A Compositional Process Control Model and its Application to Biochemical Processes*

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Abstract. A compositional generic process control model is presented which has been applied to control enzymatic biochemical processes. The model has been designed at a conceptual and formal level using the compositional development method DESIRE, and includes processes for analysis, planning and simulation. It integrates qualitative and quantitative techniques. Its application to enzymatic chemical processes is described.

Keywords
Practical applications, reusable models, compositional, process control

1 Introduction

Process control is a task that has many application domains, like production processes in industry (e.g., chemical industry, car industry), any automated process that uses a conveyor belt or assembly-line, but also in hospitals (e.g., brain-scanners, intensive-care) and remote robot control (e.g., space shuttles, the docking of space-crafts, nuclear reactors, deep-sea exploratory vessels) for environments that are hostile for human beings or for situations in which humans are not capable of receiving and interpreting sensory information quickly enough to make the right decisions.

Applications for process control often are developed in an ad hoc manner, with no explicit specification at a conceptual level or built in facilities for reuse or verification. In this paper, a reusable model for process control is described which has been designed using the compositional development method DESIRE; see (Brazier, Jonker and Treur, 1998) for the underlying principles, and (Brazier, Dunin-Keplicz, Jennings and Treur, 1995) for an extensive case study. The model covers analysis of the current state (and history) and the possibility to simulate a possible plan before actually selecting and executing it.

The model is generic in two senses: it is generic with respect to the processes or tasks, and it is generic with respect to the information structures and knowledge. Genericity with respect to processes or tasks refers to the level of process abstraction: a generic model abstracts from processes at lower levels. A more specific model with respect to processes is a model within which a number of more specific processes, at a lower level of process abstraction are distinguished. This type of refinement is called *specialisation*. Genericity with respect to knowledge refers to levels of knowledge abstraction: a generic model abstracts from more

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specific information structures and knowledge. Refinement of a model with respect to the knowledge in specific domains of application, is refinement in which knowledge at a lower level of knowledge abstraction is explicitly included. This type of refinement is called *instantiation*. Reuse of such a generic model can take place by

- adding domain-specific information structures and knowledge (instantiation)
- adding more specific sub-processes within the processes defined by the generic model (specialisation)
- adding or deleting components (reconfiguration)

In addition to the possibility to reconfigure, also verification is supported by the compositional structure of the design.

The process control model presented has been reused in the domain of enzymatic reactions, in particular for penicillin production processes. The prototype implementation developed integrates qualitative methods acquired in the form of expert knowledge, and quantitative techniques (a numerical simulation model). In Section 2 the problem of process control is discussed, and the example domain of application addressed is presented. In Sections 3 through 5 the processes in the generic model are presented, together with their composition relation. In Section 6 the generic information types are presented. In Sections 7 and 8 it is shown how it has been instantiated by information structures and knowledge on the specific application domain.

2 Problem description: process control and biochemical production processes

For effective control of a process, a good understanding of the current situation of that process is vital. Furthermore, most often it is also important to have access to previous situations of the process, so that a prediction can be made of future situations of the process if no action is undertaken. Knowing, for instance, the previous four values of the temperature of a chemical process, makes it possible recognise that the temperature is rising. Using this knowledge, action can be undertaken to regulate the temperature at a stage before the situation gets out of hand. Thus it might be possible to prevent undesired situations. Furthermore, the process can be kept closer to an optimal situation. Process control can be used to keep the process within acceptable bounds, but also to optimize a process.

The two basic generic information elements for process control are observations and actions. Observation information (for example, acquired by sensors) is needed to assess the current situation. Based on the assessment of the situation (but also previous situations), actions must be performed to control the process.

Process control can be performed with or without *simulation* of the plans that are determined to control the process. For example, in environmental policy making it is essential to be able to simulate the effects of proposed plans to reduce the emission of polluting elements. The effect of environmental policies can often only be measured after years. By then, it might be too late to undo these effects. A simulation enables the policy makers to have a reasonable idea of the effects of a proposed plan before a definite choice for a policy is made.

2.1 Domain of application: enzymatic reactions

In chemical industry more and more production processes for medicins are based on enzymatic reactions. For example, benzylpenicillin is an antibiotic that is directly used as a medicin. It can be produced from 6-amino penicillin acid (6-APA) and phenyl acetate. Also, benzylpenicillin can be broken down to 6-amino penicillin acid and phenyl acetate. This is an interesting reaction as well, as 6-amino penicillin acid is a precursor voor several antibiotics. So, both benzylpenicillin and 6-amino penicillin acid are products that have commercial value. To give an impression: The company Gist Brocades produced in 1984 about 15-20 % of the world production of benzylpenicillin. The world production is about 12.500.000 kg a year. Biological processes take place in huge kettles of thousends of liters. In this application we restrict ourselves to the production of benzylpenicillin. The reaction is described by the following:

benzylpenicillin $\leftrightarrow$ 6-amino penicillin acid + phenyl acetate

The reaction is a balance reaction, where the balance is determined by the pH of the mixture. The reaction takes place in water until an equilibrium is reached at a certain pH, depending on the starting concentrations. Since it is an enzymatic reaction, the mixture needs to contain penicillin amidase for the reaction to take place.

