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Membrane Systems with Marked Membranes

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Abstract

Membrane computing is a biologically inspired computational paradigm. Motivated by brane calculi we investigate membrane systems which differ from conventional membrane systems by the following features:

(1) biomolecules (proteins) can move through the regions of the systems, and can attach onto (and de-attach

from) membranes, and (2) membranes can evolve depending on the attached molecules. The evolution of membranes is performed by using rules that are motivated by the operation of pinocytosis (the pino rule) and the operation of cellular dripping (the drip rule) that take place in living cells.

We show that such membrane systems are computationally universal. We also show that if only the second feature is used then one can generate at least the family of Parikh images of the languages generated by programmed grammars without appearance checking (which contains non-semilinear sets of vectors).

If, moreover, the use of pino/drip rules is non-cooperative (i.e., not dependent on the proteins attached to membranes), then one generates a family of sets of vectors that is strictly included in the family of semilinear sets of vectors.

We also consider a number of decision problems concerning reachability of configurations and boundness.

*Keywords:* Membrane Computing, Brane Calculi

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# Introduction

Membrane computing is a biologically inspired computational paradigm introduced by Gh. Pa˘un in 1998, [[10](#_bookmark29)]. The model is based on a hierarchical structure of nested membranes, inspired by the structure of living cells. In each region (enclosed by a membrane) some objects are present, modeling the presence of molecules inside the compartments of living cells. Moreover, each region has an associated set of multiset rewriting rules. These rules are motivated by chemical reactions that occur inside the regions of living cells. Membranes play a crucial role in living cells: the cell membrane separates, and hence protects the cell from its environment and the inner membranes delimit the structure of various organelles of the cell, e.g., the nuclear membrane separates the nucleus from the rest of the cell.

Membranes are not only “containers” but they also regulate the flow of molecules into and out of the cell. This is facilitated by proteins that are embedded in mem- branes and which provide channels for the transport of molecules through mem- branes.

In brane calculi, presented in [[3](#_bookmark22)], several operations (*pino, exo, phago, mate, drip, bud* ) involving membranes with embedded proteins are considered and formal- ized in the framework of process calculi. The important difference with membrane computing is that the evolution of the system happens *on* the membranes and *not inside* the compartments (regions) delimited by them. The computational power of several brane calculi operations has been investigated in [[2](#_bookmark23)] where universality has been obtained for systems using *phago* and *exo*. In [[4](#_bookmark25)] these operations from brane calculi have been represented in the membrane computing framework and then studied by using tools from formal language theory.

In this paper we investigate operations involving membranes with embedded proteins, but we also add the ability of proteins to attach/de-attach to/from the membranes, and also to move through the membranes. Hence, in our case, the evolution of the system takes place both on the membranes and inside the regions, which is natural from a biological point of view.

More specifically, we consider *protein-membrane rules* – rules that modify the structure of (the membranes of) the system where the modifications are based on the multisets of proteins embedded in the membranes (we say that such multisets *mark* the membranes). In particular, we consider the *pino* and *drip* rules inspired by the operation of *pinocytosis* and the operation of cellular *dripping*, respectively. Both pinocytosis and dripping split off a membrane from another membrane, however, in pinocytosis, this new (empty) membrane is found inside the original membrane, while in dripping, this new membrane is found outside the original membrane. We also use *protein movement rules*, that model the attachment, de-attachment and movement of the proteins. Also these rules are applied according to the proteins marking the involved membranes. The protein movement rules do not change the membrane structure of the system, but they can change the multisets of embedded proteins marking the membranes of the system.

The paper is structured in the following way. In Section [2](#_bookmark5) we provide preliminar-

ies concerning formal languages, recalling in particular the definition of programmed grammars often used in the proofs. In Section [3](#_bookmark6) we recall the formal definition of pino and drip rules, and introduce the protein movement rules, and in Section [4](#_bookmark7) we introduce membrane systems based on these rules which – the model is called *membrane system with marked membranes, protein-membrane rules, and protein movement rules*, abbreviated as *Ppp* system.

