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Applications of ϵ-Semantics to Biological Systems[1]

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Abstract

Hybrid automata are a natural model for both representing and analyzing systems that exhibit a mixed discrete continuous behaviours. However, the assumption of being able of performing infinite precision measurements over them soon leads to undecidability results and, sometimes, produces evolutions that are artifacts of the model and do not correspond to any observable phenomena. A class of finite precision semantics, named ϵ-semantics, is a way to handle these problems by formally representing noise, partial information, and finite precision instruments. This paper extends the classical reachability algorithm based on these semantics. Moreover, it reduces the computation of two specific ϵ-semantics to the decidability of a first-order theory and suggests how to decrease the complexity of the involved formulæ. Finally, it provides two practical applications of the proposed techniques to the biological domain.

Keywords: Hybrid Systems, ϵ-Semantics, Reachability problem

1. Introduction

The growing area of systems biology requires the development of techniques and formal models suitable for the description of biological systems. Often, such class of natural phenomena, can be captured through an abstraction process that involves hybrid systems, i.e., systems consisting of interactions between discrete and continuous components. Hybrid automata are mathematical models particularly suitable to the description of hybrid systems. Therefore, the study and the analysis of biological systems can be reduced to the resolution of reachability problems of hybrid automata.

Unfortunately, due to the undecidability of such problem, there are no algorithms able to compute, in a finite amount of time, the reachability set of a hybrid automaton.

Several techniques tackling the undecidability of the reachability problem have been proposed in recent years. One of the most studied approaches consists in the approximation of the original reachability set of hybrid automata. Such approximations can be performed in different manners: numerical calculation, symbolic computation or geometrical analysis are just few examples between all the approximation techniques offered in the literature. The most important factors to be considered are the quality of the approximation with respect to the original reachability set and the relationship between the approximated automaton and the behaviors of the modeled system.

ϵ-Semantics is a class of semantics that obviate the undecidability of the reachability problem over hybrid automata with bounded invariants. They were not originally meant to be proper approximations of the standard one, but, on the contrary, they were introduced to better mime the behaviors of real systems by adopting some natural-inspired constraints. Due to their peculiarity, these semantics are able to capture some indeterminacy which is intrinsic in the real word and, because of that, their use appears to be particularly useful in the study of biological systems.

In our framework, ϵ-semantics affect polynomial dynamics that are part of hybrid automata. Specifically, the ϵ-semantics evaluation of a formula can be attributed to the standard evaluation of a formula that is the result of a particular translation applied to the starting one. Such translated formula characterizes exactly in the standard semantics the ϵ-semantics of the considered formula. Unfortunately, this translation process increases the formulæ complexities, introducing an enlarged number of variables and quantifier operators. This aspect causes a prolongation of the computational times required to calculate the reachability set, operation which is performed exploiting tools for the quantifiers elimination.

Part of this work is to identify approximation semantics of particular interest for which the complexity of the evaluation can be contained. We will identify some simplification applicable to the translated formulæ to both decrease the number of the quantifier operators and reduce the complexity of the ϵ-semantics evaluations. These optimizations will be exploited in the analysis of two real biological cases, demonstrating the fact the ϵ-semantics represent a valid tool in the the study of biological systems.

The paper is organized as follows. Section 2 introduces notation and defines hybrid automata. In Section 3, we present the notion of ϵ-semantics and provide a reachability algorithm for hybrid automata based on it that extends the applicability of the classical algorithm to a wider class of hybrid automata. Section 4 describes two examples of ϵ-semantics, it shows that these two semantics are definable in the standard theory, and builds the formulæ that define them. As suggested by Section 5, in some specific, but frequent, cases, the complexity of these formulæ can be decreased. In Section 6 we study two real biological cases, a neural oscillator and a glycemic control system, exploiting all the techniques presented in the previous sections and, finally, Section 7 makes some concluding remarks and suggests future work.

2. Hybrid Automata

We first need to introduce some basic notions and conventions. Capital letters X, X_i, Y, Y_i, W, and W_i, denote variables ranging over the reals, while bolded letters $\mathbf{X}$, $\mathbf{X_i}$, $\mathbf{Y}$, $\mathbf{Y_i}$, $\mathbf{W}$, and $\mathbf{W_i}$, denote tuples of real variables. We assume that all those variables that occur bound in a formula do not occur free, and vice versa. This enables us to label variables, rather than occurrences, as free or bound. We write $\varphi[X_1, \dots, X_m]$ to stress the fact that the set of free variables of the formula φ is a subset of the set of variables $\{X_1, \dots, X_m\}$. By extension, $\varphi[\mathbf{X_1}, \dots, \mathbf{X_n}]$ indicates that the variables of tuples $\mathbf{X_1}, \dots, \mathbf{X_n}$ are free in φ. We denote the formula obtained from $\varphi[\mathbf{X_1}, \dots, \mathbf{X_n}]$ by simultaneously replacing all the variables $\mathbf{X_1}, \dots, \mathbf{X_n}$ by $\mathbf{s_1}, \dots, \mathbf{s_n}$, where $\mathbf{s_i}$ is either a constant or a variable, by writing $\varphi[\![\mathbf{s_1}, \dots, \mathbf{s_n}]\!]$.

The notions of first-order formula, models, and theory are defined in the standard way (see [1, 2]). A formula without free variables is called a *sentence*. A *theory* $\mathcal{T}$ is a set of sentences such that if φ is a logical consequence of $\mathcal{T}$, then $\varphi \in \mathcal{T}$. A theory $\mathcal{T}$ admits the *elimination of quantifiers* if, for any formula φ, there exists in $\mathcal{T}$ a quantifier free formula ϱ such that φ is equivalent to ϱ with respect to $\mathcal{T}$. A theory $\mathcal{T}$ is *decidable* if there exists an algorithm for deciding whether a sentence φ belongs to $\mathcal{T}$ or not.

Example 1. *Consider the formula* $\varphi \overset{def}{=} \exists X \left(a * X^2 + b * X + c = 0\right)$. *It is well known that* φ *is in the theory of reals with* $+$, $*$, *and* $\geq$ *if and only if the unquantified formula* $b^2 - 4ac \geq 0$ *holds.*

In this work we refer to the first-order theory of $\langle \mathbb{R}, +, *, =, < \rangle$, also known as the *Tarski's theory* or the theory of *semi-algebraic sets*, which is decidable and admits quantifier elimination. Even if we will implicitly refer to Tarski's theory, all our results hold for any decidable theory over the reals.

