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Acquisition of Adaptation Knowledge for Breast Cancer Treatment Decision Support

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Abstract. The elaboration of a treatment in cancerology depends on decision protocols. These protocols are often adapted rather than used straightforwardly. This paper deals with the acquisition of the knowledge exploited during protocol adaptations. It shows that this knowledge acquisition process can be based on similarity paths, that are used for representing the matchings between decision problems (e.g., source and target problems within a case-based reasoning process).

1 Introduction

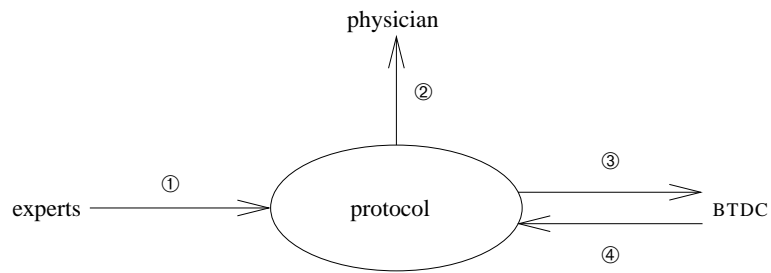
Case-based reasoning (CBR) consists in reusing the solutions of already solved problems in order to solve a new problem [15]. Such a reasoning relies on a retrieval phase (selection of a memorised solved problem with its solution) and an adaptation of the solution of the retrieved problem, in order to solve the new problem. In many CBR systems, the adaptation is based on complex and domain-dependent adaptation knowledge which has to be acquired and modelled.

This paper presents the acquisition and modelling of adaptation knowledge for the system KASIMIR/CBR whose application domain is breast cancer treatment. Beyond this application, our ambition is to present some elements of an adaptation knowledge acquisition methodology.

Section 2 describes how breast cancer treatment is managed in the *Alexis Vautrin hospital* (cancer therapy centre). The Kasimir project, context of this study, is presented in section 3. The principle of the adaptation process is presented in section 4. Section 5 plays a central role in this paper: it presents the adaptation knowledge acquisition and modelling. The discussion of section 6 comments the contribution of this work. Section 7 concludes the paper.

2 Breast Cancer Treatment in *Alexis Vautrin Hospital*

In *Alexis Vautrin hospital*, breast cancer treatment is based on a *protocol*. The links between the physicians and the protocol are schematically presented in figure 1.



- ① Creation and updating of the protocol based on evidence-based medicine principles
- ② Straightforward (“daily”) use of the protocol
- ③ Adaptation-based use of the protocol
- ④ Protocol evolutions involved by the adaptations performed during meetings of the BTDC

Fig. 1. The protocol and how it is used.

① The protocol is created by a pluridisciplinary group of experts in breast cancer, who use the principles of the so-called evidence-based medicine [2] for the most frequent situations of patients with breast cancer. This means that these experts exploit published studies about breast cancer. Another task of this group of experts is to update periodically the protocol taking into account new knowledge in oncology.

② The protocol can be considered as a set of rules helping the physicians in their daily practice. It determines the “standard way” to consider and treat the patient, or options when no standard is available.

③ Unfortunately, the straightforward use of the protocol gives satisfaction in only about 70 % of the cases. The other cases –the “out of protocol cases”– are (a) the cases for which the rules do not provide any answer (or provide incomplete answers) and (b) the cases for which the solutions proposed by the rules raise some difficulties (contraindication, impossibility of applying completely a treatment, etc.). Most of the time, the out of protocol cases are handled by adaptation of the protocol rules. A role of the BTDC –breast therapeutic decision committee– is to perform these adaptations. This committee gathers every week several specialists involved in breast cancer (specialists in medical treatment, surgery, radiotherapy, etc.). The acquisition and modelling of adaptation knowledge involved during the meetings of the BTDC constitute the subject of this paper.

④ The adaptations performed during the meetings of the BTDC may be the cause of protocol evolutions [16]. Indeed, if an adaptation is applied systematically for certain types of cases, it should be possible to integrate it into the protocol (modification of a threshold used in a rule, use of new parameters about the patient, replacement of a rule by two more accurate new rules, etc.). This remark has led to a collaboration between specialists of cancer, of ergonomics and of computer science, in order to design a protocol evolution helping system based on the examination of the adaptations performed in the BTDC. Note that this vision of the protocol evolution is incomplete –other types

of evolutions exist— and schematic —the BTDC is not the unique entity taking a decision about evolution, in particular, the group of experts plays also a role at that level.

