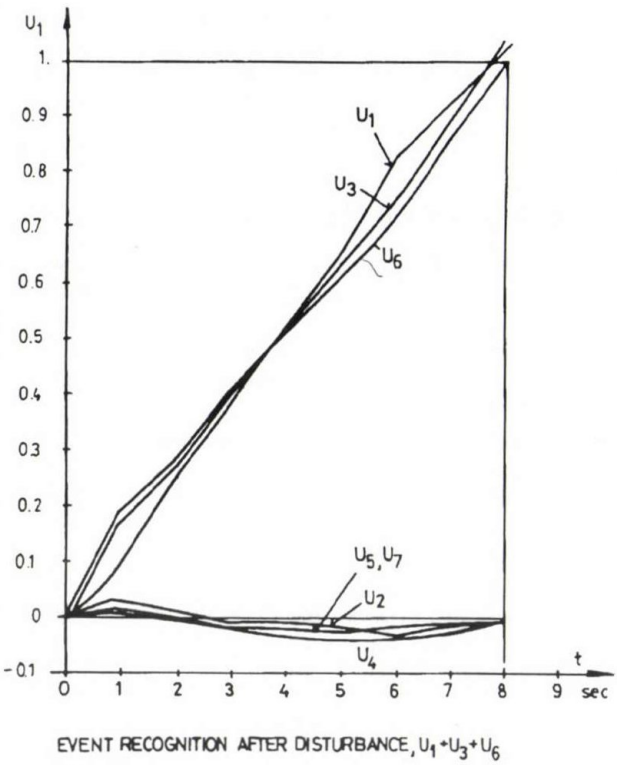

Figure 12. Event Recognition after disturbance: $u_1 = 1$, $u_3 = 1$, $u_6 = 1$

5. APPLICATION OF COMPUTATIONAL STATISTICS TO THE INVESTIGATION OF TUMORS OF THE DIGESTIVE SYSTEM

Statistical analysis and within this exploratory data analysis play an important role in preventive medicine and in daily therapeutic work. In the course of human life different diseases may develop. Among them tumors those in the digestive system have a special importance. A major purpose of our activity in the field of their investigation was to develop computational methods which increase the efficiency of preventive medical work, the accurate recognition of diseases and serve the daily medical treatment, with effective application possibility [11], [12].

Laboratory findings, complaints, symptoms and accomplished examinations of 400 patients of the Department of Surgery of the "Jáhn Ferenc" Hospital, Budapest were available concerning tumors of the digestive system. The majority of the investigated data was categorical that is of qualitative character. Since the complaints are rather subjective and the medical examinations are expensive, we wanted to choose the relevant ones. More generally, our purpose was to analyze the complaints, the symptoms, the results of the examinations performed and laboratory findings to discover the connections, relations between the diagnosed diseases and the treatment, and to investigate the groups of similar patients and the classes of related variables. A possible technique was reported earlier [13], [14].

Our aim was to classify the patients into disjoint subgroups on the basis of the above data in such a way that patients having similar complaints, symptoms and examination results should belong to the same subgroup.

Supposing that these groups coincide with the main diagnostic groups with a relatively high probability, an expert system can be built up.

One of the most common ways of classification is discriminant analysis. In order to be able to apply the usual discriminant techniques, we used dual scaling techniques for the categorical variables.

5.1. Statistical Analysis of the Data

20 complaints, 21 symptoms, and 20 examinations were investigated. The variables within these three groups are not independent. Our aim was to reveal their hidden structure and to find relations between them.

Dual scaling applied for this purpose is the categorical analogue of factor- and canonical analysis for normally distributed variables. We proceed in the following way:

Let n denote the number of variables (in our case $n = 20$). For an integer $k < n$ we are looking for k-dimensional quantifications of the patients and those of the variable-categories, so that patients having many complaints (or symptoms or examination results) in common should be close in Euclidean metric in the k-dimensional space, where they are represented by their quantifications.

The dual scaling technique of the multiple correspondence analysis determines the eigenvalues of the special $tn \times tn$ contingency table called Burt-table (where t is the maximal number of categories of the variables). These eigenvalues give the proportion of variances of the so-called correspondence factors. Let k denote the number of significant factors.

Then in the k-dimensional space of the first k non-trivial factors the patients and the variable-categories can be represented together fulfilling the requirement that patients having many complaints (or symptoms or examination results) in common should be close in Euclidean metric in the k-dimensional space.

