ICEA Design and Implementation Document

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1 Introduction

1.1 The problem: medical perspective

The aim of the ICEA[1] research project is the design, clinical implementation and evaluation of a decision-support system that is capable of assisting ICU doctors in dealing with patients who are mechanically ventilated and display symptoms and signs possibly related to the development of pneumonia. This form of pneumonia is known in the literature as *ventilator-associated pneumonia*, or VAP for short [1].

The treatment of VAP in patients is seen as a significant problem by ICU doctors. Firstly, many of these patients are severely ill. Secondly, the presence of multi-resistant bacteria in clinical wards, in particular the ICU, makes prescription of antibiotics with a spectrum as narrow as possible essential; the prescription of broad-spectrum antibiotics promotes the development of antimicrobial resistance, and should therefore be avoided when possible.

Choosing an appropriate therapy for pneumonia not only involves the issue of susceptibility of pathogens to antibiotic agents, and antimicrobial spectrum, but also of possible side effects of prescribed drugs. In the case of antibiotic therapy possible side effects are: renal failure, diminished hearing, epileptic seizures and allergic reactions varying from skin rash to anaphylactic shock.

What adds very much to the difficulty of the problem is that in many cases it is not even clear whether a patient has ventilator-associated pneumonia or not; the accurate diagnosis of ventilator-associated pneumonia is currently seen as an important clinical challenge. The diagnosis is difficult because of lack of a simple, cheap yet accurate diagnostic test; the disease is therefore diagnosed by taking a number of different clinical features into account [2]. Moreover, patients must usually be treated before the results of sputum cultures become available, which takes at least 48 hours.

The probabilistic and decision-theoretic models designed for the system are based on a combination of the theory of (causal) probabilistic networks [3, 4], also known as Bayesian (belief) networks [6], and decision theory [7]. A preliminary version of the model is described in detail in Ref. [5].

1.2 Design rationale for the system

The decision-support system that is described in this document is intended to be operating with the ICUs of the University Medical Centre, Utrecht. As such, it is necessary that the system is integrated with the clinical information system that is being used in three of the four ICUs. This system, which is being sold by firm *Eclipsys*, previously called *Emtek*, is a full-fletched system that functions as an electronic patient records system (EPR). As no paper patient records are used any more within the three ICUs deploying Eclipsys, the Eclipsys system contains a wealth of patient information which can be exploited for decision-support purposes.

The front-end of the Eclipsys system consists of a GUI with pop-up menus, tables and some graphics, allowing clinicians to enter patient data and to inspect patient data, mostly in textual form, but sometimed – for certain laboratory data – in graphical form, as a time plot. The back-end of Eclipsys is the relational database management system Sybase. This

[1]ICEA is an acronym, standing for 'An *I*ntentive *C*are, *E*xpert system for the prescription of *A*ntibiotics. The project is funded by the Netherlands Research Council, NWO.

not only offers modern facility for secure data storage, updating and retrieval, but also an SQL interface, allowing external systems access to the data.

It seems to be sensible to make use of the facilities of Eclipsys as much as possible within the decision-support system, as this would reduce the amount of data to be entered by the clinician using the decision-support system, as most patient data would already be available in Eclypsis. However, it is less obvious that the decision-support system should be integrated with current fron-end of Eclipsys, in particular because this would make separate development difficult if not impossible. As a consequence, it was decided to develop a separate user-interface for the decision-support system using modern distributed information system technology, as frequently used as part of the Internet, in our case PHP. PHP is a server-side HTML-embedded cross-platform scripting language, which allows one to generate content of HTML pages dynamically.

PHP is actually used as the language to link various parts of the system together. The majority of the functionality of the system is offered by HUGIN, a commercially available Bayesian-network and decision-network package, that is used in the ICEA project to implement the inference engine for the decision-support system. This part of the system processes patient data, and offers various types of advice based on the results computed after instantiating the Bayesian network model of VAP with the patient data. This advice is presented to the user.

The final components for the system are a HTTP server, and a Web browser. The HTTP server that is used in the project is Apache. This system has the advantage that its source code is available in the public domain, and PHP modules can be easily integrated with Apache, and are available in the public domain. The Web browser acts as the user interface to the decision-support system. This has the advantage that most users will be able to work with the system without much training. In addition, this approach saves on time in user-interface development.

Summarised, the basic system consists of four components:

- Hugin module
- PHP module
- Sybase
- HTTP server (Apache)
- Web browser

2 Architecture

In this section, the global functionality of the entire system is described. The global archirecture of the system is shown in Figure 1.

3 Design

The detailed functionality of the individual modules and the data flow between the modules will be described in this section.

