Artificial Intelligence Techniques for Monitoring Dangerous Infections

Evelina Lamma, Paola Mello, Anna Nanetti, Fabrizio Riguzzi, Sergio Storari, and Gianfranco Valastro

***Abstract*—The monitoring and detection of nosocomial infections is a very important problem arising in hospitals. A hospital-acquired or nosocomial infection is a disease that develops after admission into the hospital and it is the consequence of a treatment, not necessarily a surgical one, performed by the medical staff. Nosocomial infections are dangerous because they are caused by bacteria which have dangerous (critical) resistance to antibiotics. This problem is very serious all over the world. In Italy, almost 5–8% of the patients admitted into hospitals develop this kind of infection. In order to reduce this figure, policies for controlling infections should be adopted by medical practitioners. In order to support them in this complex task, we have developed a system, called MERCURIO, capable of managing different aspects of the problem. The objectives of this system are the validation of microbiological data and the creation of a real time epidemiological information system. The system is useful for laboratory physicians, because it supports them in the execution of the microbiological analyses; for clinicians, because it supports them in the definition of the prophylaxis, of the most suitable antibi-otic therapy and in monitoring patients' infections; and for epidemiologists, because it allows them to identify outbreaks and to study infection dynamics. In order to achieve these objectives, we have adopted expert system and data mining techniques. We have also integrated a statistical module that monitors the diffusion of nosocomial infections over time in the hospital, and that strictly interacts with the knowledge based module. Data mining techniques have been used for improving the system knowledge base. The knowledge discovery process is not antithetic, but complementary to the one based on manual knowledge elicitation. In order to verify the reliability of the tasks performed by MERCURIO and the usefulness of the knowledge discovery approach, we performed a test based on a dataset of real infection events. In the validation task MERCURIO achieved an accuracy of 98.5%, a sensitivity of 98.5% and a specificity of 99%. In the therapy suggestion task, MERCURIO achieved very high accuracy and specificity as well. The executed test provided many insights to experts, too (we discovered some of their mistakes). The knowledge discovery approach was very effective in validating part of the MERCURIO knowledge base, and also in extending it with new validation rules, confirmed by interviewed microbiologists and specific to the hospital laboratory under consideration.**

***Index Terms*—Classification, data mining, decision support systems, microbiology, knowledge-based systems.**

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E. Lamma and F. Riguzzi, and S. Storari are with the University of Ferrara, 44100 Ferrara, Italy (e-mail: elamma@ing.unife.it; friguzzi@ing.unife.it; sstorari@ing.unife.it).

P. Mello and A. Nanetti are with the University of Bologna, 40138 Bologna, Italy (e-mail: pmello@deis.unibo.it; ananetti@med.unibo.it).

G. Valastro is with Dianoema S.p.A. Via De' Carracci 93, 40131 Bologna, Italy (e-mail: gvalastro@dianoema.it).

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I. Introduction

THE monitoring and detection of nosocomial infections is a very important problem arising in hospitals. In the US, nosocomial infections are third in the list of most costly and deadly infectious diseases after AIDS and food-borne illnesses. A hospital-acquired or nosocomial infection is a disease which develops after the admission of the patient into the hospital, and is the consequence of a treatment, not necessarily a surgical one, performed by the medical staff. A community infection, in constast, is an infection acquired by the patient before the admission to the hospital. A disease is usually considered a nosocomial infection if its symptoms appear more than 48–72 hours after the admission to the hospital.

Nosocomial infections are much more dangerous than community infections because they are caused by bacteria which have a dangerous (critical) resistance to antibiotics. Usually, nosocomial infections are resistant to more than one antibiotic, while community infections are resistant to very few antibiotics. As a consequence, the cure of a community infection does not normally present problems, whereas it may prove difficult to cure a nosocomial one. There are now bacterial strains which are resistant to all known antibiotics but one [1]. In Italy, this problem is very serious: almost 5–8% of the patients admitted to hospitals develop a nosocomial infection [2].

Nosocomial infections have steadily grown for nearly two decades, in spite of many measures—such as shorter hospital stays—that were expected to have an attenuating effect [3]. Now it is widely argued that the only sustainable defense against this danger is greater vigilance, public education, and a significant reduction in "antibiotic pressure" in the community. In order to support medical practitioners in the complex task of controlling nosocomial infections, we have developed a system called MERCURIO that manages different aspects of the problem. MERCURIO is a commercial software package that is the result of the engineering of a research system developed in the scope of the project TDMIN involving Dianoema S.p.A. [4], an Italian information technology company operating in the health care market, and the Department of Electronics, Informatics and Systemistics (DEIS) at the University of Bologna. The objectives of this system are the validation of microbiological data and the creation of a real time epidemiological information system. The system is useful for laboratory physicians because it supports them in the execution of the microbiological tests; for clinicians, because it supports them in the definition of the most suitable antibiotic therapy and in the monitoring of patients' infections; and for epidemiologists because it allows them to identify outbreaks and to study infections.

In order to achieve these objectives we have adopted artificial intelligence techniques and, in particular, expert system and data mining techniques. An expert system approach has been applied in order to achieve clarity (the possibility of explaining in detail the answers given), flexibility (the possibility of easily updating the knowledge base), and reliability (the correctness of the answers given). We have also applied statistical methodologies. Statistics about infection frequencies are useful from two points of view: on one hand, they can be used in order to monitor the diffusion of nosocomial infections over time in the hospital; on the other hand, they are a valid help for clinicians to perform a first diagnosis.

As a result of project activity, we have built a system mainly composed of: an epidemiological database, designed for storing epidemiological data; a knowledge based system, called ESMIS, for real time validation and monitoring; a statistical module, for performing statistical analyses and identifying outbreaks.

ESMIS is an expert system for microbiological infection surveillance. We have described the ESMIS specifications and features in [5] in detail. In this paper we show the overall system, its implementation and its performances obtained on a testing trial. For bacterial infections, the stored data usually includes: information about the patient (sex, age, hospital unit where the patient has been admitted to), the kind of material (specimen) to be analyzed (e.g., blood, urine, bronchial aspiration, pus, etc.) and its origin (the body part where the specimen was collected), the date in which the specimen was collected and, for every different bacterium identified, its species and its antibiogram. The antibiogram [6] represents the results of the test on the bacterium of a series of antibiotics and it is usually represented by a set of couples (antibiotic, result), where four types of results to antibiotics can be recorded: R when resistant, I when intermediate, S when susceptible, and null when not tested.

ESMIS provides automatic data validation and real-time alarming. Given a newly isolated bacterium and the related antibiogram, the system performs five main tasks: it validates the culture results, reports the most suitable list of antibiotics for therapy, issues alarms regarding the newly isolated bacterium, issues alarms regarding the patient's clinical situation, and identifies potential epidemic events inside the hospital.

The ESMIS knowledge base has been obtained from NCCLS guidelines and from experts' suggestions. NCCLS [7], [8] is an international standard organization recognized by almost all laboratories as the reference in routine work, and it publishes an annual compendium containing testing guidelines for microbiological laboratories.

In order to improve the validation process, we have applied knowledge discovery techniques to microbiological data with the purpose of discovering new validation rules not yet included in NCCLS guidelines, but considered plausible and correct by interviewed experts. In particular, we have applied the knowledge discovery process in order to find (association) rules relating to each other the susceptibility or resistance of a bacterium to different antibiotics. This knowledge discovery process is not antithetic, but complementary to the manual elicitation of rules from the NCCLS guidelines: it allows both to validate some of them, and to extend them with new rules. In this respect, the microbiologists have begun to be aware of new correlations among some antimicrobial test results which were not noticed before. The new discovered rules are more tailored to the hospital situation, and this is very important, since some resistances to antibiotics are specific to particular, local hospital environments.