Given a language $\mathcal{L}$, a *semantics* of it is a function $[\cdot]$ from the set of formulæ of $\mathcal{L}$ to the power set of $\mathbb{R}^*$ such that $[\varphi[X_1,\dots,X_n]] \subseteq \mathbb{R}^n$. Any theory $\mathcal{T}$ over a language $\mathcal{L}$ induces the semantics $[\varphi[X_1,\dots,X_n]] \overset{def}{=} \{\langle s_1,\dots,s_n\rangle \mid \varphi[\![p_1,\dots,p_n]\!] \in \mathcal{T}\}$. The formula $S[\mathbf{X}]$ *represents* (also *defines*) in $[\cdot]$ the set $[S[\mathbf{X}]]$. If there exists a formula $S[\mathbf{X}]$ such that $[S[\mathbf{X}]] = \mathbb{S}$, then the set $\mathbb{S}$ is said *definable* in $[\cdot]$. In the case of the first-order language $\langle \mathbb{R}, +, *, =, <\rangle$, the semantics induced by the Tarski's theory is also called *standard semantics* and we denote it by using the notation $\{\!|\cdot|\!\}$. Whenever we do not explicitly mention any semantics, we are referring to the standard one.

We also use some standard notions from topological and metric spaces (see [3]). Given a set $\mathbb{S} \subseteq \mathbb{R}^n$, $conv(\mathbb{S})$ denotes the convex hull of $\mathbb{S}$, while, with the symbol δ, we refer to the *standard euclidean metric* over $\mathbb{R}^n$. From now on, although we implicitly refer to δ, our results can be generalized to any metric definable in Tarski's theory. With the notation $B(p,\epsilon)$ we indicate the set of points at distance smaller than ϵ from p, i.e., the open sphere of radius ϵ centered in $p \in \mathbb{R}^n$. By extension, $B(\mathbb{S},\epsilon)$, where $\mathbb{S}$ is a subset of $\mathbb{R}^n$, denotes the Minkowski sum of $B(0,\epsilon)$ and $\mathbb{S}$.

2.1. Syntax, Semantics, and Reachability

In this section we give the formal definition of hybrid automata. In the literature there are many different definitions of hybrid automata. Even if the most common differences between those formalisms reside in the descriptions of continuous and discrete transitions, the semantics attributed to the transitions are almost the same. Here we define hybrid automata through first-order formulæ over the reals and, in particular, semi-algebraic formulæ.

Definition 1 (Hybrid Automata - Syntax)**.** *A hybrid automaton H of dimension $d(H) \in \mathbb{N}$ is a tuple $H = \langle \mathbf{X}, \mathbf{X}', T, \mathcal{V}, \mathcal{E}, Inv, Dyn, Act, Res\rangle$ where:*

- $\mathbf{X} = \langle X_1, \dots, X_{d(H)}\rangle$ *and* $\mathbf{X}' = \langle X'_1, \dots, X'_{d(H)}\rangle$ *are two tuples of variables ranging over the reals* $\mathbb{R}$*;*
- T *is a variable ranging over* $\mathbb{R}_{\geq 0}$*;*
- $\langle \mathcal{V}, \mathcal{E}\rangle$ *is a finite directed graph. Each element of* $\mathcal{V}$ *will be dubbed* location*;*

- *each location $v \in \mathcal{V}$ is labeled by the two first-order formulæ $Inv(v)[\mathbf{X}]$ and $Dyn(v)[\mathbf{X}, \mathbf{X}', T]$ such that if $Inv(v)[\![p]\!]$ is true then $Dyn(v)[\![p, q, 0]\!]$ is true if and only if $p = q$;*
- *each edge $e \in \mathcal{E}$ is labeled by the formulæ $Act(e)[\mathbf{X}]$ and $Res(e)[\mathbf{X}, \mathbf{X}']$ which are called* activation *and* reset*, respectively.*

Intuitively, the formula $Dyn(v)[\mathbf{X}, \mathbf{X}', T]$ characterizes the dynamics associated to the location v, while $Inv(v)[\mathbf{X}]$ denotes the set of the values admitted during the continuous evolution of the automaton inside v. The formulæ $Act(e)[\mathbf{X}]$ and $Res(e)[\mathbf{X}, \mathbf{X}']$ identifies the set of continuous values from which the automaton can jump over the edge e and a map that should be applied to the continuous values from which the automaton crosses the edge e. The following section details the formal meaning of these formulæ and describes the semantics of hybrid automata.

Hybrid automaton dynamics are usually described by using differential equations (see, e.g., [4, 5]). However, in many cases, solutions or approximated solutions of the differential equations are computed before proceeding with any reasoning on the automata (see, e.g., [5]). Whenever such solutions are polynomials, we obtain automata which fall under our definition.

Differently from [6], we require that $Dyn(v)[\![p, q, 0]\!]$ *implies* $p = q$. Intuitively, this means that if we are in p at time 0, we can reach a point different from p through a continuous dynamic only if we let time flow. This assumption allows us to both get flow continuity at time 0 and slightly simplify the reachability formulæ with respect to the ones defined in [6].

2.2. Hybrid Automaton Semantics

Intuitively, the formula $Dyn(v)[\mathbf{X}, \mathbf{X}', T]$ holds if there exists a continuous flow going from $\mathbf{X}$ to $\mathbf{X}'$ in time T. Our semantics admits an infinite number of continuous flows which can also be self-intersecting.

Definition 2 (Hybrid Automata - Semantics)**.** *A* state ℓ *of H is a pair $\langle v, r\rangle$, where $v \in \mathcal{V}$ is a location and $s = \langle s_1, \ldots, s_{d(H)}\rangle \in \mathbb{R}^{d(H)}$ is an assignment of values for the variables of $\mathbf{X}$. A state $\langle v, s\rangle$ is* admissible *if $Inv(v)[\![s]\!]$ is true. We have two kind of transitions:*

- *the* continuous transition relation $\xrightarrow{t}_C$*:*
  $\langle v, s\rangle \xrightarrow{t}_C \langle v, r\rangle \iff$ *there exists $f : \mathbb{R}_{\geq 0} \to \mathbb{R}^{d(H)}$ continuous function such that $s = f(0)$, there exists $t \geq 0$ such that $r = f(t)$, and for each $t' \in [0, t]$, both $Inv(v)[\![f(t')]\!]$ and $Dyn(v)[\![s, f(t'), t']\!]$ hold;*

- *the* discrete transition relation $\xrightarrow{(v,u)}_D$:
  $\langle v, s\rangle \xrightarrow{(v,u)}_D \langle u, r\rangle \iff (v,u) \in \mathcal{E}$ *and both the formulæ* $Act((v,u))[\![s]\!]$ *and* $Res((v,u))[\![s,r]\!]$ *holds.*

A trace is a sequence of continuous and discrete transitions. A point r is reachable from a point s if there is a trace starting from s and ending in r. We write $\ell \to_C \ell'$ and $\ell \to_D \ell'$ to mean that there exists a $t \in \mathbb{R}_{\geq 0}$ such that $\ell \xrightarrow{t}_C \ell'$ and that there exists an $e \in \mathcal{E}$ such that $\ell \xrightarrow{e}_D \ell'$, respectively. Moreover, we write $\ell \to \ell'$ to denote either $\ell \to_C \ell'$ or $\ell \to_D \ell'$.

