Organisation Modelling for the Dynamics of Complex Biological Processes

Tibor Bosse, Catholijn M. Jonker, Jan Treur

Vrije Universiteit Amsterdam, Department of Artificial Intelligence
De Boelelaan 1081a, 1081 HV Amsterdam, The Netherlands
Email: {tbosse, jonker, treur}@cs.vu.nl URL: http://www.cs.vu.nl/~{tbosse, jonker, treur}

Abstract. This paper shows how an organisation modelling approach can be used to model the dynamics of biological organisation, in particular the circulatory system in biological organisms (mammals). This system consists of a number of components that are connected and grouped together. Dynamic properties at different levels of aggregation of this organisation model have been identified, and interlevel relationships between these dynamic properties at different aggregation levels were made explicit. Based on the executable properties simulation has been performed and properties have been checked for the produced simulation traces. Thus the logical relationships between properties at different aggregation levels have been verified. Moreover, relationships between roles within the organisation model and realisers of these roles have been defined. This case study shows that within biological and medical domains organisation modelling techniques can play a useful role in modelling complex systems at a high level of abstraction.

1 Introduction

In biological systems often many complex distributed interacting processes take place, that together result in some form of coherent joint action. Examples of such biological systems are mammals, insect colonies and bacteria. During evolution, Nature has developed several forms of organisational structure; typical examples are the organisation of a beehive, the coordinated processes of organs in mammals, and the well-organised regulated biochemistry of a living cell. Usually such biological systems are addressed by modelling the underlying physical/chemical processes by mathematical and system theoretical techniques, for example sets of differential equations; e.g., [26]. For some small unicellular organisms, a few isolated chemical pathways are understood in sufficient kinetic detail to obtain a description (by differential equations) of their import and primary processing of nutrients; e.g., in *Escherichia coli* [22], [24], or yeast [21]. However, even if all details would be available, at best this approach provides a description that is inherently low-level and complex. The adequacy of such mathematical techniques addressing the underlying physical/chemical level can be questioned. Such approaches do not exploit the apparent organisational structure that can be identified at a conceptual level within the biological systems addressed; the types of techniques often used are not tuned to modelling at such a conceptual level of the organisation of the distributed interacting processes.

In the area of organisation modelling, to handle complex distributed dynamics of the interaction between multiple agents in human society, often some type of organisational structure is exploited. The dynamics that emerge from multiple interacting agents within human society has been studied within Social Sciences in

the area of Organisation Theory (e.g., [12], [13], [17], [19]) and within Artificial Intelligence in the area of Agent Systems (e.g., [2], [25]). To manage complex, decentralised dynamics in human society, organisational structure is a crucial element: organisation provides a structuring and co-ordination of the processes in such a manner that a process or agent involved can function in a more adequate manner. The dynamics shown by a given organisational structure is much more dependable than in an entirely unstructured situation. To exploit such organisational structures in a society particularly in modelling of these processes, within the agent systems area a number of conceptual modelling approaches have been developed, where a specific form of organisational structure is taken as a central concept. One of the recently developed organisational modelling approaches is the Agent/Group/Role (AGR) approach introduced in [3], extended with operational semantics in [4], and with a specification language for dynamic properties in [5].

Like in human societies, as discussed above, many biological systems take the form of complex organised distributed interacting processes. Therefore a natural research question addressed in this paper is whether organisational modelling techniques provide adequate means to model such biological systems at a conceptual-organisational level. If such an approach succeeds, it may be expected that it results in models of a much higher level than those addressing the biological processes at the level of their physiology or chemistry. A relating hypothesis is that such higher-level models can be simulated and analysed much more easily than the more complex mathematical models. These are the issues addressed in this paper. To explore these issues, in a rather arbitrary manner one specific available organisation modelling framework has been chosen and one specific organised biological phenomenon on which this organisation modelling framework was applied.

The chosen organisation modelling framework is the one described in [10], addressing both analysis and simulation of AGR-models, and supported by a software environment; a formal foundation can be found in [10]. This dynamic modelling environment allows to

- specify dynamic properties for the different elements and levels of aggregation within an AGR organisation model
- relate these dynamic properties to each other according to the organisational structure
- use dynamic properties in executable form as a declarative specification of a simulation model and perform simulation experiments
- automatically check dynamic properties for simulated or empirical traces

The goal of this paper is, in particular, to illustrate how this dynamic modelling framework for organisations, whilst being a conceptual approach, can also be used to model complex organised dynamics in biological systems involving several interacting processes.

The chosen case study for such a biological system, concerns the most primary dynamics of the circulatory system in biological organisms (mammals in particular). This biological system shows sufficient complexity to be an interesting challenge. In the literature, many different kinds of cardiovascular (CV) models exist, typically based on modelling the physiology by differential equations. The first modern CV models were based on the *Windkessel* theory (the idea that arterial elasticity has a buffering effect on the pulsatile nature of blood flow), e.g. [16], [18], [20]. Another modern approach, that is influential in CV modelling today, makes use of hydrodynamic pulse-wave models [6], [10], [16], [18]. Furthermore, a distinction can

be made between so-called transmission line models [27], segmental models [7], [15], [23], [28] and hybrid models. What all these approaches have in common is that they use rather complex models based on differential equations at the level of detailed physiology to describe the dynamics of this system.

In contrast, the current paper shows that the organisation modelling approach, although initially meant for purely social systems, provides adequate models in this type of application area as well. Realisers of roles within such an organisation models are active components of the biological system. As a result, this kind of biological organisations can also be considered in a way as (pseudo-)social systems, especially in the sense that the processes involved within these active components have to co-operate in a well-organised manner in order to produce the desired or required behavior for the overall system.

In Section 2 a brief introduction of the AGR organisation modelling approach can be found and illustrated for the context of the circulatory system. In Section 3 the dynamic properties at different levels of aggregation of this organisation model are identified. In Section 4 the relationships between these dynamic properties at different levels are presented. Section 5 describes how part of the dynamic properties can be used to enable a simulation of the circulatory system. In Section 6 the remaining properties are validated against the simulation of Section 5. Finally, Section 7 provides a description of how specific agents can be allocated to roles within the AGR approach.