3 Towards a Knowledge Management System of Breast Cancer Treatment Protocol

In order to model the protocol evolution by analysis of the protocol adaptations that has been performed for specific cases, it is necessary to model (1) the protocol and (2) the knowledge on which adaptation is based.

The modelling of the protocol has led to the system KASIMIR/RBR. It can be considered that the protocol is represented in this system by a set of rules $R = (\text{Prem} \rightarrow \text{Ccl}^\circ)$. Prem and Ccl° respectively are the premiss and the conclusion of the rule R . Prem is a set of conditions for the selection and the application of the rule R . Ccl° is the therapeutic solution. The development of KASIMIR/RBR has been done in a generic perspective. The representation of the adaptations performed during the BTDC sessions must give birth to the system KASIMIR/CBR. The general organisation of KASIMIR/CBR has been planned, as described in [8]. This system will perform a CBR task. The cases from the case base *are* the protocol rules $R = (\text{Prem} \rightarrow \text{Ccl}^\circ)$ (for a discussion about this unusual application of CBR, in which rules are considered as cases, see [8]). Prem represents a generic problem and corresponds to a generic patient. Ccl° is a generic therapeutic solution of the problem Prem . KASIMIR/CBR has to suggest a set of possible adaptations of the protocol for a specific target problem.

In a more distant future, a third system should take into account the adaptation knowledge in order to propose evolutions of the protocol. Since this knowledge changes with time, an adaptation knowledge acquisition methodology should be useful. One of the objectives of this paper is to propose some elements of such a methodology.

The Kasimir project is presented with more details in [9].

4 Adaptation Principle

Before the description of adaptation knowledge acquisition, the principle of the implementation of adaptation, as it is planned, has to be described. This principle has been developed during the conception and implementation of the RESYN/CBR system of synthesis planning in organic chemistry [11].

CBR aims at solving problems in an application domain. Let tgt , be a problem to be solved (a *target* problem). Let $(\text{srce}, \text{Sol}(\text{srce}))$ be a case retrieved from the case base that must be adapted to solve tgt : srce is a problem and $\text{Sol}(\text{srce})$ is a solution of srce . Adapting $\text{Sol}(\text{srce})$ in order to solve tgt consists in building a solution $\text{Sol}(\text{tgt})$ of tgt derived from $\text{Sol}(\text{srce})$.

The first adaptation step consists usually in *matching* srce and tgt , i.e., in pointing out how these problems are similar and how they are dissimilar. In our approach, the matching result is a *similarity path*, i.e. a sequence of relations

$$pb_0 \ r_1 \ pb_1 \ r_2 \ pb_2 \ \dots \ pb_{q-1} \ r_q \ pb_q$$

such that:

- The pb_i 's are problems and the r_i 's are binary relations between problems;
- $pb_0 = srce$ and $pb_q = tgt$;
- For each $i \in \{1, 2, \dots, q\}$, a piece of *adaptation knowledge* is available for adapting the solution $Sol(pb_{i-1})$ of pb_{i-1} into a solution $Sol(pb_i)$ of pb_i .

The second adaptation step simply consists in “following” the similarity path in the solution space, involving the adaptation chain: $1^\circ / Sol(srce) = Sol(pb_0)$ into $Sol(pb_1)$, $2^\circ / Sol(pb_1)$ into $Sol(pb_2)$, ... $q^\circ / Sol(pb_{q-1})$ into $Sol(pb_q) = Sol(tgt)$.