Definition 3 (Hybrid Automata - Reachability)**.** *A* trace *of length* n *of* H *is a sequence of admissible states* $\ell_0, \ell_1, \ldots, \ell_n$*, with* $n \in \mathbb{N}_{>0}$*, such that:*

- *for each* $j \in [1, n]$ *it holds* $\ell_{j-1} \to \ell_j$*;*
- *for each* $j \in [1, n-1]$ *if* $\ell_{j-1} \not\to_D \ell_j$*, then* $\ell_j \to_D \ell_{j+1}$*.*

In H*,* $s \in \mathbb{R}^{d(H)}$ reaches $r \in \mathbb{R}^{d(H)}$ *if there exists a trace* $\ell_0, \ldots, \ell_n$ *of* H *such that* $\ell_0 = \langle v, s\rangle$ *and* $\ell_n = \langle u, r\rangle$*, for some* $v, u \in \mathcal{V}$*. A set* $\mathbb{I} \subseteq \mathbb{R}^{d(H)}$ reaches $\mathbb{F} \subseteq \mathbb{R}^{d(H)}$ *if there exists* $s \in \mathbb{I}$ *which reaches* $r \in \mathbb{F}$*.*

Notice that we impose a condition such that, in a trace, two continuous transitions do not occur consecutively. In all those hybrid automata whose flows are solutions of autonomous differential equations, the continuous transition relation is transitive, which means that different consecutive continuous transitions can be reduced to a single continuous one. Definition 1 allows also automata whose continuous transition relation is not transitive. For instance, if the solution of the differential-based dynamics is $\langle X_0 + T, X_1 + T^2\rangle$, the set of points reachable from $\langle 0, 0\rangle$ is $R = \{\langle t, t^2\rangle | t \in \mathbb{R}_{\geq 0}\}$. However, for every $r \in \mathbb{R}$, there exists a tuple $\langle t, r * t\rangle$ in R. It follows that, if the semantics admitted two or more successive continuous transitions, the reachability set would have been $\mathbb{R}^2$ which is not the expected one.

Let us notice that the definition of $\to_C$ requires the existence of a continuous function f which satisfies both the formuæ *Inv* and *Dyn*. If we consider only functional automata (i.e., automata whose dynamics have the form $Dyn(v)[\mathbf{X}, \mathbf{X}', T] \stackrel{def}{=} \mathbf{X}' = f_v(\mathbf{X}, T)$) such an existence can be expressed by an opportune first-order language. However, there exist non functional automata for which this is not the case. Hybrid automata in Michael's form [6] generalize functional automata still admitting a reduction of the continuous reachability problem over them to a satisfiability problem. On the one hand, they allow to express dynamics involving unknown parameters, which may be useful in many practical applications (e.g., systems biology). On the other hand, they enable us to both over-approximate and under-approximate the reachable set by exploiting the techniques presented in [7] and [8].

3. ϵ-Semantics

The ability of characterizing dense regions of arbitrarily small size, is the main cause of the undecidability of the reachability problem over hybrid automata. As noticed in [8], such ability may be misleading in some cases. The continuous quantities used in hybrid automata are very often abstractions of large, but discrete, quantities. For instance, in the study of biological systems, the ability of handling values with infinite precision is a model artifact rather than a real property of the original system.

Theorem 1 ([8])**.** *Let $\mathcal{T}$ be a decidable first-order theory over reals and H be a $\mathcal{T}$-hybrid automaton with bounded invariants. If there exists $\epsilon \in \mathbb{R}_{>0}$ such that, for each $\mathbb{I} \subseteq \mathbb{R}^{d(H)}$ and for each $i \in \mathbb{N}$, either $RSet_H^{i+1}(\mathbb{I}) = RSet_H^{i}(\mathbb{I})$ or there exists a $a_i \in \mathbb{R}^{d(H)}$ such that $B(a_i, \epsilon) \subseteq RSet_H^{i+1}(\mathbb{I}) \setminus RSet_H^{i}(\mathbb{I})$, then there exists $j \in \mathbb{N}$ such that $RSet_H^{i}(\mathbb{I}) = RSet_H^{j}(\mathbb{I})$ and the reachability problem over H is decidable.*

Since our hybrid automata characterization is based on first-order formulæ, it is reasonable to reinterpret the semantics of semi-algebraic automata by giving each formula a "dimension of at least ϵ". ϵ-semantics [8] are a class of approximated semantics, which guarantee the decidability of reachability in the case of hybrid automata with bounded invariants.

Definition 4. *Let $\mathcal{T}$ be a first-order theory and let $\epsilon \in \mathbb{R}_{>0}$. For each formula $\psi \in \mathcal{T}$ with d free variables, let $\{\!|\psi|\!\}_\epsilon$ be a subset of $\mathbb{R}^d$ such that:*

(ϵ)either $\{\!|\psi|\!\}_\epsilon = \varnothing$ or there exists $p \in \mathbb{R}^d$ such that $B(p, \epsilon) \subseteq \{\!|\psi|\!\}_\epsilon$

($\cap$)$\{\!|\phi \wedge \varphi|\!\}_\epsilon \subseteq \{\!|\phi|\!\}_\epsilon \cap \{\!|\varphi|\!\}_\epsilon$ *($\cup$)$\{\!|\phi \vee \varphi|\!\}_\epsilon = \{\!|\phi|\!\}_\epsilon \cup \{\!|\varphi|\!\}_\epsilon$*

($\forall$)$\{\!|\forall X \psi[X, \mathbf{X}]|\!\}_\epsilon = \{\!|\bigwedge_{r \in \mathbb{R}} \psi[\![r, \mathbf{X}]\!]|\!\}_\epsilon$ *($\exists$)$\{\!|\exists X \psi[X, \mathbf{X}]|\!\}_\epsilon = \{\!|\bigvee_{r \in \mathbb{R}} \psi[\![r, \mathbf{X}]\!]|\!\}_\epsilon$*

($\neg$)$\{\!|\psi|\!\}_\epsilon \cap \{\!|\neg\psi|\!\}_\epsilon = \varnothing$

Any semantics satisfying the above conditions is an ϵ-semantics for $\mathcal{T}$.

