Online Application for Simulating Intelligent Support for Medicine Intake

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ABSTRACT

In this paper, we present two contributions around an intelligent ambient system to assist people in adherence to medication prescription. First, we describe a computational model for monitoring medicine intake based on activities of a person, which is an extension of earlier work. Second, we present a web-based application that allows evaluating the benefits of such a model in an intelligent ambient system. We use this application to show the feasibility of an intelligent system for medicine intake support by comparing situations with and without intelligent support.

Categories and Subject Descriptors

I.6 [SIMULATION AND MODELING] I.6.3 [**Applications**]

Keywords

intelligent medication assistance, RTMEMS

1. MOTIVATION

A challenge for medicine usage management is to achieve in a non-intrusive manner that patients for whom it is crucial that they take medicine regularly, indeed do so. Examples of specific relevant groups include independently living elderly people, psychiatric patients or HIV-infected persons. One of the earlier solutions reported in the literature provides the sending of automatically generated SMS reminder messages to a patient's cell phone at the relevant times; e.g., [8]. A disadvantage of this approach is that patients are disturbed often, even if they do take the medicine at the right times themselves, and that due to this after some time a number of patients start to ignore the messages.

A more sophisticated approach can be based on a recently developed automated medicine box that has a sensor that detects whether a medicine is taken from the box, and can communicate this to a server; cf. SIMpill [5][†]. This enables to send SMS messages only when at a relevant point in time no medicine intake is detected. This is also called a Real-time Medication Event Monitoring System (RTMEMS). A next step is to let a computing device find out more precisely what relevant times for medicine intake are. One way is to base this on prespecified prescription schemes that indicate at what time points medicine should be taken. However, this may be inflexible in cases that a patient did not follow the scheme precisely, or if activities of the patient require a different scheme.

To obtain a more robust and flexible approach, we have proposed an application of an automated medicine box in combination with a computational model that determines the (estimated) medicine level over time [6]. This system incorporates an intelligent agent that includes a dynamic system model to estimate the medicine level in the patient's body by simulation. Based on this it is able to dynamically determine at what point in time the patient should take medicine, and given that, to analyse whether the patient intends to take medicine too early or too late, and to take measures to prevent this.

In this paper we introduce an extended version of the initial computational model, in which also the activities of a patient are taken into account. Secondly, we present a web-based application that is build around this model and can be used to simulate and evaluate intelligent ambient support for medicine intake. We first introduce the intelligent support system itself (Section 2), followed by a description of the main characteristics of the model in Section 3. Section 4 presents the web-based application, which is then used in Section 5 to illustrate the usability of the support system in a two different scenarios. Finally, Section 6 concludes the paper.

2. INTELLIGENT SUPPORT FOR MEDICINE INTAKE

The intelligent support system is designed as an agent-based application. Figure 1 presents an overview of the entire system as considered and the interaction with the patient. The top right corner shows the patient, who interacts with the medicine box, and communicates with the patient cell phone. The Medicine Box detects whether medicine is taken out of the medicine box. The Medicine Box Agent (MBA) observes this medicine box. In case, for example, the patient intends to take the medicine too soon after the previous dose, it finds out that the medicine should not be taken at the moment (i.e., the sum of the estimated current

[*] This product is already commercially available from Simpill, http://www.simpill.com/

medicine level plus a new dose is too high), and communicates a warning to the patient by a beep. Furthermore, all information obtained by this agent is passed on to the Usage Support Agent (USA), which maintains a model of the estimated medicine level in the patient. Optionally, the USA can use observations about the activities of a patient (e.g. hearth rate, movement) in the determination of the estimated medicine level. All information about medicine usage is stored in the patient database by this agent. If the patient tries to take the medicine too early, a warning SMS with a short explanation is communicated to the cell phone of the patient, in addition to the beep sound already communicated by the Medicine Box Agent.