Implementing the adaptation function requires (a) the implantation of matching that points out a similarity path, and (b) the acquisition and the modelling of adaptation knowledge. This knowledge, as seen above, aims at the design of $Sol(pb_i)$ from $Sol(pb_{i-1})$, knowing on one hand pb_{i-1} and pb_i , and on the other hand the relation r_i relating the two problems. This relation determines the adaptation function \mathcal{A}_{r_i} to be used:

$$\mathcal{A}_{r_i} : (pb_{i-1}, Sol(pb_{i-1}), pb_i) \mapsto Sol(pb_i)$$

Thus the adaptation knowledge is composed of ordered pairs (r_i, \mathcal{A}_{r_i}) called *reformulations* [12]. A reformulation (r, \mathcal{A}_r) can be seen as an “adaptation rule”:

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if  $pb \ r \ pb'$  //  $pb$  is related to  $pb'$  by  $r$ 
  then  $\mathcal{A}_r(pb, Sol(pb), pb') = Sol(pb')$  //  $Sol(pb)$  is adapted into  $Sol(pb')$  by  $\mathcal{A}_r$ 

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The problems $pb_1, pb_2, \dots, pb_{q-1}$ are reified during the matching process. For KASIMIR/CBR, these *intermediate problems* corresponds to *virtual patients*: they are introduced during the reasoning.

Finally, it must be noticed that an adaptation has a *cost* indicating that the solution $Sol(tgt)$ of tgt may be worse than the solution $Sol(srce)$ of $srce$. The precise meaning of this cost depends on the application domain. For KASIMIR/RBR, this cost is characteristic of the risk, taken during adaptation, of a bad treatment choice. A reformulation can be accompanied by informations on its cost. In particular, a method for computing a numerical cost evaluating the adaptation is needed and it is used to select, during the retrieval phase, the case that is the least costly to adapt. Furthermore, some qualitative informations about this cost may be useful for the explanation of the reasoning to the user; it enables to highlight the advantage and disadvantage of the application of a reformulation. For KASIMIR/CBR, these arguments are in concern in particular with the therapeutic risk associated with a treatment.

The acquisition of reformulations is described in the next section, with an example illustrating the different issues presented above.

5 Study of BTDC adaptations

This section aims at describing the activity of adaptation knowledge acquisition. The main steps of the adaptation knowledge acquisition are presented in section 5.1. Section 5.2 presents a detailed example. Section 5.3 presents briefly some pieces of adaptation knowledge that have been acquired.

5.1 Adaptation Knowledge Acquisition Sessions

The adaptation of the protocol are performed during the meetings of the BTDC (cf. section 2, ②). Summaries of these meetings have been written and analysed by a psycho-ergonomist (see [16]). The adaptation knowledge acquisition sessions consisted in the study of these summaries in presence of experts in cancerology, of a psycho-ergonomist and of computer science specialists. Schematically, such a session can be decomposed into four phases:

phase 1: Presentation of the summary by the psycho-ergonomist, with corrections and precisions from the experts.

phase 2: Discussion and explanation of the reasoning leading to an adaptation.

phase 3: Re-description of this reasoning by the computer specialists and discussions on the variations of this reasoning.

phase 4: Analysis of the reasoning from the perspective of general adaptation knowledge propositions (this last phase usually takes place after the session).

It must be noticed that the specialist of psycho-ergonomics is also a physician, fact that facilitates her interactions with the experts and the communication between experts and computer specialists, giving her a status of interpreter. A previous work on a knowledge-based system in organic synthesis in chemistry has shown the usefulness of such an interpreter [13]. In these works, it is important that the experts have some idea about the modelling. Indeed, contrasting to the approach “cognitician-expert”, where the first person monopolises the power related to the computer, it is essential that the expert has some knowledge and some consciousness of the tools used, of their advantages and limits, especially for the knowledge representation formalisms and reasoning types. So, during the transfer of expertise, the traditional problems of misunderstanding between computer specialists and the experts are attenuated if not completely suppressed: the former cannot promise to the latter all the things that the latter would expect to have. This knowledge acquisition approach is distributed and honest, in the sense that it considers that the expert is a real associate, who has a role to play in the modelling of the knowledge.

5.2 A Detailed Example

The example presented in this section is an actual example with two modifications. First, the name of the patient has been changed: he has been called Jules. Second, the case has been slightly modified to simplify the description of the corresponding adaptation. (In this context, the term “case” is taken in a medical sense and corresponds to the notion of target problem in CBR). In fact, this case has been treated in its whole complexity. Furthermore, some pieces of information were omitted because they did not play any direct role in the reasoning.

