

People and Ideas in Medical Informatics - A Half Century Review

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Summary

Objective. Reviewing the onset and the rapid changes to make realistic predictions on the future of medical informatics.

Methods. Pointing to the contributions of the early pioneers, who had their roots in other disciplines and by illustrating that from the onset an interdisciplinary approach was characteristic for our field.

Results. Some of the reasons for the changes in medical informatics are that nobody was able to predict the advent of the personal computer in the 1970s, the world-wide web in 1991, and the public start of the Internet in 1992, but foremost that nobody expected that it was not primarily the hardware or the software, but human factors that would be crucial for successful applications of computers in health care. In the past sometimes unrealistic expectations were held, such as on the impact of medical decision-support systems, or on the overly optimistic contributions of electronic health records. Although the technology is widely available, some applications appear to be far more complex than expected. Health care processes can seldom be fully standardized. Humans enter at least in two very different roles in the loop of information processing: as subjects conducting care - the clinicians - and as subjects that are the objects of care - the patients.

Conclusions. Medical informatics lacks a specific methodology; methods are borrowed from adjacent disciplines such as physics, mathematics and, of course, computer science. Human factors play a major role in applying computers in health care. Everyone pursuing a career in biomedical informatics needs to be very aware of this. It is to be expected that the quality of health care will increasingly be assessed by computer systems to fulfill the requirements of medical evidence.

Keywords

Interdisciplinarity, pioneers in medical informatics, computer simulation, biosignal processing, electronic health records

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Introduction

After having been around for almost half a century, much can be told about medical informatics. Our field has been and continues to be in a state of rapid development. After medical informatics came into being, several other informatics-related branches also sprouted from the tree of medicine, such as genomics and proteomics. At the same time other branches, such as physiology or anatomy, were intertwined with yet other ones. Perhaps, sooner or later this will also occur to medical informatics.

Instead of reviewing the history of medical informatics it might be more interesting to discuss ideas of individuals and their initiatives, as well as reasons for successes and failures. Therefore, in the following I want to present a few snapshots of the rapid evolution of our discipline by pointing to pioneers in the field. It will become clear that the present situation in medical informatics is not comparable with that of 50 years ago. The early workers in medical informatics all had their roots in other disciplines, and after having started using computers in their research they became involved in medical informatics. This also applies to the author of this article. Therefore I will discuss how this gradual change took place.

Prelude

Around the end of the 1950s, when studying physics at Delft University of Technology in the Netherlands, Cees Verhagen, the professor of the department where I conducted my experi-

mental work, regularly invited researchers from abroad to present their work. In this way students and staff could widen their views. For instance, I remember a lecture on artificial intelligence and neural networks, given in 1961 by Bernard Widrow of MIT's Lincoln Lab. He discussed methods that would later be adopted widely by researchers in medical informatics. At that time our discipline as such was not yet in existence, although people like Bob Ledley and Lee Lusted already had started research [1, 2] that laid the groundwork for our discipline. Also Morrie Collen was already active in conducting research in multiphasic health screening at Kaiser Permanente [3]. Hubert Pipberger at the VA Hospital in Washington [4], Cesar Caceres [5] at Washington University, Ralph Smith at the Mayo Clinic, and Ray Bonner of IBM had all started research for computer analysis of electrocardiograms, one of the earliest applications of artificial intelligence and pattern recognition in medicine. Verhagen in Delft had the idea that, perhaps in the future, computers would be able to think quasi-independently, as a result of artificial intelligence research, even improving and replicating themselves. Up to now this dream has remained as pure speculation, in spite of the remarkable, though somewhat unconventional, ideas of Ray Kurzweil, who believes that the next step in evolution will be a combination of brain and computer [6]. My own ideas on such predictions are quite different, if not the opposite.