In order to verify the reliability of the mixed elicitation method, manual and automatic, we performed a test of ESMIS on data collected by the Clinical, Specialist and Experimental Medicine Department—Microbiology Section at the University of Bologna, Italy. Data were collected during a six month period. In this paper, we report the results obtained in terms of accuracy and specificity.

During the last few years, many infection event surveillance systems have been developed in order to monitor microbiological analysis results and/or in order to early identify infection and epidemiological events early. However, none of these systems addresses all the aspects of this complex phenomenon. Examples of these systems are GermWatcher [9], which performs only antibiogram validation, and TheraTrac 2 AES [10], [11], which provides services similar to the one provided by MERCURIO, but has a "closed" knowledge base that makes it difficult to adapt it the opinions and needs of the microbiological laboratory manager. In addition, no one uses our innovative approach for automatic microbiological knowledge elicitation.

This paper is organized as follows. In Section II, we discuss the state of the art of current real time systems for the validation of microbiological data. Section III describes the MERCURIO system and its objectives, the knowledge to be managed, and its architecture. In Section IV-A, we illustrate the ESMIS expert system, the first MERCURIO module. In Section IV-B, we present the other MERCURIO system modules. In Section V, we describe how we have applied data mining techniques in order to address knowledge acquisition and updating problems. In Section VI, we illustrate the results of the experimentation activity performed on the MERCURIO system considering real microbiological data. In Section VII, we discuss a number of works related to ours. In Section VIII, we show some possible directions for future work. Finally, in Section IX, we conclude.

II. State of the Art of Microbiological Support Systems

In the microbiological application field, during the last few years, many real time validation systems have been developed in order to monitor microbiological analysis results and to identify infections and epidemiological events at an early stage. All these systems have features that make them unsuitable for efficiently and correctly solving of all the problems related to nosocomial infections. Significant examples of these systems are WHONET 5 [12], GermWatcher [9], TheraTrac 2 [10], and VITEK AES [11].

WHONET 5 [12] is a database software for the management of microbiology laboratory test results. The software was developed for the management of routine laboratory results but

has also been used for research studies. The system focuses on the analysis of data, particularly of the data resulting from antimicrobial susceptibility testing.

GermWatcher [9] is an expert system that applies both local and international culture-based criteria for detecting potential nosocomial infections. Its knowledge base was obtained by the analysis of some documents, written by CDC's NNIS [13] (Center for Disease Control, National Nosocomial Infection Surveillance), providing explicit culture-based and clinical-based definitions for the most significant nosocomial infections.

TheraTrac 2 [10] is designed to support the pharmacy in the monitoring of the therapy proposed by clinicians, and in the identification of alternative therapies with better performance and/or cost. The system provides automatic data transfer and real-time, on-screen updates of alarm conditions. It directly interacts with the VITEK Advanced Expert System (AES) [11], an expert system for antibiogram validation, that is integrated in particular analytical instruments. AES interprets the results of antibiotic susceptibility tests using a knowledge base that contains most of the known resistance mechanisms. The AES system starts from the minimum inhibitory concentration levels given by the instruments and classifies them into three levels: susceptible, intermediate and resistant.

AES performs three main tasks.

1) Biological validation: detection of antibiotic resistance phenotypes and technical error warnings.
2) Proposal of therapeutic corrections: possible user initiated modification of the classification of the result into susceptible, intermediate, resistant for enhanced prediction of antibiotic efficacy *in vivo*.
3) Therapeutic comments: recommendations based on the official NCCLS guidelines.

By analyzing the systems working in the microbiological application field, we can observe the following problems.

The WHONET system only performs statistical evaluation of long term infection evolution inside the hospital and does not take care of antibiogram validation, international guidelines application, patient infection monitoring, and contagion detection.

GermWatcher only performs antibiogram validation, but it does not raise any alarm regarding infection evolution, so it gives the hospital personnel only a limited view of the nosocomial infections phenomena.

AES knowledge base cannot be modified by laboratory physicians.

III. The Mercurio System

The objectives of MERCURIO are the validation of microbiological data and the real time monitoring of nosocomial infection events. In particular, the system must

1) identify critical situations for a single patient (e.g., unexpected antibiotic resistance of a bacterium) or for hospital units (e.g., contagion events), and warn the microbiologist; and
2) provide reports about the amount of nosocomial infections in the various areas of the hospital.

In order to achieve these objectives, we analyzed the microbiological aspects and problems related to the treatment of microbiological data inside a hospital in more detail. As a result of this study, we have identified some subproblems which involve different time periods: short, medium, and long term.

Short term problems mainly involve the validation of antibiotics test results according to international guidelines. The quality of antibiogram results is critical because clinicians use them directly for therapy definition. The system should check that all the necessary antibiotics have been tested, and that the results of the tests are correct according to NCCLS rules. The results can be wrong if they are not in accordance with the predictions based on the results of other antibiotics. For example, tetracycline is representative for all tetracyclines: if a bacterium is found resistant to tetracycline, then it is resistant to all the tetracyclines, regardless of the results of the tests on them.

Medium term problems mainly involve the monitoring of the patients' status and the evolution of infections. Alarms should be raised in the case in which dangerous events are discovered by comparing the result of the current analysis with the result of the previous analysis. For example, an alarm should be raised if a bacterium is found with a significant change in its antibiogram with respect to the previous test: this change may be explained by an error in the previous or actual antibiogram, by a bacterium mutation, or by a new bacterium infection. This event should immediately trigger a repetition of the antibiogram in order to verify the correct bacterium species and response. The clinician will react to this alarm by changing the therapy. Another alarm should also be raised if a bacterium infection persists for a relatively long period (for example 15–30 days): also in this case the actual therapy is not suitable and should be changed.

Another medium term problem is the identification of infection transmission in the hospital (contagion). We have a contagion when the same bacterium is found on two or more patients. In this case, the epidemiologist should be alerted so that he can try to identify the causes of the contagion: for example incautious nursing or bad hygienic conditions inside hospital wards.

A long term problem is the one of identifying outbreaks of an infection. An outbreak happens when the same bacterium causes a number of new infection events significantly greater than the normal. To this purpose, the number of infection events found is compared to the number of events predicted using statistical techniques. If the number of infections found is above the predicted one, then an outbreak alarm is raised and communicated to the epidemiologist.

In Section III-A, we briefly describe the medical knowledge we have considered, while in Section III-B, we illustrate the architecture of the system.

A. Knowledge Considered

The knowledge considered in MERCURIO consists of: microbiological data, strain data, antibiotic data, hospital discharge forms, and international microbiological laboratory guidelines.

1) Microbiological Data: For a microbiological analysis, the stored data usually includes: information about the patient

(sex, age, and hospital unit where the patient has been admitted), the kind of material (specimen) to be analyzed (e.g., blood, urine, bronchial aspiration, pus, etc.), its origin (the body part where the specimen was collected), the date when the specimen was collected, and, for each different bacterium identified, its species and its antibiogram.