Jules is a man with a cancer at the left breast. The first characteristics making him an out of protocol case is his sex. Indeed, the huge majority of persons suffering from breast cancer are women, so the protocol –coming for the main part from statistical studies– has been elaborated for them. The idea is then to *do as if* Jules was a women and to reason with this working hypothesis (which may be temporary). Note that the

use of expressions like “We do as if...” by the experts points out the possible presence of adaptation knowledge.

Another characteristic of Jules is that his tumour localisation in his left breast is unknown. This raises a difficulty since it is important, from the radiotherapist viewpoint, to know whether the tumour is external, central or internal. More precisely, the most pessimistic assumption –the one that makes the radiotherapy needing more precautions– is that the tumour is internal or central. The experts make this assumption. Thus, if they are wrong, it would only involve that useless precautions would have been taken.

To summarise, two characteristics making Jules an out of protocol case have been successively (and temporarily) suppressed. This can be reformulated by introducing two virtual patients: (1) a virtual patient Julie who is just like Jules but is a women, (2) a virtual patient Juliette who is just like Julie except for the tumour localisation (the localisation of Julie tumour is unknown whereas the localisation of Juliette tumour is internal or central). Juliette corresponds to the protocol, meaning that there is a rule of the protocol $R = (\text{Prem} \rightarrow \text{Ccl}^\circ)$ such that Prem holds for Juliette –denoted by $\text{Prem} \leftarrow \text{Juliette}$ (the conditions Prem are entailed by the description Juliette). Thus the following similarity path relates the protocol to Jules:

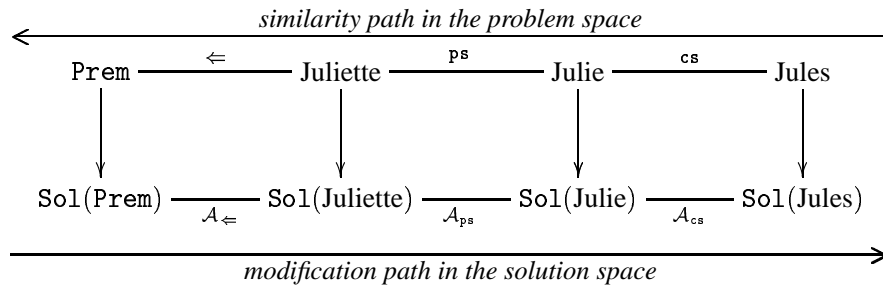
$$\text{Prem} \leftarrow \text{Juliette} \text{ ps } \text{Julie} \text{ cs } \text{Jules}$$

where ps and cs are relations between problems and where

$$\begin{aligned} \text{Jules} &= [\text{sex} = \text{male} & \text{tumour localisation} = \text{unknown} & \dots] \\ \text{Julie} &= [\text{sex} = \text{female} & \text{tumour localisation} = \text{unknown} & \dots] \\ \text{Juliette} &= [\text{sex} = \text{female} & \text{tumour localisation} = \text{internal or central} & \dots] \end{aligned}$$

Prem is a generic patient (or a class of patients) for which the treatment $\text{Sol}(\text{Prem}) = \text{Ccl}^\circ$ is a radiotherapy taking into account the internal or central position of the tumour and a hormonotherapy using tamoxifen.

When the similarity path is built –from Jules to Prem , reading from right to left–, the reverse path in the solution space must be followed, i.e., from the treatment $\text{Sol}(\text{Prem})$ of Prem to a treatment $\text{Sol}(\text{Jules})$ of Jules, reading from left to right:



Reformulation ($\leftarrow, \mathcal{A}_{\leftarrow}$) The treatment $\text{Sol}(\text{Prem})$ can be applied to Juliette since $\text{Prem} \leftarrow \text{Juliette}$. The piece of knowledge reified by the reformulation ($\leftarrow, \mathcal{A}_{\leftarrow}$) can be written: “A treatment designed for a general case can be applied to a specific case of this general case.” (This reformulation is not a new piece of knowledge: it is the basis of the deductive reasoning of KASIMIR/RBR.)