In those early years I was very much attracted by biomedical engineering and medical physics, an area that was in rapid development. Computer tomography

(CT) was still to be developed and 3D ultrasound was in its infancy. Another lecture during my study in physics that raised my interest was given by two researchers in medical physics from the University of Amsterdam, Henk van der Tweel and Jan Strackee. Their lecture strengthened my decision to try to pursue a career in medical physics and bioengineering. After having been nominated in 1973 to the first chair in medical informatics in our country at the Free University Amsterdam, I took the initiative with Jan Strackee to establish training in medical informatics at the two Amsterdam universities [7]. A few years later, in 1987, our entire group moved from the Free University Amsterdam to the Erasmus University Rotterdam, where we would primarily concentrate on scientific research and the training of PhD students. The Amsterdam training was to be continued at the University of Amsterdam.

To understand what follows, I return once more to the initial years of my research. After having completed my studies in physics in 1963, a period followed of most exciting bioengineering research. It was the time that Europe, less than 20 years after the war, was still in full expansion. There was plenty of funding for new research and a great need for people with a scientific background. Therefore, the 1960s were a magnificent time for our research team and we were involved in several interesting research areas, such as perinatal medicine [8, 9], cardiology [10], patient monitoring [11, 12], neuro-physiology and pulmonology. Dealing with such problems required a thorough knowledge of the underlying processes, which I acquired by both studying the fundamentals of medicine and collaborating with researchers from other disciplines and with clinicians. An interdisciplinary approach is characteristic of our field. That is why we see in medical informatics people from a wide range of backgrounds. This early period, which I spent at the Institute of Medical Physics in Utrecht, was the prelude for research in the area that was later to be called medical

informatics^a. Before addressing some aspects of the early R&D in our field, let me first make a short excursion to the rapid developments in hardware and software, the vehicles on which our models and information systems ride.

Evolution in Systems

Who of the present workers in medical informatics does recollect the use of 5- or 7-hole paper tapes or punched cards, 5¼ or 3½ inch diskettes, DEC-tapes or digital magnetic tapes of the 1970s and 1980s? Who still remembers the time that the speed of computers was measured in thousands of instructions per second, that computers had magnetic core memory, and that removable magnetic disks had a storage capacity of a mere hundred thousand bytes? Besides, who can still read the old digital files, produced by a mainframe or minicomputer of those early years? Perhaps, the most impressive observation is that Moore's Law (that the number of transistors on integrated circuits doubles every two years) has held now for half a century. Figure 1 shows a picture of a PDP-15 computer of the early 1970s with four DEC-tape readers. It operated with 'words' of 18 bits.

Indeed, an incredible large number of changes have taken place in computer hardware. But this is no less the case with respect to the software. Are there still people around in our field who wrote programs in Assembler, FORTRAN, COBOL, Pascal, or ALGOL? Are there still systems operational in the original versions of MUMPS or Basic?

The changes since these early days have been tremendous. Yet, nobody was able to predict the advent of the personal computer in the 1970s, the world-wide web in 1991, and the public start of the Internet in 1992. Who at that time had ever heard of computer viruses and computer crime? Who was concerned about

computer security, data confidentiality and privacy protection? Nobody had expected the fast proliferation and processing speed of computers and their applications to all aspects of society, including health care. Who could have predicted, that it was not the hardware nor the software, but the manware or the human factor, that would be the crucial factor for successful applications in the medical domain? It has become very clear during the past 50 years, that computers – in any field – can only be successful when processes can be formalized and procedures standardized.

In the early years of my research in biomedical engineering the first minicomputers appeared, often developed in university laboratories. The Digital Equipment Corporation (DEC) was a spin-off from MIT's Lincoln Lab that I mentioned above. In the course of many years DEC was very successful in marketing their computers, all of them called 'programmed digital processor' (PDP), starting with the PDP-1. We have used many generations of PDPs, in particular the PDP-11 series, which later evolved into powerful workstations. IBM was mainly business-oriented, with the exception of its early IBM 1800 and 1130, which were also used in biomedical research.

The successes of a research team in biomedical informatics are determined by virtue of the different skills its members possess: people with a background in medicine, biology, physics, mathematics, chemistry, pharmacy, informatics, programming, or engineering. A typical research group in our field has a multidisciplinary composition. Each team member should be able to collaborate with his colleagues from other disciplines, but at the same time he or she should be an expert in at least one specific, individual discipline. A beautiful example of true multidisciplinary research is the following.