2) Strain Data: One of the problems that MERCURIO tries to address is the classification of the infecting bacteria into strains. The strain classification is important in order to correlate apparently different infection events which are instead caused by the same bacterium. MERCURIO constructs a catalogue of bacteria strains, considering the bacteria species and antibiogram, as will be described in Section IV-B-2. This new information is used by MERCURIO in order to find cooccurrences among different infection events, as will be described in Section IV-A. The system records the number of strains identified for each day with respect to a hospital ward or to the overall hospital.

3) Antibiotic Knowledge: Antibiotics are represented hierarchically following the ATC5 specifications [14]. The ATC5 code specifies which active principle characterizes each antibiotic. Other information recorded for each antibiotic is: the daily defined dose (DDD), the cost of the DDD, the way of administration, and other characteristics used by ESMIS to compute the list of the most effective antibiotics to use for each infection.

4) Hospital Discharge Forms: For each patient stay into the hospital, a hospital discharge form collects the following information: patient personal data, identified pathologies, clinical therapies performed, and the hospital ward. This kind of information is collected by every hospital because it is mandatory in Italy.

5) International Microbiological Laboratory Guidelines: The knowledge regarding the tests performed by microbiological laboratories has been elicited from NCCLS guidelines [7], [8]. NCCLS guidelines are basically composed of: a list that specifies the antibiotics to be tested, a list that specifies antibiotic test interpretation, and a list of exceptions regarding particular antibiotic test results.

B. Mercurio Architecture

MERCURIO collects the microbiological data from a laboratory information systems (LIS). MERCURIO has been adapted to work with two different LISs: Italab C/S, developed by Dianoema S.p.A. [4], and the LIS developed by another company. The LIS collects the analysis results from automatic analysers connected to the system or from manual input. The data from the LISs are stored by MERCURIO in an internal database, in which the information is coded following the most widely recognized international standards. In order to let the system work with a particular LIS, the hospital laboratory manager has to provide the system with a translation from LIS hospital codes to MERCURIO codes. Once inside the internal database, the microbiological information is analyzed by several system modules, as shown in Fig. 1: an expert system called ESMIS, a statistical module and a strain identification module. In Section IV, we will describe these modules in more details.

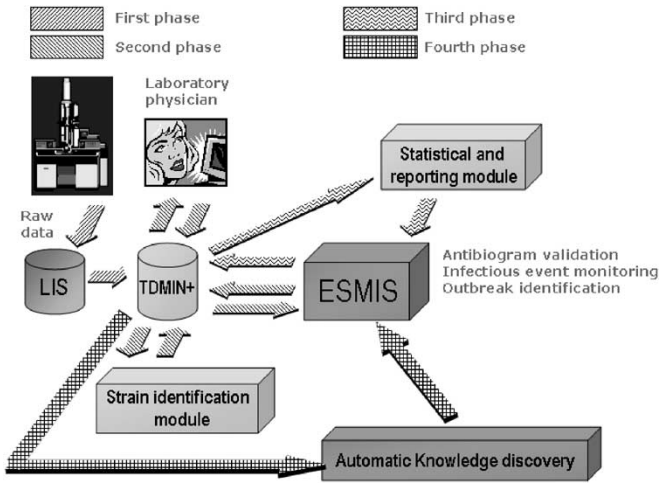

Fig. 1. Architecture of the MERCURIO system.

The infection event processing within MERCURIO involves four main phases.

In the first phase, the raw data coming from the LIS is transferred to MERCURIO's internal database (TDMIN+) to be organized in infection events.

In the second phase, each infection event is analyzed by a module that, starting from the bacterium species and antibiogram, classifies the bacterium into the corresponding strain. After strain classification, each infection event is analyzed by EMSIS that executes a first set of short and long term tests that will be described in greater detail in Section IV-A. Infection events, now enriched by ESMIS evaluations, are shown to the microbiological laboratory physician, who has to decide which is the correct bacterium antibiogram to be presented to the clinician for therapy definition, and which alarms issued by ESMIS have to be shown to him/her. In order to try to reduce human and machine errors, every time the microbiological laboratory physician changes an antibiogram result, the antibiogram is reprocessed by ESMIS. Such a process is described in detail in Section IV-A.

In the third phase, each infection event, now associated to the final antibiogram, is analysed by a statistical and reporting module, described in Section V, that generates some reports and makes forecasts on infection trends in wards and in the entire hospital. The infection event is then reprocessed by ESMIS that performs the long term tests.

The fourth phase is not performed in daily routine but only periodically, as scheduled by the laboratory manager. In this phase, described in Section V, knowledge discovery techniques are applied to a set of infection events in order to automatically elicit new and interesting knowledge to be integrated in the ESMIS knowledge base.

IV. MERCURIO MODULES

In the following sections, we go through a detailed description of each module, and we describe the ESMIS expert system in greater detail.

A. The ESMIS Expert System

ESMIS was built to solve short, medium, and long term problems. Given a newly isolated bacterium and the related antibiogram, ESMIS solves three short term problems.

1) Validation of the culture results: the system finds untested but necessary antibiotics (rack test task), identifies impossible antibiotic results for particular species, and tests common relationships among antibiotic results;
2) intelligent reporting of the most suitable list of antibiotics: the system associates a suitability to each antibiotic, obtained considering a number of features: cost of the antibiotic, infection site, bacterium species and hospital ward; and
3) issuing alarms regarding the newly isolated bacterium: the system provides information regarding the bacterium, such as dangerous resistance (resistance to a particular last generation antibiotic) and multiresistant (bacterium resistant to more than one antibiotic).

Given a newly isolated bacterium and the related antibiogram, ESMIS solves two medium term problems:

1) Issuing single patient alarms: the system issues alarms considering the infection history of the patient. The alarms are
   a) polimicrobic population: if two or more bacterium species were found in two different (consecutive) time points in the same sample material; and
   b) resistance acquisition: if the newly identified bacterium is resistant to more antibiotics than the previous one of the same species.
   In the latter case the clinician could decide to modify the therapy.
2) Issuing hospital ward alarms: the system checks whether the same bacterium strain was found in the same ward or in different wards; i.e., whether a contagion has happened.

Given the set of bacteria isolated in the current day, ESMIS solves the long term problem of identifying outbreaks of an infection. An outbreak happens when the same bacterium causes a number of new infection events significantly greater than the normal (the normal value is predicted using statistical techniques [15]). If the number of found infections is above the predicted one, then an outbreak alarm is raised and communicated to the epidemiologist.

1) System Architecture and Knowledge Base: ESMIS interacts with the environment in four ways: it checks for changes in the configuration data (composed of antibiotic data, bacterium data, testing protocols), it imports a set of non-validated antibiograms from the database, it validates these antibiograms, and it issues alarms and returns evaluations back to the database, together with comments and explanations. Moreover, it presents this information to the laboratory personnel during the validation task.

The NCCLS compendium contains a set of antibiotics to be tested on a specific species divided in: main reporting antibiotics (basic, advanced, specific, and for urinary tract infections); antibiotic subgroups (antibiotics with similar characteristics); and antibiotic equivalences (antibiotics with the same test result).

The NCCLS compendium also contains notes associated to specific bacteria and/or antibiotics that represent exceptions to be considered during the antibiogram validation (for example, a difference between the "*in vivo*" and the "*in vitro*" results of an antibiotic against a specific bacterium).

All this data plus data regarding bacteria (single bacterium data and bacterium classification) are stored in database tables. ESMIS checks if changes are made to information stored in these tables, and, if needed, updates its knowledge base in order to be always consistent with them.

