Behavioural Equivalences over Mobile Membranes with Delays

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Abstract. Mobile membranes with delays represent a biological inspired formalism able to model systems involving timing, explicit locations and mobility. We define a number of behavioural equivalences over this formalism, and prove some relationships between these equivalences.

1 Introduction

During the last years, membrane computing [3, 6] has been applied to Biology. It may have an important impact in understanding how biological systems work, giving also a way to describe, manipulate, analyse and verify them. Behavioural equivalence is an important concept in biology needed for analysing and comparing the organs behaviour. For example, an artificial organ is the functional equivalent of the natural organ, meaning that both behave in a similar manner.

Using mobile membranes, we are interested either in locations, times of evolution, mobility objects, or in combinations of these concepts. Thus we define several equivalences, showing that some of them are finer that others, and that some of them are incomparable. Defining several equivalences, we offer flexibility in selecting the right one when verifying biological systems and comparing them.

What we do in this paper is a first step towards establishing the formal framework used in software verification for biological systems sensitive to timeouts.

2 Systems of Mobile Membranes with Delays

Systems of simple mobile membranes [4] are a particular class of membrane computing [6], while several types of mobile membranes were studied in detail in [2]. We use a rule-based model of computation called systems of mobile membranes with delays in order to model complex biological processes.

Definition 1. *A system of mobile membranes with delays is a construct* $\Pi = (O_t, H, \mu, w_1, \ldots, w_n, R)$, $n \geq 1$ *(the degree of the system), where:*

1. $O_t = O \times \mathbb{N}$ *is a set of objects with delays, where* O *is an alphabet of objects, and* $(a, t_a) \in O_t$ *represents an object* a *together with its delay* $t_a \geq 0$*;*

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2. *H is a finite set of labels for membranes;*
3. *$\mu \subset H \times H$ describes the* membrane structure*, such that $(i, j) \in \mu$ denotes that the membrane labelled by j is contained in the membrane labelled by i;*
4. *$w_1, w_2, \ldots, w_n$ are multisets over O_t, describing the initial multisets of objects with delays placed in the n regions of μ;*
5. *R is a finite set of evolution rules of the following forms, where $h, m \in H$, $(a, 0), (\overline{a}, 0), (c, t_c), (b, t_b), (a, t_a), (a, t_a - 1) \in O_t$:*
   (a) $[\,(a,0)\,]_h[\,(\overline{a},0)\,]_m \rightarrow [\,[\,(c,t_c)\,]_h(b,t_b)\,]_m$ *endocytosis*
   an elementary membrane h containing $(a, 0)$ enters membrane m containing $(\overline{a}, 0)$; $(a, 0)$ is rewritten to (c, t_c), and $(\overline{a}, 0)$ is rewritten to (b, t_b);
   (b) $[\,[\,(a,0)\,]_h(\overline{a},0)\,]_m \rightarrow [\,(c,t_c)\,]_h[\,(b,t_b)\,]_m$ *exocytosis*
   an elementary membrane h containing $(a, 0)$ exits membrane m containing $(\overline{a}, 0)$; $(a, 0)$ and $(\overline{a}, 0)$ are rewritten to (c, t_c) and (b, t_b), respectively;
   (c) $[\,(a,0)\,]_h \rightarrow [\,(c,t_c)\,]_h[\,(b,t_b)\,]_h$ *elementary division*
   if containing $(a, 0)$, a membrane h is divided into two membranes with the same label m, and $(a, 0)$ is rewritten to (b, t_b) and (c, t_c);
   (d) $[\,(a,t_a)\,]_h \rightsquigarrow [\,(a,t_a-1)\,]_h$ *delay decrementing*
   if $t_a > 0$ then (a, t_a) placed inside membrane h is rewritten to $(a, t_a - 1)$.

In terms of computation, we are working with membrane configurations (ranged over by $M, N, \ldots$) and with the free monoid O_t^* (ranged over by $u_t, v_t, \ldots$).