To produce benzylpenicillin the mixture needs to contain the same amount of 6-APA as it contains phenyl acetate. Furthermore, the mixture must contain so much phenyl acetate that it has a pH-degree lower than 5. An example: if pH=4.4, then 88% of the 6-APA is transformed into benzylpenicillin. Because the mixture will contain less and less acetate by this reaction, the pH will rise (i.e., the mixture will become less acid). Therefore, if the production is to continue, the pH must be kept low, so phenyl acetate is to be added. Furthermore, if phenyl acetate is added, the same amount of 6-APA must be added as well.

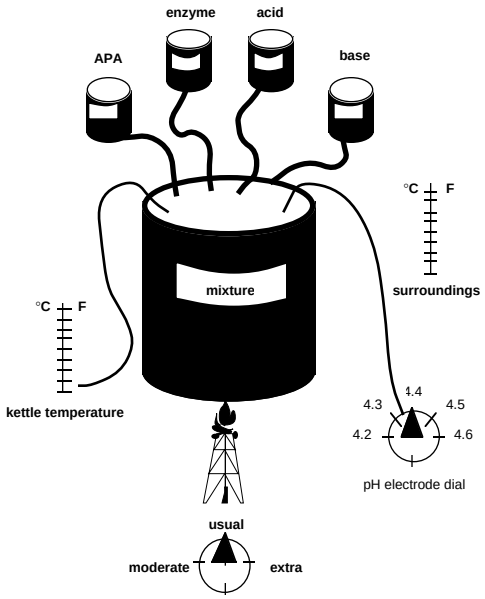

Figure 1 Formation

The enzyme is very sensitive to acids, it deteriorates rapidly if the pH drops below 4.3. Furthermore, the enzyme only functions good if the temperature is close to 25˚C.

To monitor and control the production process correctly, see Figure 1, there are two thermometers (one for the temperature in the kettle, and one for the temperature of the surroundings), one pH-electrode (to measure the pH in the kettle), a dial to set the heating of the kettle, four smaller kettles containing 6-APA, enzyme, acetate and sodium hydroxide (NaOH) respectively. The sodium hydroxide is a base, and can therefore be used to raise the pH if necessary. Each of these kettles can be made to release a standard amount of material.

2.2 The requirements

The process control system has to be able to analyse the state of a process in terms of the assessments specified for the domain of application. On the basis of these assessments the system is to determine a plan of actions with which the process is to be controlled. These plans must be tested first before being applied to the process in the external world. Therefore, the process control system has to contain a simulation of the world process.

The task of analysing (or monitoring) the process must be exercised on the process running in the external world as well as on the simulated process. The analysis has to be performed on the process in the real world in order to determine a plan for that process. The plan is tested on the simulation, and the simulation results have to be analysed in order to adapt the plan before executing it on the process in the external world. Depending on the domain of application it might be important to store information on observation results over time. Given that for complex processes observation might be costly and/or time consuming, the system has to determine when and which observations are to be performed both on the process in the external world as well as on the simulated process.

The task of determining which plan is to be executed depends entirely on the domain of application. For some domains it suffices if a plan consists of a selected number of actions that can be performed simultaneously, the results of executing such a plan become known quite quickly. In other domains of application (like environmental control) a plan has to be a long term plan consisting of sets of actions that have to executed after each other and pending the right circumstances.

The simulation of the process has to be quick enough so that the plan is still useful for the process in the real world. On the other hand it has to give a reasonable prognosis of the effect of the plan on the process running in the external world. A problem is that very accurate simulations are (often) time consuming. These two constraints have to be balanced within the process control system.

3 Process control processes at different levels of abstraction

Within the generic model the following levels of process abstraction are considered.