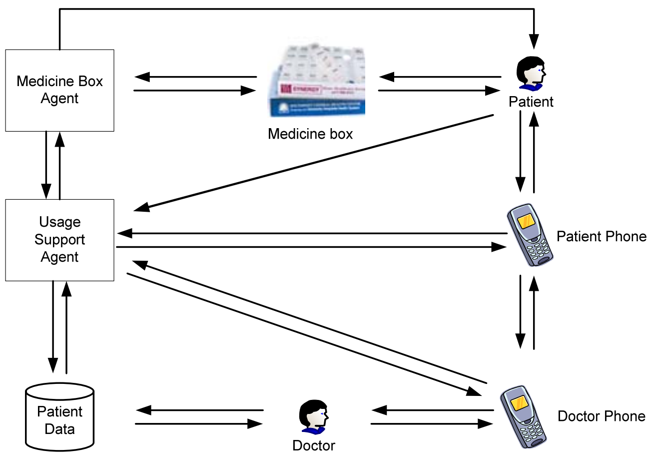

Figure 1. Multi-Agent System: Overview

On the other hand, in case the Usage Support Agent finds out that is a need to take the medicine (i.e., the medicine concentration is estimated too low for the patient and no medicine was taken yet), it can take measures as well. First of all, it can warn the patient by communicating an SMS to the patient cell phone. This is done some time before the estimated medicine concentration in the patient is getting too low. In case that after some time the patient still does not take medicine, the agent can communicate an SMS to cell phone of the appropriate doctor. The doctor can look into the patient database to see the medicine usage, and in case the doctor feels it is necessary to discuss the state of affairs with the patient, he or she can contact the patient via a call using the doctor cell phone to the patient cell phone.

The system as proposed above is described by using cell phones as a feedback mechanism to the patient and the doctor. Of course, a variety of options are available besides the use of a cell phone, for instance landline phones, the television, an alarm bell, etc. For each specific patient or doctor the most suitable device can be chosen.

3. MODEL

This section describes the rules that are the basis of the two agents present in the application. These rules are taken from [6]. First, the rules of the Medicine Box Agent are discussed. Note that for the sake of clarity these rules are specified in a semi-formal format.

First of all, the observed usage of medicine is communicated to the Usage Support Agent in case the medicine is not taken too early, as specified in MBA1.

MBA1: Medicine usage communication

If the Medicine Box Agent has a belief that the patient has taken medicine from a certain position in the box, and that the particular position contains a certain type of medicine M, and taking the medicine does not result in a too high medicine concentration of medicine M within the patient, then the usage of this type of medicine is communicated to the USA.

In case medicine is taken out of the box too early, a warning is communicated by a beep and the information is forwarded to the Usage Support Agent (MBA2 and MBA3).

MBA2: Too early medicine usage prevention

If the Medicine Box Agent has the belief that the patient has taken medicine from a certain position in the box, that this position contains a certain type of medicine M, and taking the medicine results in a too high medicine concentration of medicine M within the patient, then a warning beep is communicated to the patient.

MBA3: Early medicine usage communication

If the Medicine Box Agent has a belief that the patient was taking medicine from a certain position in the box, and that the particular position contains a certain type of medicine M, and taking the medicine would result in a too high concentration of medicine M within the patient, then this is communicated to the Usage Support Agent.

Domain-specific rules for the Usage Support Agent are shown below. The Usage Support Agent's specific functionality is described by three sets of temporal rules. In order to reason about the usage information, this information is interpreted (USA1), and stored in the database (USA2).

USA1: Prepare storage usage

If the agent has a belief concerning usage of medicine M and the current time is T, then a belief is generated that this is the last usage of medicine M, and the intention is generated to store this in the patient database.

USA2: Store usage in database

If the agent has the intention to store the medicine usage in the patient database, then the agent performs this action.

Temporal rules were specified for taking the appropriate measures. Three types of measures are possible. First, in case of early intake, a warning SMS is communicated (USA3). Second, in case the patient is too late with taking medicine, a different SMS is communicated, suggesting to take the medicine (USA4). Finally, when the patient does not respond to such SMSs, the doctor is informed by SMS (USA5).

USA3: Send early warning SMS

If the agent has the belief that an intention was shown by the patient to take medicine too early, then an SMS is communicated to the patient cell phone that the medicine should be put back in the box, and the patient should wait for a new SMS before taking more medicine.