In Section [5](#_bookmark8), we investigate the computational power of *Ppp* systems which use only protein movement rules, and in Section [6](#_bookmark10) of *Ppp* systems using only pino (or drip) rules. In Section [7](#_bookmark13), we discuss *Ppp* systems using both types of rules. In Section [8](#_bookmark16) we prove several decidability results concerning reachability of configurations and boundness of *Ppp* systems with pino, drip rules, and protein movement rules. In the last section we discuss the results obtained in this paper and formulate a number of research directions.

This paper does not contain any proofs – all the proofs can be found in the full version of this paper [[1](#_bookmark24)].

# Preliminaries

We will briefly recall the main notions and results of formal language theory used in this paper. For more details the reader can consult standard books, such as [[8](#_bookmark30)], [[13](#_bookmark31)], [[7](#_bookmark28)], and the handbook [[12](#_bookmark32)].

Given a set *A*, we denote by |*A*| its cardinality and by P(*A*) the power set of *A*. The empty set is denoted by ∅.

all strings over *V* . The empty string is denoted by *λ*. The *length* of a string *w* ∈ *V* ∗ As usual, an *alphabet V* is a finite set of symbols. By *V* ∗ we denote the set of is denoted by |*w*|, while the number of occurrences of *a* ∈ *V* in *w* is denoted by

|*w*|*a*. For a language *L* ⊆ *V* ∗, the set *length*(*L*)= {|*w*|| *w* ∈ *L*} is called the *length*

*set* of *L*. Given a string *w*, a string *u* is a *subword* of *w* if there exist two strings

*x, y*, possibly empty, such that *w* = *xuy*. The string *u* is a *scattered subword* of

that *u* = *x*1 ··· *xk*, and *w* = *y*0*x*1*y*1 ··· *xkyk*. We use *Sub*(*w*) to denote the set of all *w* if and only if there exist strings *x*1*,... , xk*, and *y*0*,... , yk*, possibly empty, such subwords of *w*, while *Scub*(*w*) denotes the set of the scattered subwords of *w*.

Given an alphabet *V* = {*a*1*, a*2*,... , an*}, with every string *w* ∈ *V* ∗ we can associate the *Parikh vector* Ψ*V* (*w*) = (|*w*|*a*1 *,* |*w*|*a*2 *,... ,* |*w*|*an* ), where the ordering (*a*1*,... , an*) of *V* is assumed. Given a language *L* ⊆ *V* ∗, the *Parikh image* of *L* is defined as Ψ*V* (*L*)= {Ψ*V* (*w*) | *w* ∈ *L*}.

If *FL* is a family of languages, then *PsFL* denotes the family of Parikh images of

sets of languages in *FL*. Note that each *L* ∈ *PsFL* is a set of vectors with a fixed languages in *FL* (w.r.t. a given alphabet *V* ), and *NFL* denotes the family of length dimension. We denote by *FIN* , *REG*, *CF* , *CS*, and *RE* the family of finite, regular,

context-free, context-sensitive, and recursively enumerable languages, respectively. Accordingly, the family of Parikh images of languages in *RE* is denoted by *PsRE* (this is the family of all recursively enumerable sets of vectors of natural numbers). The family of all recursively enumerable sets of natural numbers is denoted by

*NRE*. As usual, two language generating/accepting devices are called *equivalent* if they generate/accept the same language.

