

Formal Design and Simulation of an Ambient Multi-Agent System Model for Medicine Usage Management

Mark Hoogendoorn, Michel Klein, and Jan Treur

Vrije Universiteit Amsterdam, Department of Artificial Intelligence
De Boelelaan 1081a, 1081 HV Amsterdam, The Netherlands
{mhoogen, michel.klein, treur}@cs.vu.nl

Abstract. A formally specified multi-agent-based model for medicine usage management is presented and formally analysed. The model incorporates an intelligent ambient agent model that has an explicit representation of a dynamic system model to estimate the medicine level in the patient's body by simulation, and is able to analyse whether the patient intends to take the medicine too early or too late.

1 Introduction

The fast developing area of Ambient Intelligence [2, 1, 13] is an interesting application area for agent-based methods. In this paper a formally analysed ambient multi-agent system model for the domain of medicine usage management is presented. The main problem addressed in this health domain is to achieve in a non-intrusive, human-like 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., [14]. 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 after some time a number of patients start to ignore the messages. More sophisticated approaches make use of a recently developed automated medicine box that has a sensor that can detect whether a medicine is taken from the box, and can communicate this to a server; cf. SIMpill [8]. This paper explores and analyses possibilities to use automated devices such as an automated medicine box, servers and cell phones as non-human agents, in addition to human agents such as the patient and a supervising doctor. The aim is to obtain a form of medicine usage management that on the one hand achieves that the patient maintains the right amount of medicine, whereas the human factors are also incorporated in an adequate manner, e.g. that a patient is only disturbed if it is really required, thus providing a human-like ambience.

The ambient multi-agent system model for medicine usage management as discussed was formally specified in an executable manner and formally verified using dedicated tools. The system hasn't been actually deployed in a real life situation. The model developed can be used as a blueprint for specific applications in the domain of

medicine usage management. The model incorporates an intelligent ambient agent model that has an explicit representation of a dynamic system model to estimate the concentration of the medicine in the patient's body by simulation, and is able to analyse whether the patient intends to take medicine too early or too late. For actual deployment, the model might have to be extended with other aspects of the patient, e.g. his physical activity and his food consumption, which all has impacts on the drug doses.

In this paper, Section 2 describes the modelling approach. In Section 3 the Multi-Agent System is introduced, whereas Section 4 presents the specification at the multi-agent system level. The specification of the ambient agent is presented in Section 5. Furthermore, Section 6 presents simulation results, and finally, Section 7 is a discussion.

2 Modelling Approach

This section briefly introduces the modelling approach used to specify the multi-agent model. Two different aspects are addressed. First of all, the process aspects, and secondly, the information and functionality aspects. Thereafter, the language used for execution of a model and the specification and verification of dynamic properties is briefly introduced.

2.1 Process and Information/Functionality Aspects

Processes are modelled as components in the generic model. A component can either be an active process, namely an *agent*, or a source that can be consulted, which is a *world component*. In order to enable interaction between components, *interaction links* between such components can be specified. From the perspective of information, *interfaces* of components are specified by *ontologies*. Using ontologies, the *functionalities* of components in order to perform the tasks of the component can be specified as well.

2.2 Specification Languages

In order to execute and verify multi-agent models, an expressive language is needed. To this end, the language called TTL is used [10, 3]. This predicate logical language supports formal specification and analysis of dynamic properties, covering both qualitative and quantitative aspects. TTL is built on atoms referring to states, time points and traces. A *state* of a process for (state) ontology Ont is an assignment of truth values to the set of ground atoms in the ontology. The set of all possible states for ontology Ont is denoted by $STATES(Ont)$. To describe sequences of states, a fixed *time frame* T is assumed which is linearly ordered. A *trace* γ over state ontology Ont and time frame T is a mapping $\gamma : T \rightarrow STATES(Ont)$, i.e., a sequence of states γ_t ($t \in T$) in $STATES(Ont)$. The set of *dynamic properties* $DYNPROP(Ont)$ is the set of temporal statements that can be formulated with respect to traces based on the state ontology Ont in the following manner. Given a trace γ over state ontology Ont , the state in γ at time point t is denoted by $state(\gamma, t)$. These states can be related to state properties via

the formally defined satisfaction relation \models , comparable to the Holds-predicate in the Situation Calculus: $\text{state}(\gamma, t) \models p$ denotes that state property p holds in trace γ at time t . Based on these statements, dynamic properties can be formulated in a formal manner in a sorted first-order predicate logic, using quantifiers over time and traces and the usual first-order logical connectives such as $\neg, \wedge, \vee, \Rightarrow, \forall, \exists$. A special software environment has been developed for TTL, featuring both a Property Editor for building and editing TTL properties and a Checking Tool that enables formal verification of such properties against a set of (simulated or empirical) traces.