2 The Organisation Structure of the Circulatory System

This section presents the organisation structure for the biological case study undertaken to investigate the usefulness of the AGR multi-agent organisation modelling approach to biological systems: the circulatory system in mammals. After a description of the functioning of the circulatory system, the AGR approach is briefly introduced. Next, the approach is applied to the circulatory system by identifying the organisational structure, expressed by AGR in terms of roles, groups, and interactions between these elements, and the agents realising these roles.

2.1 The Circulatory System

The circulatory system takes care for a number of capacities, such as providing nutrients and oxygen to the body and taking wastes (e.g., CO_2) out of the body; e.g., [18], [20]. The main property to focus on in this example is that the system provides oxygen for all parts of the body. The organisation of the circulatory system S is analysed as consisting of the following active components (or agents) that by showing their reactive and pro-active behavior all play their roles within the overall process:

- heart
- capillaries in lungs and other organs
- arteries
  - pulmonary artery channels (from the heart to the capillaries in the lungs)
  - aorta channels (from heart to the capillaries in the body)
- veins

- pulmonary veins (from the capillaries in the lungs to the heart)
- inferior and superior vena cava (from the capillaries in the body to the heart)

These active components work together due to some structure, as schematically depicted in Figure 1. Note that Figure 1 only describes the material structure of the circulatory system; the components depicted are physical components. Such pictures do not account for the role that the different physical components play in the organised process as a whole. For example the similarity in roles of the components in the systemic cycle (left hand side) and in the pulmonary cycle (right hand side) are not made precise. To clarify such functional and organisational aspects and similarities, the organisational structure will be described in the next subsections.

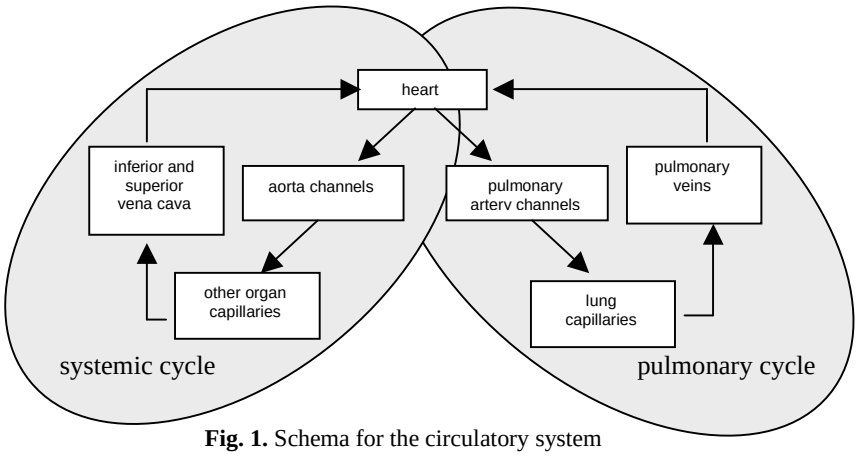

Fig. 1. Schema for the circulatory system

2.2 AGR Organisational Structures

To model an organisation, the Agent/Group/Role (AGR) approach, adopted from [3] is used. The *organisational structure* is the specification of a specific multi-agent organisation based on a definition of groups, roles and their relationships within the organisation:

- An organisation as a whole is composed of a number of *groups*.
- A group structure identifies the *roles* and (*intragroup*) *interaction between roles*, and *transfers* between roles needed for such interactions.
- In addition, *intergroup* role relations between roles of different groups specify the connectivity of groups within an organisation.

The modelling approach is further explained and illustrated by the application to the circulatory system in mammals.

2.3 Groups and Roles within the Circulatory System

The left-hand side and the right-hand side of the picture in Figure 1 are organised according to a similar structure:

- The *heart* initiates the flow,
- which is led by (aorta, resp. pulmonary artery) *arteries* or *channels* to
- *organs* (lung, resp. other organs) where exchange takes place,
- from where the flow is led by (pulmonary, resp. inferior and superior vena cava) *veins*
- back to the *heart.*

Here, in each of the two sides the heart plays two roles, one of a well, initiating the flow, and one of a drain, where the flow disappears (and will re-appear in the other side).

The similarity of the two parts of the circulatory system enables to model their common structure in an abstract manner in the form of a more generic *group structure* G which has two instantiations within the circulatory system: one for the left hand side (called *systemic cycle*, used for oxygen supply, among others), and one for the right hand side (called *pulmonary cycle*, used for oxygen uptake, among others). Modelling the system from this perspective provides several advantages over the material perspective shown in Figure 1. For instance, the possibility to describe both main cycles by a single, generic group structure allows us to identify certain similarities between the two cycles. Moreover, such generic structures could enable comparative studies with systems in other organisms than mammals.

Generic Group Structure G

The generic group structure G (see Figure 2) consists of the following five *roles*: *well, supply guidance, exchange, drain guidance, drain.*

Transfers and intragroup role interactions within G

The transfers underlying the interactions between roles are depicted in Figure 2. A short explanation of these interactions is as follows:

well – supply guidance role interaction

If the well comes up with a new flow, then this flow will be picked up by the supply guidance, and transported further.

supply guidance – exchange role interaction

If the supply guidance delivers a flow, then the exchange role will take out substances from this flow and will insert other substances in the flow.

exchange – drain guidance role interaction

The flow resulting from the exchange will be picked up by and transported by the drain guidance.

drain guidance – drain role interaction

If the drain guidance delivers a flow, then this is picked up by the drain (which lets it disappear).

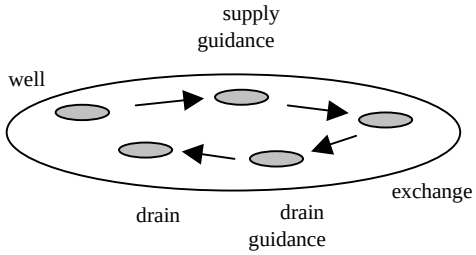

Fig. 2. Roles and transfers within the generic group structure G

Group instances and role instances

Two instances of the generic group structure G are used: the *pulmonary cycle group instance* G_p and the *systemic cycle group instance* G_s. Based on the generic group structure G, for each of the group instances different role instances are defined. These role instances are denoted by using the group instance name as a prefix; i.e., the role instances *systemic cycle well*, *systemic cycle supply guidance*, *systemic cycle exchange*, *systemic cycle drain guidance*, *systemic cycle drain* within the systemic cycle group instance, and similar for the pulmonary group instance.