A context-free *programmed grammar with appearance checking* is a construct

resp.), *S* ∈ *N* is the start symbol, and *P* is a finite set of productions of the form *G* = (*N, T, S, P* ), where *N* (*T* , resp.) is a finite set of nonterminals (terminals, (*b* : *A* → *x, Eb, Fb*), where *b* is a label, *A* → *x* with *A* ∈ *N* and *x* ∈ (*N* ∪ *T* )∗ is a

context-free production, and *Eb*, *Fb* are two sets of labels of productions of *G* (*Eb*

(*b* : *A* → *x, Eb, Fb*) is applied as follows: if *A* is present in the sentential form, then is called the *success ﬁeld* and *Fb* the *failure ﬁeld* of the production). A production the production *A* → *x* is applied and the next production is chosen from those with

the labels in *Eb*, otherwise, the sentential form remains unchanged and we choose

A derivation step is denoted by ⇒ while ⇒∗ denotes the reflexive and transitive the next production from the set of productions labeled by some element of *Fb*. closure of ⇒. If no failure field is given for any of the productions, then we obtain

a programmed grammar *without appearance checking*.

By *PR* we denote the family of languages generated by programmed grammars without appearance checking, and by *P Rac* we denote the family of languages gen- erated by programmed grammars with appearance checking. Proofs of the following results can be found in [[7](#_bookmark28)].

Lemma 2.1 *CF* ⊂ *PR* ⊂ *PRac* = *RE.*

We assume the reader to be familiar with the basic notions of membrane com-

puting, see, e.g., [[11](#_bookmark33)].

# Membrane Operations with Marked Membranes

In [[3](#_bookmark22)] several membrane operations involving membranes and embedded proteins have been modeled in the framework of process calculi. In [[4](#_bookmark25)] these operations have been expressed in the framework of membrane systems.

We will briefly recall these operations, however in a slightly modified form: while in [[3](#_bookmark22)] and [[4](#_bookmark25)] a region (enclosed by a membrane) can contain other membranes but not objects, we allow a region to contain objects.

As usual in membrane computing, a membrane is represented by a pair of square brackets, [ ]. To each membrane [ ] we associate a multiset *u* (over a certain alphabet *V* ) and this is denoted by [ ]*u*. We say that the membrane is *marked* with *u* (*u* is called a *marking* ). The objects of *V* are called *proteins* or, simply, *objects*. The contents of a membrane can consist of proteins and/or other membranes.

The *protein-membrane rules* over *V* are of the following form (the subscript *i*

stands for *internal*, *e* for *external* ):

*pinoi* :[ ]*uav* → [[ ]*ux*]*v,*

*pinoe* :[ ]*uav* → [[ ]*v*]*ux,*

*drip* :[ ]*uav* → [ ]*ux*[ ]*v.*

where *a* ∈ *V* , and *u, x, v* ∈ *V* ∗ (thus the restriction of having the right-hand sides

of the rules non-empty, as in [[4](#_bookmark25)], has been relaxed here). If *uv* = *λ*, then we have a *non-cooperative rule*; we add the prefix (*ncoo*) to denote it. Thus (*ncoo*)*pinoi* :

[ ]*a* → [[ ]*x*] is a non-cooperative *pinoi* rule.

The described rules are applicable to any membrane whose marking *includes* the

multiset indicated in the left hand side of the rules; all the proteins not specified in the rules are not affected by the use of the rules, but they are *randomly distributed* between the two resulting membranes. When using any rule of any type, we say that the membrane from its left hand side is *involved* in the rule; the membrane involved is “consumed” while the membranes from the right hand side of the rule are “produced”. Similarly, the protein *a* specified in the left hand side of the rules is consumed, and it is replaced by the multiset of proteins *x* (that might be empty). After the application of a *pinoi* or *pinoe* rule, the contents of the consumed membrane is moved into the region of the created external membrane (thus, mem- brane [ ]*v* for *pinoi* and membrane [ ]*ux* for *pinoe*), and after the application of a *drip* rule, the contents of the consumed membrane is moved into the region of the

produced membrane [ ]*v*.