There is no ϵ-semantics over-approximating $\{\!|\cdot|\!\}$, i.e., there is no $\{\!|\cdot|\!\}_\epsilon$ such that $\{\!|\psi|\!\}_\epsilon \supset \{\!|\psi|\!\}$ for any formula ψ. As a matter of fact, by rule $(\neg)$, $\{\!|\psi|\!\}_\epsilon \cap \{\!|\neg\psi|\!\}_\epsilon = \varnothing$. Hence, if $\{\!|\psi|\!\}_\epsilon \supset \{\!|\psi|\!\}$, then $\{\!|\neg\psi|\!\}_\epsilon$ should be a subset of $\{\!|\neg\psi|\!\}$.

It is well known that, in the standard semantics, the reachability problem over hybrid automata with bounded invariants is not decidable. This is not the case if we use ϵ-semantics in place of the standard one and, in particular, [8] introduced an algorithm that, provided the computability of the ϵ-semantics, evaluates the reachable set of functional automata having transitive dynamics. These constraints imposed on the dynamics were not related to the applicability of the suggested strategy to more general automata, but they were due to the focus of interest of the original article. Indeed, Algorithm 1 supports any hybrid automata in Michael's form, even those whose dynamics are not transitive.

The `while` loop of Algorithm 1 is repeated until the set of active locations is exhausted. This happens when the set $\{\!|N(v')[\mathbf{X}] \wedge \neg R(v')[\mathbf{X}]|\!\}_\epsilon$ becomes empty for all the active locations v' (line 14), i.e., set of states reached for the first time during the last iteration is smaller than an ϵ-sphere. Since all the sets $\{\!|Inv(v)|\!\}_\epsilon$ are bounded by hypothesis, we conclude from Theorem 1 that soon or later such a condition will be reached and Algorithm 1 eventually terminates. The correctness of it easily follows from the same arguments that were used for the original algorithm.

4. Two Relevant ϵ-Semantics

This section presents two computable instances of ϵ-semantics: the *sphere semantics* and the *dilated erosion semantics*.

Definition 5 (Sphere semantics)**.** *Let $\mathcal{T}$ be a first-order theory over the reals and let $\epsilon > 0$. The* sphere semantics *of ψ, $(\!|\psi|\!)_\epsilon$, is defined by structural induction on ψ as follows:*

- $(\!|t_1 \circ t_2|\!)_\epsilon \overset{def}{=} B\left(\{\!|t_1 \circ t_2|\!\}, \epsilon\right)$*, for* $\circ \in \{=, <\}$
- $(\!|\psi_1 \wedge \psi_2|\!)_\epsilon \overset{def}{=} \bigcup_{B(p,\epsilon) \subseteq (\!|\psi_1|\!)_\epsilon \cap (\!|\psi_2|\!)_\epsilon} B\left(p, \epsilon\right)$
- $(\!|\psi_1 \vee \psi_2|\!)_\epsilon \overset{def}{=} (\!|\psi_1|\!)_\epsilon \cup (\!|\psi_2|\!)_\epsilon$
- $(\!|\forall X \psi[X, \mathbf{X}]|\!)_\epsilon \overset{def}{=} (\!|\bigwedge_{r \in \mathbb{R}} \psi[\![r, \mathbf{X}]\!]|\!)_\epsilon$
- $(\!|\exists X \psi[X, \mathbf{X}]|\!)_\epsilon \overset{def}{=} (\!|\bigvee_{r \in \mathbb{R}} \psi[\![r, \mathbf{X}]\!]|\!)_\epsilon$
- $(\!|\neg\psi|\!)_\epsilon \overset{def}{=} \bigcup_{B(p,\epsilon) \cap (\!|\psi|\!)_\epsilon = \varnothing} B\left(p, \epsilon\right)$

It is known that the sphere semantics is an ϵ-semantics [8]. This semantics is neither an over-approximation nor an under-approximation of the

Algorithm 1 Reachability$(H, I(\cdot)[\mathbf{X}], \{\!|\cdot|\!\}_\epsilon)$

Require: $\{\!|Inv(v)|\!\}_\epsilon$ is bounded for all $v \in \mathcal{V}$, $cReach(v)[\![p,q]\!]$ holds iff $\langle v,p\rangle \to_C \langle v',q\rangle$, $dcReach(e)[\![p,q]\!]$ holds iff $e = (v,v')$ and there exists a $s \in \mathbb{R}^*$ such that $\langle v,p\rangle \xrightarrow{e}_D \langle v',s\rangle \to_C \langle v',q\rangle$

Ensure: At the end of the computation $R(v)[\![p]\!]$ holds off $\langle v,p\rangle$ is reachable

for $v \in \mathcal{V}$ **do**
    $R(v)[\mathbf{X}] \leftarrow \exists \mathbf{X}'(cReach(v)[\![\mathbf{X}', \mathbf{X}]\!] \wedge I(v)[\![\mathbf{X}']\!])$
    $N(v)[\mathbf{X}] \leftarrow \bot$
end for
$active\_\mathcal{V} \leftarrow \mathcal{V}$
while $active\_\mathcal{V} \neq \varnothing$ **do**
    $new\_active \leftarrow \varnothing$
    for $v \in active\_\mathcal{V}$ **do**
        $R(v)[\mathbf{X}] \leftarrow R(v)[\mathbf{X}] \vee N(v)[\mathbf{X}]$
        $N(v)[\mathbf{X}] \leftarrow \bot$
    end for
    for $(v,v') \in \mathcal{E}$ such that $v \in active\_\mathcal{V}$ **do**
        $N(v')[\mathbf{X}] \leftarrow N(v')[\mathbf{X}] \vee \exists \mathbf{X}'(dcReach(\langle v,v'\rangle)[\![\mathbf{X}', \mathbf{X}]\!] \wedge R[\![\mathbf{X}']\!])$
        if $\{\!|N(v')[\mathbf{X}] \wedge \neg R(v')[\mathbf{X}]|\!\}_\epsilon \neq \varnothing$ **then**
            $new\_active \leftarrow new\_active \cup \{v'\}$
        end if
    end for
    $active\_\mathcal{V} \leftarrow new\_active$
end while
return $R(\cdot)[\mathbf{X}]$

standard semantics and, for instance, $\{\!|X < 3|\!\} \subset (\!|X < 3|\!)_\epsilon$ and $(\!|\neg(X < 3)|\!)_\epsilon \subset \{\!|\neg(X < 3)|\!\}$.