Allocation of agents to role instances

The relation between Figure 2 and Figure 1 is such that to each role instance depicted in Figure 2, a specific agent is allocated in Figure 1. This is the case for both the pulmonary cycle group instance and the systemic cycle group instance. In particular, for the systemic cycle group instance the allocation of agents to role instances is as follows:

heart	- systemic cycle well
aorta channels	- systemic cycle supply guidance
organ capillaries	- systemic cycle exchange
inferior and superior vena cava	- systemic cycle drain guidance
heart	- systemic cycle drain

For the pulmonary cycle group instance the allocation of agents to role instances is as follows:

heart	- pulmonary cycle well
pulmonary channels	- pulmonary cycle supply guidance
lung capillaries	- pulmonary cycle exchange
pulmonary veins	- pulmonary cycle drain guidance
heart	- pulmonary cycle drain

The allocation of agents to role instances is discussed in more detail in Section 7.

2.4 Connectivity between groups: intergroup role interactions

The connectivity between the groups within the organisation structure is realised by two intergroup role interactions: from the drain role instance within one group to the well role instance in the other group, in both directions; see Figure 3.

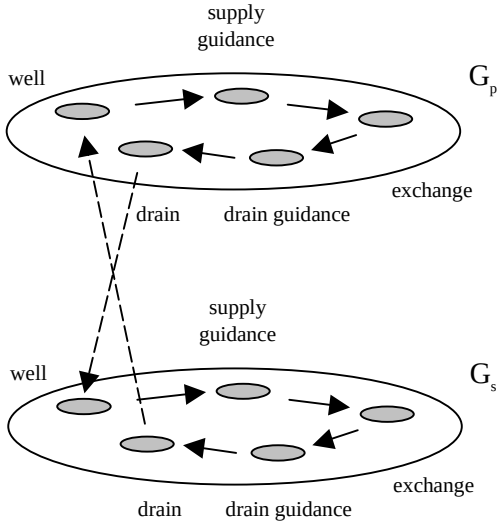

Fig. 3. Intergroup role interactions

In a generic sense such an intergroup role interaction can be explained by stating that the flow taken out by the drain role instance in one group instance is supplied within the other group instance by the well role instance. For the two group instances in the example these interactions are briefly explained as follows.

- *pulmonary cycle drain – systemic cycle well role interaction*
  The oxygen-rich blood flow taken out by the pulmonary cycle drain role instance within the pulmonary cycle group instance is supplied to the systemic cycle well role instance within the systemic cycle group instance
- *systemic cycle drain – pulmonary cycle well role interaction*
  The oxygen-poor blood flow taken out by the systemic cycle drain role instance within the systemic cycle group instance is supplied to the pulmonary cycle well role instance within the pulmonary cycle group instance

3 Dynamic Properties at Different Levels within the Organisation

To describe the functioning of the circulatory system S as an organisation, the following types of dynamic properties can be used (in the paper limited to properties related to oxygen supply which is a core function of the circulatory system):

- dynamic properties of the organisation as a whole

- dynamic properties for groups and intergroup role interactions
- properties of roles, transfer properties and intragroup role interactions within a group.

Moreover, usually some environmental assumptions are needed. The argument "s" when appearing in the name of a property refers to the instance of that property suitable for the systemic cycle group, similarly the argument "p" refers to the pulmonary cycle group.

3.1 Environment Assumptions

For the circulatory system S two reasonable environmental assumptions are:

EA1 **Oxygen availability**
At any point in time oxygen is present in the lungs

EA2(i) **Stimulus occurrence (with maximal interval i)**
For any point in time t there exists a time point with $t < t' \leq t + i$ such that at t' a stimulus occurs.

3.2 Dynamic Properties of the Organisation as a Whole

Global properties can be expressed for proper functioning of the flow through the cycles (taken at the well), and for resulting oxygen provision through the capillaries.

GP1(w) **Well successfulness (with maximal interval w)**
After an initiation time t0, for any point t there exists a time point t' with $t < t' \leq t + w$ such that at t' a fluid with ingredients I is generated by the well.

Here I is a specification of ingredients, for example by a list of them, possibly with indications of concentrations.

Note that this global property depends on the organisation as a whole, not only on the group of the well. This property can be instantiated both for the well within the pulmonary cycle group ($GP1(p, w_p)$), and for the well within the systemic cycle group ($GP1(s, w_s)$).

GP2(d) **Oxygen delivery successfulness (with maximal interval d)**
After an initiation time t0, for any point t there exists a time point t' with $t < t' \leq t + d$ such that at t' by exchange oxygen is delivered to the organs.

3.3 Intergroup Role Interaction Properties

Intergroup role interaction properties relate roles in different groups. They typically express a dynamic relation between the input of one role in one group to the output of another role in another group. For the organisation of the circulatory system S consisting of two group instances as depicted in Figure 3 the following intergroup role interaction property has been specified. Again, this property can be instantiated both

for the well within the pulmonary cycle group (IrRI(p, c_p, r_p)), and for the well within the systemic cycle group (IrRI(s, c_s, r_s)).

IrRI(c, r) **Drain– well intergroup role interaction**

At any point in time t0
- if at some $t \leq t0$ the drain within some group instance G_i received a fluid volume V with ingredients I
- and between t and t0 no stimulus occurred
- and at t0 a stimulus occurs
- then there exists a time point t1 with $t0 + c \leq t1 \leq t0 + r$ such that at t1 the well within the other group instance G_j generates a fluid volume V with ingredients I

3.4 Dynamic Properties of Groups

Within an overall organisation, each group's contribution can be formulated in the form of some group property. An example of such a group property is the following.