Perinatal Medicine

My own research started in 1963 in the field of perinatal medicine. Computers

^a Many other terms were given to our field, such as health- or nursing informatics, (biomedical) informatics, e-Health, or medical computer science.



Fig. 1 The PDP-15 computer that we used in the early 1970s for our research in electrocardiology. It had four DEC-tape readers for the storage of data and programs, and operated with 'words' of 18 bits.

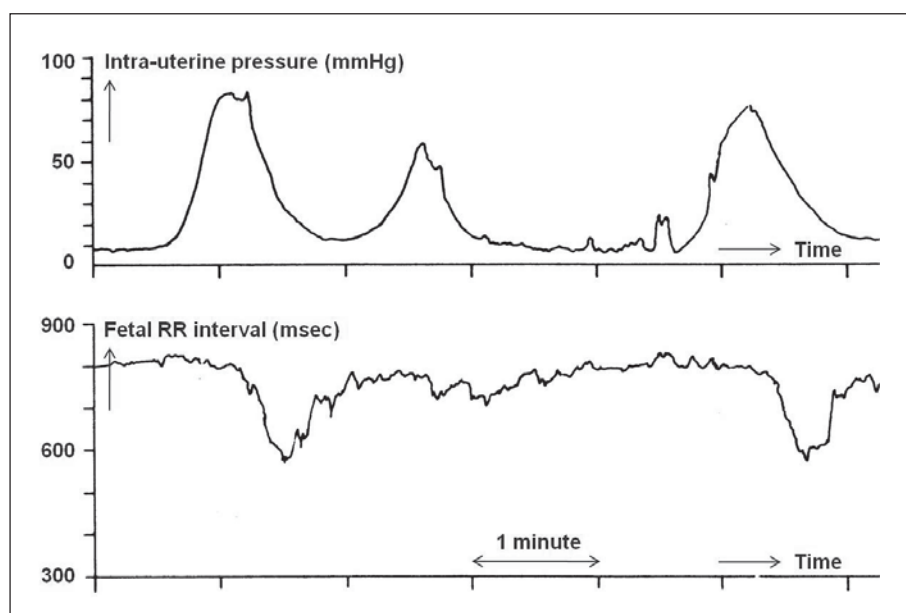


Fig. 2 A typical example of the fetal heart rate (expressed as RR-intervals) changing under the influence of an increasing intra-uterine pressure and umbilical cord occlusion.

were not yet available and we had to build all instruments and processing equipment ourselves from scratch. In later years we started using the early digital computers for the processing of biomedical signals, but in the first years we used analog and hybrid computers for modeling. An exciting research area in which our team was involved was the study of control mechanisms in the fetal circulation during birth. During that period of life, major changes take place. In our research

we developed monitoring equipment [13], computer models [14] and performed animal experiments with pregnant sheep. Because digital computers were not yet available we constructed our own special-purpose processing systems. But later in the 1960s digital computers became affordable to use in the R&D in our emerging discipline.

The goal of our research was (1) to get insight in the condition of the fetus during pregnancy and birth in order to

understand the sometimes dramatic events that take place during delivery, and (2) to develop instruments to be able to record biosignals reflecting the contractions of the uterus and the condition of the fetal heart and the circulation. Figure 2 gives a typical example of the fetal heart rate (expressed as RR-intervals) that may change under influence of an increasing intra-uterine pressure and umbilical cord occlusion.

When a fetus is developing, it grows from only a few cells to a newborn of about 3.5 kilograms. A similar growth applies to all its organs, including the fetal heart, which starts beating at about 22 days after conception. After about 10 weeks it is detectable by ultrasound and by 12 weeks its ECG can sometimes already be recorded from the mother's abdominal wall. In the early days of our perinatal research we developed instrumentation that could detect fetal ECGs with amplitudes of only a few microvolts, whereas the maternal ECG has amplitudes at least a thousand times greater. This required the avoidance and cancellation of noisy disturbances from active abdominal muscles as well as from external sources, including the maternal ECG. In a collaborating obstetric department we even had to install a Faraday cage within an experimental labor room, in order to reduce electromagnetic radiation from the outside world. It was around this time that we developed the first digital fetal monitor, not with the chips of today, but by constructing it ourselves with transistors, hard-wiring the connections for data processing.