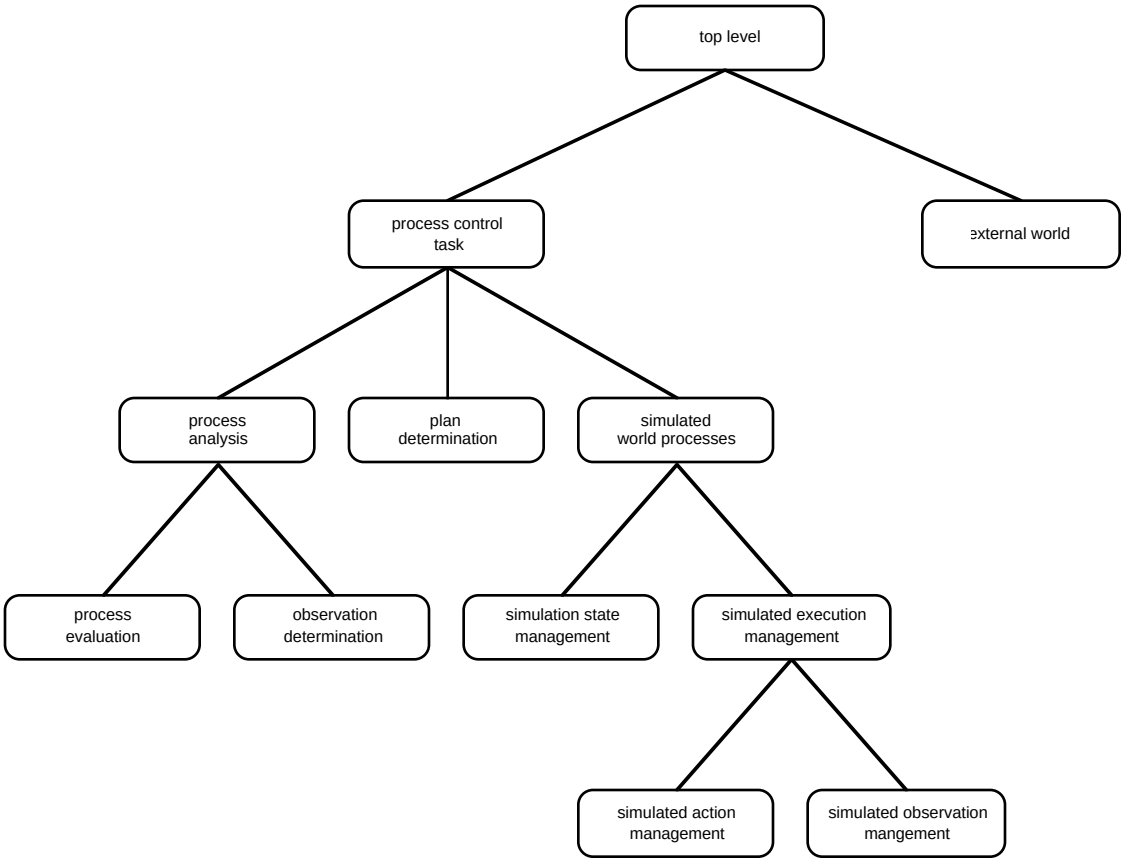

Figure 2 Levels of process abstraction

The information that can be obtained from observations using the sensors is modelled by the information type observation result info (in the example: observation information on temperature and pressure). The information type observation result info is used both in the output interface of the component external world and in the input interface of the component process control task.

process	*input information types*	*output information types*
process control task	observation result info	observation info action info
external world	observation info action info	observation result info

Figure 3 Interface information types: top level

The information types observation info and action info model information on the observations and actions to be performed in the external world. These information types are used in the output interface of process control task and the input interface of external world.

process	*input information types*	*output information types*
process analysis	observation result info simulation result info plan descriptions	assessments observation info simulation observation info
plan determination	assessments	plan descriptions action info simulation action info
simulated external world	simulation action info simulation observation info observation result info	simulation result info

Figure 4 Interface information types: process control task

Within the component process control task information types are defined that are used by its three internal components. The information type assessments is used in the output interface of the component process analysis and in the input interface of plan determination. Assessments represent information on the state of the process. The information type observation result info is used as an input of simulated external world to callibrate the simulation models used.

process	*input information types*	*output information types*
plan evaluation	observation result info simulation result info plan descriptions	assessments
observation determination	observation result info simulation result info plan descriptions	observation info simulation observation info

Figure 5 Interface information types: process analysis

Within simulated world two sub-processes are considered: simulated execution management, where the actual simulation steps are calculated, and simulation state management, where the simulated state is maintained and updated after each simulation step. The actual simulated observations are executed by this component, whereas the management of simulated observations (e.g., determing whether a simulated observation should only be performed once or continuously) is performed by simulated execution management. The execution of simulated actions (i.e., calculating their effects) is performed by simulated execution management.

process	*input information types*	*output information types*
simulated execution management	simulation action info simulation observation info observation result info	next simulation state description continuous simulation observation info incidental simulation observation info
simulation state management	current simulation state info continuous sim obs focus info incidental sim obs focus info	current simulation state

Figure 6 Interface information types: simulated external world

Note that two types of observations can be performed: *incidental observations* that return an observation result for only the current point in time, and *continuous observations* that continuously return all updated observation results as soon as changes in the world occur.

process	*input information types*	*output information types*
simulated action management	simulation action info	next simulation state description
simulated observation management	simulation observation info observation result info simulation result info	simulation result info continuous simulation observation info incidental simulation observation info

Figure 7 Interface information types: simulated execution managment

4 Process composition relation: information links

The process composition relation defines how the behaviour of a component emerges from the behaviours of its sub-components. The definition of a process composition relation consists of a static part (the information links) and a dynamic part (task control). Information links are discussed in two sections: all information links on the top level, and all information links within component process control task and all sub-components thereof.

4.1 Information links: top level

At the top level, two components are modelled, see Figure 8: process control task and external world. They interact with each other in a bidirectional manner. The information on observation results is transferred from the external world to the process control task by the link world observation information. The information on the observations and actions to be performed is transferred from the process control task to the world by the link selected actions and observations.

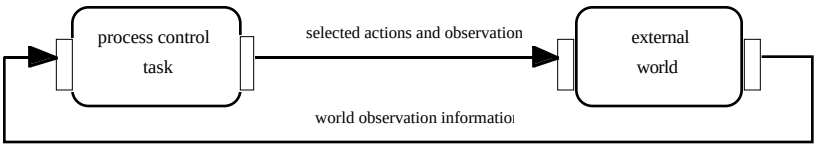

Figure 8 Information links: top level

4.2 Information links: process control task

The component process control task is composed of the components process analysis, simulated world processes, and plan determination, see Figure 9.