Definition 6 (Erosion and DE Semantics)**.** *Let ψ be a formula and $\epsilon \in \mathbb{R}_{>0}$. The* erosion semantics *of ψ is the set $\rangle\psi\langle_\epsilon$ defined by structural induction on ψ itself as follows:*

- $\rangle t_1 \circ t_2\langle_\epsilon = \bigcup_{B(p,\epsilon)\subseteq\{\!|t_1\circ t_2|\!\}} \{p\}$
- $\rangle\psi_1 \wedge \psi_2\langle_\epsilon = \rangle\psi_1\langle_\epsilon \cap \rangle\psi_2\langle_\epsilon$
- $\rangle\psi_1 \vee \psi_2\langle_\epsilon = \rangle\psi_1\langle_\epsilon \cup \rangle\psi_2\langle_\epsilon$
- $\rangle\forall X\psi[X,\mathbf{X}]\langle_\epsilon = \bigcap_{r\in\mathbb{R}} \rangle\psi[\![r,\mathbf{X}]\!]\langle_\epsilon$
- $\rangle\exists X\psi[X,\mathbf{X}]\langle_\epsilon = \bigcup_{r\in\mathbb{R}} \rangle\psi[\![r,\mathbf{X}]\!]\langle_\epsilon$
- $\rangle\neg\psi\langle_\epsilon = \bigcup_{B(p,\epsilon)\cap\{\!|\psi|\!\}=\varnothing} \{p\}$

The dilated erosion semantics*, or simply,* DE semantics*, of ψ is the set $\rangle\!\rangle\psi\langle\!\langle_\epsilon \stackrel{def}{=} \bigcup_{p\in\rangle\psi\langle_\epsilon} B(p,\epsilon)$.*

As $\rangle\delta(X,0) < \epsilon\langle_\epsilon$ does not contain a sphere of radius ϵ, but it is not empty, the erosion semantics is not an ϵ-semantics. However, the DE semantics is an ϵ-semantics and it under-approximates the standard semantics.

Lemma 1. *For any first-order formula ψ and $\epsilon \in \mathbb{R}_{>0}$, $\rangle\!\rangle\psi\langle\!\langle_\epsilon \subseteq \{\!|\psi|\!\}$. Moreover, the DE semantics $\rangle\!\rangle\cdot\langle\!\langle_\epsilon$ is an ϵ-semantics.*

Proof. First, we demonstrate that the DE semantics is an under-approximated semantics, i.e., for any first-order formula ψ and $\epsilon \in \mathbb{R}_{>0}$, $\rangle\!\rangle\psi\langle\!\langle_\epsilon \subseteq \{\!|\psi|\!\}$. The proof is given by structural induction on ψ itself.

$t_1 \circ t_2$, for $\circ \in \{=,<\}$. By definition of DE semantics, $\rangle\!\rangle t_1 \circ t_2\langle\!\langle_\epsilon = B(\rangle t_1 \circ t_2\langle_\epsilon, \epsilon)$ $= B\left(\bigcup_{B(p,\epsilon)\subseteq\{\!|t_1\circ t_2|\!\}} \{p\}, \epsilon\right) = \bigcup_{B(p,\epsilon)\subseteq\{\!|t_1\circ t_2|\!\}} B(p,\epsilon) \subseteq \{\!|t_1 \circ t_2|\!\}$.

$\psi_1 \wedge \psi_2$. $\rangle\!\rangle\psi_1 \wedge \psi_2\langle\!\langle_\epsilon = B(\rangle\psi_1 \wedge \psi_2\langle_\epsilon, \epsilon) = B(\rangle\psi_1\langle_\epsilon \cap \rangle\psi_2\langle_\epsilon, \epsilon) \subseteq B(\rangle\psi_1\langle_\epsilon, \epsilon) \cap B(\rangle\psi_2\langle_\epsilon, \epsilon) = \rangle\!\rangle\psi_1\langle\!\langle_\epsilon \cap \rangle\!\rangle\psi_2\langle\!\langle_\epsilon$. By inductive hypothesis, $\rangle\!\rangle\psi_1\langle\!\langle_\epsilon \subseteq \{\!|\psi_1|\!\}$ and $\rangle\!\rangle\psi_2\langle\!\langle_\epsilon \subseteq \{\!|\psi_2|\!\}$, hence $\rangle\!\rangle\psi_1\langle\!\langle_\epsilon \cap \rangle\!\rangle\psi_2\langle\!\langle_\epsilon \subseteq \{\!|\psi_1|\!\} \cap \{\!|\psi_2|\!\} = \{\!|\psi_1 \wedge \psi_2|\!\}$.

$\psi_1 \vee \psi_2$. By definition, $\rangle\!\rangle\psi_1 \vee \psi_2\langle\!\langle_\epsilon = B(\rangle\psi_1 \vee \psi_2\langle_\epsilon, \epsilon) = B(\rangle\psi_1\langle_\epsilon \cup \rangle\psi_2\langle_\epsilon, \epsilon) = B(\rangle\psi_1\langle_\epsilon, \epsilon) \cup B(\rangle\psi_2\langle_\epsilon, \epsilon) = \rangle\!\rangle\psi_1\langle\!\langle_\epsilon \cup \rangle\!\rangle\psi_2\langle\!\langle_\epsilon$. Now, by inductive hypothesis we know that $\rangle\!\rangle\psi_1\langle\!\langle_\epsilon \subseteq \{\!|\psi_1|\!\}$ and $\rangle\!\rangle\psi_2\langle\!\langle_\epsilon \subseteq \{\!|\psi_2|\!\}$, thus $\rangle\!\rangle\psi_1\langle\!\langle_\epsilon \cup \rangle\!\rangle\psi_2\langle\!\langle_\epsilon \subseteq \{\!|\psi_1|\!\} \cup \{\!|\psi_2|\!\} = \{\!|\psi_1 \vee \psi_2|\!\}$.

$\forall X\psi[X,\mathbf{X}]$. By the definition of DE semantics and inductive hypothesis, $\rangle\!\rangle\forall X\psi[X,\mathbf{X}]\langle\!\langle_\epsilon = B(\rangle\forall X\psi[X,\mathbf{X}]\langle_\epsilon, \epsilon) = B(\bigcap_{r\in\mathbb{R}} \rangle\psi[\![r,\mathbf{X}]\!]\langle_\epsilon, \epsilon) =$

$B\left(\rangle\bigwedge_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]\langle_\epsilon,\epsilon\right) = \rangle\!\rangle\bigwedge_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]\langle\!\langle_\epsilon$. Applying the inductive step demonstrated in the conjunction case, we can state that $\rangle\!\rangle\bigwedge_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]\langle\!\langle_\epsilon \subseteq \{\!|\bigwedge_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]|\!\}$ which in terms of the standard semantics corresponds to the formula $\{\!|\forall X\psi[X,\mathbf{X}]|\!\}$.

$\exists X\psi[X,\mathbf{X}]$. By the definition of DE semantics and inductive hypothesis, $\rangle\!\rangle\exists X\psi[X,\mathbf{X}]\langle\!\langle_\epsilon = B\left(\rangle\exists X\psi[X,\mathbf{X}]\langle_\epsilon,\epsilon\right) = B\left(\bigcup_{r\in\mathbb{R}}\rangle\psi[\![r,\mathbf{X}]\!]\langle_\epsilon,\epsilon\right)$, which is equal to $B\left(\rangle\bigvee_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]\langle_\epsilon,\epsilon\right) = \rangle\!\rangle\bigvee_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]\langle\!\langle_\epsilon \subseteq \{\!|\bigvee_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]|\!\}$, that, by the standard semantics, corresponds to $\{\!|\exists X\psi[X,\mathbf{X}]|\!\}$.