USA4: SMS to patient when medicine not taken on time

If the agent has the belief that the level of medicine M is C at the current time point, and the level is considered to be too low, and the last message has been communicated before the last usage, and at the current time point no more medicine will be absorbed by the patient due to previous intake, then an SMS is sent to the patient cell phone to take the medicine M.

USA5: SMS to doctor when no patient response to SMS

If the agent has the belief that the last SMS to the patient has been communicated at time T, and the last SMS to the doctor was communicated before this time point, and furthermore, the last recorded usage is before the time point at which the SMS has been sent to the patient, and finally, the current time is later than time T plus a certain delay parameter for informing the doctor, then an SMS is communicated to the cell phone of the doctor that the patient has not taken medicine M.

The last properties concern the medicine level within the patient's body. First, the agent maintains a dynamic model for the concentration of medicine in the patient over time in the form of a belief about a leads to after relation.

USA6: Maintain dynamic model

*The Usage Support Agent believes that if the medicine level for medicine M is C, and the usage effect per time step of the medicine is E, then after duration D the medicine level of medicine M is C+E*D minus G*(C+E*D)*D with G the decay value.*

This property is also specified in a formal fashion:

internal(usage_support_agent)|belief(leadsto_to_after(
 medicine_level(M, C) ∧ usage_effect(M, E) ∧ decay(M, G),
 medicine_level(M, (C+E) - G*(C+E)*D), D)

Hereby, the agent has an internal belief about the dynamic model of the medicine level.

A topic not addressed in [6] is how the decay values and the usage effect are influenced by the activities of the patient. This requires that the activities of a patient are somehow monitored, for example by an device that registers the hearth rate or movements of a patient.

Below, a set of generic rules are given that are able to specify the influence of such activities on these parameters. The rules are specified in a temporal format using the LEADSTO language [1]. The basic building blocks of this language are temporal (or causal) relations of the format $\alpha \rightarrow_{e,\ f,\ g,\ h} \beta$, which means:

if	state property α holds for a certain time interval with duration g,
then	after some delay (between e and f) state property β will hold for a certain time interval of length h.

with α and β state properties of the form 'conjunction of literals' (where a literal is an atom or the negation of an atom), and e, f, g, h non-negative real numbers. In case these parameters are not specifically mentioned, the default values of 0,0,1,1 respectively are chose. Using this language, first, the decay value accompanying the current activity is represented. Under certain activities the decay might be lower than other activities:

DM1: determine decay factor

If the current activity is A, and medicine M has a certain decay value during this activity, then this is the decay value for medicine M used in the model at this time point.

internal(usage_support_agent)|belief(current_activity(A)) ∧
internal(usage_support_agent)|belief(has_decay_value_during(M, G, A))
↠ decay(M, G)

A second set of properties concerns the usage effect. Some activities make that medicine is absorbed more slowly by the body (i.e. lower usage effect per time step, but for a longer period), or faster. For example, while eating medicine is often more slowly absorbed than while not eating. Similarly, when the patient is very active and has a high blood flow, the medicine is absorbed at a higher rate. Therefore, a number of aspects need to be maintained:

- the dose the patient has taken;
- the dose which has not yet been absorbed within the patients body;
- the speed with which the dose that still needs to be absorbed will be absorbed per time point.

First, the unabsorbed dose is determined after the patient has taken a certain dose of medicine, as expressed in property DM2. Note that in these properties, it is assumed that the unabsorbed dose does not decay over time, since it is not absorbed in the patients body yet, after which the decay starts. This decay could however be incorporated in the properties in a straightforward manner.

DM2: determine unabsorbed dose

If the patient takes dose D of medicine M, and there is currently a certain unabsorbed dose left (which might be 0), then the sum of these two is the current unabsorbed dose, and the total dose at this time point.

internal(usage_support_agent)|belief(patient_just_taken_medicine(M)) ∧
internal(usage_support_agent)|belief(patient_taken_dose(M, D)) ∧
current_unabsorbed_dose(M, DCURRENT)
↠ current_unabsorbed_dose(M, D + DCURRENT)

How fast this dose is absorbed is determined by looking at the current activity. The activity determines how much of the medicine will be absorbed within 1 time step. Of course, in case there is no dose left, no more medicine will be absorbed.