The k-dimensional quantifications of the patients are called scores, while those of the variable-categories are called loadings. On the basis of these loadings some physical meaning can be assigned to the factors and at the same time the most important complaints (or symptoms or examinations) — those having large weights in the first factors — can be chosen. These variables characterize the patients best and cause the main interactions between the variables.

5.2. Classification of the Patients

65 % of the 400 patients belonged to one of the following five diagnostic groups:

tumor ventriculi (1519),
tumor sigmae (1533),
tumor colontos (1539),
tumor recti (1541),
ulcus duodeni (5320),

where the numbers in brackets are the International Classification Codes of the illnesses in question.

Studying the profiles of the complaints, symptoms and examinations in these 5 diagnostic groups we found that the groups do not differ significantly with respect to any of the above variables.

However, when we substituted the complaints, symptoms and examinations by their most relevant correspondence-factors, we found that the diagnostic groups had similar profiles with respect to these factors. It is very hopeful: on the one hand it is the condition of obtaining good classification of the patients on the basis of their correspondence-scores belonging to the most relevant factors, while on the other hand the well-known classification methods elaborated for continuous variables can be applied.

The most important laboratory findings (such as haematocrit, haemoglobin and number of white cells) can also be attached as continuous data. The patients were classified by the k-means method. For the whole sample we obtained that it is worth while taking the number of clusters to be 8. We found that 5 of the 8 clusters showed a good accordance with the above diagnostic groups, but patients belonging to other diagnostic groups (each having at most 2-3 persons) were not homogeneous, some of them belonged to the big groups while others constituted other clusters. When we proceeded on the algorithm for 5 clusters and for the patients of 5 main diagnostic groups, by cross-tabulation we found that 3 of the clusters showed good accordance with the diagnostic groups 1519, 1541 and 5320. (If we had more patients of the other groups, probably better results might have been obtained).

The above classification result led us to perform discriminant analysis for the 5 main diagnostic groups. In the case of the 3 diagnostic groups (showing good accordance with our clusters) the probability of good classification was relatively high (93,3 % for 1519, 58 % for 1541 and 75 % for 5320). The average probability of the correct classifications was 76,4 %.

Thus on the basis of the discriminant coefficients a new patient could be diagnosed with the above probability. If this probability is "high", this forecasting can be developed into a knowledge-based expert system.

5.3. Bases of an Expert System

The performed exploratory data analysis is useful in many respects. It helps the physician

- to reduce the number of complaints (or symptoms or examination results) to be registered,
- to choose the most important complaints (or symptoms or examination results),
- to reveal hidden relations between the complaints (or symptoms or examination results),
- to build up a computer-aided registration and diagnostic facility, which gives merely a hint to the physician: if he were a computer having the total mass of the sorted available information he would guess the illness with high probability. This machine-opinion can be revised by performing the above analysis again adding new patients to the sample.

Important elements of the expert system to be developed later are the obtained experience and the above-mentioned diagnostic capacity based on this. However, according to the evolutionary technique usual in producing expert systems, we have prepared the quick prototype of a surgical expert system of limited capacity. It is rule-based and unsuited for taking probabilities into account, and comprises only the most common diseases. It was prepared with the aid of a frame ystem. In the future we would like to produce an adaptive knowledge-based expert system which includes also the statistical analysis and can treat probabilities too.

6. APPENDIX

t time
n number of compartments in a system
Q_j amount of substance in compartment j (mass)
q_j amount of tracer in compartment j (mass)
$a_j = \frac{q_j}{Q_j}$ abundance ratio for a stable isotope, or specific activity for a radioactive tracer, in compartment j
$\frac{a_j}{a_j(0)}$ relative specific activity of tracer in compartment j
k_{ij} rate constant for transport into compartment i from compartment j (time^{-1})
R_{ij} rate of transport of unlabelled substance into compartment i from compartment j (mass time^{-1})
$q_j(0)$ the amount of tracer in compartment j when $t = 0$ (mass)
$a_j(0)$ the specific activity of the tracer in compartment j when $t = 0$
X_i coefficient of the i^{th} exponential term
λ_i constant of the i^{th} exponential term (time^{-1})

The abundance ratio of the tracer a_j, can be given in the following form:

$$a_j = \frac{q_j}{Q_j}$$

If the tracer is radio-active, then the specific activity = (counting efficiency) × (aboundance ratio):

$$a_j = E\frac{q_j}{Q_j}$$

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Zoltán Benyó received his degree in electrical engineering at the Technical University of Budapest in 1961. Since then he has been teaching at the University, first as an assistant professor, then as senior lecturer, and since 1976 as an associate professor in the Department of Process Control. He teaches various courses in process control theory and biomedical engineering. He has published about 100 papers, and has presented his results at many conferences in Hungary and abroad. He is the author of 15 textbooks (some with co-authors).