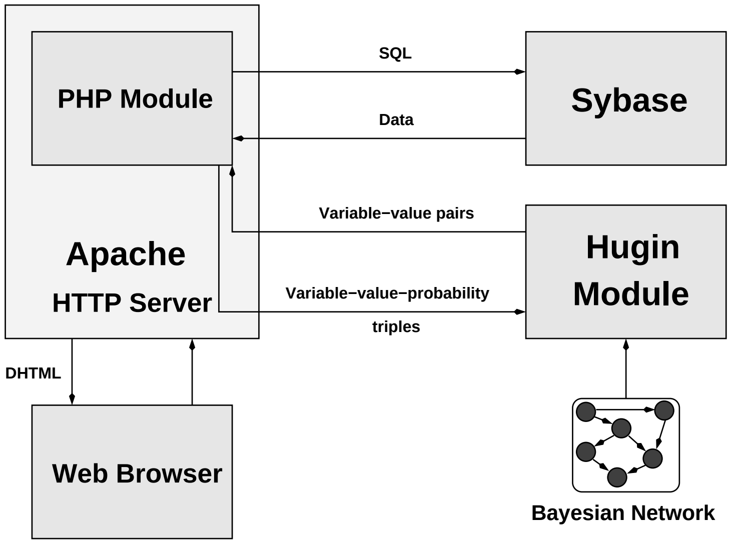

Figure 1: Global archirecture of the system.

3.1 Modules

Description of input, output and process of every module.

3.2 Bayesian-network model

The global structure of the Bayesian-network model is shown in Figure 2.

Appendix A lists the variables incorporated in the model.

4 Implementation

4.1 PHP

Describtion of the layout of the PHP files constituting the ICEA information system.

4.1.1 User point of view

Several states:

- *Requesting advice*: The doctor is presented a form with all possible input variables (see section 'input variables'). Some of these variables are taken from the ICEA-database and pre-selected as default (and made bold, so at any time you can see what the ICEA-database data were).
- the doctor corrects and makes additions to the suggested values.
- Possibly, the doctor is asked his medical opinion about the matter. The chance that this will happen is configurable
- The model is executed, and the doctor is presented the following data:

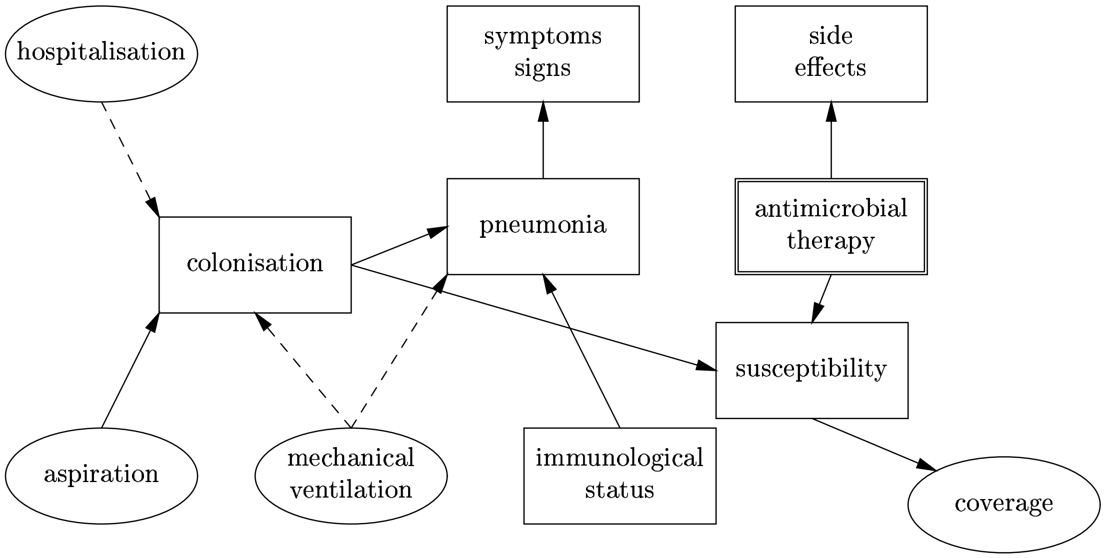

Figure 2: Global structure of the Bayesian-network model of VAP.

  - The likelihood of the patient having pneumonia (form is modifyable, either true/false, or 'exact' chance, see function 'render_pneumonia_chance'
    * For each pneumonia-causing organism the likelihood that specific
    * organism is the cause, sorted from highest likelihood to lowest.
    * Chances are included.
    * For a number of possible medications the few with the best effectiveness (??????)

- Possibly, the doctor is asked his medical opinion about the matter. The chance that this will happen is configurable

4.1.2 File layout

HTTP/phpinfo.php: informatie over onze installatie van PHP

HTTP/.htaccess: niet interessant

HTTP/corrigeer.php: invoerpagina

HTTP/execute.php: controle invoer, aanroepen execute_model()

HTTP/style.css: niet interssant

inc/model: het model zelf (model.net) + info over de invoer-variabelen (bbn_vars.csv)

inc/model.php: algemene info over model, o.a. parsing van bbn_vars.csv (dus, het bijhouden van info over BBN-variabelen)

inc/init.php: niet interessant

inc/hugin.php: voert het model uit, vooralsnog met een hoop debug-info inc/emtek.php: probeert gegevens uit de Sybase DB te halen

inc/config.php.dist: niet interessant

inc/config.php: database-access info

inc/layout.php: niet interessant

4.2 Hugin

4.3 Sybase interface

5 Evaluation

References

[1] Bartlett JG. *Management of Respiratory Tract Infections.* Baltimore: Williams & Wilkins, 1997.