DM3(1): determine usage effect and unabsorbed dose

If the patient has not just taken medicine M and the current unabsorbed dose of the medicine is DCURRENT, and the current activity A allows for a maximum absorption of the medicine of DMAX, and DCURRENT is more than the maximum absorbed then the current unabsorbed dose is DCURRENT – DMAX and the usage effect.

internal(usage_support_agent)|¬belief(patient_just_taken_medicine(M)) ∧
current_unabsorbed_dose(M, DCURRENT) ∧
activity_admits_absorption_of(M, A, DMAX) ∧ DMAX > DCURRENT
↠ current_unabsorbed_dose(M, DCURRENT-DMAX) ∧
 usage_effect(M, DMAX)

Of course, also a variant of this property is expressed in case fewer dose is unabsorbed.

DM3(2): determine usage effect and unabsorbed dose

If the patient has not just taken medicine M and the current unabsorbed dose of the medicine is DCURRENT, and the current activity A allows for a maximum absorption of the medicine of DMAX, and DCURRENT is lower of equal to the maximum absorbed then the current unabsorbed dose is 0 and the usage effect is DCURRENT.

internal(usage_support_agent)|¬belief(patient_just_taken_medicine(M)) ∧
current_unabsorbed_dose(M, DCURRENT) ∧
activity_admits_absorption_of(M, A, DMAX) ∧ DMAX ≤ DCURRENT
↠ current_unabsorbed_dose(M, 0) ∧
 usage_effect(M, DCURRENT)

The final property of the Usage Support Agent is to communicate the concentration to the Medicine Box Agent:

USA7: Communicate Current Concentration

If the agent has the belief that the level of medicine M is C at the current time point then the agent informs the medicine box agent about this level.