2) ESMIS Implementation: ESMIS has been implemented using an expert system programming approach. This artificial intelligence technique has been applied to the medical field since 1980 [16]. In an expert system, also called knowledge based system (KBS), knowledge about the problem is translated into special data structures and rules. An inference engine applies these rules to the available data in order to produce solutions.

In order to choose the best instrument for implementing ESMIS, we evaluated three different tools described in detail in [17]. The evaluation led us to choose Kappa-PC 2.4 by Intellicorp [18] because it offers a good features/cost ratio and a simple and powerful programming language. Moreover, it works in interpreted and compiled mode, can reason both forward and backward, and communicates easily with databases through ODBC.

Regarding the ESMIS knowledge base, since the guidelines of the NCCLS compendium can change each year, ESMIS rules are designed as templates: rules are general and are dynamically instantiated referring to database entries that represent NCCLS guidelines. Therefore, the rules can be updated with the last guidelines version by simply updating the corresponding database table. Thus, the need to have qualified people continuously updating the knowledge is avoided since it is sufficient to update NCCLS table entries which are stored in the MERCURIO database. The following are examples of rules present in the ESMIS knowledge base.

1) There are two types of rack test rules: mainstream rule and exception rules.
— Mainstream rules verify if at least one antibiotic from each subgroup was tested.
— Exception rules are used to represent exceptions to the rack test specified in NCCLS document notes. One example is:

```
IF InfectionSite = Urinary Tract
AND
 Tested(Erythromycin)
THEN DisplayComment(Erythromycin
was
tested but it is not relevant)
```

2) Single patient alarms.
— For implementing the resistance acquisition test we use the following rule: Considering the patient infection history

```
IF SpeciesOfLastBacterium =
BacteriumSpecies(IdentifiedBacterium)
AND
ResistanceNumOfLastBacterium <
ResistanceNumOfNewBacterium
```

REP.GRP.	ANTIBIOTIC	STRUM. RES.	ESMIS RES.	DER.	TO REPORT	RACK NOTE	VALID. NOTE	REPORT NOTE
C41	RIFAMPIN	S	S	no	no	--	--	N_REP1
B41	VANCOMYCIN	S	S	no	*	--	--	--
B21	CLINDAMYCIN	R	R	no	*	--	--	--
B11	CLARITHROMYCIN	R	R	no	*	--	--	--
---	NETILMYCIN	S	>R<	no	*	N_RACK1	N_VALI1	--
A11	OXACILLIN	R	R	no	*	--	--	--
A21	PENICILLIN	R	R	no	*	--	--	--
B31	SULFA/TRIMETH	R	R	no	*	--	--	--
---	CLOXACILLIN	-	>R<	*	no	--	--	N_REP2
---	DICLOXACILLIN	-	>R<	*	no	--	--	N_REP3

Fig. 2. Antibiogram results after ESMIS evaluation.

```
THEN IssueAlarm(Therapy is failed!
The Bacterium
has increased the number of antibiotic
resistances
```

3) Esmis Reports and Graphical User Interface: Fig. 2 shows an example of ESMIS evaluation report in which we find the results of the tests executed on a *Staphylococcus Aureus* bacterium. For each modifications performed by ESMIS, there is a reference to a note that contains the name of the rule applied and its description. In Fig. 2, an inconsistency arises between Netilmycin (belonging to the Aminoglycoside antibiotic group) and Oxacillin. The validation note about this inconsistency is indicated by the reference N_VALI1.

Below the report, ESMIS shows the referenced notes, for example:

VALIDATION NOTE: N_VALI1 $\longrightarrow$ 1: (Vali_Stafi_23_5)
If Oxacillin test result is Resistance (R) then test results for Aminoglycoside should be Resistant too. The expected test result is R.

This note shows the name of the activated rule, Vali_Stafi_23_5, and the comment which describes its meaning.

One important aspect of ESMIS is the interaction with the laboratory personnel. The interaction has the following aims: to simplify the overall laboratory work, to help in finding antibiotic test errors, to help in the generation of reports, and to aid in the early detection of dangerous infection events. The microbiologist has the possibility of modifying each antibiotic test result proposed by ESMIS. Each time she/he modifies a result, ESMIS is rerun on the new data to check for new inconsistencies that may possibly arise.

B. Other Mercurio Modules

The other modules of the MERCURIO systems are a database, a statistical module, and a strain identification module.

1) Mercurio Database: The MERCURIO database structure is designed to store all the information regarding infection events that are acquired in real time from different LISs. The database associates infection event data, according to the typical design of a datawarehouse, to other information such as antibiotic knowledge, hospital discharge forms, and international microbiological laboratory guidelines (described in Section III-A). All the information is coded according to the ICD-9-CM international standard [19]. As described in Section IV-A, the international guidelines are stored in the database in special tables in order to be used by the ESMIS inference engine for dynamically instantiating template rules.

The DMBS used is Oracle 8.1, and the other modules use ODBC to access the database.

2) Strain Identification Module: One of the problems that MERCURIO tries to address is the classification of the infectious bacteria in strains. Strain classification is important in order to correlate apparently different infection events that instead are caused by the same bacterium. The most precise classification method is the genetic analysis of the bacterium genome. Such an investigation, however, is currently too costly; therefore, the most common classification uses the antibiogram associated to the bacterium. According to this information, a strain is a combination of a bacterium species and a particular set of results in the associated antibiogram. For a particular bacterium species, it may be necessary to restrict the set of antibiotics (inside the antibiogram) to be used for identifying a strain. The strain identification module follows these considerations in order to analyze each isolated bacterium and assign the relative strain to it. This new information is used by the other modules in order to find cooccurrence between different infection events.

This strain identification module is also used to improve the quality of the reports. In order to compute more effective reports on the microbiological data, it is necessary to count each infection event only once. Therefore, the repeated isolation in a short period of the same bacterium with the same or very similar resistance profile on the same biological material collected from the same patient is considered as a single infection episode. The similarity function and filtering parameters are configured, by default, according to the guidelines provided by NCCLS, but they can also be configured according to particular hospital epidemiology guidelines.

The strain identification module can easily be modified in order to be adapted to the case where strains are identified by means of genetic analyses. This will improve the quality of the alarms and statistics produced by MERCURIO.

3) Statistical and Reporting Module: Statistical analysis is very important and widely used in medicine. In the microbiological field, statistics about infection frequencies are useful from two points of view: on one hand, they can be used in order to monitor the diffusion of nosocomial infections over time in the hospital; on the other hand, they are a valid help for clinicians to perform a first diagnosis.

The MERCURIO statistical and reporting module is very rich and versatile: the users can compose their elaborations freely by selecting the target data, and decide how to aggregate this information and how to textually and/or graphically represent it. For example, some interesting reports are the following.

1) Prevalence: it measures the number of individuals of a population that, in a given period of time, are affected by a particular illness. Prevalence is useful to estimate the damage induced by an illness in a population, the difficulties in the realization of a plan for a cure, or the cost/benefit ratio of the plan before starting it.

2) Biological Materials or Origins Distribution/Bacteria: for every biological material or origin it represents the distribution of bacteria isolated on it.
3) Bacteria/Antibiotics: for every isolated bacterium, it represents the distribution of the achieved antibiotic test results on it (susceptible, intermediate, resistant).

These statistical elaborations may also be correlated with other available information such as: sex and age of the patient, information about the hospital ward and, where available, clinical information.