AN ARTIFICIAL NEURAL NETWORK FOR ECG SIGNAL PROCESSING*

J. CSICSVÁRI, P. BOROS, A. MÉHES and A. PFENING

TECHNICAL UNIVERSITY OF BUDAPEST

A new algorithm is proposed to detect a specific part of the ECG signal, the so-called QRS complex. A backpropagation neural network (BPNN) was applied for learning and identification. Other possible applications of the BPNN in the ECG signal processing are also discussed.

1. INTRODUCTION

Electrocardiogram (ECG) has been commonly used in medicine for a long time. It contains crucial information about the heart even in identification of heart diseases or monitoring the heart in an intensive care unit. There are some diseases which can be identified only after examination of a several hours long ECG signal, i.e. there are some arhythmias that may occur only for a few tenth of a second 2-3 times a day. In this case, an automated diagnosis is of crucial importance.

In processing, ECG signal accuracy and speed are two major criteria. Several algorithms have been developed for this purpose but it seems that ECG is so complex that there is no general algorithm which works properly on any signal. Trainable algorithms seem to overcome these limitations.

2. BACKPROPAGATION NEURAL NETWORK

Neural networks (NN) are promising tools for the solution of the learning problem. Most widely, the backpropagation neural network (BPNN) is used to realize neural learning. This kind of network was succesfully trained to solve difficult tasks like pronouncing English text or recognizing handwritten characters [1], [2].

BPNN is usually a 3 layer network containing an input, a hidden and an output layer. Each layer contains neurons which are considered as the elementary units of the NN. Each neuron has input connections from the previous layer and output connections to the next layer (see Fig. 1).

The activity of a neuron is determined by the activity of the neurons in the previous layer, expressed by the values of the connection weights. Let $a_i[j]$ be the activity of the i-th neuron in the j-th layer and $w_{ij}[k]$ be the connection weight between the i-th neuron in the k-th layer and the j-th neuron of the $(k-1)$th layer. Then let

$$I_i[s] = \sum_j w_{ij}[s]\ a_j[s-1]$$

Then $a_i[s] = f(I_i[s])$ where f is a sigmoid transfer function:

$$f(x) = 1/(1+\exp(-x)).$$

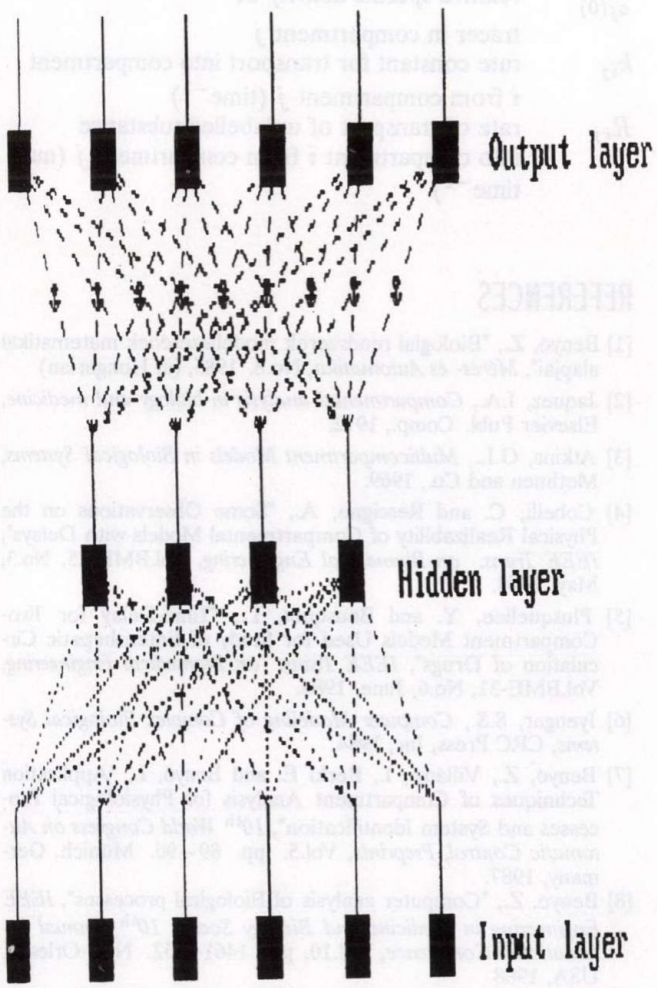

Figure 1. Backpropagation network

The training procedure is the following: activity at the input layer is fixed according to an input template. Activity of the output layer is compared to the desired output template we would like to get in response to the input. When any difference is detected by these comparisons, the weights in the NN are modified so that the difference between the output pattern and the desired output template must decrease. As an iterative process the comparisons and modifications are repeated several times on the training set. Let d_k be the desired and o_k be the real activity of the k-th output neuron. Then w_{ij} is