$\neg\psi$. $\rangle\!\rangle\neg\psi\langle\!\langle_\epsilon = B\left(\bigcup_{B(p,\epsilon)\cap\{\!|\psi|\!\}=\varnothing}\{p\},\epsilon\right) = \bigcup_{B(p,\epsilon)\cap\{\!|\psi|\!\}=\varnothing} B(p,\epsilon) \subseteq \{\!|\neg\psi|\!\}$.

Let us now demonstrate that the DE semantics is effectively an ϵ-semantics, i.e., that it satisfies all the requirements of Definition 4.

Requirement (ϵ) is trivially satisfied since any DE semantics evaluation is performed applying an ϵ-expansion. This means that a formula is either empty or large at least as an ϵ-sphere. Let $\psi = \psi_1 \wedge \psi_2$ be a conjunction. By definition, $\rangle\!\rangle\psi_1\wedge\psi_2\langle\!\langle_\epsilon = B\left(\rangle\psi_1\wedge\psi_2\langle_\epsilon,\epsilon\right) = B\left(\rangle\psi_1\langle_\epsilon\cap\rangle\psi_2\langle_\epsilon,\epsilon\right) \subseteq B\left(\rangle\psi_1\langle_\epsilon,\epsilon\right)\cap B\left(\rangle\psi_2\langle_\epsilon,\epsilon\right) = \rangle\!\rangle\psi_1\langle\!\langle_\epsilon\cap\rangle\!\rangle\psi_2\langle\!\langle_\epsilon$. Thus, requirement ($\cap$) is satisfied. Similarly, if $\psi = \psi_1\vee\psi_2$ is a disjunction, then $\rangle\!\rangle\psi_1\vee\psi_2\langle\!\langle_\epsilon = B\left(\rangle\psi_1\vee\psi_2\langle_\epsilon,\epsilon\right) = B\left(\rangle\psi_1\langle_\epsilon\cup\rangle\psi_2\langle_\epsilon,\epsilon\right) = B\left(\rangle\psi_1\langle_\epsilon,\epsilon\right)\cup B\left(\rangle\psi_2\langle_\epsilon,\epsilon\right) = \rangle\!\rangle\psi_1\langle\!\langle_\epsilon\cup\rangle\!\rangle\psi_2\langle\!\langle_\epsilon$, which means that also the requirement ($\cup$) is satisfied. Let $\psi = \forall X\psi[X,\mathbf{X}]$ be a quantified formula. Thus, $\rangle\!\rangle\forall X\psi[X,\mathbf{X}]\langle\!\langle_\epsilon = B\left(\rangle\forall X\psi[X,\mathbf{X}]\langle_\epsilon,\epsilon\right) = B\left(\bigcap_{r\in\mathbb{R}}\rangle\psi[\![r,\mathbf{X}]\!]\langle_\epsilon,\epsilon\right) = B\left(\rangle\bigwedge_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]\langle_\epsilon,\epsilon\right) = \rangle\!\rangle\bigwedge_{r\in\mathbb{R}}\psi[\![r,\mathbf{X}]\!]\langle\!\langle_\epsilon$. The case of formulæ closed by the existential quantifier operator is symmetrical to the universal one, where the unions and disjunctions play the roles of intersections and conjunctions, respectively. Hence, also requirements ($\forall$) and ($\exists$) are satisfied. Finally, since the DE semantics is an under-approximation semantics, we know that $\rangle\!\rangle\psi\langle\!\langle_\epsilon \subseteq \{\!|\psi|\!\}$ and $\rangle\!\rangle\neg\psi\langle\!\langle_\epsilon \subseteq \{\!|\neg\psi|\!\}$. Moreover, by the standard semantics, since it holds that $\{\!|\psi|\!\}\cap\{\!|\neg\psi|\!\} = \varnothing$, then $\rangle\!\rangle\psi\langle\!\langle_\epsilon\cap\rangle\!\rangle\neg\psi\langle\!\langle_\epsilon = \varnothing$ must hold too. Hence, requirement ($\neg$) is always satisfied. □

The evaluation of both $(\!|\cdot|\!)_\epsilon$ and $\rangle\!\rangle\cdot\langle\!\langle_\epsilon$ can be reduced to the evaluation of the standard semantics. For any first-order theory $\mathcal{T}$ such that $B(p,\epsilon)$ is $\mathcal{T}$-definable and any $\phi\in\mathcal{T}$, we can build two first-order formulæ, $\widehat{(\phi)}_\epsilon$ and $\widetilde{(\phi)}_\epsilon$, in $\mathcal{T}$, such that $(\!|\phi|\!)_\epsilon = \left\{\!\left|\widehat{(\phi)}_\epsilon\right|\!\right\}$ and $\rangle\!\rangle\phi\langle\!\langle_\epsilon = \{\!|\widetilde{(\phi)}_\epsilon|\!\}$. This means that, whenever $\mathcal{T}$ is decidable, both $(\!|\cdot|\!)_\epsilon$ and $\rangle\!\rangle\cdot\langle\!\langle_\epsilon$ are symbolically computable.

We need to distinguish two kind of variables: the variables of the original formula (named W, W_i, $\mathbf{W}$ and $\mathbf{W_i}$), whose evaluations are perturbed by the sphere semantics, and the auxiliary variables (named Y, Y_i, $\mathbf{Y}$ and $\mathbf{Y_i}$) introduced to translate the sphere semantics into the standard one. It is possible to see the later as symbolic constants, even if they will be quantified in the translated formula. We will use them to characterize the ϵ-semantics of the formulæ $\bigwedge_{r\in\mathbb{R}} \varphi[\![r,\mathbf{W}]\!]$ and $\bigvee_{r\in\mathbb{R}} \varphi[\![r,\mathbf{W}]\!]$ in the standard semantics.

4.1. From sphere into standard semantics

Let $\mathcal{T}$ be a first-order theory over the reals, $\varphi[\mathbf{Y},\mathbf{W}]$ be any first-order formula $\mathcal{T}$-definable, and $\epsilon \in \mathbb{R}_{>0}$. We define $\widehat{(\varphi)}_\epsilon[\mathbf{Y},\mathbf{W}]$ by structural induction on $\varphi[\mathbf{Y},\mathbf{W}]$ itself.