Some examples of aggregation are families of bacteria, families of antibiotics, and different granularities in infection origin sites. It is possible to start from a big aggregation level and dynamically increase the level of details following a "drill down" approach.

In addition to traditional statistics, predictive models, based on the analysis of historical time series of infection events, have been used to identify the "normal" trend of infection events. The forecasts of these predictive models have been used in cooperation with the reasoning performed by ESMIS for identifying "abnormal" infection events and early identifying outbreaks inside the hospital. These predictive models may be modified according to particular local epidemiologist considerations and experience. The statistical and reporting module is described in more detail in [15].

V. Data Mining Techniques for the Mercurio Project

The NCCLS compendium has been built considering data regarding many laboratories around the world, so it contains general guidelines that may not be able to completely and correctly interpret the infections developed inside a particular hospital environment. For this reason, it was necessary to verify if the rules obtained from the NCCLS document are representative of the local hospital infections, and if there are other correlations in the local hospital infection data that are both not considered in the NCCLS document and unknown to the microbiology experts.

In order to address these problems, we have applied data mining to local hospital infection data. In particular, we have extracted association rules from data. Association rules relate the susceptibility or resistance to different antibiotics to each other. The knowledge discovery approach here described is not antithetic, but complementary to the elicitation of NCCLS rules: it proved to be very effective in validating some NCCLS rules and also in extending them by "discovering" new rules not yet considered. The discovered knowledge has made the microbiologists aware of new correlations among antimicrobial test results that were previously unnoticed. Moreover, newly discovered rules, since they take into account the history of the considered laboratory, are more tailored to the hospital situation, and this is very important since some resistances to antibiotics are specific to particular, local hospital environments.

The discovered association rules have been transformed into alarm rules (through a syntactic transformation); they have been confirmed by experts and then used for data validation in ESMIS. Association rules describe correlation among events and can be regarded as probabilistic rules. Events are "correlated" if they are frequently observed together. Good examples from real life are databases of sales transactions. In this case, the aim is to find which items are usually bought together and to use this information to develop successful marketing strategies.

Given a table T, an association rule [20] is a rule of the form

$$A_1 = v_{A_1} \quad A_2 = v_{A_2}, \ldots, A_j = v_{A_j} \Rightarrow$$
$$B_1 = v_{B_1} \quad B_2 = v_{B_2}, \ldots, B_k = v_{B_k}$$

where $A_1, A_2, \ldots, A_j, B_1, B_2, \ldots, B_k$ are attributes of the table T and $v_{A_1}, v_{A_2}, \ldots, v_{A_j}, v_{B_1}, v_{B_2}, \ldots, v_{B_k}$ are values such that $v_{A_i}(v_{B_h})$ belongs to the domain of the attribute $A_i(B_h)$.

A record r of T satisfies a conjunction $A_1 = v_{A_1}, A_2 = v_{A_2}, \ldots, A_j = v_{A_j}$ if all the equivalences are true given the values of r.

The rule $X \Rightarrow Y$ holds with support s in table T if and only if $s\%$ of records in T satisfies $X \cup Y$. The rule $X \Rightarrow Y$ holds with confidence c in table T if and only if c% of records in T that satisfy X also satisfy Y.

Given the table T, the task of mining association rules can be reformulated as finding all association rules with at least a minimum support (called *minsup*) and a minimum confidence (called *minconf*), where *minsup* and *minconf* are user-specified values. Of course, the higher the support of a rule, the more general the situation that the rule can represent. Moreover the higher the confidence, the fewer are the exceptions to the rule. In order to learn association rules for validating microbiological data, we have exploited the WEKA system [21] (Waikato environment for knowledge analysis), a collection of machine learning algorithms for solving data mining problems. It contains algorithms for performing classification, numeric prediction, clustering and learning association rules. As regards association rule learning, WEKA employs the APRIORI algorithm [20].

A. Generation of Alarm Rules

Generated association rules represent frequent patterns occurring in the database. The discovered rules are related to each other according to the following generality relation: rule R1 is more general than rule R2 if they have the same consequent, but the conditions in R2's antecedent are a superset of those in R1's antecedent. For instance, consider the four rules.

1.) `Amoxicillin+ClavulanicAcid=S, Clindamycin=S` $\longrightarrow$ `Oxacillin=S`
2.) `Amoxicillin+ClavulanicAcid=S, Clindamycin=S Trimethoprim+Sulfamethoxazole=S` $\longrightarrow$ `Oxacillin=S`
3.) `Amoxicillin+ClavulanicAcid=S, Clindamycin=S, Penicillin=R` $\longrightarrow$ `Oxacillin=S`
4. `Amoxicillin+ClavulanicAcid=S, Clindamycin=S, Penicillin=R, Trimethoprim`

`+Sulfamethoxazole=S`
$\longrightarrow$
`Oxacillin=S`
(for the sake of simplicity, we have omitted support and confidence in the reported rules).

Rule 4 is the most specific, rule 1 is the most general, and rules 2 and 3 are intermediate (and not comparable with each other). The most general association rules represent normal and minimal patterns which occur frequently in the database. After having extracted association rules, we found the most general ones; i.e., those that are not more specific than any other rule. We then applied syntactic transformations to the most general rules in order to produce alarm rules, to be used in ESMIS for data validation. Abnormality, which we want to capture in the data validation process, is represented by antibiograms which do not satisfy some discovered rule; i.e., they satisfy the antecedent of the rule but not its consequent (the implication is not true). Therefore, if an association rule such as $X \Rightarrow Y$ represents the regular (and usually quite frequent) situation, the rule: $X, \mathrm{not}(Y) \Rightarrow \mathrm{alarm}(Y)$ (where the consequent is complemented and moved to the antecedent) represents an abnormal situation. When X and $\mathrm{not}(Y)$ occur simultaneously, an alarm has to be raised because the value for Y should be true instead of false, when X is true. The condition $\mathrm{not}(Y)$ is obtained in the following way: when Y is a singleton condition, we consider the result for an antibiotic in an antibiogram as two-valued, where R is the complementary value of S and *vice-versa*. For instance, the alarm rule produced from rule 1 is

1) `Amoxicillin+ClavulanicAcid=S, Clindamycin=S, Oxacillin=R` $\longrightarrow$ `alarm(Oxacillin=S)`

When Y contains more than one condition, $\mathrm{not}(Y)$ is kept as is. Usually general rules have high support and confidence, while specific rules have low support and confidence.

B. Trivial Rules

In our experiments, described in Section VI-B, the number of discovered rules is about several thousand, while the interesting rules are usually about a few tens: the number of uninteresting or trivial rules is thus quite high and the process of identifying interesting rules among the trivial ones is quite long. In order to solve this problem, we have developed a filtering program which can guide the microbiological experts in focusing on certain rules, allowing the selection of rules that satisfy certain conditions. A condition is obtained as a combination of templates by means of logical operators AND, OR, and NOT. A template is an equation $\mathrm{attribute} = \mathrm{value}$ that must be on the right or left side. In a template, it is possible to specify a set of attributes for *attribute*, e.g., it is possible to specify an equivalence of the form $\mathrm{family\_of\_antibiotics} = \mathrm{value}$. This filtering system allows to eliminate uninteresting rules not on the basis of support and confidence but on the basis of the microbiologists' interests. This is very important, since the interesting rules may represent rare events and thus have low support and confidence.