We were most gratified in being able to monitor the condition of the fetus during birth in real time. When we first collected data from the fetus, they were quite strange to all of us. The reaction of the fetus to uterine contractions sometimes appeared to be very dramatic, and it took a while, and several international meetings to understand the meaning of the signals. It also required basic studies and experiments, not possible in a clinic with women undergoing labor. Therefore, we decided to study in depth the physiology of the fetal circulation and to con-

duct experiments with unborn lambs, while in parallel developing computer models of the fetal circulation, which is very different from the adult circulation. In our animal research, no sheep or lamb needed to be sacrificed. On the contrary; many lambs, once born, were brought up by the family of one of our team, my PhD student and later colleague Ton Veth. Figure 3 presents the flow diagram of the model of the fetal circulation in which the effect of cord occlusion could be simulated on an analog computer. The fetal circulation contained arterial and venous compartments as well as a placental compartment. The fetal heart was modeled as one compartment and the heart rate was controlled by baroreceptor feedback, cord occlusion causing an increase in blood pressure and a reduced venous return. As much as possible the findings from the animal experiments were implemented in the model. In later years the model was simulated on a digital computer by using IBM's CSMP (continuous system modeling program) software package.

Before conducting such complex studies – in the animal experiments easily 10 to 15 people were involved – it was important to carefully formulate the hypotheses underlying the research. Otherwise one has to pay a price in terms of disappointing outcomes. In short: wrong a priori assumptions (or the lack of them) are reflected in negative outcomes. The results of our perinatal research were published in different journals, clinical and bioengineering [15], since medical informatics journals were not yet in existence. However, gradually the field of medical informatics emerged and conferences in the field were organized. The first scientific journal, later to be called *Methods of Information in Medicine*, had already been started in 1961 by Gustav Wagner in Heidelberg.

European Medical Computing

In 1966 I attended the very first European conference on computers in medicine in Helsingør, Denmark. It is the lo-

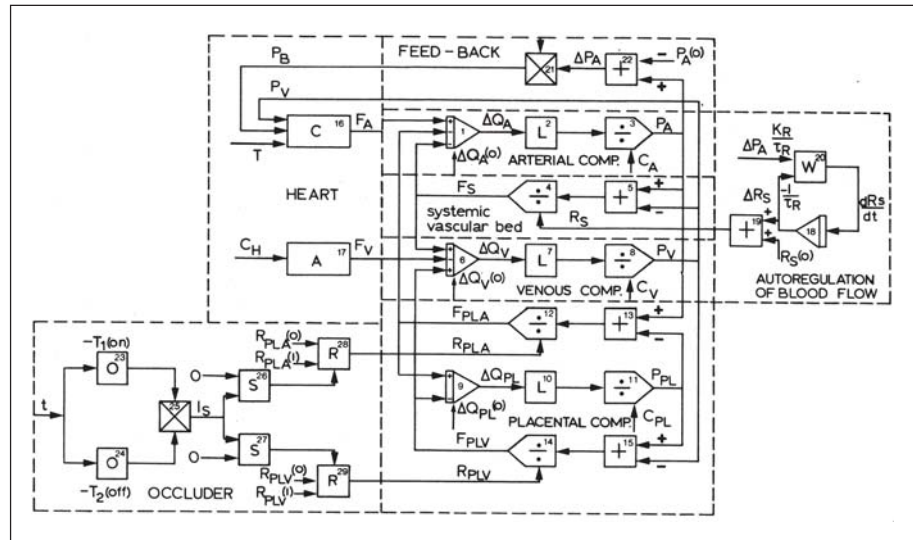


Fig. 3 Flow diagram of the model of the fetal circulation in which the effect of cord occlusion could be simulated on an analog computer. The fetal circulation contained arterial and venous compartments as well as a placental compartment. The fetal heart was modeled as one compartment and the heart rate was controlled by baroreceptor feedback. Cord occlusion caused an increase in blood pressure and a reduced venous return. As much as possible the findings from the animal experiments were implemented in the model.