[2] Bonten MM, Bergmans CJJ, Ambergen AW, De Leeuw PW, Van der Geest S, Stobberingh EE, Gaillard CA. Factors for pneumonia and colonization of respiratory tract and stomach in mechanically-ventilated ICU patients. *Am J Respir Crit Care Med* 1996; 154: 1339–1346.

[3] Lauritzen SL,Spiegelhalter DJ. Local computations with probabilities on graphical structures and their application to expert systems. *Journal of the Royal Statistical Society (Series B)* 1987; 50: 157–224.

[4] Lucas PJF, Van der Gaag LC. *Principles of Expert Systems.* Wokingham: Addison-Wesley, 1991.

[5] Lucas PJF, de Bruijn NC, Schurink K, Hoepelman IM. A Probabilistic and decision-theoretic approach to the management of infectious disease at the ICU. *Artificial Intelligence in Medicine* 2000; 19(3): 251–279.

[6] Pearl J. *Probabilistic Reasoning in Intelligent Systems.* San Mateo, California: Morgan Kaufman, 1988.

[7] Smith JQ. *Decision Analysis.* London: Chapman and Hall, 1988.

A Bayesian-network variables

A.1 INPUT A - PATIENT SPECIFIC

These variables are incorporated into the user-interface.

```
1. TEMPORAL PARAMETERS
   -------------------


HOSPITALIZATION
 <5days_COPD+REC_HOS
```

```
 >=5days_COPD+REC_HOS
 <5days_AFD+IC
 >=5days_AFD+IC
 >=5days_IC

MECHANICAL_VENTILATION
 >144hours
 96-144hours
 48-96hours
 24-48hours
 0-24hours
 NO

2. SYMPTOMS AND SIGNS OF PNEUMONIA
   -------------------------------

TEMPERATURE
 >38.5
 NORMAL
 <36.0

ANTIPYRETIC_DRUGS
 NO
 YES

RADIOLOGICAL_SIGNS
 NO
 YES

LEUKOCYTOSIS
 NO
 YES

SPUTUM
 NO
 YES

SPUTUM_PMNS
 >25
 <=25

pO2/FiO2
 >240
 <=240

SPUTUM_COLOUR
 PURULENT
```

NON_PURULENT

3. ADDITIONAL SIGNS AND LAB DATA

ASPIRATION
 NO
 YES

EPILEPTIC_SEIZURE_HISTORY
 NO
 YES

DETERIORATED_HEARING
 NO
 YES

DIMINISHED_HEARING_HISTORY
NO
YES

RENAL_FAILURE_HISTORY
 NO
 YES

PENICILLIN_HISTORY
 NO
 YES

CEPHALOSPORIN_HISTORY
 NO
 YES

COMPLEMENT
 LOW
 NORMAL

IMMUNOGLOBULIN
 DEFICIENT/INADEQUATE
 ADEQUATE

PHAGOCYTOSIS_DYSFUNCTION
 NO
 YES

HEMA_S.AUREUS

```
 NO
 YES
```

A.2 INPUT B: NON-PATIENT-SPECIFIC

These variables are not included in the user-interface.

Fill in every value for the MEDICATION variable and determine $P(\text{UTILITY})$. Order in decreasing $P(\text{UTILITY} = \text{yes})$ value.

```
MEDICATION
 AMIKACIN
 AMOXICILLIN
 AUGMENTIN
 AUGMENTIN+GENTAMYCIN
 AZTREONAM
 BENZYL_PENICILLIN
 BENZYL_PENICILLIN+GENTAMYCIN
 CEFALOTIN
 CEFTAZIDIM
 CEFTAZIDIM+TOBRAMYCIN
 CEFTRIAXON
 CEFTRIAXON+GENTAMYCIN
 CEFUROXIM
 CIPROFLOXACIN
 CLINDAMYCIN
 CLINDAMYCIN+AZTREONAM
 CLINDAMYCIN+CIPROFLOXACIN
 CO-TRIMOXAZOL
 ERYTHROMYCIN
 FLUCLOXACILLIN
 FLUCLOXACILLIN+GENTAMYCIN
 GENTAMYCIN
 IMIPENEM
 MEROPENEM
 METRONIDAZOL
 PIPERACILLIN
 PIPERACILLIN+AMIKACIN
 PIPERACILLIN+TOBRAMYCIN
 RIFAMPICIN
 TAZOCIN
 TOBRAMYCIN
 VANCOMYCIN
 NONE
```

A.3 OUTPUT

These variables are included in the user-interface.

```
PNEUMONIA
 NO
 YES

P(PNUEMONIA) and when > 0.30: text "pneumonia likely".

P(Pneumonia for individual organisms). These concern the variables
*_P, such as H.INFLUENZAE_P; there are 7 of such variables in the network.

P(UTILITY = yes | EVIDENCE, MEDICATION) where for MEDICATION every possible
drug is filled in.

SUGGESTED BEST DRUG(COMBINATION).
```