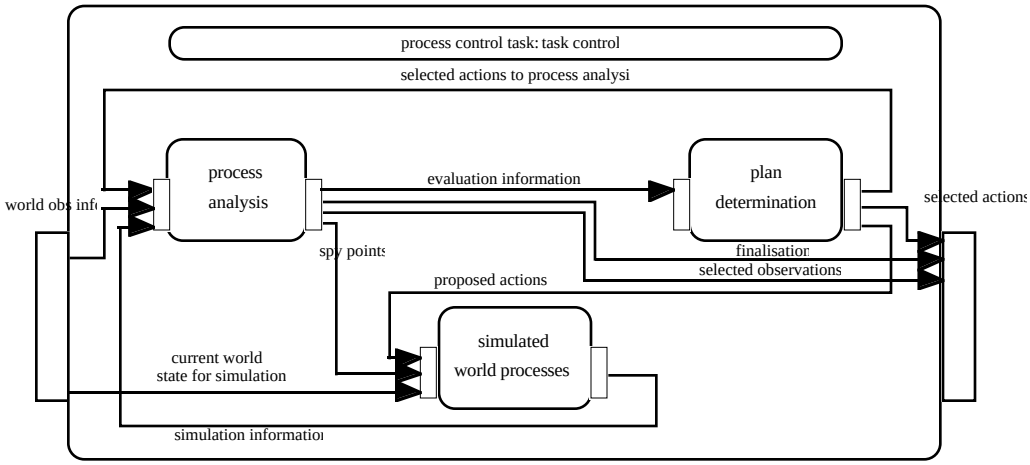

Figure 9 Information links: process control task

The component process analysis within the process control task is composed of two components: process evaluation and determine observations, see Figure 10.

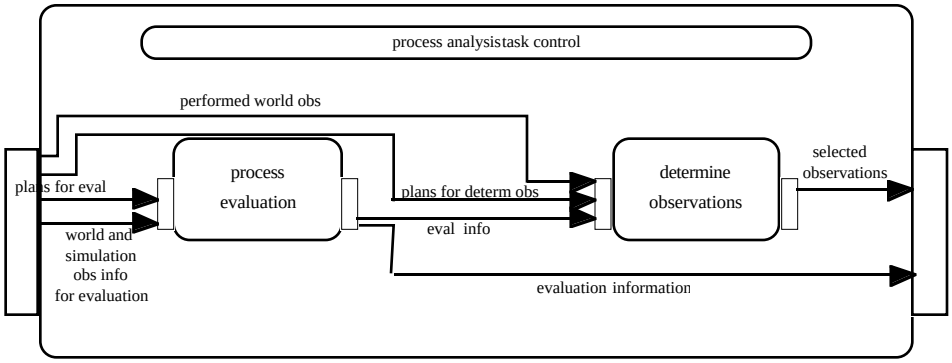

Figure 10 Information links: process analysis

The component simulated world processes within process control task is composed of two components: simulated execution management and simulation state management, see Figure 11.

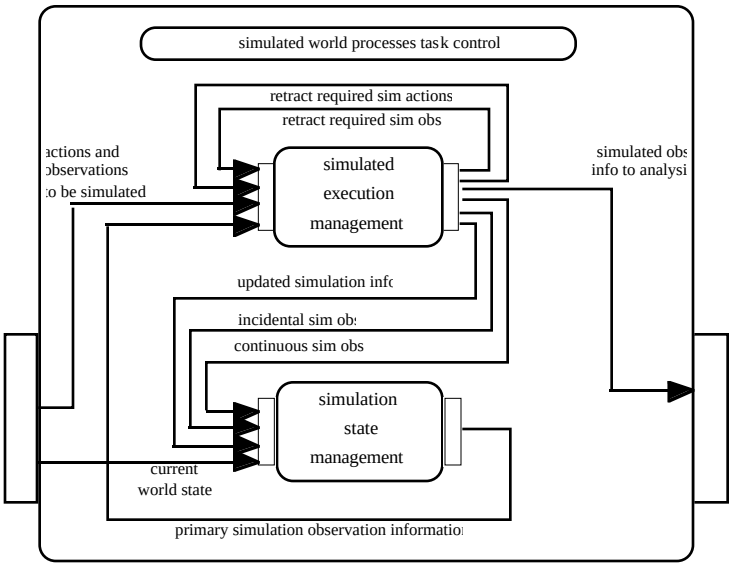

Figure 11 Information links: simulated world processes

The component simulated execution management is composed of two components: simulated observation management and simulated action management, see Figure 12.

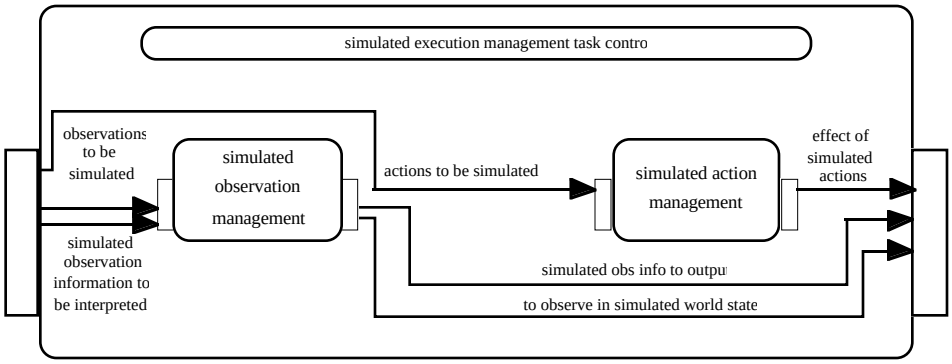

Figure 12 Information links: simulation management

5 Process composition relation: task control

Task control within the process control system is discussed globally. It is sketched when components are processing information.