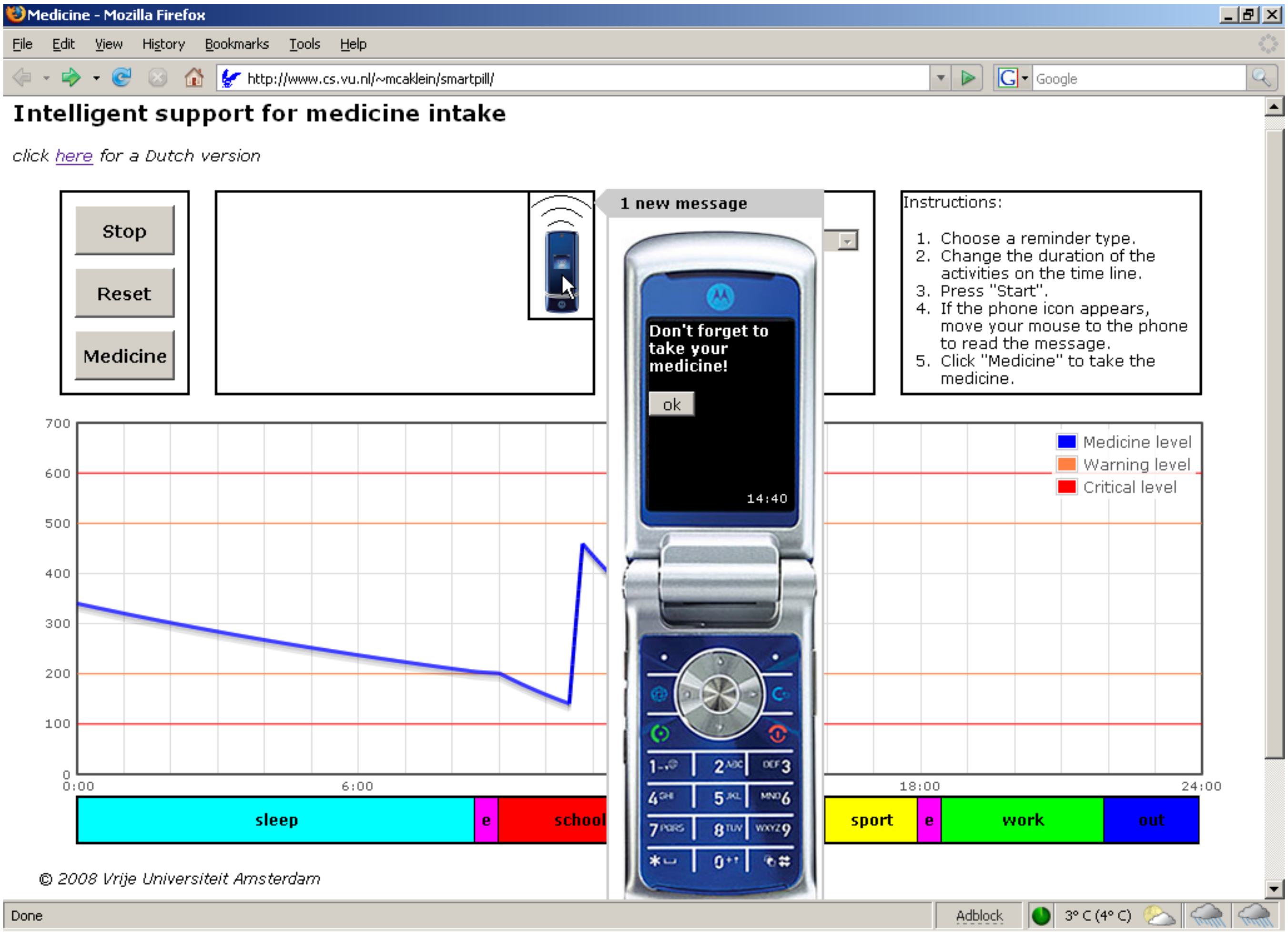

Figure 2. Screenshot of the web-based application that shows the medicine level and mimics an SMS warning.

4. WEB-BASED APPLICATION

Based on the model described above an interactive web-based application has been build.† This application serves two purposes. First, it can be used in an educational setting to explain the main concepts in the model, the interaction between activities and medicine concentration in the blood, and the effect of irregular medicine intake. Second, it can be used to evaluate the benefits of an intelligent support system. This can be done by comparing the system with a 'traditional SMS-reminder system', which only sends reminders at fixed time points, or by simulating specific 'forgetting behaviour' of a patient.

Figure 2 shows a screenshot of the web application. The horizontal axis in the main graph in the application represents the time (one day, from midnight to midnight) and the vertical axis represents the medicine concentration in the blood of a patient. The red lines show the critical values: the medicine level should always be in between these values. The orange lines represent the warning levels: if the medicine level drops below the lowest warning value, then a reminder should be sent to the patient; above the highest warning level it is unsafe to take an additional dose of medicine. The timeline below the graphs specifies the activities of the patient during the day.

Before starting the application, the user first has to choose a specific reminder type. The possible options are "None", which means no reminders at all, "Every X hours", where the user can specify the fixed interval between two reminders in numbers of hours, and "Medicine level based", which uses the model in the Usage Support Agent to determine when a warning should be sent. In addition, the user can change the planning of the day, by dragging the borders between the activities in the timeline at the bottom of the screen.

When clicking the button "Start", the application will slowly draw the estimated level of medicine in the blood of the patient over time. The effect of the activities on the decay is taken into account, as is the reduced absorption during some activities. For example, in Figure 2 can be seen that decay during the activity "sleep" is less than during the activity "school". If the type of reminder is set to "Medicine level based" a warning will be given when the medicine level drops below a certain "warning level", which is still above the critical level. In case of a warning an icon of a mobile phone appears in the screen. When moving the mouse over the icon, a picture of a phone with a message pops up. It is

† See http://www.cs.vu.nl/~mcaklein/smartpill/

the responsibility of the user to react to this message. If the user clicks the button “Medicine”, medicine intake is simulated, resulting in an increase of the medicine level during a pre-set time. This variable, and all other constants, such as the decay factor during specific activities, can be set at initialization of the application.

5. USAGE SCENARIOS

To illustrate the added value of the system, we will now describe two scenario’s of in which a patient with a specific day planning and forgetting behaviour uses a specific variant of the system.