GR(u, v, u', v') **Group successfulness**

At any point in time t,
- if at t the well generates a fluid volume V with ingredients I
- then there exist time points $t' \leq t''$ with $t + u \leq t' \leq t + v$ and $t + u' \leq t'' \leq t + v'$ such that at t' ingredient A is added to the environment and ingredient B taken from the environment
- and at t'' the drain receives a fluid volume V with ingredients I - A + B

Here V is an amount of fluid and I is a specification of ingredients, as before. The notation I - A + B is used for the specification of the ingredients of I except A and augmented by B. The group specific property instances according to group instances are called GR(s, u_s, v_s, u'_s, v'_s) and GR(p, u_p, v_p, u'_p, v'_p). For the pulmonary group instance GR(p) the air is environment, A is carbonacid, and B is oxygen, for the systemic group instance GR(s) the environment is formed by the organs of the body, A is oxygen, and B is carbonacid. The difference in meaning of A and B for instantiations according to group instances is valid in other properties as well.

The dynamic properties of the different groups and of their interactions modelled by intergroup role interactions, contribute to the overall properties of S.

As discussed in [5], some dynamic group properties have a specific form in that they relate one role in the group to another role in the group. The two types of such properties that are relevant (transfer properties and intragroup role interaction properties) are discussed in the following section.

3.5 Transfer and Intragroup Role Interaction Properties

Intragroup role interaction properties characterise how roles (have to) interact. They typically relate the output of one role to the output of another role. This is slightly more abstract than role behavior and transfer properties.

IaRI(a1, b1) **Well implies supply guidance**

At any point in time t
if the well generates a fluid volume V with ingredients I
then there exists a time point t' with $t + a1 \leq t' \leq t + b1$ such that at t'
the supply guidance generates a fluid volume V with ingredients I

IaRI2(a2, b2) Supply guidance implies exchange

At any point in time t
if the supply guidance generates a fluid volume V with ingredients I
then there exists a time point t' with $t + a2 \leq t' \leq t + b2$ such that at t'
ingredient A is added to the object and ingredient B taken from the object
and the exchange generates a fluid volume V with ingredients I - A + B

IaRI3(a3, b3) Exchange implies drain guidance

At any point in time t
if the exchange generates a fluid volume V with ingredients J
then there exists a time point t' with $t + a3 \leq t' \leq t + b3$ such that at t'
the drain guidance generates a fluid volume V with ingredients J

Transfer properties express that the different roles are connected in an appropriate manner to enable proper interaction. For each of the four arrows in Figure 3 a transfer property expresses that the proper connection exists between the output of one role and the input of the other role. In a general form delays can be taken into account for the transfers. However, for this example, these delays for transfers are assumed to be 0 (input state property is assumed identical to previous output state property), i.e., all gi's and hi's are 0.

TR1(g1, h1) Well connects to supply guidance

At any point in time t
if the well generates a fluid volume V with ingredients I
then there exists a time point t' with $t + g1 \leq t' \leq t + h1$ such that at t'
the supply guidance receives a fluid volume V with ingredients I

This property is not fulfilled, for example, if the well opening is not connected to the supply guidance, so that the generated fluid volume streams away in the environment without reaching the supply guidance.

TR2(g2, h2) Supply guidance connects to exchange

At any point in time t
if the supply guidance generates a fluid volume V with ingredients I
then there exists a time point t' with $t + g2 \leq t' \leq t + h2$ such that at t'
the exchange receives a fluid volume V with ingredients I

TR3(g3, h3) Exchange connects to drain guidance

At any point in time t
if the exchange generates a fluid volume V with ingredients I
then there exists a time point t' with $t + g3 \leq t' \leq t + h3$ such that at t'
the drain guidance receives a fluid volume V with ingredients I

TR4(g4, h4) Drain guidance connects to drain

At any point in time t

if the drain guidance generates a fluid volume V with ingredients I
then there exists a time point t' with $t + g4 \leq t' \leq t + h4$ such that at t'
the drain receives a fluid volume V with ingredients I

3.6 Role Behavior Properties

Role behavior properties abstract from the specific agent allocated to a role, but characterise which behavior an agent fulfilling this role needs to have. Such properties typically relate the input of a role to the output of the same role.

supply guidance behavior

The arteries contribute in transportation. This means that that if their input receives blood, then their output generates blood with the same ingredients.

RB1(e1, f1) Supply guidance effectiveness
At any point in time t
if the supply guidance receives a fluid volume V with ingredients I
then there exists a time point t' with $t + e1 \leq t' \leq t + f1$ such that at t'
it generates a fluid volume V with ingredients I

exchange behavior

RB2(e2, f2) Exchange effectiveness
At any point in time t
if the exchange receives a fluid volume V with ingredients I
then there exists a time point t' with $t + e2 \leq t' \leq t + f2$ such that at t'
ingredient A is added to the object (environment, i.e., lung or organ)
and ingredient B is taken from the object
and it generates a fluid volume V with ingredients I - A + B

drain guidance behavior

RB3(e3, f3) Drain guidance effectiveness
At any point in time t
if the drain guidance receives a fluid volume V with ingredients I
then there exists a time point t' with $t + e3 \leq t' \leq t + f3$ such that at t'
it generates a fluid volume V with ingredients I

4 Relationships between Dynamic Properties at Different Levels

The idea is that dynamics of the whole organised (multi-agent) system is generated by lower level properties, in particular by the group properties and intergroup interaction properties. In turn, group dynamics is generated by role behavior and transfer within a group. This is elaborated in more detail by identifying logical relationships between these dynamic properties.

4.1 Overall Properties: Oxygen Delivery Successfulness

The global property GP2 (oxygen delivery successfulness) depends on the systemic cycle instance of global property GP1 (well successfulness), assuming proper group functioning of the same group instance. To be more precise, the following relationship holds:

$$GP1(s, w) \;\&\; GR(s, u_s, v_s, u'_s, v'_s) \;\Rightarrow\; GP2(d)$$

with $d = w + v_s$.