We also define rules that can attach/de-attach proteins to/from the membranes, and rules to move the proteins through the membranes of the system. The *protein movement rules* over *V* can have one of the following forms (the subscript *i* stands for *inside*, *o* for *outside*):

*attachi* :[ *a*]*u* → [ ]*ua, attacho* :[ ]*ua* → [ ]*ua,*

*de*−*attachi* :[ ]*ua* → [ *a*]*u, de*−*attacho* :[ ]*ua* → [ ]*ua, moveout* : [*a*]*u* → [ ]*ua,*

*movein* :[ ]*u a* → [*a*]*u,*

with *a* ∈ *V* , *u* ∈ *V* ∗.

The effect of the rules *attachi* and *attacho* is to attach the protein *a* to the

corresponding membrane if the marking of the membrane *includes u*.

The rules *moveout* (*movein*) move the protein *a* outside (inside, resp.) if the marking of the corresponding membrane *includes u*. We use *prot* to denote the set of protein movement rules.

# Membrane Systems with Marked Membranes

In this section we define membrane systems (also called P systems) having mem- branes marked with multisets of proteins, and using the protein-membrane rules and the protein movement rules introduced in Section [3](#_bookmark6).

Formally, a *membrane system with marked membranes, protein-membrane rules, and protein movement rules, in short Ppp system*, is a construct

Π= (*V, μ, u*1*,... , um, R,F* )*,*

* *V* is a finite, nonempty alphabet of proteins;
* *μ* is a membrane structure with *m* ≥ 1 membranes;
* *u*1*,* ··· *, um* ∈ *V* ∗ are the markings of the *m* membranes of *μ* at the beginning of the computation (the *initial markings* of Π);
* *R* is a finite set of protein-membrane rules and protein movement rules over the alphabet *V* ;
* *F* ⊆ *V* is the set of *protein-flags*, simply called *flags* (marking the *output mem- branes*).

We will also use *V*Π, *μ*Π, *R*Π, and *F*Π to denote *V* , *μ*, *R*, and *F* respectively.

A *conﬁguration* of Π consists of a membrane structure, the markings of the membranes, and the multisets of proteins present inside the regions. In what follows, configurations are denoted by writing the markings as subscripts of the right hand parentheses which identify the membranes, e.g., [ [ ]*ab*[*aaa*]*b*[ ]*bb*]*a* is an example of a configuration.

We suppose that in the *initial conﬁguration* the regions are empty, thus the initial configuration is defined by *μ* and *u*1*,... , um*.

As standard for membrane systems, we assume the existence of a global clock which marks the timing of steps (single *transitions*) for the whole system.

A single transition of Π from a configuration to a new one is performed by apply- ing, *to each membrane of the system, either* (*i*) *the protein movement rules in the nondeterministic maximally parallel manner, or* (*ii*) *one of the protein-membrane rules*.

The choice between using protein movement rules or using a protein-membrane rule, for each membrane, is done in a nondeterministic way if both types of rules can be applied for a given membrane. A membrane remains unchanged (only) if no rules can be applied to it.

The application in the nondeterministic maximally parallel manner of the pro- tein movement rules means that, for the chosen membrane, the proteins (the ones marking the membrane and those present in the enclosed region) are assigned with the rules in such a way that, after the assignment is done, no other protein movement rule is applicable to the proteins that have no rules assigned to them. If a protein can be used by several rules, then it is assigned to one of them in a nondeterministic way.

As usual, a sequence of transitions forms a *computation*. A computation which starts from the initial configuration is *successful* if it halts, that is, it reaches a *halting conﬁguration*, i.e., a configuration where no rule can be applied, anywhere in the system. In the halting configuration we consider the *output membranes* – these are membranes whose markings contain at least one flag from *F* .

Then, the *result* of a successful computation is the set of vectors describing the multiplicities of proteins present in the markings of the output membranes. Because of the non-determinism in the choice of rules, one can get a set of (successful) computations, and thus a set of results.

Collecting all the results, for all possible successful computations, we get *the set of vectors generated* by Π, and denoted by *Ps*(Π).