- $(\widehat{(t_1 \circ t_2)[\mathbf{Y},\mathbf{W}]})_\epsilon \overset{\text{def}}{=} \exists \mathbf{W_0}((t_1 \circ t_2)[\![\mathbf{Y},\mathbf{W_0}]\!] \wedge \delta(\mathbf{W_0},\mathbf{W}) < \epsilon)$, $\circ \in \{=,<\}$;
- $(\widehat{\phi[\mathbf{Y},\mathbf{W}] \wedge \psi[\mathbf{Y},\mathbf{W}]})_\epsilon \overset{\text{def}}{=} \exists \mathbf{W_0}(\forall \mathbf{W_1}(\delta(\mathbf{W_0},\mathbf{W_1}) < \epsilon \rightarrow$ $(\widehat{(\phi)}_\epsilon \wedge \widehat{(\psi)}_\epsilon)[\![\mathbf{Y},\mathbf{W_1}]\!]) \wedge \delta(\mathbf{W_0},\mathbf{W}) < \epsilon)$;
- $(\widehat{\phi \vee \psi})_\epsilon \overset{\text{def}}{=} \widehat{(\phi)}_\epsilon \vee \widehat{(\psi)}_\epsilon$;
- $(\widehat{\forall W \phi[\mathbf{Y},W,\mathbf{W}]})_\epsilon \overset{\text{def}}{=} \exists \mathbf{W_0}(\forall \mathbf{W_1}(\delta(\mathbf{W_0},\mathbf{W_1}) < \epsilon \rightarrow$ $\forall Y (\widehat{\phi[\![\mathbf{Y},Y,\mathbf{W_1}]\!]})_\epsilon) \wedge \delta(\mathbf{W_0},\mathbf{W}) < \epsilon)$;
- $(\widehat{\exists W \phi[\mathbf{Y},W,\mathbf{W}]})_\epsilon \overset{\text{def}}{=} \exists Y (\widehat{\phi[\![\mathbf{Y},Y,\mathbf{W}]\!]})_\epsilon$;
- $(\widehat{\neg\phi[\mathbf{Y},\mathbf{W}]})_\epsilon \overset{\text{def}}{=} \exists \mathbf{W_0}(\forall \mathbf{W_1}(\delta(\mathbf{W_0},\mathbf{W_1}) < \epsilon \rightarrow$ $\neg(\widehat{\phi[\![\mathbf{Y},\mathbf{W_1}]\!]})_\epsilon) \wedge \delta(\mathbf{W_0},\mathbf{W}) < \epsilon)$.

We now prove that the sphere semantics of φ and standard semantics of $\widehat{(\varphi)}_\epsilon$ are the same and that, provided the decidability of φ, we can symbolically compute the sphere semantics of it.

Theorem 2 (Semantics Equivalence [9])**.** *Let $\mathcal{T}$ be any first-order theory and δ be a $\mathcal{T}$-definable distance. The sphere semantics $(\!|.|\!)_\epsilon$ of $\mathcal{T}$ is $\mathcal{T}$-definable in the standard semantics and, in particular, $(\!|\varphi[\mathbf{X}]|\!)_\epsilon = \{\!\!|\widehat{(\varphi)}_\epsilon[\mathbf{X}]|\!\!\}$ for any formula $\varphi[\mathbf{X}] \in \mathcal{T}$ and all $\epsilon \in \mathbb{R}_{>0}$.*

Example 2. *Let us consider the formula $\varphi[X] \overset{def}{=} X > 0 \wedge X < 2$. We have that $(\widehat{X > 0})_\epsilon \equiv \exists X_0(X_0 > 0 \wedge \delta(X_0,X) < \epsilon) \equiv X_0 + \epsilon > 0$. By applying the same rule, $(\widehat{X < 2})_\epsilon \equiv \exists X_0(X_0 < 2 \wedge \delta(X_0,X) < \epsilon) \equiv X - 2 - \epsilon < 0$. Finally, since ϵ is a positive real, $(\widehat{X > 0 \wedge X < 2})_\epsilon \equiv \exists X_0(\forall X_1(\delta(X_0,X_1) < \epsilon \rightarrow X_1 + \epsilon > 0 \wedge X_1 - 2 - \epsilon < 0) \wedge \delta(X_0,X) < \epsilon) \equiv X > -\epsilon \wedge X \leq 2 + \epsilon$.*

Let us notice that the formula $\widehat{(\psi)}_\epsilon$ is syntactically more complex than ψ. This is mainly due to the possible introduction of new quantifier alternations.

4.2. From DE into standard semantics

Both erosion semantics and DE semantics are definable in the Tarski's theory, i.e., if ψ is a formula of the first-order language of the reals equipped of sum, product and comparison relations, then there exist two formulæ $\widetilde{\psi}_\epsilon$ and $\overline{\psi}_\epsilon$ such that $\rangle\!\rangle\psi\langle\!\langle_\epsilon = \{\!|\widetilde{\psi}_\epsilon|\!\}$ and $\rangle\psi\langle_\epsilon = \{\!|\overline{\psi}_\epsilon|\!\}$. Moreover, we can compute both of them. As a matter of fact, it is easy to prove that $\widetilde{\psi}_\epsilon[\mathbf{X}] = \exists \mathbf{X_0}\left(\delta(\mathbf{X}, \mathbf{X_0}) < \epsilon \wedge \overline{\psi}_\epsilon[\![\mathbf{X_0}]\!]\right)$.

As concern the formula $\overline{(\psi[\mathbf{Y}, \mathbf{W}])}_\epsilon$, we define it by structural induction on ψ as follows:

- $\overline{((t_1 \circ t_2)[\mathbf{Y}, \mathbf{W}])}_\epsilon \stackrel{def}{=} \forall \mathbf{Y_1}(\delta(\mathbf{Y_1}, \mathbf{W}) < \epsilon \rightarrow (t_1 \circ t_2)[\![\mathbf{Y}, \mathbf{Y_1}]\!])$;
- $\overline{((\psi_1 \wedge \psi_2)[\mathbf{Y}, \mathbf{W}])}_\epsilon \stackrel{def}{=} \overline{(\psi_1[\mathbf{Y}, \mathbf{W}])}_\epsilon \wedge \overline{(\psi_2[\mathbf{Y}, \mathbf{W}])}_\epsilon$;
- $\overline{((\psi_1 \vee \psi_2)[\mathbf{Y}, \mathbf{W}])}_\epsilon \stackrel{def}{=} \overline{(\psi_1[\mathbf{Y}, \mathbf{W}])}_\epsilon \vee \overline{(\psi_2[\mathbf{Y}, \mathbf{W}])}_\epsilon$;
- $\overline{(\forall W \psi_1[\mathbf{Y}, W, \mathbf{W}])}_\epsilon \stackrel{def}{=} \forall Y \overline{(\psi_1[\![\mathbf{Y}, Y, \mathbf{W}]\!])}_\epsilon$;
- $\overline{(\exists W \psi_1[\mathbf{Y}, W, \mathbf{W}])}_\epsilon \stackrel{def}{=} \exists Y \overline{(\psi_1[\![\mathbf{Y}, Y, \mathbf{W}]\!])}_\epsilon$;
- $\overline{(\neg\psi[\mathbf{Y}, \mathbf{W}])}_\epsilon \stackrel{def}{=} \neg\exists \mathbf{Y_0}(\delta(\mathbf{Y_0}, \mathbf{W}) < \epsilon \wedge \psi[\![\mathbf{Y}, \mathbf{Y_0}]\!])$.