To logically specify simulation models and to execute these models in order to get simulation traces, the language LEADSTO, an executable subset of TTL, is used; cf. [4]. 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.

3 Overview of the Multi-Agent System

Figure 1 presents an overview of the entire system as considered. Two world components are present in this system: the medicine box, and the patient database; the other components are agents. The top right corner shows the patient, who interacts with the medicine box, and communicates with the patient cell phone. The (ambient) Medicine Box Agent monitors whether medicine is taken from the box, and the position thereof in the 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 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 (ambient) Usage Support Agent. All information about medicine usage is stored in the patient database by this agent. If the patient tried 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.

On the other hand, in case the Usage Support Agent finds out that the medicine is not taken early enough (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 soon after the patient should have taken the medicine. In case

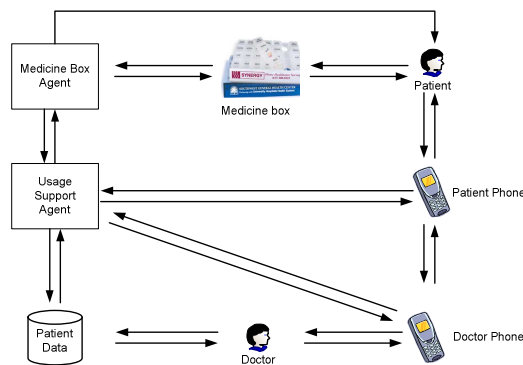


Fig. 1. Multi-Agent System: Overview

the patient still does not take medicine (for example after a number of hours), 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.

4 Specification of the Multi-Agent Level

In order for the various components shown in Figure 1 to interact in an appropriate manner, generic temporal rules at the global level are specified that model the interaction between the various components. First of all, Table 1 shows the ontology needed to express such rules. Using the ontology, the following generic temporal rules were specified.

Action Propagation from Agent to World

$$\forall X:\text{AGENT} \forall W:\text{WORLD} \forall A:\text{ACTION} \\ \text{output}(X)|\text{performing_in}(A, W) \wedge \text{can_perform_in}(X,A,W) \rightarrow \text{input}(W)|\text{performing}(A)$$

Observation Focus Propagation: from Agent to World

$$\forall X:\text{AGENT} \forall W:\text{WORLD} \forall I:\text{INFO_EL} \\ \text{output}(X)|\text{observation_focus_in}(I, W) \wedge \text{can_observe_in}(X,I,W) \rightarrow \text{input}(W)|\text{observation_focus}(I)$$

Observation Result Propagation from World to Agent

$$\forall X:\text{AGENT} \forall W:\text{WORLD} \forall I:\text{INFO_EL} \\ \text{output}(W)|\text{observation_result_from}(I, W) \wedge \text{can_observe_in}(X,I,W) \rightarrow \text{input}(X)|\text{observed_result_from}(I, W)$$

Communication Propagation Between Agents

$$\forall X,Y:\text{AGENT} \forall I:\text{INFO_EL} \\ \text{output}(X)|\text{communication_from_to}(I,X,Y) \wedge \text{can_communicate_with_about}(X,Y,I) \\ \rightarrow \text{input}(Y)|\text{communicated_from_to}(I,X,Y)$$

5 Specification of the Ambient Agents

The Ambient Agent Model used is based on a combination of the Generic Agent Model GAM described in [5], and the generic process control model in [11]. To express the agent's internal states and processes, the ontology shown in Table 2 was specified.

Table 1. Ontology for Interaction at the Global Level

SORT	Description
ACTION	an action
AGENT	an agent
INFO_EL	an information element, possibly complex (e.g., a conjunction of other info elements)
WORLD	a world component
Predicate	Description
performing_in(A:ACTION, W:WORLD)	action A is performed in W
observation_focus_in(I:INFO_EL, W:WORLD)	observation focus is I in W
observation_result_from(I:INFO_EL, W:WORLD)	observation result from W is I
observed_result_from(I:INFO_EL, W:WORLD)	the observed result from W is I
communication_from_to(I:INFO_EL, X:AGENT, Y:AGENT)	information I is communicated by X to Y
communicated_from_to(I:INFO_EL, X:AGENT, Y:AGENT)	information I was communicated by X to Y
can_observe_in(X:AGENT, I:INFO_EL, W:WORLD)	agent X can observe I within world component W
can_perform_in(X:AGENT, A:ACTION, W:WORLD)	agent X can perform action A within world component W
can_communicate_with_about(X:AGENT, Y:AGENT, I:INFO_EL)	agent X can communicate with agent Y about info element I