$$w_{ij}[s](t) = w_{ij}[s](t-1) - \Delta w_{ij}[s](t)$$

after an iteration step and

$$\Delta w_{ij}[2](t) = \eta(d_i - o_i)\ f'(I_i[2])\ x_j[1]$$

* The paper is based on an award winning competition paper presented at the Scientific Student Conference 1990, Technical University of Budapest.

for the weights between the output and the hidden layer, and

$$w_{ij}[1](t) = \\ = \eta \sum_k ((d_k - o_k) w_{ki}[2] f'(I_k[2])) f'(I_i[1]) x_j[0]$$

$$\eta = 0.3 \ldots 0.4$$

between the input and the hidden layer.

3. QRS DETECTION WITH BPNN

In this section we would like to present an application of the NN to ECG processing.

An example of an ECG signal is shown in Fig. 2. This signal has 5 primitives: P, Q, R, S, T waves. One elementary problem of the ECG processing is how to detect the QRS complex. Several algorithms have been worked out to identify QRS but none of them could perform 100% accuracy due to the great variety of ECG signals and biological 'noise' (muscle activity such as tremor, sweating) [3], [4], [5].

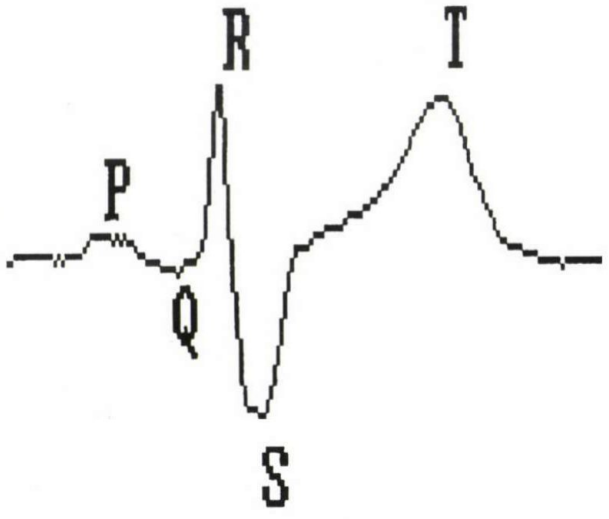

Figure 2. An example of an ECG signal

We trained BPNN to detect QRS. We have examined 2 networks. The output layer of both networks contained one neuron. The input values were regarded to belong to a QRS if and only if they produced an output response higher than 0.5. In the case of the first NN, 5 selected values of the first derivatives of the ECG were used as input. First, three consecutive positive derivatives were selected and then, as additional two input parameters, the next two negative derivatives were also chosen. The first input value had to exceed a predetermined amplitude treshold. This means that there was a preprocessing phase before we applied the NN.

In the case of the second NN, 11 consecutive sampled values of ECG were applied as input parameters.

In the case of both NN, the training set contained about 100 patterns. About 30 percent of them represented the QRS.

We had six different records of ECG (sampled with 250 Hz) and the training set comprised four of them. After 1000 iterations in the case of the first NN, and 5000 iterations in the case of the second one, the BPNNs detected QRS with 100 percent accuracy. The performance of other algorithms introduced to detect the QRS [3] was never found to be better than 90 percent.

Fig. 3 and 4 show some detection results of our NNs on two ECG records from sick patients.