5.1 Scenario 1: high-school pupil

In the first scenario, we consider a high-school pupil at a Friday, who goes to school during the day, does some sports afterwards, has a job in the evening and goes out at night. His prescription specifies that he has to take is medicine three times per day. For his convenience, he always takes his medicine during his meals.

Figure 3 shows the level of medicine (blue line) during the day. One could see that this schedule works reasonably well: almost during the whole day the medicine level is between the critical levels (red line), except just after lunch and at the end of the day. Note however, that the whole night following this day the level will be too low, as the next intake moment is during breakfast.

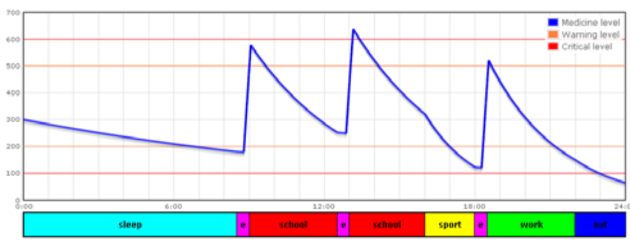

Figure 3. Medicine intake during meals.

If he would use a reminder-system based on fixed intervals, he could specify that he would like to receive a reminder every eight hours. The development of the medicine level in this scenario (assuming that all reminders results in medicine intake) is shown in Figure 4. This scheme works a bit better: most of the time the medicine level is within the safe zone, only during a short time in the evening the level is too low.

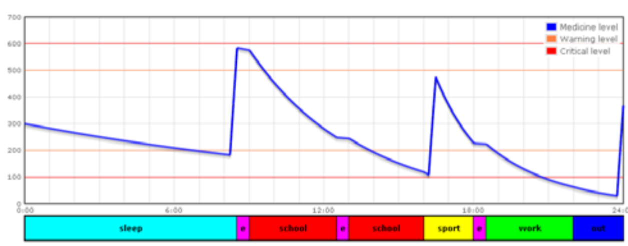

Figure 4. Medicine intake based on a reminder every eight hours.

Finally, let’s consider the effect of the model-based reminder system. Now, a reminder is sent if the medicine level drops below the warning level (orange line). Again, we assume that every reminder is followed up by a medicine intake. Figure 5 shows the medicine level over time.

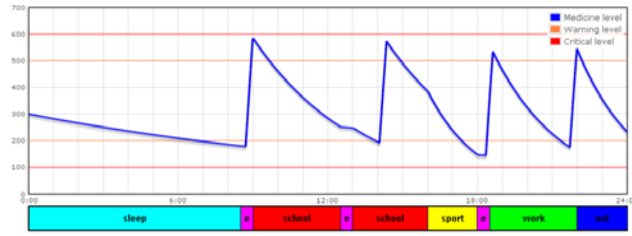

Figure 5. Medicine intake after warning based on medicine level.

In this case, we see that the medicine level is always within the safe zone, of course. However, we also note that medicine is taken four times a day instead of three times. Apparently, the activities of this patient require more medicine than is foreseen. This partly explains the fact that the medicine level was sometimes too low in the previously described situations. However, one can clearly see that a higher dose would have resulted in too high levels of medicine.

5.2 Scenario 2: elderly woman

In the second scenario, we look at an elderly woman, obviously with a much less active life. She wakes up quite early in the morning, has to wait till her breakfast is served, and spend her day mainly with sitting and reading. In the afternoon she has a short nap and goes out for a short stroll. Her medicine prescription says that she has to take her pills (dose 238 mg) during all meals. If this is followed everything works out quite well, as can be seen in Figure 6: the medicine level always stays within the safe zone, and the level at the end of the day is more or less equal to the level at the start of the day.

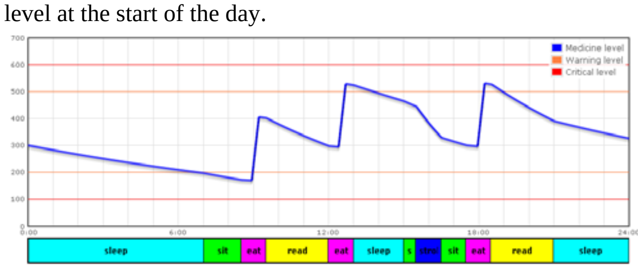

Figure 6. Medicine intake during the meals for an elderly woman.