cation of the castle that inspired Shakespeare for his play *Hamlet*, with its famous phrase 'to be or not to be'. During that conference I got acquainted with Hubert Pipberger, mentioned above, who had started research on the computer analysis of the vectorcardiogram, also a research topic of our team. Our contacts would result in a close collaboration with Hubert Pipberger that would last for many years. From Hubert I learned the axiom 'research is people', the truth of which would become more and more evident over the years: human ideas lie at the root of all human endeavors and certainly at the basis of scientific research. Such ideas are always founded on what are hopefully clearly phrased assumptions or a priori information. To re-emphasize: when something is wrong with the basic assumptions one should not be surprised if research outcomes are disappointing or even false. Regrettably, negative outcomes are seldom published in the scientific literature so that others have to frequently repeat the same errors.

The conference in Helsingør amplified a paradigm shift in our research, but first of all I had to study the state of the art in medical computing. Having re-

ceived a grant from the World Health Organization I studied medical computer applications in Europe. A study tour of about three months to research labs and hospitals in different countries resulted in a substantial report, called 'Computers in European Hospitals' [16]. An anecdote related to this is the following. Two years ago I received a letter from Clem McDonald with a copy of my 1967 report, which he had found while tidying his desk at the Regenstrief Institute in Indianapolis [17], after having been nominated director of the *Lister Hill Research Center* of the National Library of Medicine in Bethesda: 'Dear Jan, I ran across this report recently – thought you might get a kick out of it. Hope you are well. Regards, Clem.' About Clem I could tell several stories, including our walk together in the crowd of people on the Mall in Washington during the 'one million men march', but let it suffice to say that I consider Clem with other colleagues such as Bob Ledley, Morris Collen, Homer Warner, Octo Barnett and Don Lindberg as the early US pioneers in our field. It is interesting to note that my first visits in 1968 to Homer in Salt Lake City and Octo at

MGH were not related to medical informatics, but to our common interests in computer modeling in cardiology.

My trip in Europe brought me to Stockholm where I met, among others, Paul Hall and Hans Selander at Karolinska Hospital who were developing one of the first hospital information systems; and to Tybjerg Hansen of Copenhagen's University Hospital, who used an IBM 1800 for research in physiology and planned to develop applications for hospital administration. In Copenhagen I also visited Fritz Buchthal and his younger colleague Annelise Rosenfalck. They did neurophysiologic research and used a small Olivetti 101 computer that could only process 120 machine instructions in a row. With Annelise I established in the 1990s under the umbrella of IMIA a series of working conferences called 'Biosignal interpretation', which has been very successful over the years, with the Proceedings appearing in 'Methods' [18]. Fritz Buchthal and Annelise had little laboratory space. It is striking that the most advanced research often is not conducted in spacious and well-equipped labora-

tories, but that success is primarily determined by the individuals working in those labs; 'research is people'. Of course, I could comment on many other interesting people I met during my WHO tour in London, Paris and Geneva and their equally interesting ideas, but in the following I would like to concentrate on one colleague in particular, François Grémy, who is one of the European pioneers and is well known for his role in the founding of IMIA.

In 1967 I visited François for the first time in his *Département de Biophysique* in Paris. It was at the time that I studied the analysis of electro-encephalograms in the laboratory of Antoine Rémond at the *Hôpital de la Salpêtrière*. The visit to François was to become a contact and a friendship for life. He differed from most other researchers I had met, having a much wider interest than 'just' scientific research. We shared a common interest in philosophy. Much later, in 1996, when I was invited to speak at his farewell meeting from the University of Paris I added to my address the following: '*Je sais que mon cher ami François Grémy n'aime pas seulement la Science mais, en devenant un petit peu plus âgé,*

de plus en plus la Philosophie'^b and then cited Blaise Pascal, who said that '*man is not just a reed, the most fragile in nature, but a thinking reed*'.^c Our field needs people like François who know that we live in a world much larger and richer than that of science, let alone medical informatics. François moved to a small city in southern France, where I was able to visit him a few years ago with Marion Ball, as shown in Figure 4. François was instrumental in the founding of the Technical Committee 4 (TC-4) of IFIP, the *International Federation for Information Processing*. TC-4 organized the first World Conference of Medical Informatics in 1974 in Stockholm, under the chairmanship of François Grémy, and was after that transformed into the International Medical Informatics Association (IMIA). After the Stockholm conference, the era of medical informatics can be considered to be well under way. It would lead to hundreds of thousands of computers – networked mainframes, workstations, PCs, etcetera – in hospitals, primary care settings and research laboratories.