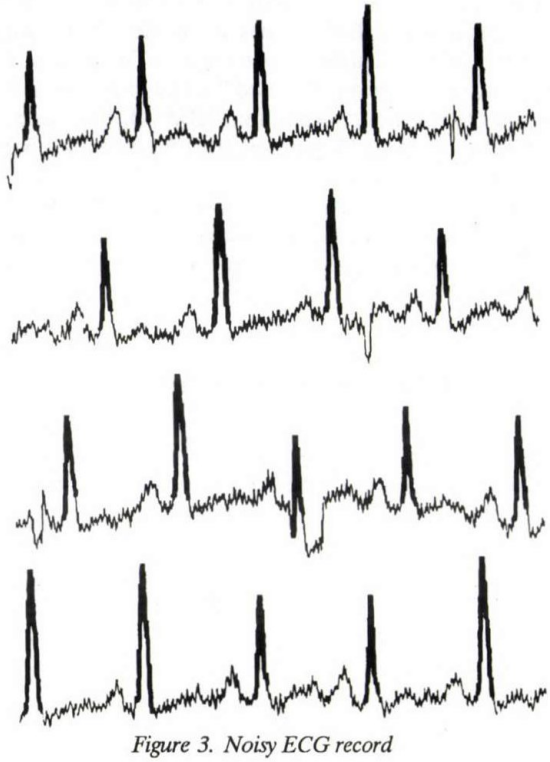

Figure 3. Noisy ECG record

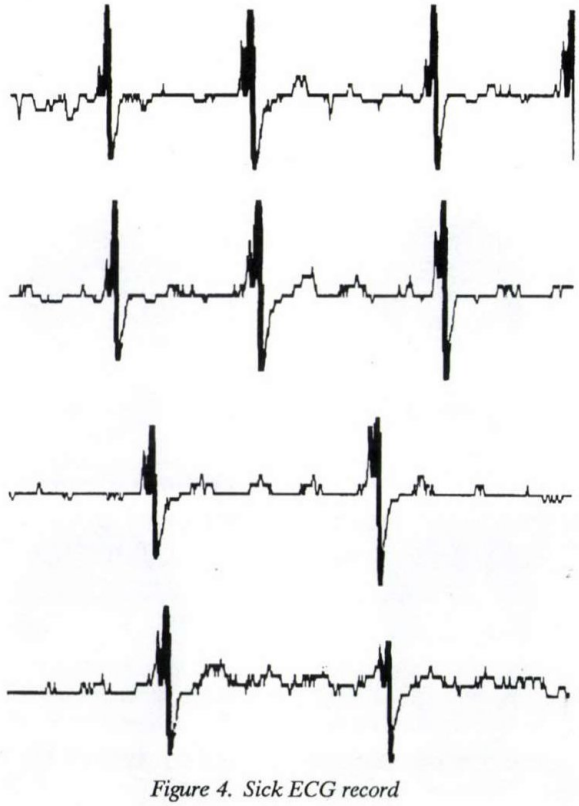

Figure 4. Sick ECG record

4. DISCUSSION

We must emphasize that our results do not mean that our network can work correctly on any ECG record but they strongly indicate that back propagation NN

- is able to learn any kind of QRS, and, after a brief learning procedure,
- it can correctly detect the QRS on a long record.

Another important problem is how to realize BPNN. Only simulation of BPNNs was available for us, with no possibility of their hardware realization. This simulation of the networks, however, resulted in new algorithms to detect the QRS. On a conventional IBM-AT, the learning of the NN takes about 15 minutes, but the detection is much more faster. The first version of the NN can detect even on-line. Although the second version of the NN was found to work much more slowly, there are some accelerator boards commercially available and there is a programmable Intel chip in the market with 64 artificial neurons which seems to permit the hardware realization of the NN.

5. FURTHER APPLICATIONS

It seems that the NN, due to its learning ability, can be efficiently used to process ECG. Recently we are working on a possible application of the BPNN to support STI (Syptolic Time Interval) analyzers. For these analyzers, certain points in the ECG must be marked, and it is possible that the NN can correctly find these points. Our initial results are encouraging.

It may be possible to use the BPNN as an arhythmia recognizer. However, this is a difficult problem, and the recognizer needs a large arhythmia data-base and probably a long learning procedure.

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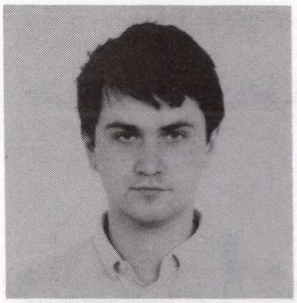
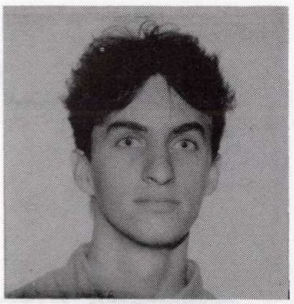
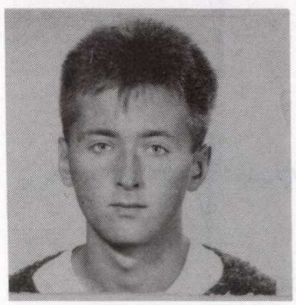
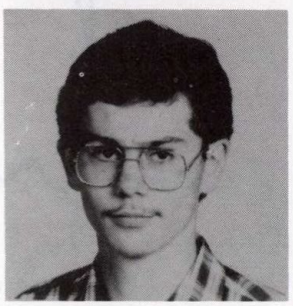








József Csicsvári, Tibor Boros, András Méhes and András Pfening are 5th year students studying informatics at the Faculty of Electrical Engineering of the Technical University of Budapest. They were awarded several times for their works presented at the Students' Conference of the Faculty. Due to their excellent results they are recipients of the Republican Award and the Medal for Hungarian Progress in Technology. To pursue studies abroad, all of them have already spent some period in different countries.