5.1 Task control: top level

All processes and information links at the top level are awake, i.e., both the external world and the process control task process information as soon it arrives. This enables the process control task to interpret new observation result information as soon as possible. Furthermore, plans can be determined as quickly as possible, and long term effects can be predicted by use of the simulation task.

5.2 Task control: process control task

Within process control task a cycle of process activations takes place continuously. Each cycle starts with an activation of process analysis with task control focus analysis of current plans, that is, process analysis first checks the effects on the process running in the external world of the plan that is currently being executed and determines which incidental observations have to be performed. If this check is satisfactory, the simulation is activated, to give a prognosis of the rest of the current plan with respect to the last observation result information from the external world, after which a new cycle begins. If, however, the current plan is no longer satisfactory, component plan determination is activated with task control focus new plan. Component plan determination comes up with a new plan, sends it to the simulation and the analysis components. If plan determination finished determination of a new plan, process analysis is activated with task control focus pre-analysis new plan. Component process analysis determines which observations have to be performed on the simulation that are relevant for the new plan. Then the simulation is activated with the new plan and the latest observation results. Component simulated world processes provides simulation results after which component process analysis is activated again, but now with task control focus analysis new plan. Component process analysis check the new plan, if it is satisfactory it makes the new plan the current plan and allows it to be executed in the external world and a new cycle begins. If the check is unsatisfactory, component plan determination is activated with task control focus new plan, starting a new sub-cycle for the production of a satisfactory new plan. Information links are activated as relevant for the above cycle. However, the mediating information link world obs info to component process analysis is made awake to enable the component to react directly to the latest information (to be able to react to emergency situations at any time).

The processes within process analysis are activated in a row, first proces evaluation, then observation determination. All information links are awake. Components within simulated world processes are activated in a cycle as long as is necessary to provide the necessary simulation observation result information. The components within simulated execution management are awake during the activation period of their parent component.

6 Knowledge composition: generic information types

In this section the generic information types used in the process control model are briefly discussed. In Figure 3 the interface information types at the top level were named. Based on the *observation result information* the process controller is to decide which actions are to be performed. The process controller receives statements about what has been observed of the state of the process.The generic information type observation results is used to express observation result information, see Figure 13. The graphical representation form of information types is an extension of a variant of the conceptual graph representation language (Sowa, 1984). This representation format can be translated into order-sorted predicate logic.

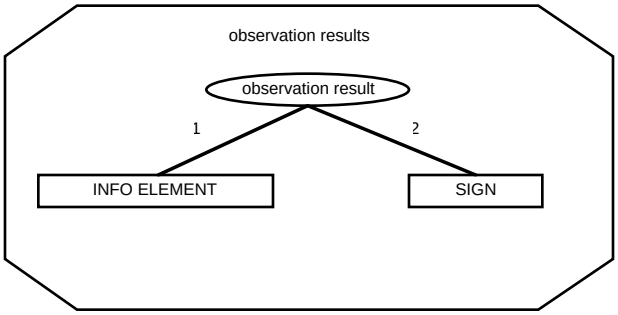

Figure 13 Generic information type: observation results

The aim is to be able to express statements like "the observation result is that it is true that the pressure is low" and "the observation result is that it is false that the pressure is high". The information type observation results includes the sorts INFO ELEMENT and SIGN. The sort SIGN is also specified in the information type truth indication. By referencing the information types truth indication and observation results within the information type observation result info the objects pos and neg are available in information type observation result info. Similarly, terms are needed of the sort INFO ELEMENT in order to express statements about statements in the language defined by the domain specific information type domain info. These terms are available in information type observation result info by referencing the information type domain meta-info. In the generic model the information type domain info remains empty. If the model is applied this information type is instantiated with domain-specific information structures.

The information type action info makes use of the generic nformation type actions to be performed and is meant to enable the reasoning about actions. In the information type actions to be performed the sort ACTION is introduced and the relation to be performed is added to be able to reason about actions, see Figure 14. This information type is generic; no reference is made to domain specific information types. The information type action info is composed of this generic information type and the domain specific information type domain actions. In the generic model this information type remains empty. If the model is applied, this information type is instantiated with the domain-specific action names. For example, the atom to_be_performed(add(enzyme)) refers to one of the actions used in the application domain addressed in Section 7.

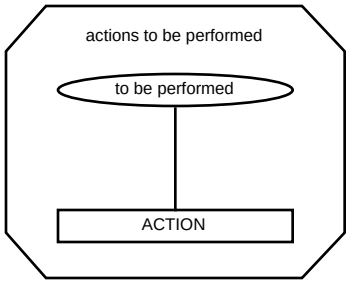

Figure 14 Generic information type: actions to be performed

Similarly the other information types, named in Figures 3, 4, 5, 6, 7 have been specified. For example, the information type assessments defines the relation assessment that is used to express output of the analysis process. For instances of the use of these generic information types in knowledge bases, see Section 7.

7 Application domain specific knowledge

In this section the relevant knowledge in the application domain of enzymatic reactions is described, and related to the generic model.

