Diagnostic Games, a Tool for Clinical Experience Formalization in Interactive "Physician – IT-specialist " Framework

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Abstract

The specific characteristics of data processing in clinical decision problems require special approaches. This was the insight that made Izrail Gelfand and his colleagues look for new methods of formalization that would allow to discover the intrinsic structures in clinical data. A special technique for collaborative work of IT specialists and physicians named "diagnostic games" (DG) was developed for this purpose. This approach including the DG and related ideas of an "adequate language" and "structural units" is presented in this paper. The preliminary setting of clinical decision problem of surgical timing in patients with ruptured subarachnoid aneurysm is introduced as a subject for further formalization.

Keywords: machine learning, diagnostic games, knowledge acquisition, subarachnoid aneurysmal haemorrage, structural units

1. Introduction

Machine Learning (ML) methods are widely used in the area of biomedical research. Powerful algorithms learning from data have been developed and applied to various problems of decision support. Nevertheless, the issue of adequate formalization in clinical decision making problems and the issue of small size samples, typical for this area, still remains.

That's why in this paper we explore the following topics:

a) introduction to the "diagnostic games" (DGs) - a technique for physician's knowledge acquisition and formalization;

b) formulation of the principles and technical aspects of DGs;

c) positioning of this technique in the machine learning paradigm;

d) presentation of the problem of choice of appropriate timing of surgery treatment for patients with subarachnoid aneurysmal haemorrage (SAH).

The sections 2.1 to 2.3 lay the background for the discussion by presenting the idea of DG and some of its most important theoretical aspects: adequate language and structural units. The remainder of the paper is thought as a contribution to the formulation of the main principles and rules of the DGs and to the topics in b) – d) listed above.

2. DIAGNOSTIC GAMES

2.1 Some specific difficulties of data processing in clinical problems.

The idea to use intensive experimental methods of knowledge acquisition and formalization emerged from a long collaboration between mathematicians and physicians in the laboratory of renowned contemporary mathematician Izrail Gelfand at Moscow University in the 1970s and from the experience of using ML algorithms in the context of clinical decision support. In this article we pursue this line of work. The idea originally stemmed from the problems posed by a direct ML approach in this domain.

Working on clinical problems researchers are often confronted with some specific difficulties of data processing. First of all, in the majority of clinical problems, the number of features is comparable or larger than a sample size. Often a researcher has to deal with hundreds of features and only dozens of patients. Consequently, the ratio (number of features/ number of patients) is too high to yield statistically significant results.

To obtain datasets of a sufficient size, data appear in fact to be collected at different medical institutions and put together in a large dataset. Special methods of control are needed to avoid the heterogeneity of the resulting samples.

The next problem is the non-independency of the features describing an individual patient, which is expressed by the recurrent redundancy in the dataset. The redundancy of the data usually goes along with lack of information. Another, very typical problem for applying ML algorithms comes from the abundance of missing data. In this situation various imputation methods can be used [13, 14] prior to inducing a predictive model by the application of ML methods. However, the problem reappears when one wants to apply this model to a new patient with other, unavailable predictor values.

How can we avoid these difficulties?

We want to approach problems of clinical decision making from a different perspective. This approach was first developed in collaborative works of I.Gelfand and his colleagues with clinicians and was given the name of ***"diagnostic game".*** This technique was described in details in [1] .Some aspects of DGs may be found in the publications [2, 3].

The general shape of DG technique resembles some of *experimental psychological techniques* proposed earlier in [4] in order to formalize human methods for interpreting the results of psychological tests.

2.2 *Adequate language and Structural organization of the data*

The idea behind DG is based on two common observations. The first one is that the physician can find his way in an enormous amount of incoming information. In fact, the amount of data he obtains may be very considerable just at the general examination of patient alone, even when he doesn't turn to additional methods of investigation. Nevertheless, in many cases the physicians cope successfully with the abundance of information. Hence it is judicious to pay attention to this aspect of clinical experience. The second observation about clinical doctors concerns the way the information can be transmitted from one physician to another. Talking to each other, physicians are able to convey in a few sentences literally all essential points about a given patient. It is important that, even in the context of a short phone conversation, physicians successfully transmit the relevant information on the concrete case.

The above-mentioned abilities of physicians are possible for two reasons. First, doctors have a capacity to single out the most essential factors in every specific situation. Second, they use notions displaying a proper degree of integrity that permit them not to "get swamped" in details and at the same time avoid losing important information.

We suggest that what is exposed above means that the language of physicians properly conveys their cognitive representation of the given situation.