IMPEDANCE CARDIOGRAPH

ICG-M401 NONINVASIVE HEMODYNAMIC MONITORING SYSTEM

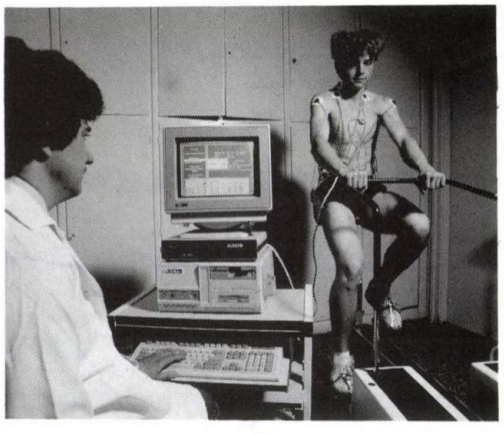
IMPEDANCE CARDIOGRAPHY

Description

Electrical bioimpedance is a technique that enables noninvasive measurement of blood flow by measurement of changes in the electrical conductivity of the thorax or a body segment.

Depending on the source of the electrical impedance change (i.e. first derivative of the impedance change), the result of the calculation is

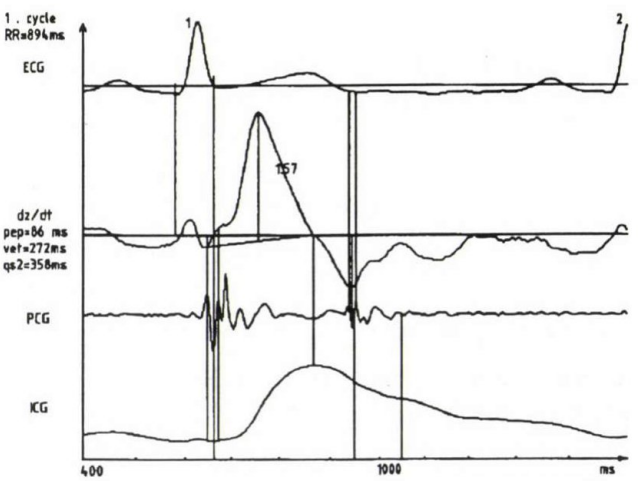
- Stroke Volume
  (SV, volume of blood pumped by the heart in one heart-beat interval),
- Pulse Volume
  (PV, volume of blood passing through the segment in one heart-beat interval)
- Cardiac Output
  (CO, blood flow through the heart in one minute).



ICG-M401 is a continuous, noninvasive hemodynamic monitoring system utilizing impedance technology. Through the use of eight electrodes the ICG-M401 produces a safe and painless high frequency low amplitude constant magnitude current that is passed through the thorax. Pulsatile changes in the electrical resistance of the thorax produces a signal that is precisely time related to the ECG, but is produced by the mechanical activity of blood flow rather than the electrical depolarization of cardiac tissue. The ICG-M401 is connected to an IBM PC/AT. The PC evaluates the signal and computer the hemodynamic parameters.

ICG-M401 GIVES YOU THE FOLLOWING HEMODYNAMIC VARIABLES

SV	**S**troke Volume
CO	**C**ardiac **O**utput
SVI	**S**troke Volume **I**ndex
CI	**C**ardiac **I**ndex
HR	**H**eart **R**ate
PEP	**P**re-Ejection **P**eriod
VET	**V**entricular **E**jection **T**ime
QS2	Electromechanical Systolic Time
PEPI	**P**re-Ejection **P**eriod **I**ndex
VETI	**V**entricular **E**jection **T**ime **I**ndex
QS2I	Electromechanical Systolic Time Index
SVR	**S**ystemic **V**ascular **R**esistance
LVSERI	**L**eft **V**entricular **S**ystolic **E**jection **R**ate **I**ndex (Contractility)
PM	**M**ean **A**rtirial **P**ressure
RPP	**R**ate **P**ressure **P**roduct