Note that in a *Ppp* system one computation can deliver a finite family of vectors

as its output because several membranes can be “flagged” as output membranes. This differs from assigning the output in “standard” membrane systems. However since the set of vectors *Ps*(Π) generated by a *Ppp* system is taken over the union of results of all successful computations, this difference “disappears” when we consider *Ps*(Π).

We denote by *P Pm*(*α, prot*), with *α* ∈ {*pinoi, pinoe, drip,* (*ncoo*)*pinoi,* (*ncoo*)*pinoe,* (*ncoo*)*drip*}*, m* ≥ 1*,* the class of *Ppp* systems using protein-membrane rules of type *α*, protein movement rules, and at most *m* membranes (*α* or *prot* are

removed if the corresponding rules are not used). Therefore *PsP Pm*(*α, prot*) is the family of sets of vectors generated by *Ppp* systems from *P Pm*(*α, prot*) (*α* or *prot*

are removed if the corresponding rules not used). If *m* is substituted by ∗ then the number of membranes considered is arbitrary.

Since one cannot mark the empty multiset by a flag, we consider the equality of families of multisets modulo the empty multiset, i.e., if two families differ only by the empty multiset, then we consider them to be equal.

A configuration of a *Ppp* system Π that can be reached by a (possibly empty) sequence of transitions, starting from the initial configuration, is called *reachable*. A multiset *w* of proteins is a *reachable marking* for Π if there exists a reachable configuration of Π which contains a membrane marked by *w*.

# Preliminary Results

We begin with some preliminary results that follow directly from the definitions and from the Turing-Church thesis.

Theorem 5.1

*PsP P*∗(*α, prot*) ⊆ *PsRE, PsP P*∗(*α*) ⊆ *PsP P*∗(*α, prot*)*. PsP P*∗((*ncoo*)*α, prot*) ⊆ *PsP P*∗(*α, prot*)*,*

*PsP P*∗((*ncoo*)*α*) ⊆ *PsP P*∗(*α*)*, α* ∈ {*pinoi, pinoe, drip*}*.*

First we consider *Ppp* systems that use only the protein movement rules. The power of such systems is very restricted, even when there is no bound on the number of membranes to be used.

Theorem 5.2 *PsP P*∗(*prot*)= *PsFIN.*

# Membrane Systems Using Protein-Membrane Rules

As stated by Theorem [5.2](#_bookmark9) the use of only protein movement rules results in a very limited generative power. In this section we turn to the dual situation: the use of protein-membrane rules only.

In this case the membrane structure can change during the computation, but the proteins cannot move through the regions of the system.

First we investigate *Ppp* systems using the non-cooperative versions of the pino and of the drip rules. In this case the power of the system is still very limited: the family of the so generated sets of vectors is strictly included in the family of Parikh images of context-free languages. Then we will study *Ppp* systems using only pino and drip rules; in this case the power of the system increases: one can generate now at least the family of Parikh images of the languages generated by programmed grammars without appearance checking.

Theorem 6.1 *PsP P*∗((*ncoo*)*α*) ⊂ *PsCF, α* ∈ {*pinoi, pinoe, drip*}*.*

The computational power of this class increases when one uses cooperative

*pinoi, pinoe* or *drip* rules. In this case the systems can generate at least the family of Parikh images of languages generated by programmed grammars without ap- pearance checking – it is known that *PsPR* strictly contains *PsCF* because it also contains non-semilinear vectors of natural numbers (see [[7](#_bookmark28)] for further details).

Formally, we have the following result.

Theorem 6.2 *PsPR* ⊆ *PsP P*∗(*α*)*, α* ∈ {*pinoi, pinoe, drip*}*.*

# Membrane Systems Using Protein-Membrane and Pro-

tein Movement Rules

We will investigate now membrane systems using both protein-membrane rules and protein movement rules. As we will demonstrate the ability to attach, de-attach, and move proteins across the system in a controlled fashion increases the generative power of the systems.