For the mathematicians who worked on clinical problems in close collaboration with physicians, under the guidance of I. Gelfand, it became clear that singling out and articulating new concepts that are goal-oriented and reflect the doctors' understanding of the problem will be a crucial step towards modeling clinical decision making . These new concepts - elements of an ***adequate language*** - can become the basis that will serve for further application of logical schemes (algorithms) and its experimental verification (testing). The notion of adequate language (AL) was first introduced in [5]) and discussed in [1, 6].

In various problems of clinical decision making we worked on, AL was obtained as a result of an interaction (namely, DGs) between physicians and mathematicians and/or computer science specialists.

It is important to note two points concerning adequate languages.

- AL cannot be elaborated either by physicians alone or without the participation of physicians.
- Though the articulation of such a "language" is not a result of a logical process, the concepts of the adequate language can be formalized.

This formulation lends these concepts an unambiguous meaning.

At this point we touch upon another very important idea: the ***structural approach*** for the study of complex living systems. As I.Gelfand underlined in [6], the structural approach is an inalienable part of the professional thinking of mathematicians: "…entering a new area, look into the structures underlying it ". That's why mathematicians and computer science specialists, particularly those who take mathematics to be part of culture, realize that their experience in discovering and handling complex structures plays the most important role for correct formalization and organization of the data in clinical decision making problems.

2.3 Structural units.

To solve clinical prognostic or diagnostic problems, it is necessary to identify structures that would adequately reflect both the inner relations in the data and the specific goals of the study.

As was said above, DGs allow discovering the main concepts: the elements of AL that can be formalized. These AL concepts expressed in terms of initial variables (features) are called "***structural units***". Now we have a model for our goal-oriented problem that includes:

- two levels of description: ***features*** (in the "lower level" description) and ***structural units*** (in the "upper level" description)
- formal transformation rules that relate these two levels.

These structural units have been found in various clinical decision making problems. For an example of a concrete study see [16].

Importantly, structural units adequately represent ***the specific goals of the study*** and ***the internal relationships in the data***.

Objects analogous to "structural units" can be found in others disciplines studying complex living and artificial systems. Some synonyms exist for this term, e.g. "synergy" in the physiology of movement, neurophysiology and cellular biology (see, for example, a contribution in [7]). In modern programming, "objects" are similar to our structural units. A salient feature of structural units is that in all these areas they have simple outer appearance and complex inner organization.

2. 4 *The technique of DG: several principles and rules*

Theoretically it could be possible that the physician describe explicitly the reasons that made him to make a certain diagnosis or recommend a certain therapy for the patient. An example of such an approach making use of the physicians' self-reported guidelines could be found in [9].

However, when one tries to analyze one's own reasoning, there may occur both analytical distortions and bias in evaluations. Furthermore, relying on the physician's introspection we run the risk of neglecting and even losing the ingredients of the decision making process that are subconscious in physicians. This way, we may also lose tacit assumptions available to the physician and his colleagues, of which however not only mathematicians or computer science specialists but even physicians from other medical schools may not be aware. "In some cases, we were once aware of the understandings which were subsequently internalized in our filling for the stuff of action. In other cases we may never have been aware of them. In both cases, however, we are usually unable to describe the knowing which our action reveals" (see in [8] p.54).

Moreover, asked how he has arrived at the diagnosis, the physician is thereby placed in unnatural conditions from the point of view of his professional activities. When the physician explains what steps should be taken in a given situation or writes a scientific paper, he acts as a person sharing his experience (or, more exactly, his verbal concepts of it). When he is in a clinical situation, at the patient's bed, his goal is to treat this concrete patient. The physician does not make decisions in a strictly logical way, he makes them “in action” (about “knowing-in-action”, and “non-logical process” see [8]).

Medical experience is elicited most adequately in the course of the patient's treatment. At this time, the information about the patient received by the physician is impossible to control for the purpose of formal analysis. A special technique has then been developed which makes the elicitation of the physician's practical experience close to his professional activities, and makes it now accessible to formal analysis. It is based on the imitation of situations occurring in the process of the treatment using formalized questionnaires

Now we can formulate the main *principles* of DG:

- During the game, the leader (a mathematician, a computer science specialist, etc. leading the DG) and the physician exchange questions and answers; the physician (as well as the leader) may react to the question with further enquiry.
- During the DG, the physician must be put into a situation most close to one in which he makes decisions with the purpose of assessing the condition and the treatment of a concrete patient; ***he is asked clinical questions about a concrete case.***
- Throughout the DG, the questionnaires, formalized clinical descriptions of patients, should be used.
- DG is conducted making specific use of the data contained in the questionnaires.