However, this woman tends to forget her pill that she has to take at lunchtime. Usually, she only realizes this at dinner, and she then takes two pills to compensate for the missed one. As we can see in Figure 7, this doesn’t work out well. The medicine level is for some period above the critical value, and the level at the end

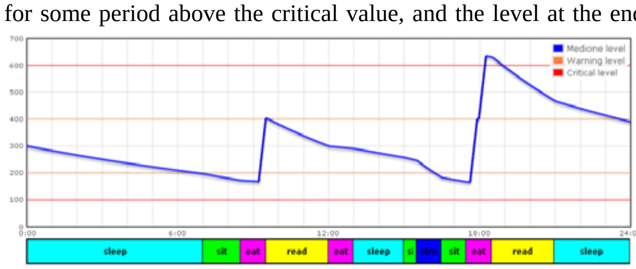

Figure 7. Forgotten pill that is compensated at the next intake moment.

of the day is higher than the level at the beginning of the day. This will result in an increased level of medicine during the next day. Actually, it can easily be checked that it would have been better if she would have taken just one pill at dinner, but she wasn't aware of this.

Let's now look at the situation in which the woman or a caregiver uses the intelligent support system. First of all, this system would have warned when taking out the second pill from the medicine box (we assume that every 'taking pill out action' can be registered in the box), because the medicine level was above the upper warning level. If we also assume that she follows up on the reminders, the following would have happened (see Figure 8).

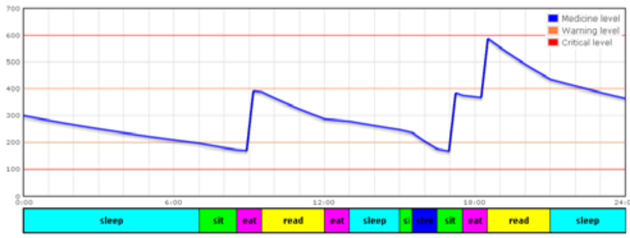

Figure 8. Reminder received for forgotten pill and system determined that the regular pill at dinner is safe.

First, she receives a reminder in the morning that she should take her pill. She is aware of this, so she takes the pill during her breakfast. Then, if she again forgets her pill at lunch, she gets a reminder during her stroll. Directly after her stroll she takes her forgotten pill. During dinner, she opens the medicine box again to take her regular pill. In this case, the system decides that it is safe to take the pill at the regular moment, as the medicine level is just below the critical value. Indeed the medicine intake does not lead to a too high medicine level.

6. DISCUSSION

In this paper, an intelligent support system for improving adherence to medication prescription was described. We introduced a computational model of medicine concentration in the blood of a patient, which takes the activities of patients into account. In addition, we presented a web-based application to evaluate the benefits of such a system. By describing two scenarios we showed how this web application indeed gives insight in the added value of an intelligent support system. Obviously, the described scenarios do not say anything about the effectiveness and usability of the intelligent support system in practice, but only serve to illustrate the difference in effect between different approaches to support medication adherence. In addition, the model for medication concentration itself, with the different effects of activities on medication, has not yet been validated.

The presented system fits well in the recent developments in Ambient Intelligence [1][2][9]. Furthermore, it also indicates that multi-agent system technology can be of great benefit in health care applications, as also acknowledged in [7]. More approaches to support medicine usage of patients have been developed. Both in [5] as well as [4] models are presented that do not simply always send an SMS that medicine should be taken such as proposed by [8]. Both approaches only send SMS messages in case the patient does not adhere to the prescribed usage. The model presented in this paper however adds an additional dimension to such a support system, namely the explicit representation and simulation of the estimated medicine level inside the patient, taking the effect of his activities into account. Having such an explicit model enables the support agent to optimally support the patient.

It is future work to see how accurately the proposed model describes the actual medicine level within the patient. Furthermore, we plan on testing the proposed system with real patients to investigate whether the adherence to medicine indeed improves compared to the more conventional approaches.

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