Fig. 4 Visiting François Grémy in 2005. From left to right: Jan van Bommel, Marion Ball, François Grémy, and An van Bommel.

Growing to Adulthood

In the 1970s the first R&D departments in medical informatics were founded in universities to develop advanced training and education programs. The domain evolved from simply computer applications in medicine to a multidisciplinary research field, where medical students, MSc and PhD students were trained. As it became clear that medical informatics was lacking a specific methodology, methods were borrowed from related adjacent scientific disciplines such as physics, statistics and, of course, computer science. Medical Informatics is

^b 'I know that my dear friend François Grémy not only loves Science, but – growing older – more and more also Philosophy.'

^c L'homme n'est qu'un roseau, le plus faible de la nature, mais c'est un roseau pensant. Blaise Pascal (1670) *Pensée* 347.

‘not a fundamental scientific area on its own, but an applied field. It is at most an ancillary science, existing for the benefit of health care in the widest sense [19]. Like medicine it, too, primarily consists of a combination of different disciplines. These different disciplines are needed to solve specific problems. Likewise, different people, disciplines and skills are required for the computer interpretation of medical signals or images and for the construction of electronic health records or for the development of hospital networks.

Two years after the 1974 World Conference MEDINFO in Stockholm, colleagues in the USA started a series of annual conferences, first held in alternate years in Washington DC and Baltimore: the *Symposium on Computer-Assisted Medical Care* or SCAMC. It was for a long time under the leadership of Thom Piemme from Washington University. During the first years these conferences drew mainly ‘local’, i.e., American participants. However, from the beginning our research group also participated in SCAMC, realizing that medical informatics is an international discipline. Besides, we already had several joint projects with our American colleagues. It would last until 1989 when a single US national society for medical informatics, AMIA was formed, thanks to the leadership of Don Lindberg [20] and the backing by his colleagues from several universities. Having started at the University of Missouri in Columbia, Don Lindberg had become the director of the *National Library of Medicine* in 1984. He also became the first president of AMIA. The Society for Medical Informatics in the Netherlands, VMBI, was founded much earlier, in 1971. Jan Roukens became its first chairman and I was also one of the co-founders, becoming chairman after him.

From the foregoing it might be clear that I felt very much at home with colleagues like François Grémy who shared my interest for philosophy. This was also the case with Jean-Raoul Scherrer in Geneva. When I made the WHO study in 1967 I also visited Geneva, but at that

time Jean-Raoul was in Brookhaven in the USA. Having returned to Switzerland, he designed his Diogène system with the intention of storing patient-related data in a structured way. He was also the originator of *Health-on-the-Net* (HON), an accreditation system for health-related websites. It was always a great pleasure to spend time with Jean-Raoul, in particular when drinking a good glass of wine, sometimes even from his own vineyard. Similar to François Grémy, Jean-Raoul had a very wide philosophical and historic interest and an iron memory for facts. After he died unexpectedly in 2002 it was a great honor for me to give the memorial lecture in Budapest at the Congress of the European Federation of Medical Informatics (EFMI) [21].

I would also like to mention some other pioneer who had great influence on medical informatics, especially in Germany: Peter Reichertz. Peter held the first chair in our discipline in Germany at the Medical University of Hannover. Years ago his current successor, Reinhold Haux, named his center in Braunschweig and Hannover after Peter Reichertz. Peter returned to Germany and established the first research and training program in medical informatics in Germany after spending a period in Columbia, Missouri, where he collaborated with Gwilym Lodwick and Don Lindberg and joined in the development of one of the first systems for radiotherapy planning, MARS. Many of the later chair-holders in medical informatics in Germany were trained by Peter Reichertz at his center in Hannover [22]. Like Jean-Raoul, Peter died too early, but laid a foundation for medical informatics that is still of great importance for the present generation.