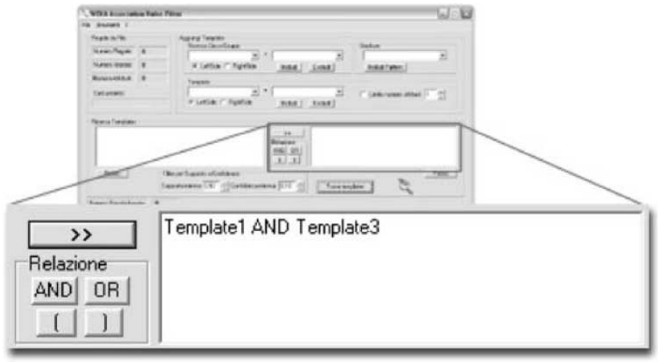

Fig. 3. Rule selection graphical user interface.

The filtering system has a graphical user interface that is represented in Fig. 3. This interface allows the user to execute all the selections operations mentioned previously.

VI. Test of Mercurio

In order to evaluate MERCURIO, we tested ESMIS and the automatic association rules extraction on six months of data collected from the Clinical, Specialist and Experimental Medicine Department—Microbiology Section at the University of Bologna.

The available dataset is composed of 368 antibiograms and has the following features:

1) 367 positive samples (a sample is positive if a bacterium has been discovered);
2) 35 different species;
3) 8904 antibiotic test results available for the evaluation of the rack test task and of the intelligent reporting task;
4) 3638 antibiotic test results available for the evaluation of the validation task; and
5) 334 patients.

The results of the rack test, the intelligent reporting task, and the validation task are provided by a domain expert. Such an expert is a microbiologist with 30 years of experience, who works in a laboratory that is certified ISO 9001.

A. ESMIS Evaluation

The ESMIS rule set is composed of: nine validation mainstram rules, 24 validation exception rules for the *Staphylococcus* species, 29 validation exception rules for the *Enterobacteriaceae* species, 15 validation exception rules for the *Pseudomonas* and other non-*Enterobacteriaceae* species, eight single patient alarm rules, six single analysis alarm rules and one contagion identification rule.

Performance evaluations have been obtained for the rack test, validation, and intelligent reporting tasks. The results of this test have also been described in [22]. The evaluation results regarding each specific task have been aggregated in four different performance indexes following an approach similar to the one explained in [23]. These indexes are generally used for characterizing the reliability of a classification system. The various tasks performed by ESMIS can, in fact, be considered

TABLE I
CONFUSION MATRIX

		Classification by the system	
		Positive	Negative
True classification (classification by the expert)	Positive	TP	FN
	Negative	FP	TN

TABLE II
CONFUSION MATRIX FOR THE VALIDATION TASK

		ESMIS	
		Positive	Negative
Laboratory expert	Positive	132	8
	Negative	2	3496

TABLE III
CONFUSION MATRIX FOR THE INTELLIGENT REPORTING TASK

		ESMIS	
		Positive	Negative
Laboratory expert	Positive	2164	1475
	Negative	217	5048

as classification tasks. Take into account, for example, the intelligent reporting task. This problem can be considered as a classification task with two classes: an antibiotic whose result is selected by the expert to be reported to the clinician is a positive example, while an antibiotic that the expert selects to be hidden from the clinician is a negative example. The classifications performed by the system and by the domain expert are compared and a confusion matrix is obtained (see Table I).

The classification provided by the expert is considered as the true classification. The confusion matrix contains four figures: TP (true positives) is the number of examples classified as positive by both the expert and the system (i.e., is the number of positive examples correctly classified as positive by the system); FN (false negatives) is the number of positive examples erroneously classified as negative by the system; FP (false positives) is the number of negative examples erroneously classified as positive by the system; and TN (true negatives) is the number of negative examples correctly classified as negative by the system.

The reliability of a classification system can be measured using the four figures defined as [23]

$$\text{Accuracy} = \frac{\text{TP}}{\text{TP} + \text{FP}} \tag{1}$$

$$\text{Sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}} \tag{2}$$

$$\text{Specificity} = \frac{\text{TN}}{\text{FP} + \text{TN}} \tag{3}$$

$$\text{FalseAlarmRate} = 1 - \text{Specificity}. \tag{4}$$

The meaning of these four figures is as follows: the accuracy (also called precision) is the fraction of examples correctly classified as positive over the total number of examples classified as positive; the sensitivity (also called recall) is the fraction of positive examples that are classified as positive; the specificity is the fraction of examples correctly classified as negative over the total number of negative examples; and the false alarm rate is the fraction of negative examples incorrectly classified as positive over the total number of negative examples. Accuracy, sensitivity and specificity have to be maximized, while false alarm rate has to be minimized.

In the rack test task, a positive example is an antibiotic that has not been tested but is considered necessary by the expert, while a negative example is an antibiotic that has not been tested and is not considered necessary by the expert.

In the validation task, a positive example is an antibiotic result that has been changed by the expert, while a negative example is an antibiotic result that has not been changed by the expert. A positive example is considered classified as positive by ESMIS if the result is changed by ESMIS and the new value is the same as the one chosen by the expert; otherwise, it is considered classified as negative.

In the intelligent reporting task, a positive example is an antibiotic result reported in the final antibiogram by the expert, while a negative example is an antibiotic result that is not reported in the final antibiogram by the expert.

Regarding the rack test task, we do not have negative examples; i.e., we do not have data regarding antibiotics that have not been tested and that have been considered unnecessary by the expert. Therefore, the only meaningful figure is sensitivity. The expert added 49 test results, and ESMIS also added all of them, so the system achieves 100% for sensitivity.

In the validation task, the system achieved the following results: 98.5% for accuracy and sensitivity, 98% for specificity, and 2% for false alarm rate. In Table II, the confusion matrix for this task is reported. Note that FN include both the test results incorrectly left unchanged by ESMIS and the results changed by ESMIS in an incorrect way (in this case 0).

In the intelligent reporting task, ESMIS achieved an accuracy of 91%, a sensitivity of 60%, a specificity of 96%, and a false alarm rate of 4%. Table III shows the confusion matrix for this task.

To summarize, the results obtained are very satisfactory. In, addition, the executed test provided many insights to the experts (we discovered some mistakes made by them).

The only figure that is not very good is sensitivity for the reporting task (60%). This value is low since one purpose of the system is to reduce the number of antibiotic results proposed to clinicians as much as possible.

B. Experiments on Association Rules

Experiments on automatic association rule extraction have been conducted on the bacteria: *Staphilococcus Aureus*, *Escherichia Coli* and *Enterobacteriaceae*. These experiments have been also described in [24], [22]. We have also experimented with the methodology that aims at helping laboratory physicians in finding the most significant rules among the huge extracted set.