Definition 2. *The set $\mathcal{M}(\Pi)$ of membrane configurations in a membrane system Π is inductively defined as follows:*

- *if $i \in H$ and u_t is a multiset over O_t then $\langle i; u_t \rangle \in \mathcal{M}(\Pi)$; $\langle i; u_t \rangle$ is called an* elementary membrane configuration*;*
- *if $i \in H$, $M_1, \ldots, M_n \in \mathcal{M}(\Pi)$, $n \geq 1$, and u_t is a multiset over O_t then $\langle i; u_t,\ M_1 \ldots M_n \rangle \in \mathcal{M}(\Pi)$; $\langle i; u_t,\ M_1 \ldots M_n \rangle$ is a* composite membrane*.*

Definition 3. *For a membrane system Π, if $M, N \in \mathcal{M}(\Pi)$ then:*

- *M* reduces *to N (denoted by $M \mapsto N$) if there exists a rule in R, applicable to membrane M such that we can obtain membrane N. We use $\mapsto$ to stand for both $\rightarrow$ and $\rightsquigarrow$. We denote by $\rightsquigarrow^n$ a sequence of $n \geq 1$ reductions $\rightsquigarrow$.*

3 Behavioural Equivalences

These equivalence relationships are useful when checking the "healthiness" of a system. For example, take two healthy systems M and N that are in a relationship of barbed bisimulation. If they are both infected with a virus and evolved into M' and N', through the barbed bisimulation, it is easy to check if they are infected with a virus of the same kind (each virus has an unique behaviour and is activated by an unique trigger).

In what follows, in order to distinguish between normal and abnormal behaviours, we define various barbed bisimulation as in [5], and specify first what is observable. To emphasize the mobility aspects, the objects involved in endocytosis and exocytosis rules are observable.

To avoid ambiguity, we consider that the objects involved in endocytosis and exocytosis rules belong to the sets of objects O_{exo} and O_{endo}, respectively, such that $O_{exo} \in O_t$, $O_{endo} \in O_t$ and $O_{endo} \cap O_{exo} = \emptyset$. In what follows, let $x \in \{endo, exo\}$ represent the possible movements, u'_t, u''_t arbitrary multisets of objects with delays, N, M, M' configurations, and $m \in H$ a membrane label.

A barb predicate $\downarrow_{x(a)}$ ($\downarrow_{x(a)@m}$, $\downarrow^{t_a}_{x(a)}$, $\downarrow^{t_a}_{x(a)@m}$) is defined by the rule:

$$M \downarrow_{x(a)} \ (M \downarrow_{x(a)@m},\ M \downarrow^{t_a}_{x(a)},\ M \downarrow^{t_a}_{x(a)@m}, \text{ respectively})$$
$$\text{iff } M \equiv \langle m; (a, t_a) \uplus u'_t, N\rangle \parallel M', \text{ where } a \in O_x.$$

Definition 4. *A barbed bisimulation $\mathcal{S}$ in terms of mobility is a symmetric binary relation over membrane configurations such that for all $(M, N) \in \mathcal{S}$, $n \in \mathbb{N}$*

1. *if $M \downarrow_{x(a)}$, then $N \downarrow_{x(a)}$ for any barb predicate $\downarrow_{x(a)}$;*
2. *if $M \rightsquigarrow^n \rightarrow M'$, then exists N' such that $N \rightsquigarrow^n \rightarrow N'$ and $(M', N') \in \mathcal{S}$.*

Two membrane configurations are barbed bisimilar, in terms of mobility, denoted $M \sim_{mob} N$, if and only if $(M, N) \in \mathcal{S}$ for some barbed bisimulation $\mathcal{S}$.

It is rather natural to strengthen the observing power of the previous defined barbs by allowing the observer to look also at the label (location) of the membrane containing the object that facilitates a movement.

The barbed bisimulation $\sim_{Lmob}$, in terms of location and mobility, is defined similarly with the barbed bisimulation $\sim_{mob}$, by using the barb predicate $\downarrow_{x(a)@m}$. This bisimulation compares membrane configurations by looking also at the label of the membrane containing an object that facilitates a movement.

Bisimulation relations are represented and studied as sets of pairs of membrane configurations. Thus the comparison between bisimilarities are set-theoretic.