7.1 Domain specific knowledge used in analysis

In enzymatic reactions the following observations can be made:

- pH
- T, the (internal) kettle temperature
- Tlab, the temperature of the laboratory
- heater

Given this observation information from the component external world the task of the component process_analysis is to analyse the process. For the domain of benzylpenicillin a knowledge base has been acquired from the domain expert which provides assessments of the process in terms of:

- kettle temperature is too high
- kettle temperature is high, but not too high
- kettle temperature is optimal
- kettle temperature is too low
- kettle temperature is low, but not too low
- pH is too high
- pH is high, but not too high
- pH is optimal
- pH is too low
- pH is low, but not too low
- no enzyme in the mixture
- enzyme in the mixture
- no reaction is taking place
- reaction is taking place
- not enough 6-APA in the mixture
- enough 6-APA in the mixture

The following knowledge base (acquired from the domain expert) determines whether or not a reaction is taking place:

if observation_result(kettle_temp(too_high_kettle), pos) **then** assessment(kettle_temp_too_high)
and assessment(no_enzyme_present);

if observation_result(kettle_temp(too_low_kettle), pos) **then** assessment(kettle_temp_too_low)
and assessment(no_enzyme_present);

if observation_result(pH<4.3, pos) **then** assessment(no_enzyme_present)
and assessment(pH_too_low);

if assessment(no_enzyme_present) **then** assessment(no_reaction_going);

if observation_result(pH>4.6, pos) **then** assessment(no_reaction_going)
and assessment(pH_too_high);

if observation_result(pH=4.3, pos) **then** assessment(pH_low);

if observation_result(pH=4.4, pos) **then** assessment(pH_optimal);

if observation_result(pH=4.5, pos) **then** assessment(pH_high);

if observation_result(pH=4.6, pos) **then** assessment(pH_high);

if observation_result(kettle_temp(high_kettle), pos) **then** assessment(kettle_temp_high);

if observation_result(kettle_temp(normal_kettle), pos) **then** assessment(kettle_temp_optimal);

if observation_result(kettle_temp(low_kettle), pos) **then** assessment(kettle_temp_low);

if assessment(kettle_temp_optimal)
and assessment(pH_optimal)
and previous_assessment(no_enzyme_present)
and not previous_action(add(enzyme)) **then** assessment(no_enzyme_present);

if assessment(kettle_temp_optimal)
and assessment(pH_optimal)
and previous_assessment(no_enzyme_present)
and previous_action(add(enzyme)) **then** assessment(enzyme_present);

if previous_assessment(enzyme_present)
and not observation_result(kettle_temp(too_high_kettle))
and not observation_result(pH(less_than_4_3))
and previous_action(add(enzyme)) **then** assessment(enzyme_present);

if assessment(kettle_temp_optimal)
and assessment(pH_optimal)
and previous_assessment(enzyme_present)
and not previous_action(add(APA)) **then** assessment(no_reaction_going)
and assessment(APA_shortage);

7.2 Domain specific knowledge used in planning

The process can be influenced in the following manners:

- addition of: acid, base, 6-APA, or enzyme
- changing the heater.

Given the information from the component process_analysis the component plan_determination is to produce a plan to correct the process. For the domain of benzylpenicillin the component plan_determination can have to correct the following situations:

- kettle temperature above optimum but not too high
- kettle temperature too high
- kettle temperature below optimum but not too low
- kettle temperature too low
- pH above optimum but not too high
- pH too high
- pH below optimum but not too low
- pH too low
- no enzyme in the mixture
- no reaction is taking place
- not enough 6-APA in the mixture

The following table (acquired from the domain expert) represents the knowledge used for action selection (see next page).

reaction	enzyme	kettle temp	pH	action type			
				temp	pH	enzyme	apa
+	+	above optimum	above optimum	decrease	acid	naught	naught
			ok	decrease	naught	naught	naught
			below optimum	decrease	base	naught	naught
		ok	above optimum	nil	acid	naught	naught
			ok	nil	naught	naught	naught
			below optimum	nil	base	naught	naught
		below optimum	above optimum	increase	acid	naught	naught
			ok	increase	naught	naught	naught
			below optimum	increase	base	naught	naught
-	+	above optimum	above optimum	decrease	acid	naught	naught
			ok	decrease	naught	naught	naught
			below optimum	decrease	base	naught	naught
		ok	above optimum	nil	acid	naught	naught
			ok	nil	naught	naught	add
			below optimum	nil	base	naught	naught
		below optimum	above optimum	increase	acid	naught	naught
			ok	increase	naught	naught	naught
			below optimum	increase	base	naught	naught
-	-	above optimum	above optimum	decrease	acid	naught	naught
			ok	decrease	naught	naught	naught
			below optimum	decrease	base	naught	naught
		ok	above optimum	nil	acid	naught	naught
			ok	nil	naught	add	naught
			below optimum	nil	base	naught	naught
		below optimum	above optimum	increase	acid	naught	naught
			ok	increase	naught	naught	naught
			below optimum	increase	base	naught	naught

The combination reaction + and enzyme - is impossible.
Based on this table, the following knowledge base was specified.