In the past sometimes unrealistic expectations have been held regarding the possible contributions of medical informatics to health care such as on the impact of medical decision-support systems and expert systems. The results in this branch appeared to be very modest, to say the least. The same applies to the overly optimistic expectations regarding the introduction of electronic health

records. Although the technology is widely available, all such developments appeared to be far more complex than expected. Many aspects were underestimated, such as the influence of human factors and the obstacle of cumbersome interfaces between man and machine. Let me devote a short section to the equally complex field of electronic health records (EHRs).

Electronic Health Records

We initiated our R&D for the development of EHRs at the beginning of the 1980s. We started this research in primary health care, and it is still ongoing in clinical medicine. Let me briefly describe the different stages of our R&D and point to some important aspects that may be of wider interest.

The structure of the provision of health care in the Netherlands is, in a way, ideal for the introduction of EHRs. Each citizen is in principle connected with just one primary care practice, where one or more general practitioners (GPs) coordinate her or his health care, keep a comprehensive patient record, and refer the patient, if necessary, to a specialist or a hospital. In our R&D on EHRs we concentrated from the very onset on the entire patient record, including the patient history. We had, from the beginning, a close collaboration with GPs and industrial partners. The latter were involved early on, because an R&D department is neither able to, nor should be responsible for, the implementation and maintenance of information processing systems in health care. We also had the intention of broadening our research later on to clinical EHRs in hospitals. From the outset we had a very close collaboration with primary care centers with the intention to shape a network for research. Later on, we expanded our research to projects on the quality of health care, the integration of EHR systems with decision support systems [23, 24], and post-marketing surveillance of drugs. This research is still ongoing in the Netherlands

and has expanded to the European level.

In the first half of the 1990s we started the next development, intended to implement an EHR system for clinical use, based on the concept of structured data entry. This rather basic research also took us about 10 years, before it resulted in a system that could be used for clinical care settings in the widest sense, because of its conceptual approach [25]. The development of a clinical EHR system that ideally comprises all patient-related data, from the patient history up to diagnostic and therapeutic results, appears to be an extremely complex enterprise. This is also the experience of many other research groups and industries worldwide. It is an area still full of pitfalls and difficulties. Perhaps, the most complex issue is that a clinical EHR system – in contrast to primary care – needs to be implemented for a variety of different clinical specialties, for which the patient's history is often different, incorporating requirements of clinicians with very different backgrounds and ideas. It has become clear that there exist fundamental differences between automation in health care and, for instance, in banking, traffic control, or industry. Health care processes can seldom be fully standardized. Humans enter at least in two very different roles in the loop of information processing: as subjects carrying out care - the clinicians - and as subjects who are the object of care - the patients. Everyone pursuing a career in biomedical informatics needs to be very aware of this.

In primary care we have been very successful, so that today 100% of all GPs in the Netherlands use information systems containing an EHR, most of them exchanging their data with other GPs, and many of them with our team participating in a research network [26]. In clinical care there still remain major challenges. The complexity of clinical patient care is much larger, much less standardization is possible, and all clinical specialties are in the process of continuous change, because medical science itself is constantly being renewed. EHRs in a

clinical environment, therefore, should permit much more freedom to the clinician to implement her or his own ideas. This freedom, however, is in sharp contrast with the requirements for formalization and standardization.

Our R&D in the field of EHRs has also shown that it is important not to give up when major difficulties arise as a result of, for instance, conflicts between freedom and standardization, or due the lack of financial support or adequate clinical collaboration. My advice then is: don't give up; perseverance is essential.

Expectations

Just as for medical research in the broadest sense, medical informatics R&D is in constant evolution. For instance, it is only about twenty years ago that basic medical research was primarily concerned with problems in physiology, anatomy, or embryology; fundamental research in biomedicine was generally carried out at the level of organs and organisms. Nowadays, the challenges are of a totally different nature, with many research projects primarily conducted at the level of biomolecules and cells. This is partly the result of the sequencing of the genome and the proteome. Genomics and proteomics have had a profound effect on modern clinical research and population-based research. As a consequence, a new branch of informatics in medicine has emerged under the name of bioinformatics. Despite these changes it will still take a considerable amount of time before the newly gained insights in biomolecular and bioinformatics research will be translated into clinical and medical practice, i.e., into new diagnostic and therapeutic techniques, that is, into translational medicine.