1) Staphilococcus Aureus: The considered dataset for *Staphilococcus Aureus* contains 7009 records having, among the attributes, 41 different antibiotics. This dataset has been filtered by removing useless anitibiograms i.e., those in which the bacterium was susceptible to each antibiotic (apart from

Penicillin, to which the *Staphilococcus Aureus* can be sometimes susceptible and sometimes resistant). This filtering has been suggested by the microbiologists interviewed, and it has reduced the dataset to 3734 records. We run WEKA with *minsup* equal to 0.1 and with decreasing *minconf*. The number of most general rules found was around 6500. Out of these, 10 are among the 27 rules that are present in the NCCLS report (and in the ESMIS knowledge base) regarding *Staphilococcus Aureus*. In particular, we have discovered the rules that relate the results of the two classes of antibiotics Oxacillin and Penicillin (when a bacterium is resistant to Oxacillin it must also be resistant to any kind of Penicillin), and the resistance result for Oxacillin and Penicillin with B-lactamase inhibition (when a bacterium is resistant to Oxacillin it must also be resistant to any Penicillin with B-lactamase inhibition). For instance, the following two instances of these general rules were found (the first has confidence equal to 1, the second equal to 0.99):

```
Oxacillin=R, not ([Amoxicillin
+ClavulanicAcid=R,
Penicillin=R]) ⟶
alarm([Amoxicillin+ClavulanicAcid=R,
Penicillin=R]
Clarithromycin=R, Oxacillin=R,
not ([Amoxicillin+ClavulanicAcid=R,
Ceftriaxone=R, Penicillin=R]) ⟶
alarm([Amoxicillin+ClavulanicAcid=R,
ceftriaxone=R, Penicillin=R])
```

Furthermore, among the discovered rules, microbiologists have identified two rules which were not present in ESMIS knowledge base, but were considered relevant for ESMIS. The identified rules were (the first with confidence equal to 1, the second equal to 0.99):

```
Teicoplanin=S, Vancomycin=R ⟶
alarm(Vancomycin=S)
Vancomycin=S,
Teicoplanin=R ⟶
alarm(Teicoplanin=S)
```

which relate the results of two (last-generation) antibiotics (i.e., Teicoplanin and Vancomycin) to each other.

2) Escherichia Coli: The dataset for *Escherichia Coli* contains 7165 records having, among the attributes, 25 different antibiotics. The filtering process, the same as that used for *Staphilococcus Aureus*, reduced the number of records to 3285. From these data, with a *minsup* equal to 0.8 (and *minconf* equal to 1) around 3500 most general rules were discovered. Among these, we did not find any of the 7 NCCLS rules present in ESMIS for this microorganism. However, two rules not present in ESMIS were considered relevant for the system by microbiologists:

```
Cefotaxime=S, Ceftazidime=R ⟶
alarm(Ceftazidime=S)
Ceftazidime=S, Cefotaxime=R ⟶
alarm(Cefotaxime=S)
```

These two of rules relate the results of two classes of antibiotics to each other; i.e., Cefotaxime and Ceftazidime (when a bacterium is susceptible to Cefotaxidime it must also be susceptible to Ceftazidime, and vice-versa). With lower support, but with *minconf* still equal to 1, we have also discovered a rule already considered in ESMIS in accordance with the NCCLS compendium—the one relating the resistance to Piperacillin with the resistance to Ampicillin when the bacterium is isolated from the urinary tract.

3) Enterobacteriaceae: We have also done further experiments by considering four different bacteria belonging to the *Enterobacteriaceae* family: *Enterobacter Cloacae, Klebsiella Oxytoca, Klebsiella Pneumoniae* and *Proteus Mirabilis*. The considered dataset contains 3387 records having 28 different antibiotics among the attributes. The filtering process, the same as the one used for *Staphilococcus Aureus*, reduced the number of records to 2656. From this data, with *minsup* equal to 0.68 (and *minconf* equal to 1) we have discovered around 2500 most general rules. Among the discovered rules, we did not find any of the seven NCCLS rules present in ESMIS for these microorganisms. However, we have found two rules not present in ESMIS that were considered relevant for the system by microbiologists. These are the same as those found for the *Escherichia Coli*: the rules relating to each other the results of Cefotaxime and Ceftazidime. With lower support, but with *minconf* still equal to 1, we have also discovered one rule already considered in ESMIS according to the NCCLS compendium, relating the resistance to Cefotaxime with the resistance to Cephalotin.

VII. Related Work

In this section, we describe a number of systems that achieve some of the objectives of MERCURIO.

A. Knowledge-Based Systems Related to Esmis

We have found numerous works concerning the application of a knowledge based approach to medical tasks. The medical expert systems described in detail in this subsection are: DNSev [25], [26], VALAB [27], and Pro.M.D. [28].

The DNSev expert system has been developed by Dianoema S.p.A. and DEIS - University of Bologna in order to support the laboratory physicians during the process of validation of biochemical analyses. In the biochemical laboratory of a modern hospital, the quality of the analyses results is fundamental. In this respect, an important step in the process is validation, in which laboratory physicians check the results of analyses in order to verify that no error occurred during their production.

The objectives achieved by DNSev are: support of the validation of analysis results (medical laboratory expertise in the process is translated into rules and automatically applied by DNSev); help for laboratory automation (checks that are usually manually executed are now automatically executed); clarity (each raised alarm is documented in order to explain it to laboratory physicians); flexibility (new types of reasoning can easily be added to the system by simply upgrading its knowledge base); reliability (checks may be tailored to patient characteristics); time saving; and cost reduction. During the development of DNSev, the knowledge acquisition and elicitation task was performed by interviewing laboratory physicians, and also by using available documents and laboratory guidelines. During the first tests, the system achieved a time saving of around 63%

for each analysis request and a reduction of around 20–25% of the overall number of analyses to be manually examined by laboratory physicians.

VALAB is a knowledge-based system, very similar to DNSev, that performs automatic validation of the biochemical analyses performed in a laboratory. VALAB intervenes in the last stage of the process before the results are transmitted to clinicians. VALAB goals are to reduce the time between the arrival of the samples to be analyzed and the dispatch of the validated results, and to increase the reliability of the results of analyses. VALAB rules deal with a set of biological variables, or analyses. Each analysis is associated with a pair of normal limits (upper and lower), within which the result must lie for a positive validation. The expertise contained in VALAB adjusts these normal limits from the initial value to a current value. Adjusting these limits takes into account the age and sex of the subject, and the result of other analyses performed. When all the factors have been inserted, and therefore the normal limits have been fixed, the result should be within these limits. If this is the case, then the validation is positive; otherwise it is negative. Other criteria are used by VALAB for analyzing a set of results. The complete set of criteria is associated with the following parameters: extreme limits (limits outside which the values are unacceptable in all cases), reference limits (limits of normality, adaptable to each case at hand), percentage above which the difference between the present and previous results is deemed significant, and clinical or therapeutic information. Each biological variable is associated with these parameters. They allow multiple checks to be performed on the results of a group of analyses.

Pro.M.D. stands for "prolog system for the support of medical diagnostics." With this system, the laboratory physician is able to convert his own theoretical understanding and efficient problem-solving strategies into the rules of a knowledge base. Pro.M.D. is characterized by a rule based, declarative knowledge representation, the separation of the knowledge base and inference engine, a database, and an explanation function. The most important part of its knowledge base are condition or production rules in the form *if [condition] then [action]*. The Pro.M.D. Access System offers an automatic conversion of the knowledge base into Microsoft Access database tables and forms, used for data input by the user or filled with data received from the LIS. The Pro.M.D. inference engine delivers an interpretation text that can successively be edited if necessary. The general explanatory report structure consists of four main text blocks: introduction, patho-biochemical characterization, interpretation, and diagnostic suggestions. Each of these main modules is divisible into smaller modules. This tool is associated with a particular knowledge notation technique called NOTABENE.