knowledge base plan_determination_kb

if assessment(kettle_temp_too_high) **then** to_be_performed(set_temperature(moderate));

if assessment(kettle_temp_high) **then** to_be_performed(set_temperature(moderate));

if assessment(kettle_temp_too_low) **then** to_be_performed(set_temperature(extra));

if assessment(kettle_temp_low) **then** to_be_performed(set_temperature(extra));

if assessment(kettle_temp_optimal) **then** to_be_performed(set_temperature(usual));

if assessment(pH_too_high) **then** to_be_performed(add(acid));

if assessment(pH_high) **then** to_be_performed(add(acid));

if assessment(pH_too_low) **then** to_be_performed(pH, add_base);

if assessment(pH_low) **then** to_be_performed(add(base));

if assessment(pH_optimal) **then not** to_be_performed(add(base))
and not to_be_performed(add(acid)) ;

if assessment(reaction_going) **then not** to_be_performed(add(apa));

if assessment(enzyme_present) **then not** to_be_performed(add(enzyme));

if assessment(no_reaction_going)
and assessment(enzyme_present)
and not assessment(kettle_temp_optimal) **then not** to_be_performed(add(apa));

if assessment(no_reaction_going)
and assessment(enzyme_present)
and not assessment(pH_optimal) **then not** to_be_performed(add(apa));

if assessment(no_reaction_going)
and assessment(enzyme_present)
and assessment(pH_optimal)
and assessment(kettle_temp_optimal) **then** to_be_performed(add(apa));

if assessment(no_reaction_going)
and assessment(no_enzyme_present)
and not assessment(kettle_temp_optimal) **then not** to_be_performed(add(enzyme));

if assessment(no_reaction_going)
and assessment(no_enzyme_present)
and not assessment(pH_optimal) **then not** to_be_performed(add(enzyme));

if assessment(no_reaction_going)
and assessment(no_enzyme_present)
and assessment(pH_optimal)
and assessment(kettle_temp_optimal) **then** to_be_performed(add(enzyme));

8 The simulation model

In Figure 16 the enzymatic reaction for the production of benzylpenicillin is given.

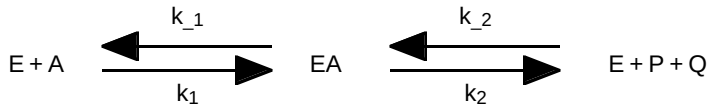

Figure 16 Enzymatic Reaction

Notation	*Entity*	*Measure*
E	enzym: penicillin amidase	mol / liter (concentration)
A	benzylpenicillin	mol / liter
EA	intermediate result	mol / liter
P	phenyl acetic acid	mol / liter
Q	6-APA	mol / liter
k	reaction rate constant	/ sec

From the reaction specification in Figure 16 it is clear that four reaction rate constants play a role. However, an additional deactivation rate constant k_3 plays a role, due to the deterioration of the enzyme according to temperature and pH.

For the computation of the concentration of the different substances in the solution, the following differential equations hold:

$$\frac{dc_A}{dt} = - k_1 c_E c_A + k_{-1} c_{EA}$$

$$\frac{dc_P}{dt} = - k_{-2} c_E c_P c_Q + k_2 c_{EA}$$

$$\frac{dc_Q}{dt} = - k_{-2} c_E c_P c_Q + k_2 c_{EA}$$

$$\frac{dc_{EA}}{dt} = k_1 c_E c_A - k_{-1} c_{EA} + k_{-2} c_E c_P c_Q - k_2 c_{EA}$$

$$\frac{dc_E}{dt} = -k_1 c_E c_A + k_{-1} c_{EA} - k_{-2} c_E c_P c_Q + k_2 c_{EA} - k_3 c_E$$

Figure 17 Differential equations

Make these differential equations discrete, the concentrations of the substances in the solution at time $t + dt$ (time in minutes) can be approximated by:

$$c_A(t + dt) = c_A(t) + (- k_1 c_E c_A + k_{-1} c_{EA})dt$$

$$c_P(t + dt) = c_P(t) + (- k_{-2} c_E c_P c_Q + k_2 c_{EA})dt$$

$$c_Q(t + dt) = c_Q(t) + (- k_{-2} c_E c_P c_Q + k_2 c_{EA})dt$$

$$c_{EA}(t + dt) = c_{EA}(t) + (k_1 c_E c_A - k_{-1} c_{EA} + k_{-2} c_E c_P c_Q - k_2 c_{EA})dt$$

$$c_E(t + dt) = c_E(t) + (-k_1 c_E c_A + k_{-1} c_{EA} - k_{-2} c_E c_P c_Q + k_2 c_{EA} - k_3 c_E)dt$$

where dt is the duration of 1 step measured in minutes.

Experimental results show that, if the temperature is between 5°C and 30°C, the reaction rate constants behave approximately linear with respect to temperature. The reaction rates are 0 at 0°C, as the mixture in the kettle then freezes. Therefore, we chose to use the following linear equations for the reaction rate constants:

$$k_1 = 0.04 * c * (T - 273)$$
$$k_{-1} = 5000 * c * (T - 273)$$
$$k_{-2} = 6 * c * (T - 273)$$
$$k_2 = 1 * c * (T - 273)$$

where the rates correspond to reaction rates per minute. Although it seems as if k_{-1} is much higher than the others, it's effect is less than that of k_{-2}. Both have more effect than k_1 and k_2, which is as one would hope if penicilline is to be produced.

The case i = 3 is special: the enzym deteriorates rapidly if the pH leaves the vicinity of 4.4 and if the temperature within the kettle rises above 25°C. This was modelled by:

$$k_3 = c \left(1 - \frac{1}{1 + z(pH - 4.4)^2} \right) + c \frac{1}{2} \left(1 + \frac{T - 303}{\sqrt{(1 + (T - 303)^2)}} \right)$$

The parameter z determines how fast the deterioration goes. For this application the value 25 for the parameter z was estimated.