So property GP2(d) is implied by two other properties, i.e., GP1(s, w) and GR(s, u_s, v_s, u'_s, v'_s). This implication are depicted in Figure 4. A sketch of a proof of this implication is as follows. Suppose GP1(s, w) holds. Then, after an initiation time t0, for any point t there exists a time point t' with $t < t' \leq t + w$ such that at t' a fluid with ingredients I is generated by the well of the systemic cycle. And if GR(s, u_s, v_s, u'_s, v'_s) holds as well, this means that the systemic cycle works correctly. Thus, from the fluid generated by the well, oxygen is finally taken and delivered to the organs. It can be concluded that after an initiation time t0, for any point t there exists a time point t' with $t < t' \leq t + d$ such that at t' by exchange oxygen is delivered to the organs, which is exactly what GP2(d) states. Furthermore, it is known that w is the maximum time interval for fluid generation by the well, and v_s is the maximum time interval for oxygen supply by the systemic cycle. Hence, it follows logically that $d = w + v_s$.

The relationships that GP1(s, w) and GR(s, u_s, v_s, u'_s, v'_s) have with other properties are depicted in Figures 5 and 6.

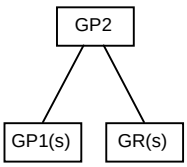

Fig. 4. Oxygen delivery successfulness related to global property GP1(s) and a group property.

4.2 Overall Properties: Well Successfulness

Well successfulness depends on proper functioning of the whole cycle; it needs as input that a fluid volume is received. If the whole cycle functions well, the group properties, intergroup role interaction properties, and environmental assumption EA2 guarantee that this well functioning is maintained. However, the process needs a starting point. This starting point is assumed for the well within both groups at time point t = 0 in the following form:

Init(w_{init}) **Well initialisation**

There exists a time point t with $0 \leq t \leq w_{init}$ such that at t
the well in the pulmonary group instance generates a fluid volume V with any ingredients I
and the well in the systemic group instance generates a fluid volume V'

with any ingredients I'

Using these properties the following relationships can be established (see also Figure 5).

$Init(w_{init})$ & $GR(s, u_s,v_s,u'_s,v'_s)$ & $GR(p, u_p,v_p,u'_p,v'_p)$ & $IrRI(s, c_s,r_s)$ & $IrRI(p, c_p,r_p)$ & $EA2(i) \Rightarrow GP1(s, w_s)$

with $w_s = max(w_{init}, max(i, v'_p)+r_s)$.

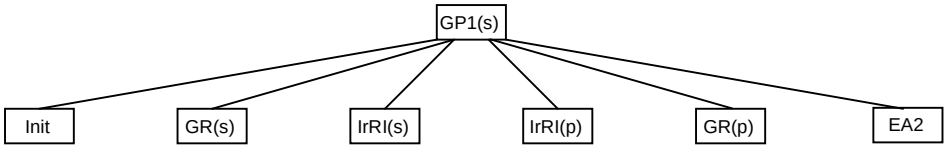

Fig. 5. Global property GP1(s) related to other properties

4.3 Group Properties

A group property is related in an integrative manner to a combination of intragroup role interaction properties.

$IaRI1(s, a1_s, b1_s)$ & $IaRI2(s, a2_s, b2_s)$ & $IaRI2(s, a3_s, b3_s) \Rightarrow GR(s, u_s,v_s,u'_s,v'_s)$

with $u_s = a1_s + a2_s$, $v_s = b1_s + b2_s$, $u'_s = a1_s + a2_s + a3_s$, $v'_s = b1_s + b2_s + b3_s$.

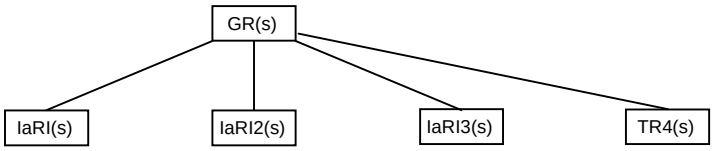

Fig. 6. Group property related to intragroup interaction properties

Intragroup role interaction properties relate to role behavior properties and transfer properties in the following manner.

$TR1(s)$ & $RB1_s(s, e1_s, f1_s) \Rightarrow IaRI1(s, e1_s, f1_s)$
$TR2(s)$ & $RB2(s, e2_s, f2_s) \Rightarrow IaRI2(s, e2_s, f2_s)$
$TR3(s)$ & $RB3(s, e3_s, f3_s) \Rightarrow IaRI3(s, e3_s, f3_s)$

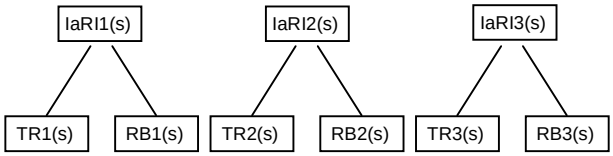

Fig. 7. Intragroup interaction properties related to role behavior and transfer properties

4.4 Overview

In Figure 8 an overview can be found for all dynamic properties relating to $GP1_s$.

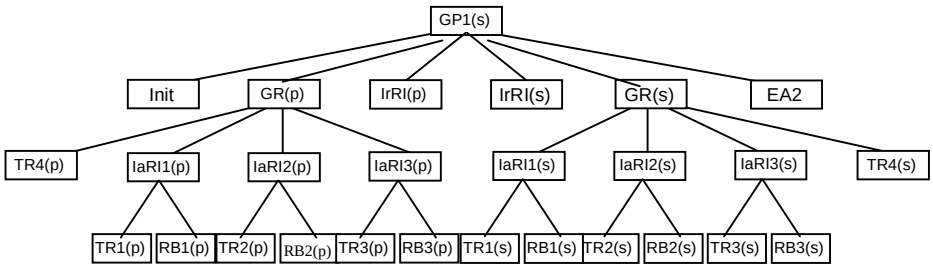

Fig. 8. Overview of the interlevel relationships for global property GP1(s)

5 Simulation

A software environment has been created to enable the simulation of executable organisation models specified at a high conceptual level [10]. The input of this simulation environment is a set of dynamic properties in a specific, executable format. In [9] the language TTL was introduced as an expressive language for the purpose of specification and checking of dynamic properties. For the purpose of simulation, to obtain computational efficiency the format used for dynamic properties is more restricted than the TTL format used to specify various types of dynamic properties: they are in so-called *leads to* format; cf. [10]. This is a real time-valued variant of Executable Temporal Logic [1]. Roughly spoken, in *leads to* format the following can be expressed:

> *if a state property α holds for a time interval with duration g,*
> *then after some delay (between e and f) another state property β will hold for a time interval h*

This specific temporal relationship *leads to* is applicable forward as well as backward in time. Hence, if α and β are state properties, and α leads to β, this also means that if β holds for a time interval of length h, then α held during some time interval with length g, of which the starting point was between e and f before the starting point of the second interval. A formal definition of this *leads to* relation is as follows. Here state($\mathcal{T}$, t) denotes the state at time t in trace $\mathcal{T}$, and S $\models \alpha$ that in a state S state property α holds. Moreover, *Traces* denotes the set of all possible traces.