*Ppp* systems from *PsP P*∗((*ncoo*)*αi, prot*)*, α* ∈ {*pinoi, pinoo, drip*}, can generate at The first indications of the increased generative power is given by Theorem [7.1](#_bookmark14): least the family of Parikh images of context-free languages (compare this result with

Theorem [6.1](#_bookmark11)).

Theorem 7.1 *PsCF* ⊆ *PsP P*∗((*ncoo*)*α, prot*)*,α* ∈ {*pinoi, pinoe, drip*}*.*

If *Ppp* systems are equipped with both protein-membrane and protein movement

rules, then they are computationally complete, in the sense that they are able to generate the family of Parikh images of recursively enumerable languages.

So, informally, it seems that the ability to move the proteins (in a controlled way) through the regions of the system is important for reaching computational completeness. On the other hand, it is interesting to notice that the generative power of protein movement rules, when used alone, is very “weak” (Theorem [5.2](#_bookmark9)). By comparing the following proof with the proof of Theorem [6.2](#_bookmark12) we clearly notice similarities. The main difference is the second group of rules, used to simulate the

appearance checking mechanism present in the programmed grammar.

Theorem 7.2 *PsP P*∗(*α, prot*)= *PsRE, α* ∈ {*pinoi, pinoe, drip*}*.*

# Decision Problems

Since the set of proteins attached to a membrane determines the set of rules that can be applied to this membrane, we will consider now the following decision problem: Is it decidable whether or not an arbitrary multiset *w* is a reachable marking for an arbitrary *Ppp* system?

We will demonstrate that this problem is decidable for *Ppp* systems using (*i*) only pino and/or drip rules, or (*ii*) only protein movement rules, while it is not decidable for *Ppp* systems using both pino (or drip) rules and protein movement rules.

Theorem 8.1 *It is undecidable whether or not, for any Ppp system* Π *and any multiset w of proteins over V*Π*, w is a reachable marking of* Π*.*

If *Ppp* systems use only protein movement rules, only pino rules, or only drip rules, then the above problem becomes decidable.

Theorem 8.2 *It is decidable whether or not, for any Ppp system* Π *from P P*∗(*prot*)

*and any multiset w of proteins over V*Π*, w is a reachable marking of* Π*.*

Theorem 8.3 *It is decidable whether or not, for any Ppp system* Π *from P P*∗(*α*)*, α* ∈

{*pinoi, pinoe, drip*}*, and any multiset w of proteins over V*Π*, w is a reachable mark- ing of* Π*.*

We conclude this section by investigating two more decision problems. The first problem concerns the reachability of a configuration in *Ppp* systems. The second problem concerns the boundness of *Ppp* systems.

First, we observe that, given an arbitrary *Ppp* system Π and an arbitrary con- figuration *C* of Π, one can compute an upper bound *map*Π(*C*) on the number of applications of pino and drip rules that can be used in deriving *C* from the initial configuration of Π (in case that *C* is reachable in Π).

Clearly, one can generate in a systematic fashion all reachable configurations of Π containing no more than *r* membranes. Since each application of a pino or drip rule increases the number of membranes this generation process takes a bounded number of steps. If *C* appears among these configurations, then it is reachable, otherwise *C* is not reachable in Π.

Thus, we have the following result:

Theorem 8.4 *It is decidable whether or not, for any Ppp system* Π *and any con- ﬁguration C of* Π*, C is a reachable conﬁguration of* Π*.*

It is perhaps worthwhile to discuss Theorem [8.4](#_bookmark20) in the light of the universality result stated in Theorem [7.2](#_bookmark15). The reason that Theorem [8.4](#_bookmark20) holds is that, for a given configuration *C*, one can, a priori, provide an upper bound *mc* such that *C* is reachable in Π if and only if it is reachable by computations that do not exceed *mc* steps.