Table 2. Ontology Used within the Ambient Agent Model

Predicate	Description
belief(I:INFO_EL)	information I is believed
world_fact(I:INFO_EL)	I is a world fact
has_effect(A:ACTION, I:INFO_EL)	action A has effect I
Function to INFO_EL	Description
leads_to_after(I:INFO_EL, J:INFO_EL, D:REAL)	state property I leads to state property J after duration D
at(I:INFO_EL, T:TIME)	state property I holds at time T
critical_situation(I:INFO_EL)	the situation concerning I is critical

An example of an expression that can be made by combining elements from this ontology is $\text{belief}(\text{leads_to_after}(I:\text{INFO_EL}, J:\text{INFO_EL}, D:\text{REAL}))$ which represents that the agent has the knowledge that state property I leads to state property J with a certain time delay specified by D. Using this ontology, the functionality of the agent has been specified by generic and domain-specific temporal rules.

5.1 Generic Temporal Rules

The functionality within the Ambient Agent Model has the following generic specifications.

$$\begin{aligned} & \forall X:\text{AGENT}, I:\text{INFO_EL}, W:\text{WORLD} \\ & \quad \text{input}(X)|\text{observed_result_from}(I, W) \wedge \text{internal}(X)|\text{belief}(\text{is_reliable_for}(W, I)) \rightarrow \text{internal}(X)|\text{belief}(I) \\ & \forall X, Y:\text{AGENT}, I:\text{INFO_EL} \\ & \quad \text{input}(X)|\text{communicated_from_to}(I, Y, X) \wedge \text{internal}(X)|\text{belief}(\text{is_reliable_for}(X, I)) \rightarrow \text{internal}(X)|\text{belief}(I) \\ & \forall X:\text{AGENT} \forall I, J:\text{INFO_EL} \forall D:\text{REAL} \forall T:\text{TIME} \\ & \quad \text{internal}(X)|\text{belief}(\text{at}(I, T)) \wedge \text{internal}(X)|\text{belief}(\text{leads_to_after}(I, J, D)) \rightarrow \text{internal}(X)|\text{belief}(\text{at}(J, T+D)) \end{aligned}$$

When the sources are assumed always reliable, the conditions on reliability can be left out. The last rule specifies how a dynamic model that is represented as part of the agent's knowledge can be used by the agent to perform simulation, thus extending its beliefs about the world at different points in time.

For the world components the following generic formal specifications indicate how actions get their effects and how observations provide their results:

$$\begin{aligned} & \forall W:\text{WORLD_COMP} \forall A:\text{ACTION} \forall I:\text{INFO_EL} \\ & \quad \text{input}(W)|\text{performing_in}(A, W) \wedge \text{internal}(W)|\text{has_effect}(A, I) \rightarrow \text{internal}(W)|\text{world_fact}(I) \\ & \forall W:\text{WORLD_COMP} \forall I:\text{INFO_EL} \\ & \quad \text{input}(W)|\text{observation_focus_in}(I, W) \wedge \text{internal}(W)|\text{world_fact}(I) \\ & \quad \rightarrow \text{output}(W)|\text{observation_result_from}(I, W) \\ & \forall W:\text{WORLD_COMP} \forall I:\text{INFO_EL} \\ & \quad \text{input}(W)|\text{observation_focus_in}(I, W) \wedge \text{internal}(W)|\text{world_fact}(\text{not}(I)) \\ & \quad \rightarrow \text{output}(W)|\text{observation_result_from}(\text{not}(I), W) \end{aligned}$$

5.2 Domain-Specific Temporal Rules

Domain-specific rules are both shown for the Medicine Box Agent and the Usage Support Agent.

Medicine Box Agent. The Medicine Box Agent has functionality concerning communication to both the patient and the Usage Support Agent. 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 Usage Support Agent. Formally:

```
internal(medicine_box_agent)|belief(medicine_taken_from_position(x_y_coordinate(X,Y))) ^
internal(medicine_box_agent)|belief(medicine_at_location(x_y_coordinate(X, Y), M)) ^
internal(medicine_box_agent)|belief(medicine_level(M, C)) ^
max_medicine_level(maxB) ^ dose(P) ^ C + P ≤ maxB
→0,0,1,1 output(medicine_box_agent)|communication_from_to(
    medicine_used(M), medicine_box_agent, usage_support_agent)
```

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.

```
internal(medicine_box_agent)|belief(medicine_taken_from_position(x_y_coordinate(X,Y))) ^
internal(medicine_box_agent)|belief(medicine_at_location(x_y_coordinate(X, Y), M)) ^
internal(medicine_box_agent)|belief(medicine_level(M, C)) ^
max_medicine_level(maxB) ^ dose(P) ^ C + P > maxB
→0,0,1,1 output(medicine_box_agent)|communication_from_to(
    sound_beep, medicine_box_agent, 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.