The current pH is given by:

$$pH = - \log(\sqrt{(c_P 1.7 \times 10^{-5})})$$

Computing backwards from the optimum pH of 4.4, we see that then c_p should be 0.000093229 mol/liter. Since these are unpleasant figures to work with, we normalize the computation of pH in such a way that if we choose $c_p = 100$, then pH = 4.4:

$$pH = - \log(\sqrt{(0.00000093229 \times c_P \times 1.7 \times 10^{-5})})$$

The change in the kettle temperature T per dt depends on the temperature of the laboratory and the state of the heater:

$$\Delta T / dt = c * \beta * heater - c * \alpha * (T - Tlab)$$

In the current model we estimated β to be 300000, and α to be 50000.

The heater can have the following values: 1, 2, and 3. The temperature of the laboratory fluctuates, but is assumed to be somewhere between 10°C and 30°C.

9 Conclusions

The generic model for process control presented in this paper was designed on the basis of earlier experiences in the control of ship building processes (Brazier, Klerk, Langen and Treur, 1994). On the basis of the generic model, the application to the control of enzymatic reactions, in particular in antibiotics production was designed in a relatively short time; most of the effort was spent in building the simulation model. The application integrates qualitative methods (acquired from our domain expert) and quantitative techniques (the simulation model based on differential equations). The prototype implementation that was automatically created on the basis of the design, using the DESIRE software environment, has been tested in a simulated environment, but not yet in the real environment.

This project has shown that the generic model for process control indeed provides a strong form of reusability, and improves the efficiency of the development process of applications to a large extent. The generic and compositional nature of the process control model supports reusability of the model as a whole, but also of separate components within the model.

To prove that an application with this model works properly, the compositional verification method introduced in (Jonker and Treur, 1998) can be used, in a similar manner as how this has been done for a generic model of diagnosis; see (Cornelissen, Jonker and Treur, 1997). This compositional verification method relates dynamic properties of a system as a whole to properties of system components, and properties of components to sub-components, and so on. Finally the dynamics of the system as a whole can related to properties of the knowledge used to specify the primitive components, and environmental and domain assumptions. The formulation of these properties and the proofs of their relations can be performed in a generic manner. The generic and compositional structure of the model presented here provides an appropriate basis for this, in addition to existing techniques, for example in specification and verification of reactive systems; cf. (Manna and Pnueli, 1995; Pnueli, 1986). A difference of our approach with the references mentioned is that our model has a compositional structure over a number of process abstraction levels. Behavioural properties of the compositional process control model such as reactiveness and pro-activeness can also be studied in the context of intelligent agents; cf. (Jonker and Treur, 1998; Wooldrige and Jennings, 1995a,b).

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References

Brazier, F.M.T., Dunin-Keplicz, B., Jennings, N.R. and Treur, J. (1995). Formal specification of Multi-Agent Systems: a real-world case. In: V. Lesser (Ed.), *Proceedings of the First International Conference on Multi-Agent Systems, ICMAS-95*, MIT Press, Cambridge, MA, pp. 25-32. Extended version in: International Journal of Cooperative Information Systems, M. Huhns, M. Singh, (Eds.), Special issue on Formal Methods in Cooperative Information Systems: Multi-Agent Systems, vol. 6, 1997, pp. 67-94.

Brazier, F.M.T., Jonker, C.M., and Treur, J., Principles of Compositional Multi-agent System Development. In: J. Cuena (ed.), Proceedings of the 15th IFIP World Computer Congress, WCC'98, Conference on Information Technology and Knowledge Systems, IT&KNOWS'98, 1998, pp. 347-360.

Cornelissen, F., Jonker, C.M., Treur, J. (1997). Compositional verification of knowledge-based systems: a case study in diagnostic reasoning. In: E. Plaza, R. Benjamins (eds.), *Knowledge Acquisition, Modelling and Management, Proceedings of the 10th EKAW'97*, Lecture Notes in AI, vol. 1319, Springer Verlag, pp. 65-80.

Jonker, C.M., Treur, J. (1997). Compositional Verification of Multi-Agent Systems: a Formal Analysis of Pro-activeness and Reactiveness. In: W.P. de Roever, H. Langmaack, A. Pnueli (eds.), *Proceedings of the International Workshop on Compositionality, COMPOS'97* . Lecture Notes in Computer Science, vol. 1536, Springer Verlag, 1998pp. 350-380.

Manna, Z., Pnueli, A., Temporal Verification of Reactive Systems: Safety. Springer Verlag, Berlin, 1995.

Pnueli, A., (1986), Specification and Development of Reactive Systems. In: *Information Processing* 86, Elsevier/North-Holland.

Sowa, J. (1984). *Conceptual structures: Information Processing in Mind and Machine.* Addison-Wesley, Reading, Mass.

Wooldridge, M., Jennings, N.R. (eds.) (1995a) *Intelligent Agents*, Lecture Notes in Artificial Intelligence, Vol. 890, Springer Verlag, Berlin

Wooldridge, M., Jennings, N.R. (1995b) Agent theories, architectures, and languages: a survey. In: (Wooldridge and Jennings, 1995a), pp. 1-39.