Reformulation (p_s, \mathcal{A}_{ps}) Juliette is a “pessimistic specialisation” of Julie: she is characterised by the fact that the tumour position of Julie has been precised for Juliette and that this position is the one that makes the radiotherapy the more complex (without modifying the other treatments). Therefore, the treatment $S_{o1}(Juliette)$ is transferred without modification for Julie. This reformulation (p_s, \mathcal{A}_{ps}) models the “Wald pessimistic criterion” [1] which states that the decisions must be evaluated on the basis of their worst consequences. The relation p_s can be read as “is a pessimistic specialisation of” and \mathcal{A}_{ps} is a straightforward copy of treatment.

Reformulation (c_s, \mathcal{A}_{cs}) Finally, some questions are raised about the applicability of the treatment $S_{o1}(Julie)$ of Julie to Jules, her male equivalent. These questions deal with the consequences of the change of sex on the applicability of the treatment components. Following the principles developed in [3], we are interested on the *dependencies* between the descriptor “sex” of the problems and the descriptors “radiotherapy”, “hormonotherapy”, etc., of the solutions. In [3], the dependencies are defined by $\frac{\Delta y}{\Delta x}$ where Δx is the variation of a problem descriptor x and Δy is the variation of a solution descriptor y . For Julie and Jules, we are interested in $\frac{\Delta_{radiotherapy}}{\Delta_{sex}}$ and in $\frac{\Delta_{hormonotherapy}}{\Delta_{sex}}$. The knowledge given by the experts indicates that these dependencies are null: the radiotherapy and the hormonotherapy recommended for Julie remain recommended for Jules.

The reformulation (c_s, \mathcal{A}_{cs}) is based on the dependencies $\frac{\Delta \theta}{\Delta_{sex}}$, where θ is a particular treatment. The discussion on the variations (cf. phase 3 of 5.1) allows to make precise these dependencies. In this example, we try to establish what are the treatments “invariant under the change of sex” and, for the other ones, how they can be adapted. For instance, the hormonotherapy consisting in an ablation of the ovaries is not invariant under the change of sex. This treatment is substituted by a treatment that, for a man, brings some similar expected benefits.

5.3 Some other pieces of adaptation knowledge that have been acquired

Studies of adaptations performed during the BTDC sessions, like the one described in the previous section, have led to several reformulations. From a study to another, some reformulations have reappeared, which enable to make them more precise. Above, two acquired pieces of adaptation knowledge are briefly presented. More details about them together with the needs in representation they involve can be found in [10], which is the long version of this paper.

Some adaptations are based on the knowledge about the expected benefits and the undesirable effects of a treatment on a patient. Usually, the protocol gives an optimal compromise between these positive and negative effects of a treatment (given the current state of the art in medicine), but, e.g. in case of contraindications, this is not always true. For instance, if the patient has blood coagulation troubles, the haemorrhagic risk taken during a surgery is an undesirable effect with a big importance. In such circumstances, the surgery may be changed in order to lower this risk.

Another adaptation type is linked with the threshold effect. Indeed, when a numerical patient characteristic (e.g., the age) is close to a decision threshold of the protocol, the decision is doubtful (in particular, because of the uncertainty on this threshold): both decisions should be proposed to the user.

6 Discussion

This section discusses two issues related to this work. First, some elements of an adaptation knowledge acquisition methodology generalised from this study are proposed. Then, some related work are presented. A more detailed discussion is given in [10].

6.1 Elements of an adaptation knowledge acquisition methodology

Some elements of a methodology for an acquisition process of adaptation knowledge involving experts (and, if possible, an “interpreter”) and the study of specific adaptations, are summarised. It must be noticed that these elements of methodology must be evaluated on a larger scale and in other application domains.

The first issue—maybe the most important—is the decomposition of adaptation based on the notions of similarity path and of intermediate problems between the source and target problems, which involves adaptation knowledge expressed by reformulations. The adaptation knowledge acquisition that we describe is based on informal descriptions of adaptation processes performed by experts. For each of these adaptation processes, the steps of knowledge acquisition is as follows:

- Re-description of the adaptation process in several steps by introducing intermediate problems $\text{pb}_1, \text{pb}_2, \dots, \text{pb}_{q-1}$ and their respective solutions $\text{Sol}(\text{pb}_1), \text{Sol}(\text{pb}_2), \dots, \text{Sol}(\text{pb}_{q-1})$. Recall that $\text{pb}_0 = \text{srce}$ is the source problem and that $\text{pb}_q = \text{tgt}$ is the target problem.