```
internal(medicine_box_agent)|belief(medicine_taken_from_position(x_y_coordinate(X,Y))) ^
internal(medicine_box_agent)|belief(medicine_at_location(x_y_coordinate(X, Y), M)) ^
internal(medicine_box_agent)|belief(medicine_level(M, C)) ^
max_medicine_level(maxB) ^ dose(P) ^ C + P > maxB
→0,0,1,1 output(medicine_box_agent)|communication_from_to(
    too_early_intake_intention, medicine_box_agent, usage_support_agent)
```

Usage Support Agent. The Usage Support Agent's functionality is described by three sets of temporal rules. First, the agent maintains a dynamic model for the concentration of medicine in the patient over time in the form of a *leads to* relation.

USA1: Maintain dynamic model

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

```
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)
```

In order to reason about the usage information, this information is interpreted (USA2), and stored in the database (USA3).

USA2: Interpret 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.

```

internal(usage_support_agent)|belief(medicine_used(M)) ^
internal(usage_support_agent)|belief(current_time(T))
→0,0,1,1
internal(usage_support_agent)|belief(last_recorded_usage(M, T)) ^
internal(usage_support_agent)|intention(store_usage(M, T))

```

USA3: 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.

```

internal(usage_support_agent)|intention(store_usage(M, T))
→0,0,1,1 output(usage_support_agent)|performing_in(store_usage(M, T), patient_database)

```

Finally, 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 (USA4). Second, in case the patient is too late with taking medicine, a different SMS is communicated, suggesting to take the medicine (USA5). Finally, when the patient does not respond to such SMSs, the doctor is informed by SMS (USA6).

USA4: 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.

```

internal(usage_support_agent)|belief(too_early_intake_intention)
→0,0,1,1
output(usage_support_agent)|communication_from_to(put_medicine_back_and_wait_for_signal,
usage_support_agent, patient_cell_phone)

```

USA5: 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.

```

internal(usage_support_agent)|belief(current_time(T3)) ^
internal(usage_support_agent)|belief(at(medicine_level(M, C), T3)) ^
min_medicine_level(minB) ^ C < minB ^
internal(usage_support_agent)|belief(last_recorded_usage(M, T)) ^
internal(usage_support_agent)|belief(last_recorded_patient_message_sent(M, T2)) ^
T2 < T ^ usage_effect_duration(UED) ^ T3 > T + UED
→0,0,1,1 output(usage_support_agent)|communication_from_to(
sms_take_medicine(M), usage_support_agent, patient_cell_phone)

```

USA6: 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 has been 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.

```

internal(usage_support_agent)|belief(last_recorded_patient_message_sent(M, T)) ^
internal(usage_support_agent)|belief(last_recorded_doctor_message_sent(M, T0)) ^
internal(usage_support_agent)|belief(last_recorded_usage(M, T2)) ^
internal(usage_support_agent)|belief(current_time(T3)) ^
T0 < T ^ T2 < T ^ max_delay_after_warning(DAW) ^ T3 > T + DAW
→0,0,1,1 output(usage_support_agent)|communication_from_to(sms_not_taken_medicine(M),
usage_support_agent, doctor_cell_phone)

```

6 Simulation Results

In order to show how the above presented system functions, the system has been implemented in a dedicated software environment that can execute such specifications [4]. To enable creation of simulations, a patient model is used that simulates the behaviour of the patient in a stochastic manner. The model specifies four possible behaviours of the patient, each with its own probability: (1) too early intake, (2) correct intake (on time), (3) responding to an SMS warning that medicine should be taken, and (4) responding to a doctor request by phone. Based upon such probabilities, the entire behaviour of the patient regarding medicine usage can be simulated. In the following simulations, values of respectively 0.1, 0.8, 0.9 and 1.0 have been used.

Figure 2 shows the medicine level over time in an example of a simulation trace as estimated by the agent based on its dynamic model. Here the x-axis represents time whereas the y-axis represents the medicine level. Note that in this case, the minimum level of medicine within the patient is set to 0.35 whereas the maximum level is 1.5. These numbers are based on the medicine half-life value, that can vary per type of medicine. In the trace in Figure 2, it can be seen that the patient initially takes medicine at the appropriate time, this is done by performing an action:

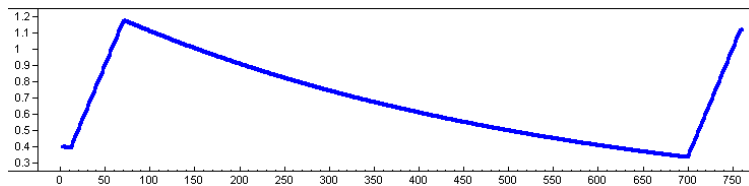


Fig. 2. Medicine level over time