Definition

(a) Let $\alpha, \beta \in$ SPROP(AllOnt). The state property α *follows* state property β, denoted by $\alpha \twoheadrightarrow_{e, f, g, h} \beta$, with time delay interval [e, f] and duration parameters g and h if

$\forall \mathcal{T} \in$ *Traces* $\forall$t1:

$[\forall t \in [t1 - g, t1) : state(\mathcal{T}, t) \models \alpha \Rightarrow \exists d \in [e, f] \forall t \in [t1 + d, t1 + d + h) : state(\mathcal{T}, t) \models \beta]$

(b) Conversely, the state property β *originates from* state property α, denoted by $\alpha \bullet\!\!-_{e, f, g, h} \beta$, with time delay in [e, f] and duration parameters g and h if

$\forall \mathcal{T} \in$ *Traces* $\forall$ t2:

$[\forall t \in [t2, t2 + h) : state(\mathcal{T}, t) \models \beta \Rightarrow \exists d \in [e, f] \forall t \in [t2 - d - g, t2 - d) \; state(\mathcal{T}, t) \models \alpha]$

(c) If both $\alpha \twoheadrightarrow_{e,f,g,h} \beta$, and $\alpha \bullet\!\!-_{e,f,g,h} \beta$ hold, then α *leads to* β this is denoted by: $\alpha \bullet\!\!\twoheadrightarrow_{e,f,g,h} \beta$.

Making use of these *leads to* properties, the software environment generates simulation traces (actually the *follows* relations are used in the simulation software; if in a specification there is only one way to reach each β, then this automatically results in *leads to* relations holding). A trace is developed by starting at time t = 0 and for each time point up to which the trace already has been constructed, checking which antecedents of executable properties hold in the already constructed trace. For these executable properties, add the consequent to the trace, i.e., extend the trace in time in such a manner that the consequent holds.

Table 1. Time parameters for *leads to* properties

Property	Minimal delay (e)	Maximal delay (f)	Duration antecedent (g)	Duration consequent (h)
RB1(p)	3	5	0	0
RB1(s)	10	20	0	0
RB2(p)	5	10	0	0
RB2(s)	5	10	0	0
RB3(p)	3	5	0	0
RB3 (s)	10	20	0	0
IrRI(p)	5	10	1	10
IrRI(s)	5	10	1	10

The relation between the specification and the constructed trace is that the trace is a model (in the logical sense) of the theory defined by the specification, i.e., all executable dynamic *leads to* properties of the specification hold in the trace.

To be able to simulate the behavior of the circulatory system, all leaves of the tree in Figure 8 have been expressed in *leads to* format. That is, all intergroup role

interaction properties, role behavior properties, transfer properties, and the special starting point property Init. The values chosen for the timing parameters are shown in Table 1.

The resulting trace is shown in Figure 9. Time is on the horizontal axis, the properties are on the vertical axis. A dark box on top of the line indicates that the property is true during that time period, and a lighter box below the line indicates that the property is false during that time period. The line labeled *stimulus_occurs*, for example, depicts the property that a heart stimulus occurs. This property is true from time point 0 to 5, from 80 to 85, from 160 to 165, and so on. Notice that this is exactly the intended dynamics according to environmental assumption EA2. Also notice that for the maximum interval s within EA2, the value 80 has been chosen within this example. Furthermore, Figure 9 shows that after a stimulus has occurred, the wells of both groups generate fluid, which is immediately received by the supply guidances (since the delays for transfers were assumed to be 0). After that, in both groups the fluid continues to the exchange. Since the systemic cycle is longer than the pulmonary cycle (the aorta channels are longer than the pulmonary artery channels), it takes more time for the supply guidance in the systemic group to generate fluid. Next, some moments after the exchange has received a fluid, it can be seen that the ingredients are actually exchanged. After that, fluid goes from the exchange to the drain guidance and finally to the drain.

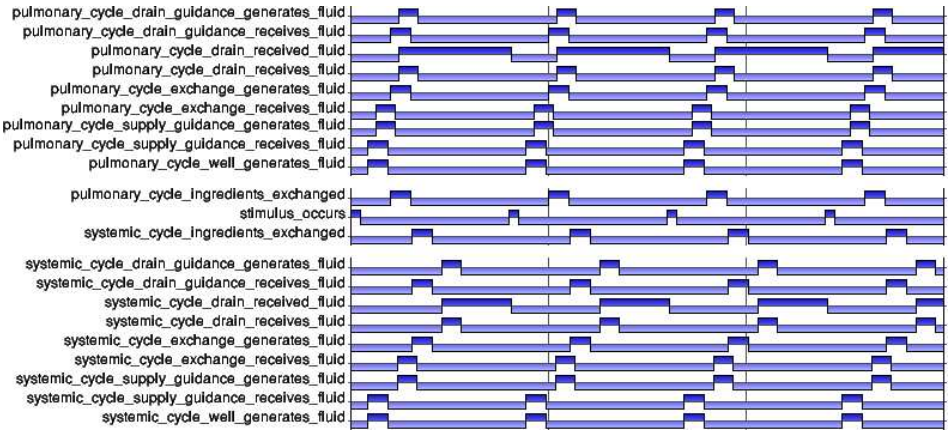

Fig. 9. Results of the simulation of executable properties of the circulatory system

6 Checking Properties

Logical relationships between properties, as depicted in the tree of Figure 8, can be very useful in the analysis of dynamic properties of an organisation (like the circulatory system in this particular case); also see [8]. For example, if for a given trace of the system the global property GP1(s) is not satisfied, then by a refutation process it can be concluded that either one of the group properties, or one of the intergroup role interaction properties, or the property Init does not hold. If, after

checking these properties, it turns out that GR(p) does not hold, then either one of the intragroup role interaction properties or TR4(p) does not hold. By this refutation analysis it follows that if GP1(s) does not hold for a given trace, then, via the intermediate properties, the cause of this malfunctioning can be found in the set of leaves of the tree of Figure 8.