The elicitation of the intermediate problems is often made from the right to the left, i.e., from pb_i to pb_{i-1} . For example, when the expert makes a working hypothesis on pb_{i-1} (“We do as if some conditions of pb_{i-1} were changed”), it can be expressed by introducing pb_i .

- For each $i \in \{1, 2, \dots, q\}$, analysis of the adaptation step

$$(\text{pb}_{i-1}, \text{Sol}(\text{pb}_{i-1}), \text{pb}_i) \mapsto \text{Sol}(\text{pb}_i)$$

This analysis aims at giving a reformulation (r_i, \mathcal{A}_{r_i}) which is either a reformulation belonging already to the adaptation knowledge base, or a new one.

The second issue is linked with the problem and solution representations. Indeed, it is useful not only to represent what a solution is but also in what it answers well (or not) the problem it is supposed to solve. For KASIMIR/CBR, this is for example the knowledge linked with the expected benefits and the undesirable effects of a treatment.

The third issue concerns the dependencies between problem descriptors x and solution descriptors y , as seen above in section 5.2, about the reformulation (c_s, \mathcal{A}_{c_s}) .

These dependencies can be symbolised by the rates $\frac{\Delta y}{\Delta x}$ and involve questions such that “How does y vary when x varies?” that are useful to question the expert.

6.2 Related Work on Adaptation Knowledge Acquisition and Modelling in CBR

The studies on adaptation knowledge acquisition and modelling seem to be rather rare. In [4] the different knowledge types useful for CBR and, in particular, for the adaptation phase, are described. The different adaptation tasks (add, suppress, substitute, reorganise, etc.) are presented there and discussed at a general level. They are useful as a guide but that must be made precise in a given applicative framework.

In [14], the knowledge about the changes in a medical context is represented. This work is very different from ours since the changes of knowledge are at the level of the domain terminology (add, replacement and suppression of terms, changes in the hierarchy, etc.), whereas our approach concerns the therapeutic adaptations, and therefore, the changes in the treatment rules.

The papers [5] and [6] describe two approaches of adaptation knowledge acquisition by learning from the case base of a CBR system. These two approaches are different from ours since they are based on two different knowledge acquisition sources: a case base for the formers and experts for the latter. Nevertheless, the idea to examine from this point of view the protocol, with automatic or interactive tools, seems to be interesting and thus constitutes a possible future work.

7 Conclusion and Future Work

This paper presents the adaptation knowledge acquisition and modelling for the system KASIMIR/CBR. This system will have to adapt a breast cancer treatment protocol for specific cases not covered by a straightforward use of the protocol. The notions of similarity path, of intermediate problem and of reformulation play an important role for these acquisition and modelling. The similarity paths and the intermediate problems (corresponding to virtual patients) allow to decompose the adaptations performed in simpler steps that can be modelled by reformulations involving general adaptation knowledge.

A first future work is to fulfill the knowledge representation needs involved by the acquired adaptation knowledge. It will also be necessary to instantiate the conceptual model schema, i.e. to establish the knowledge on which the reformulations rely (representation of pessimistic specialisations, equivalence between expected benefits of treatments, treatment variations function of the sex, etc.). This instantiation work is currently under development and is associated with the implementation of KASIMIR/CBR.

The use of this knowledge in order to be able to automatically perform these adaptations is another future work. The central problem is the similarity path elaboration. For the system RESYN/CBR [11], a technique combining hierarchical classification and search in a state space –the so-called *smooth classification*– has been used. This technique should be reusable for KASIMIR/CBR but this still requires a precise study. A first version of KASIMIR/CBR taking into account only the threshold effect thanks to *fuzzy hierarchical classification* has already been successfully developed [7].

A last future work consists in studying how the protocol examination can be helpful to suggest adaptation knowledge, following the learning approaches described in [6] and [5] and discussed in section 6.2.