Proposition 1 ($\sim_{mob} \prec \sim_{Lmob}$). *The located barbed bisimulation is strictly finer than the barbed bisimulation:*

1. *$\sim_{mob} \preceq \sim_{Lmob} \Leftrightarrow \ \forall M, N$, if $M \sim_{Lmob} N$ then $M \sim_{mob} N$;*
2. *$\sim_{Lmob} \not\preceq \sim_{mob} \Leftrightarrow \ \exists M, N$, s.t. if $M \sim_{mob} N$ then $M \not\sim_{Lmob} N$.*

Proof (Sketch).

1. The located observer (i.e., the located barb) can distinguish in both membrane configurations the same object a placed inside the same membrane m facilitating a movement, and so the located barb implies the simple barb ($M \downarrow_{x(a)@m}$ implies $M \downarrow_{x(a)}$).
2. We give the following counterexample: Take two membrane configurations M and N, and an object $\overline{a} \in O_{exo}$ s.t. $M = \langle l; (\overline{a}, t_{\overline{a}}) \uplus u'_t\rangle$ and $N = \langle k; (\overline{a}, t_{\overline{a}}) \uplus u'_t\rangle$ with $l \neq k$. Both $M \downarrow_{exo(\overline{a})}$ and $N \downarrow_{exo(\overline{a})}$ hold, and thus the two membrane configurations are barbed bisimilar: $M \sim_{mob} N$. However $M \downarrow_{exo(\overline{a})@l}$ and $N \downarrow_{exo(\overline{a})@k}$ also hold, and $l \neq k$; therefore $M \not\sim_{Lmob} N$. □

The bisimulation $\sim_{Dmob}$ is defined similarly with the bisimulation $\sim_{mob}$, by using the barb predicate $\downarrow^{t_a}_{x(a)}$. It relates membrane configurations with the same objects that execute the same movements and have the same delays.

Proposition 2 ($\sim_{mob} \prec \sim_{Dmob}$). *The delayed barbed bisimulation is strictly finer than the barbed bisimulation:*

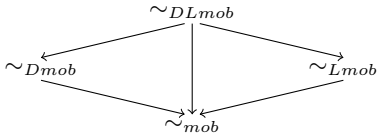
1. $\sim_{mob} \preceq \sim_{Dmob} \Leftrightarrow \forall M, N$, *if* $M \sim_{Dmob} N$ *then* $M \sim_{mob} N$;
2. $\sim_{Dmob} \not\preceq \sim_{mob} \Leftrightarrow \exists M, N$, *s.t. if* $M \sim_{mob} N$ *then* $M \not\sim_{Dmob} N$.

The bisimulation $\sim_{DLmob}$ is defined similarly with the bisimulation $\sim_{Dmob}$, by using the barb predicate $\downarrow^{t_a}_{x(a)@m}$. It relates membrane configurations with the same objects located in the same membranes that execute the same movements and have the same delays.

Proposition 3 ($\sim_{Lmob} \prec \sim_{DLmob}$). *The delayed located barbed bisimulation is strictly finer than the located barbed bisimulation:*

1. $\sim_{Lmob} \preceq \sim_{DLmob} \Leftrightarrow \forall M, N$, *if* $M \sim_{DLmob} N$ *then* $M \sim_{Lmob} N$;
2. $\sim_{DLmob} \not\preceq \sim_{Lmob} \Leftrightarrow \exists M, N$, *s.t. if* $M \sim_{Lmob} N$ *then* $M \not\sim_{DLmob} N$.

The four barbed bisimulations form a lattice in which a directed edge means "is strictly finer":



4 Conclusion

A small difference in the behaviour of a biological system could lead to a disease. Such a difference could appear because of the involved elements, their location, their actions and timing. The behavioural equivalences introduced in this paper could make the distinction between "normal" and "abnormal" behaviours, emphasizing also the elements by which behaviours differ. During the presentation, some biological examples will illustrate the use of these bisimulations.

As future work, we are interested in theoretical investigation of other behavioural equivalences and their applicability to Systems Biology. Other behavioural equivalences (other than bisimulations) can also be considered: trace equivalences, barbed congruences and testing equivalences.

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