Processed curves

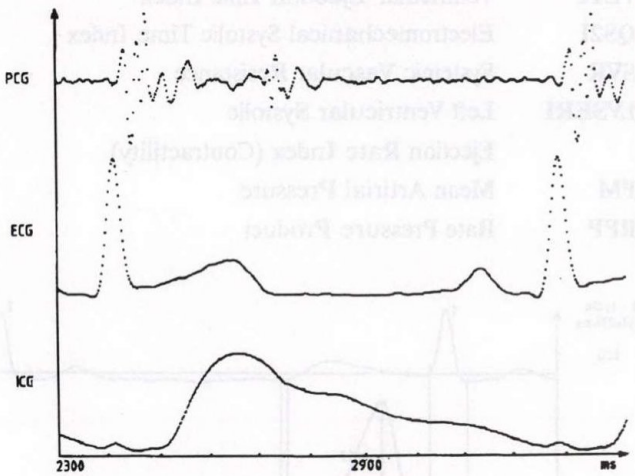
APPLICATIONS

ICG-M401 is an accurate noninvasive device, that enables hemodynamic monitoring to become a practical technique in many clinical situations where previously it was not feasible.

Clinical application of the impedance cardiography

Loading exercise tests for diagnostic purposes

- **Critical circulatory states:** recording of the salient parameters of circulation
  a) anaesthesia-during general narcosis
  b) coronary care unit
  c) perioperative period
  d) optimal adjustment of pacemaker
  e) dialysis, plasmapheresis
- **Late postoperative period:** and **infarction recovery:** determination of exercise loading establishment of working capacity
- **Clinicopharmacology:** measurement of inotrop effects
- **Physical training:** timing of high performance
- **Peripherical vascular disease:** measurement of limbs circulation

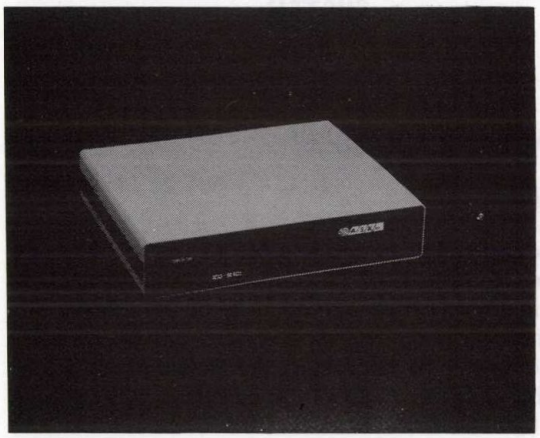


Continuous monitoring

Also appliable for pediatric application of newborns.

Technical specifications

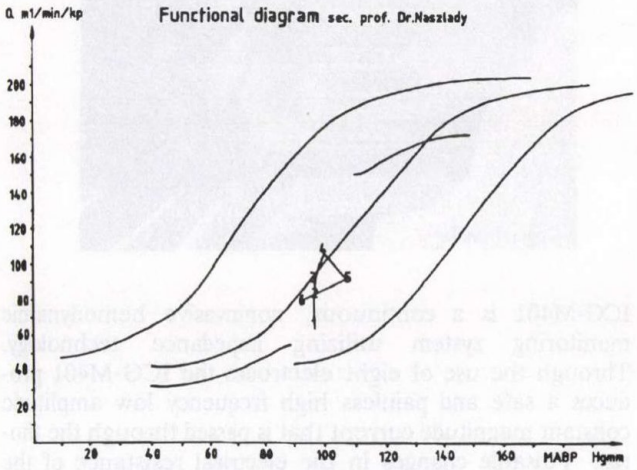
- Power supply: 110/220 V AC, 50/60 Hz
- Power consumption: max. 30 VA
- Protection class: class I
- Degree of protection: type "BF"
- Weight: approx. 4 kg
- Dimensions: 76x360x275 [mm] (HxWxD)
- Measurement current: max. 6 mA RMS 100 kHz
- A/D converter (12 bit)
- Output: serial for computer
- Required hardware:
  IBM PC or compatible
  640 KB memory
  20 MB HDD
  1.2 MB floppy disk
  VGA, EGA, Hercules or CGA graphic
- Accessories:
  supply plug
  patient cable (2m)
  serial interface for the computer
  phonosensor
  fuses (500 mA, 1 A)
  electrodes (60 pcs)



ICG-M401 NONINVASIVE HEMODYNAMIC MONITORING SYSTEM

Advantages

- correct values of salient hemodynamic parameters
- continuous and hands off monitoring
- automatic screening of
  – severe valvular regurgitations,
  – ventricular dyskinesis and
  – left–right shunts