```
output(patient)|performing_in(take_medicine_from_position(x,y_coordination(1,1)), medicine_box)
```

This information is stored in the patient database:

```
input(patient_database)|performing_in(store_usage(recorded_usage(hiv_slowers, 8)), patient_database)
```

Resulting from this medicine usage, the medicine level increases, as can be seen in Figure 3. In this simulation, the medicine takes 60 minutes to be fully absorbed by the patient. Just 240 minutes after taking this medicine, the patient again takes a pill from the medicine box. This is however too early, and as a result, the Medicine Box Agent communicates a warning beep, which is received by the patient:

```
input(patient)|communicated_from_to(sound_beep, medicine_box_agent, patient)
```

The patient does not take the medicine, and waits for an SMS, as the patient is instructed to do. The SMS is received a little while later, stating that the patient should wait with taking the medicine until a new message is sent.

```
input(patient)|communicated_from_to(put_medicine_back_and_wait_for_signal, patient_cell_phone, patient)
```

The patient awaits this message, which is sent after the medicine level is considered to be low enough such that medicine can be taken. The Usage Support Agent therefore communicates an SMS to the patient cell phone:

```
output(usage_support_agent)|communication_from_to(sms_take_medicine(hiv_slowers), usage_support_agent, patient_cell_phone)
```

This message is received by the patient:

```
input(patient)|communicated_from_to(sms_take_medicine(hiv_slowers), patient_cell_phone, patient)
```

The patient does however not respond to the SMS, and does not take its medicine. The usage support agent responds after 60 minutes, and sends an SMS to the doctor of the patient:

```
input(doctor)|communicated_from_to(sms_not_taken_medicine(hiv_slowers), usage_support_agent, doctor)
```

The doctor immediately calls the patient, and makes sure the patient understands that it is essential to take the medicine immediately. As a result, the patient takes the medicine:

```
output(patient)|performing_in(take_medicine_from_position(x_y_coordination(1,1)), medicine_box)
```

As can be seen in Figure 3, during the entire simulation the patient medicine level never exceeds the maximum level (1.6), and never goes below the minimum required level (0.35).

An example graph of the medicine level of a patient not using the support system presented in this section is shown in Figure 3. Note that this is a simulation over a longer time period (3000 minutes). As can be seen, the intake interval fluctuates a lot and the medicine level does not always stay above the desired level of 0.35.

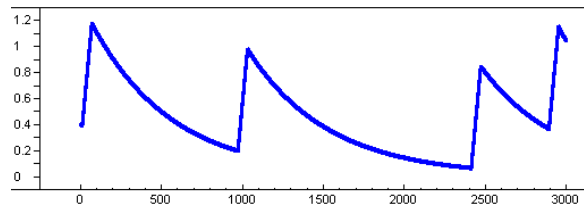


Fig. 3. Medicine level without support system

7 Discussion

In this paper, a multi-agent system model was presented that supports the users of medicine in taking their medicine at the appropriate time. The system has been specified using a formal modelling approach which enables the specification of both quantitative as well as qualitative aspects [10, 3]. To specify the model, both generic and domain specific temporal rules have been used, enabling reuse of the presented model. Evaluation of the model has been conducted by means of simulation runs using a stochastic model for patients. For a demonstration of how such results can be automatically verified, see [9].

The presented multi-agent system model fits well in the recent developments in Ambient Intelligence [1, 2, 13]. Furthermore, it also shows that multi-agent system technology can be of great benefit in health care applications, as also acknowledged in [12]. More approaches to support medicine usage of patients have been developed. Both in [12] as well as [7] models are presented that do not simply always send an SMS that medicine should be taken such as proposed by [14]. 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. Having such an explicit model enables the support agent to optimally support the patient. Evaluating the system using actual users is future work.

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