On the other hand, if we want to check whether or not a particular multiset

*w* is in the output of a successful computation of Π, then, in general, there is no

w/o *prot*

*prot*

w/o *pinoi*

(*ncoo*)*pinoi*

*pinoi*

PsFIN

⊂ PsCF

⊇ PsCF

⊇ PsPR

PsRE

Table 1

Computational power for *Ppp* systems using *pinoi* and protein movement rules (*prot*). The same table holds also for *pinoe* and *drip* operations.

upper bound *mw* such that: *w* ∈ *Ps*(Π) if and only if *w* is an output of a successful computation which takes no more than *mw* steps.

In fact, in general, there is no relationship between the size of *w* and the maximal size of a halting configuration in which *w* is marking one of the output membranes.

A *Ppp* system Π is *bounded* if there exists an integer *k*, such that, any reachable configuration of Π has less than *k* membranes.

*α* ∈ {*pinoi, pinoe, drip*}*, is bounded.* Theorem 8.5 *It is decidable whether or not an arbitrary Ppp system* Π *from P P*∗(*α*)*,*

# Concluding Remarks

We have investigated membrane systems using operations involving membranes marked with multisets of proteins. These systems use two different kinds of op- erations: the ones that involve membranes and proteins (pino and drip operations) and the ones that attach, de-attach, and move the proteins across the regions of the system (protein movement operations).

Membrane systems using both types of operations are shown to be computa- tionally complete. When the protein-membrane rules are restricted to be non- cooperative, then one generates at least the family of Parikh images of context-free languages.

We have also analyzed membrane systems whose evolution is based on only one of the two types of operations.

In particular we have shown that (in terms of Parikh sets) membrane systems using only pino (or only drip) rules are at least as powerful as programmed grammars without appearance checking.

Our current knowledge about the computational power of membrane systems considered in this paper is summarized in Table [1](#_bookmark21).

A number of problems have to be settled in order to get a more complete un- derstanding of membrane systems with marked membranes. Some of them are suggested by the results obtained in this paper.

* 1. Is the inclusion of *PsCF* ⊆ *PsP P*∗((*ncoo*)*α, prot*) *α* ∈ {*pinoi, pinoe, drip*}*,*

strict?

* 1. Is the inclusion *PsP P*∗((*ncoo*)*α, prot*) ⊆ *PsRE, α* ∈ {*pinoi, pinoe, drip*},

strict?

* 1. Is the inclusion *PsPR* ⊆ *PsP P*∗(*α*)*, α* ∈ {*pinoi, pinoe, drip*}, strict?
  2. Is the inclusion *PsP P*∗(*α*) ⊆ *PsRE, α* ∈ {*pinoi, pinoe, drip*}, strict?

Also the following “natural” decision problem should be settled for membrane

systems with marked membranes: is it possible to decide whether or not an arbi- trary multiset of proteins is a reachable marking for an arbitrary *Ppp* system from

*P P*∗((*ncoo*)*α, prot*), with *α* ∈ {*pinoi, pinoe, drip*}?

The problem is challenging since it is proved to be decidable for *Ppp* systems from

systems from *P P*∗(*α*)*, α* ∈ {*pinoi, pinoe, drip*}, i.e., using only protein-membrane *P P*∗(*prot*), i.e., using only protein movement rules (see Theorem [8.2](#_bookmark18)), and for *Ppp* rules (see Theorem [8.3](#_bookmark19)), while it is undecidable for arbitrary *Ppp* systems (Theorem

[8.1](#_bookmark17)).

A more general line of research involves the study of membrane systems having floating molecules and proteins attached to the internal or/and to the external side of a membrane (following, for instance, the idea introduced in [[6](#_bookmark27)] where projective brane calculus, with directed actions, has been introduced).

Interesting is also the idea to associate a time of execution to the considered protein rules (following, for instance, the idea of timed P systems introduced in [[5](#_bookmark26)]). We expect several interesting results along these lines of research, bridging mem-

brane systems and brane calculi.

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