The main idea of the technique is that, in the course of the game, the leader lets the doctor make a decision natural for his practice using exclusively the patients’ data that are ***controlled by the leader***. Control is achieved through disclosure or non-disclosure to the doctor of the piece of information he required and, additionally, management consists in the search and retrieval of the required information.

The management is a technical question.

The technique of DG must abide by strict *rules* in order to produce stable and reproducible results. In particular,

- at the beginning of the game the leader tells the doctor the goal of this game;
- he doesn’t tell the doctor the correct answer to the question that he asked;
- the case is discarded for the current game if the doctor recognizes the patient in the case given.

3. *DG in the context of ML*

DGs offer a possibility to investigate the doctor’s way of clinical decision making within a controlled informational environment. They can be used during different stages of work on the clinical decision problem, among which

- The problem setting: DGs help with finding questions crucial for decision making in the course of treatment;
- Work with questionnaires: DGs help to check questionnaires for completeness and to check the reproducibility of the answers in the process of filling out questionnaires by the doctors at the preliminary stage of the data preparation (“preprocessing”);
- Eliciting and articulating the main concepts of a particular AL.
- Constructing “structural units”; DGs could be especially useful in the case of small samples (insufficient for ML methods);
- Dramatically reducing the dimensionality of the initial feature space by transforming it into the “structural units space” – this is very important for the tractability of ML algorithms;

- Constructing predictive decision rules based on structural units;

  These decision rules could be used instead of or as a complement to several ML techniques (such as SVM-classifiers, feature selection algorithms, Bayesian Networks) because they look more natural for physicians who consequently trust more in them than in so-called “black box” models.

- Reconstructing missing features using DG;

  When a predictive model is based on structural units the prognosis for a clinical case with missing values for some of the features could still be valid because we use a transition to the “upper level” of our two-level model. This possibility is due to a complex inner organization of structural units exploiting interdependency and redundancy of some underlying features.

- Discovering causal relations;

This is an important advantage of DGs especially for cases where causal relations cannot be captured from the data using machine methods. DGs are efficient for causal discovery even in case where the dataset is insufficient for statistical analysis (see above in “Some specific difficulties of data processing in clinical problems”). Verification of causal relations by statistical means can further be carried out in a prospective study.

4. The problem of timing of surgery in patients with the ruptured subarachnoid aneurysm

Rupture of cerebral aneurysm is the most common cause (50-70%) of non-traumatic SAH, which is a devastating type of stroke associated with 32% to 67% fatality and 10% to 20% long term dependence in survivors due to brain damage [10].
There are two different approaches to the treatment of ruptured aneurysms: surgical therapy and endovascular treatment. The most used technique among surgical methods is clipping**.** The timing of surgery for SAH has been a major topic of controversy for a long period. A brief history of this problem is described in [11]. To understand how soon after aneurysmal rupture should clipping be attempted is in fact a difficult issue because of two competitive risks:

- the risk of rerupture
- the risk of vasospasm.

Many authorities recommended early surgery for patients with Hunt and Hess clinical grades (H&H) [15] I and II, and delayed surgery for those with H&H grade III and lower. In 1994 an early treatment within 72 hours was recommended by American Heart Association [12] even for patients with lower H&H grades.
This recommendation is increasingly followed in the US and Japan. The neurosurgeons at Burdenko Neurosurgery Institute in Moscow (Russia) followed these recommendations since 2001. They discovered that the results of surgical intervention in the first 72 hours after the rupture were far from being as good as American medical references. The material that includes 507 cases, gathered during the period 1995-2005 at the Burdenko Neurosurgical Institute, clearly reflects this situation: the outcomes within 1995-2000 are much better than within 2001-2005. Trying to explain this fact, neurosurgeons suggested that probably some of the patients who underwent early surgery had developed an early vasospasm.
Our preliminary hypothesis (which may be changed or even rejected in the course of investigation) about the clinical decision on the choice of timing of surgery could be formulated as follows:

If a patient developed an early vasospasm, the surgery is suggested to be delayed. If he didn’t develop an early vasospasm, the clinical decision depends on the assessment of the risk that the patient would develop it after surgery and on the Hunt-Hess grade before the surgery.

In the future work we are planning to present an approach to this problem based on DGs and ML techniques.

5. *Conclusion*

In this paper we introduced a new methodology for clinical decision making support. This methodology is based on a set of techniques known as Diagnostic Games. These allow to articulate an adequate language formalized into structural units with an unambiguous meaning. Finally, the clinical decision problem of surgical timing in patients with ruptured SAH is presented as a new example for further formalization using this methodology.

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