In order to determine which one of the properties encountered in this refutation process actually is refuted, some mechanism is needed to check if a certain property holds for a given trace. To this end, the simulation software described above automatically produces log files containing the traces. In addition, software has been developed that is able to read in these log files together with a set of dynamic properties (in *leads to* format), and to perform the checking process. This is done in two directions. On the one hand, each atom occurring in the trace is 'explained', i.e., the software verifies if there was a reason for its presence, according to the dynamic properties. On the other hand, for each atom a check is performed whether all atoms it implies according to the dynamic properties are actually there. As a result, the software determines not only whether the properties hold for the trace or not, but in case of failure, it also pinpoints which parts of the trace violate the properties. If a property does not hold completely, this is marked by the program. Yellow marks indicate unexpected events, occurring when certain atoms cannot be explained. Red marks indicate events that have not happened, whilst they should have happened. Checks of this kind have actually been performed for all of the higher level properties of Figure 8, i.e., for all nodes of the tree that are no leaves. They all turned out to hold for the trace of Figure 9, which validates the tree.

In addition, recently other software has been developed (and is still being improved) that is able to check traces against properties in the *TTL* format instead of the *leads to* format. Since TTL, as mentioned in Section 5, has a considerably higher expressiveness, this new software enables to check much more complex properties. For instance, for the present case study, the property "*the higher the number of stimuli, the more oxygen is delivered in the lungs*" has been checked successfully. Checks of this kind are normally performed in less than a second. Future work involves exploring the limits to the amount of complexity that the software can handle.

7 Realisation of the Organisation by Allocation of Agents

An organisation model such as the one presented in this paper provides an abstract model for the manner in which multiple interacting processes or agents generate dynamics. The specific agents are not part of such an organisation model. Instead the notion of role provides an abstract entity or placeholder for where specific agents come in. In the example domain addressed here these agents are active biological components such as the heart, lungs, and other organs. An important advantage of this abstraction is that the dynamics can be modeled independent of the specific choices of agents. The organisation model can be (re)used for any allocation of agents to roles for which:

- for each role, the allocated agent's behavior satisfies the dynamic role properties,

- for each intergroup role interaction, one agent is allocated to both roles and its behavior satisfies the intergroup role interaction properties, and
- the communication between agents satisfies the respective transfer properties.

Expressed differently, for a given allocation of agents to roles the following logical relationships between dynamic properties hold:

agent – role
from dynamic agent properties to dynamic role properties:

agent A is allocated to role r &
dynamic properties of agent A ⇒
dynamic properties of role r

As an example for the case of the circulatory system, one can think of the aorta channels as agent A and of the systemic cycle supply guidance as role r (also see the allocation schema at the end of Section 2.3).

agent – intergroup role interaction
from dynamic agent properties to dynamic intergroup role interaction properties:

agent A is allocated to roles r1 and r2 in different groups &
dynamic properties of agent A ⇒
dynamic properties of intergroup role interaction between r1 and r2

As an example, one can think of the heart as agent A and of the systemic cycle well and the pulmonary cycle drain as role r1 and r2, respectively.

agent communication – role transfer
from dynamic agent communication properties to dynamic transfer properties:

agent A is allocated to role r1 and agent B to role r2 in one group &
dynamic properties of communication from A to B ⇒
dynamic properties of transfer from r1 to r2

As an example, one can think of the aorta channels as agent A, of the systemic cycle supply guidance as role r1, of the organ capillaries as agent B and of the systemic cycle exchange as role r2.

8 Discussion

The aim of this paper was to investigate whether modelling techniques from the area of organisation modelling (already shown to be successful for human organisations in, e.g., [8], [11]) provide adequate means to model at a high level of abstraction the dynamics of biological systems in which multiple distributed interacting processes play a role. As a case study the circulatory system in biological organisms (mammals) was explored using a chosen organisation modelling framework.

In the literature, many different kinds of cardiovascular models exist, typically based on modelling the physiology by differential equations. In contrast to these mathematical models of the circulatory system our paper shows how an organisation modelling approach such as the chosen one (other organisation modelling approaches may well be as applicable as the chosen one) can be used to model the dynamics of

biological organisation for the case of the circulatory system at a high conceptual level. This system consists of a number of components that are connected and grouped together in such a manner that everything functions in a coherent manner. It was shown how active components within the circulatory system can be considered realisers of the roles within the organisation model. Dynamic properties at different levels of aggregation of this organisation model have been identified, and logical interlevel relationships between these dynamic properties at different aggregation levels were made explicit. Based on the executable properties, simulation has been performed and properties have been (automatically) checked for the produced simulation traces. Thus the logical interlevel relationships between properties have been verified. The variant of executable temporal logic (extending the approach described in [1]) used for simulation has as an advantage that it is guaranteed that a generated trace satisfies the specified executable dynamic properties. Since these dynamic properties stand in logical relationships to other (more complex, not necessarily executable) dynamic properties, this form of simulation facilitates logical analysis of the dynamics at different levels of aggregation.

In summary, it turned out that, at least for the chosen domain, the chosen organisation modelling approach provides adequate means for high-level modelling of the complexity of the dynamics of biological organisms. For example, a strong contrast in abstraction and manageability of the model was found with modelling techniques based on differential equations that provide less transparent, low-level models. This outcome was confirmed by a case study in another biological domain in which the organisation of intracellular processes was modelled.