References

1. D. Dubois, H. Prade, and R. Sabbadin. Decision-theoretic foundations of qualitative possibility theory. *European Journal of Operational Research*, 128:459–478, 2001.
2. Evidence-based medicine working-group. Evidence-based medicine. A new approach to teaching the practice of medicine. *JAMA*, 17:268, 1992.
3. B. Fuchs, J. Lieber, A. Mille, and A. Napoli. An Algorithm for Adaptation in Case-Based Reasoning. In *Proceedings of the 14th European Conference on Artificial Intelligence (ECAI-2000), Berlin, Germany*, pages 45–49, 2000.
4. B. Fuchs and A. Mille. A Knowledge-Level Task Model of Adaptation in Case-Based Reasoning. In K.-D. Althoff, R. Bergmann, and L. K. Branting, editors, *Case-Based Reasoning Research and Development — Third International Conference on Case-Based Reasoning (ICCB-99)*, LNAI 1650, pages 118–131. Springer, Berlin, 1999.
5. K. Hanney and M. T. Keane. Learning Adaptation Rules From a Case-Base. In I. Smith and B. Faltings, editors, *Advances in Case-Based Reasoning – Third European Workshop, EWCBR'96*, LNAI 1168, pages 179–192. Springer Verlag, Berlin, 1996.
6. J. Jarmulak, S. Craw, and R. Rowe. Using Case-Base Data to Learn Adaptation Knowledge for Design. In *Proceedings of the 17th International Joint Conference on Artificial Intelligence (IJCAI'01)*, pages 1011–1016. Morgan Kaufmann, Inc., 2001.
7. J. Lieber. Strong, Fuzzy and Smooth Hierarchical Classification for Case-Based Problem Solving. In F. van Harmelen, editor, *Proceedings of the 15th European Conference on Artificial Intelligence (ECAI-02), Lyon, France*, pages 81–85. IOS Press, Amsterdam, 2002.
8. J. Lieber and B. Bresson. Case-Based Reasoning for Breast Cancer Treatment Decision Helping. In E. Blanzieri and L. Portinale, editors, *Advances in Case-Based Reasoning — Proceedings of the fifth European Workshop on Case-Based Reasoning (EWCBR-2k)*, LNAI 1898, pages 173–185. Springer, 2000.
9. J. Lieber, M. d'Aquin, P. Bey, B. Bresson, O. Croissant, P. Falzon, A. Lesur, J. Lévêque, V. Mollo, A. Napoli, M. Rios, and C. Sauvagnac. The Kasimir Project: Knowledge Management in Cancerology. In *Proc. of the 4th International Workshop on Enterprise Networking and Computing in Health Care Industry (HealthComm 2002)*, pages 125–127, 2002.
10. J. Lieber, M. d'Aquin, P. Bey, A. Napoli, M. Rios, and C. Sauvagnac. Adaptation Knowledge Acquisition, a Study for Breast Cancer Treatment. Research report available on <http://www.loria.fr/equipes/orpailleur/>, LORIA, January 2003.
11. J. Lieber and A. Napoli. Using Classification in Case-Based Planning. In W. Wahlster, editor, *Proceedings of the 12th European Conference on Artificial Intelligence (ECAI'96), Budapest, Hungary*, pages 132–136. John Wiley & Sons, Ltd., 1996.
12. E. Melis, J. Lieber, and A. Napoli. Reformulation in Case-Based Reasoning. In B. Smyth and P. Cunningham, editors, *Fourth European Workshop on Case-Based Reasoning, EWCBR-98*, Lecture Notes in Artificial Intelligence 1488, pages 172–183. Springer, 1998.
13. A. Napoli, C. Laureço, and R. Ducournau. An object-based representation system for organic synthesis planning. *Int. Journal of Human-Computer Studies*, 41(1/2):5–32, 1994.
14. D. E. Oliver, Y. Shahar, M. A. Musen, and E. H. Shortliffe. Representation of Change in Controlled Medical Terminologies. *Artificial Intelligence in Medicine*, 15(1):53–76, 1999.
15. C. K. Riesbeck and R. C. Schank. *Inside Case-Based Reasoning*. Lawrence Erlbaum Associates, Inc., Hillsdale, New Jersey, 1989.
16. C. Sauvagnac. *La construction de connaissances par l'utilisation et la conception de procédures. Contribution au cadre théorique des activités métafonctionnelles*. Thèse d'Université, Conservatoire National des Arts et Métiers, 2000.