Over the years the terms that designate our field have also evolved from medical informatics, to also encompass medical telematics, biomedical informatics and eHealth. Today's research priorities focus on personalized sys-

tems and even wearable systems. We see cross-border communication (e.g. of health record summaries and e-prescriptions) and interoperability between e-health systems. In this rapidly evolving environment some significant challenges remain: in-depth research, such as on the semantics of medical data, the development of international standards, and the promotion of quality and certification.

I expect that in a couple of years medical informatics will follow the same road as other disciplines, such as medical physics, clinical chemistry and even physiology and genetics: full integration with the specialties and branches of basic and clinical medicine and health care. The involvement of patients and their families in using medical data and knowledge will continue to grow. This was the main reason why the NLM developed *PubMed* and Jean-Raoul Scherrer *Health-on-the-Net*. More and more electronic health records will contain genetic data, also of interest for one's relatives. For this reason the utmost attention should be paid to privacy and security, the more so when large patient databases are collected for research and medical data are exchanged on the Internet. I also expect that the quality of health care, provided by doctors and nurses, will increasingly be monitored by computer systems so as to ensure that it fulfills the basic requirements for medical evidence. In time the results from medical informatics will become common practice in medicine and health care. The time of the pioneers and their direct offspring will then be over. Hopefully their best ideas will have survived for the benefit of patients and health care providers.

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Historic Landmark Paper Selected by Jan H. van Bommel for the 2011 IMIA Yearbook of Medical Informatics*

Having finished my training in physics and mathematics I applied for a career in biomedical research. It was around the time that others were already active in this or related fields. I'm thinking of people like Homer Warner, Octo Barnett, François Grémy and Hubert Pipberger. But one of the most inventive and multi-talented was Bob Ledley, an unusual combination of a physicist and a dentist. At the time that he published his book 'Use of Computers in Biology and Medicine', I was already conducting research on signal processing and pattern recognition in perinatal medicine, neurophysiology and cardiology.

Ledley's book was a beautiful illustration of many of the methods that I used and was developing myself. Bob is

a true engineer, with tenacity using all the knowledge he possessed. For instance, he was the inventor of the prototype of the present whole-body CT scanner (that he called the Automatic Computerized Transverse Axial scanner), he had 20 patents to his name and was in 1997 awarded the National Medal of Technology by the President of the USA for his advanced research in biomedical computing and engineering. The book that he published in 1965 was one of the earliest if not the very first handbook in the field that was later to be called medical informatics – or one of its many synonyms. The book is primarily on the engineering aspects of our field and about half of the 926 pages contain chapters on mathematical methods used outside the biomedical field and over 200 pages discuss programming digital and analog computers. Nevertheless, already in those early years 240 pages were devoted to biological systems and the application of computers in biomedicine: biophysical processes, computer simulation, clinical data processing, and diagnostic support.

It is interesting to look at the four reasons that Ledley gave for using computers. They deal with the central question: should this problem be put on a computer? The reasons he gave were: (1) thorough knowledge of the problem, (2) knowledge of the capabilities of computers, (3) knowledge of the scientific methodological concepts upon which the statement of the problem is based, and (4) knowledge of the mathematical concepts that are to be employed in the solution. These four reasons are still fully valid, although nowadays we have become more and more aware of the human factor in applying computers in general and in biomedicine specifically. Ledley's book on using computers in biology and medicine is – even after more than 45 years – still a landmark. At the time it was published it showed that a new discipline was on the rise. Bob Ledley participated in laying its foundations.

Robert Steven Ledley. Use of Computers in Biology and Medicine. New York: McGraw-Hill Book Co.; 1965.

* The complete paper can be accessed in the Yearbook's full electronic version, provided that permission has been granted by the copyright holder(s).