References

1. Barringer, H., Fisher, M., Gabbay, D., Owens, R., and Reynolds, M., (1996). The Imperative Future: Principles of Executable Temporal Logic, Research Studies Press Ltd. and John Wiley & Sons.
2. Ferber, J., (1999). *Multiagent Systems*. Addison Wesley.
3. Ferber, J. and Gutknecht, O. (1998). A meta-model for the analysis and design of organisations in multi-agent systems. In: *Proc. of the Third International Conference on Multi-Agent Systems* (ICMAS'98), IEEE Computer Society Press, pp. 128-135.
4. Ferber, J., and Gutknecht, O. (1999). Operational Semantics of a role-based agent architecture. *Proceedings of the 6th Int. Workshop on Agent Theories, Architectures and Languages (ATAL'1999)*. In: Jennings, N.R. & Lesperance, Y. (eds.) *Intelligent Agents VI*, Lecture Notes in AI, vol. 1757, Springer Verlag, 2000, pp. 205-217.
5. Ferber, J., Gutknecht, O., Jonker, C.M., Müller, J.P., and Treur, J., (2001). Organization Models and Behavioural Requirements Specification for Multi-Agent Systems. In: Y. Demazeau, F. Garijo (eds.), *Multi-Agent System Organisations. Proceedings of the 10th European Workshop on Modelling Autonomous Agents in a Multi-Agent World, MAAMAW'01*, 2001. Lecture Notes in AI, Springer Verlag. To appear, 2002.
6. Fung, Y.C. (1984). Biodynamics: Circulation, New York, Springer-Verlag.
7. Greenway, C.V. (1982). Mechanisms and quantitative assessment of drug effects on cardiac output with a new model of the circulation. Pharm Rev 33(4):213.
8. Jonker, C.M., Letia, I.A., and Treur, J., (2002). Diagnosis of the Dynamics within an Organisation by Trace Checking of Behavioural Requirements. In: Wooldridge, M., Weiss, G., and Ciancarini, P. (eds.), *Proc. of the 2nd International Workshop on Agent-*

Oriented Software Engineering, AOSE'01. Lecture Notes in Computer Science, vol. 2222. Springer Verlag, 2002, pp. 17-32.
9. Jonker, C.M. and Treur, J. (1998). 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, 1998, pp. 350-380. Extended version in: *International Journal of Cooperative Information Systems*, vol. 11, 2002, pp. 51-92.
10. Jonker, C.M., and Treur, J., Relating Structure and Dynamics in an Organisation Model. In: J.S. Sichman, F. Bousquet, and P. Davidson (eds.), *Multi-Agent-Based Simulation II, Proc. of the Third International Workshop on Multi-Agent Based Simulation, MABS'02*, Lecture Notes in AI, vol. 2581, Springer Verlag, pp. 50-69.
11. Jonker, C.M., Treur, J., and Wijngaards, W.C.A. (2002). Temporal Languages for Simulation and Analysis of the Dynamics Within an Organisation. In: B. Dunin-Keplicz and E. Nawarecki (eds.), *From Theory to Practice in Multi-Agent Systems, Proc. of the Second International Workshop of Central and Eastern Europe on Multi-Agent Systems, CEEMAS'01*, 2001. Lecture Notes in AI, vol. 2296, Springer Verlag, 2002, pp. 151-160.
12. Kreitner, R., and Kunicki, A. (2001). Organisational Behavior, McGraw – Hill.Li, J.K.-J. (1987). Arterial System Dynamics, NewYork, New York University Press.
13. Lomi, A., and Larsen, E.R. (2001). Dynamics of Organizations: Computational Modeling and Organization Theories, AAAI Press, Menlo Park.
14. Manna, Z., and Pnueli, A. (1995). *Temporal Verification of Reactive Systems: Safety*. Springer Verlag.
15. Martin, J.F., Schneider, A.M., Mandel, J.E., et al. (1986). A new cardiovascular model for real-time applications. Trans Soc Comp Sim 3(1):31.
16. Milnor, W.R. (1989). Hemodynamics 2nd ed, Baltimore, Williams & Wilkins.
17. Mintzberg, H. (1979). The Structuring of Organisations, Prentice Hall, Englewood Cliffs, N.J.
18. Noordergraaf, A. (1978). Circulatory System Dynamics. Academic Press, New York.
19. Prietula, M., Gasser, L., Carley, K. (1997). Simulating Organizations. MIT Press.
20. Rideout, V.C. (1991). Mathematical and Computer Modelling of Physiological Systems. Prentice Hall, Englewood Cliffs.
21. Rizzi, M., Baltes, M., Theobald, U. & Reuss, M. (1997). *In vivo* analysis of metabolic dynamics in *Saccharomyces cerevisiae*: II. Mathematical model. *Biotechnol. Bioeng.* 55, 592–608.
22. Rohwer, J.M., Meadow, N.D., Roseman, S., Westerhoff, H.V., Postma, P.W. (2000). Understanding glucose transport by the bacterial phosphoenolpyruvate:glycose phosphotransferase system on the basis of kinetic measurements in vitro. J. Biol. Chem., 275(45):34909-21.
23. Slate, J.B., Sheppard, L.C. (1982). Automatic control of blood pressure by drug infusion. IEE Proc., Pt. A 129(9):639.
24. Wang, J., Gilles, E.D., Lengeler, J.W., and Jahreis, K. (2001). Modeling of inducer exclusion and catabolite repression based on a PTS-dependent sucrose and non-PTS-dependent glycerol transport systems in Escherichia Coli K-12 and its experimental verification. *J. Biotechnol*. 2001, Dec 28; 92(2): 133-58.
25. Weiss, G. (ed.) (1999). *Multiagent Systems*. MIT Press
26. Westerhoff, H.V. (2001) The silicon cell, not dead but live! Metab. Eng. 2001; 3(3):207-10.
27. Westerhof, N., Noordergraaf, A. (1969). Reduced models of the systemic arteries. Proc 8th Int Conf Med Eng, Chicago.
28. Yu, C., Roy, R.J., Kaufman, H. (1990). A circulatory model for combined nitroprusside-dopamine therapy in acute heart failure. Med Prog Tech 16:77.