Coronary disease. Preop.
Exercise loading (40 W – 100 W)

- forecast signal of myocardial ischemia, prior to development of anginal pain
- determination of actual working point of the heart related to flow and pressure by each measurement
- all the measured data storable, you can retrieve it and process it at any time
- summarising the trend of these parameters

Easy to use

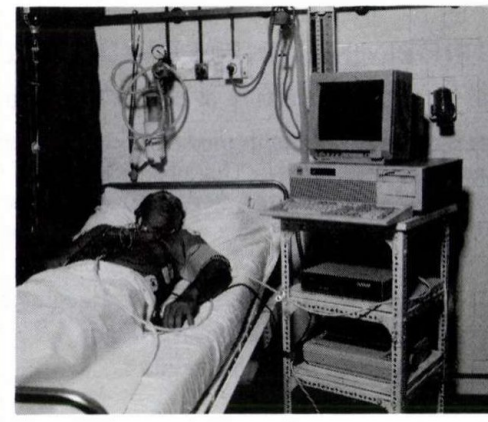
Requires twelve disposable electrodes, only.

Versatile

Can be used in Hospitals, Clinics, or Laboratories for a variety of applications.

Dynamic

Continuous, real-time monitoring, providing early detection of clinical changes.



Further information can be obtained from
ASK Ltd. H-1026 Budapest, Gábor Áron u. 55.
Phone: (361) 115-8457, 135-5984, 135-1332
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1993 EUROPEAN CONFERENCE ON CIRCUIT THEORY AND DESIGN

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The aim of the Conference is to provide in-depth overwiev of the most relevant and recent advances in CAS research activities. As a special feature, half of the time will be devoted to tutorials given by an eminent specialist in each area. Furthermore, PhD students will be given the opportunity to present their work, endorsed by the thesis adviser, in a poster session. The Conference will include the following topics:

- Circuit Design
  - Analog, Digital and Mixed Integrated Circuits
  - Switched Capacitor Networks
  - Communication Circuits
  - Neural Networks
- Signal Processing
  - Analog, Digital and Adaptive Signal Processing
  - Analog, Digital, SC and Adaptive Filtering
  - Image and Speech Processing
- Mathematical Methods
  - Linear and Nonlinear Circuit and System Theory
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Original illustrations should be submitted along the manuscript. All line drawings should be prepared on a white background in black ink. Lettering on drawings should be large enough to be readily legible when the drawing is reduced to one- or two-column width. On figures capital lettering should be used. Photographs should be used sparingly. All photographs must be glossy prints. Figure captions should be typed on a separate sheet.

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EXPONET 92
EXPANDS AT A SWIFT PACE

Germany's International Networking Trade Show doubles it's exhibition area in Frankfurt, from 24 – 26 November

After the exceedingly successful premiere of the new networking trade show "exponet" last November in Frankfurt, the organisers, dc deutsche congress in Starnberg, Germany, have already booked in exhibition area twice as big as last year for EXPONET 92 in Frankfurt (24 – 26 November). In view of the huge amount of interest, from the networking and communications areas, to exhibit at EXPONET 92, the new specialised trade show is expected to grow to over 10.000 square metres of exhibition area and to have over 200 exhibitors.

"exponet" received immediate overwhelming praise from exhibitors and visitors last year. The successful concept of attracting an unusually high number of competent and decision making managers from the I+K departments of German and European companies to the show, through several established and well visited conferences covering themes such as ISDN, cabling technology, corporate networking or LAN-connectivity, was particularly admired.

The exhibitors of the last "exponet" expressed in the poll that they were very satisfied with the quality of the expert visitors and the results of the trade show and all said that they would exhibit again at EXPONET 92. Many companies that wanted first of all to wait for the result of the first event, have now also confirmed their participation.

Along with the exhibition space and number of exhibitors, the information offered at EXPONET 92 will also increase. Alongside the conferences "ISDN 92", "Cabling Conference 92", "Switching Convention" and networking forums, in November 92 additional conferences will also take place: "EDI 92 – 4th German EDIFACT Conference", "FDDI Congress 92" as well as a conference on "Communications Measuring Technology". The organisers expect to have several thousand participants at the conferences and in total 10.000 qualified visitors at the exhibition.

Further information on EXPONET 92 is available from:
Amanda Hope-Mason — dc deutsche congress,
Postf.1125, D-8130 Starnberg,
Tel. +49 8151 13078, Fax +49 8151 28503

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