B. Systems Exploiting Data Mining

It is worth mentioning some works done in the microbiological and medical field that apply data mining techniques. Previous work on the detection of data inconsistencies in patient records has been done by applying inductive learning to a database of artherosclerotic coronary heart disease patients [29]. In particular, confirmation rules for the detection of outliers are discovered by exploiting inductive methods. The authors also consider the application of descriptor-based classifiers.

In [30], data mining techniques are applied to patient data from several hospitals and over three years in order to discover associations, e.g., among diagnoses and medical treatments, with the purpose of enhancing medical quality management.

In [31], the system PTAH is presented. This system was developed for the analysis of antibiogram data in order to help clinicians in the prescription of antibiotics for the treatment of nosocomial infections. PTAH performs four types of analysis: resistance level over time, hierarchical clustering of antibiograms, similarity of antibiograms, and effectiveness of antimicrobials over time.

In [32], the demographic clustering algorithm that is enclosed in [33] is applied in order to find interesting clusters of antibiograms.

A related work which is also worth mentioning is reported in [34], [35], where the system DMSS is described. In DMSS, the mining of association rules is applied to microbiological data in order to automatically identify new, unexpected, and potentially interesting patterns in hospital infections and public health surveillance data. A bias (possibly subject to be changed in a certain number of iterations of the mining process) is given by the experts in order to drive the search for rules. For instance, the bias may specify rules that contain a given bacterium in its left-hand part, and resistance to some antimicrobial in its right-hand part. Data are partitioned into disjoint monthly sets prior to analysis, so that the temporal trend of the confidence of rules discovered in successive months can be computed. In this way, the system uses data mining techniques to identify new, unexpected, and interesting temporal patterns for surveillance, being able to identify an increment, for instance, in the number of resistance results to a given antimicrobial for a given species.

VIII. Future Works

In the future, we plan to use algorithms for learning extensions of association rules in order to extend the ESMIS knowledge base. In particular, we will consider generalized or multi-level association rules: in this case, besides a database of transactions, a hierarchy among the items is also available. Therefore, the association rules that can be learned can contain items from different levels of the hierarchy. In the case of microbiological data, we could exploit a hierarchy among bacteria, among antibiotics, and among infection sites, and we could learn association rules that establish a relationship among families of bacteria, families of antibiotics, and families of infection sites. This rule will represent more general knowledge that can be incorporated into ESMIS.

In order to learn generalized or multi-level association rules we will exploit the algorithms that have recently been proposed [36], [37].

Another line of future research will consists in alternative ways of looking for interesting association rules among the learned ones. For example, in [38], the authors propose a method of learning association rules that contain a specific item or children of a specific item in the hierarchy. In their

approach, the algorithm directly exploits the requirements specified by the user for generating only the rules that respect the constraints. In our work, first we generated all the rules, and then we exploited a visual tool to quickly search for the interesting ones. It would be interesting to investigate whether the use of algorithm of [38] provides a better approach.

IX. Conclusion

In this paper, we have described the MERCURIO system that has been developed by Dianoema S.p.A. and DEIS—University of Bologna in order to help medical practitioners and clinicians adopt appropriate policies for controlling nosocomial infections. In particular, the objectives of this system are the validation of microbiological data and the creation of a real time epidemiological information system.

In order to achieve these objectives, we have applied an expert system, data mining, and statistical techniques.

MERCURIO is mainly composed of: an epidemiological database, designed for storing epidemiological data; a knowledge based system, called ESMIS, used for real time validation and monitoring; and a statistical module, used for performing statistical analyses and identifying outbreaks.

ESMIS has proved to be useful for laboratory physicians by supporting them in the execution of microbiological analyses, and by helping them avoid dangerous human and instrument driven mistakes. In a test trial performed on six month data, ESMIS reached very high accuracy and specificity in the validation and the intelligent reporting tasks. Regarding the rack test task, sensitivity was very good. The executed test provided many insights to experts as well (we discovered some of their mistakes).

Data mining techniques have been applied in order to automatically discover association rules from microbiological data, and to obtain alarm rules from them. The knowledge discovery approach we have followed proved to be very effective in validating part of ESMIS knowledge base (which is written in accordance with NCCLS guidelines and with microbiology experts), and also in extending it with new validation rules, confirmed by the interviewed microbiologists, and specific to the considered hospital laboratory. The contribution of this approach, is therefore, twofold: 1) it provides a way for making human experts aware of new correlations among some antimicrobial test results that were not previously noticed, previously, and 2), it can be considered an automatic method for validating and possibly extending the knowledge base of an expert system in the microbiological domain. In the experiments performed using this approach on some bacteria species, we achieved interesting results.

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Evelina Lamma graduated in electrical engineering from the University of Bologna, Bologna, Italy, in 1985, and received the Ph.D. degree in computer science in 1990.

She is Full Professor at the University of Ferrara, Ferrara, Italy, where she teaches Artificial Intelligence, and Fondations of Computer Science. Her research activity centers on logic programming languages, artificial intelligence, and agent-based programming.

Dr. Lamma was co-organizer of the 3rd International Workshop on Extensions of Logic Programming ELP92, held in Bologna in February 1992, and of the 6th Italian Congress on Artificial Intelligence, held in Bologna in September 1999. She is member of the Italian Association for Artificial Intelligence (AI*IA), associated with ECCAI.

Paola Mello graduated in electrical engineering at the University of Bologna, Bologna, Italy, in 1982, and received the Ph.D. degree in computer science in 1988. She is Full Professor at the University of Bologna, where she teaches artificial intelligence and foundations of computer science. Her research activity centers on knowledge representation, logic programming, artificial intelligence, and knowledge-based systems.

Dr. Mellos was co-organizer of the 3rd International Workshop on Extensions of Logic Programming ELP92, held in Bologna in February 1992, and of the 6th Italian Congress on Artificial Intelligence, held in Bologna in September 1999. She is member of the Italian Association for Artificial Intelligence (AI*IA), associated with ECCAI.

Anna Nanetti graduated in biologic sciences at the University of Bologna, Bologna, Italy, in 1974 and received the Ph.D. degree from the University of Bologna.

She is Assistant Professor in the Microbiology Section of the Clinical, Specialist and Experimental Medicine Department of the Faculty of Medicine and Surgery, University of Bologna, Bologna, Italy.

Fabrizio Riguzzi graduated in computer engineering at the University of Bologna, Bologna, Italy and received the Ph.D. degree in 1999.

He is Assistant Professor at the Department of Engineering of the University of Ferrara. He has been a Visiting Researcher at the University of Cyprus and at the New University of Lisbon. His researchs interest include: data mining (and in particular methods for learning from multirelational data), machine learning, and software engineering.

Sergio Storari graduated in electrical engineering at the University of Ferrara, Ferrara, Italy, in 1998 and received the Ph.D. degree from the University of Bologna, Italy, in 2004.

He is a Technician at the Department of Engineering of the University of Ferrara. His research activity centers on artificial intelligence, knowledge-based systems, data mining and multi-agent systems. He is member of the Italian Association for Artificial Intelligence (AI*IA), associated with ECCAI.

Gianfranco Valastro received the Laurea degree in electrical engineering from the University of Bologna, Bologna, Italy, in 1983.

He is the Technological Research Manager in Dianoema S.p.A. He has been the project manager of TDMIN and MERCURIO. From 1986 to 1997 he worked for the ENI group where his research activity was centered on neural networks, connectionist models and paraller computation on MIMD architectures. He was the Project Manager for the 'Signal Analysis in Oil Well Drilling using Neural Networks and Mathematical Models'.