As done for the sphere semantics, we reduce the computation of $\rangle\varphi\langle_\epsilon$ to the evaluation of the standard semantics of $\overline{\varphi}_\epsilon$.

Theorem 3. *Let $\mathcal{T}$ be any first-order theory and δ be a $\mathcal{T}$-definable distance. The erosion semantics $\rangle\cdot\langle_\epsilon$ of $\mathcal{T}$ is $\mathcal{T}$-definable in the standard Tarski's semantics and, in particular, $\rangle\psi[\mathbf{X}]\langle_\epsilon = \left\{\!\left|\overline{(\psi[\mathbf{X}])}_\epsilon\right|\!\right\}$ for any formula $\psi[\mathbf{X}] \in \mathcal{T}$ and all $\epsilon \in \mathbb{R}_{>0}$.*

Proof. By structural induction on ψ.

$\psi[\mathbf{Y}, \mathbf{W}]$ is atomic.

By the definition of the erosion semantics, $\rangle t_1 \circ t_2\langle_\epsilon = \bigcup_{B(p,\epsilon) \subseteq \{\!|t_1 \circ t_2|\!\}} \{p\}$, for $\circ \in \{=, <\}$. The righter term of the last equation is the union of the centers of all the ϵ-spheres entirely included into the standard semantics of $(t_1 \circ t_2)$. Any point $\vec{y}$ is included in such a union if and only if all the points belonging to the ϵ-sphere centered in $\vec{y}$ satisfy $(t_1 \circ t_2)$. By the standard semantics, the later sentence holds if and only if the formula $\forall \mathbf{Y_1}(\delta(\mathbf{Y_1}, \mathbf{W}) < \epsilon \rightarrow (t_1 \circ t_2)[\![\mathbf{Y}, \mathbf{Y_1}]\!])$ does the same.

$\psi[\mathbf{Y},\mathbf{W}]$ has the form $(\psi_1 \wedge \psi_2)[\mathbf{Y},\mathbf{W}]$.

By definition, $\rangle\psi_1 \wedge \psi_2\langle_\epsilon \stackrel{def}{=} \rangle\psi_1\langle_\epsilon \cap \rangle\psi_2\langle_\epsilon$, while, by inductive hypothesis both $\rangle\psi_1\langle_\epsilon \equiv \{|\overline{(\psi_1)}_\epsilon|\}$ and $\rangle\psi_2\langle_\epsilon \equiv \{|\overline{(\psi_2)}_\epsilon|\}$ hold. From the standard semantics and the definition of $\overline{(\cdot)}_\epsilon$, we deduce the thesis.

$\psi[\mathbf{Y},\mathbf{W}]$ has the form $(\psi_1 \vee \psi_2)[\mathbf{Y},\mathbf{W}]$.

Similarly to the previous case, since $\rangle\psi_1 \vee \psi_2\langle_\epsilon \stackrel{def}{=} \rangle\psi_1\langle_\epsilon \cup \rangle\psi_2\langle_\epsilon$ and by inductive hypothesis both $\rangle\psi_1\langle_\epsilon \equiv \{|\overline{(\psi_1)}_\epsilon|\}$ and $\rangle\psi_2\langle_\epsilon \equiv \{|\overline{(\psi_2)}_\epsilon|\}$ hold, we can deduce the thesis directly from the standard semantics and the definition of $\overline{(\cdot)}_\epsilon$.

$\psi[\mathbf{Y},\mathbf{W}]$ has the form $\forall W \psi_1[\mathbf{Y},W,\mathbf{W}]$.

By definition, $\rangle\forall W \psi_1[\mathbf{Y},W,\mathbf{W}]\langle_\epsilon \stackrel{def}{=} \bigcap_{r\in\mathbb{R}} \rangle\psi_1[\![\mathbf{Y},r,\mathbf{W}]\!]\langle_\epsilon$. By inductive hypothesis $\rangle\psi_1[\mathbf{Y},r,\mathbf{W}]\langle_\epsilon \equiv \overline{(\psi_1[\mathbf{Y},r,\mathbf{W}])}_\epsilon$ holds, while by the standard semantics $\bigcap_{r\in\mathbb{R}} \rangle\psi_1[\mathbf{Y},r,\mathbf{W}]\langle_\epsilon \equiv \forall Y \overline{(\psi_1[\mathbf{Y},Y,\mathbf{W}])}_\epsilon$ holds too. Hence, from the definition of erosion semantics, we can conclude that the set $\left\{\left|\forall Y \overline{(\psi_1[\mathbf{Y},Y,\mathbf{W}])}_\epsilon\right|\right\}$ is equivalent to the set $\rangle\forall W \psi_1[\mathbf{Y},W,\mathbf{W}]\langle_\epsilon$.

$\psi[\mathbf{Y},\mathbf{W}]$ has the form $\exists W \psi_1[\mathbf{Y},W,\mathbf{W}]$.

Using the same argument of the previous case, it is easy to see that the equivalence $\rangle\exists W \psi_1[\mathbf{Y},W,\mathbf{W}]\langle_\epsilon \stackrel{def}{=} \bigcup_{r\in\mathbb{R}} \rangle\psi_1[\![\mathbf{Y},r,\mathbf{W}]\!]\langle_\epsilon \equiv \left\{\left|\exists Y \overline{(\psi_1[\mathbf{Y},Y,\mathbf{W}])}_\epsilon\right|\right\}$ holds.

$\psi[\mathbf{Y},\mathbf{W}]$ has the form $\neg\psi_1[\mathbf{Y},\mathbf{W}]$.

By definition, $\rangle\neg\psi\langle_\epsilon \stackrel{def}{=} \bigcup_{B(p,\epsilon)\cap\{\psi_1\}=\varnothing}\{p\}$. The righter term of the last equation is the union of the centers of all the ϵ-spheres which do not intersect the standard semantics of ψ_1. Any point $\vec{y}$ is belongs to such union if and only if all the points included into the ϵ-sphere centered in $\vec{y}$ do not satisfy ψ. By the standard semantics, the later sentence holds if and only if the formula $\neg\exists\mathbf{Y_0}(\delta(\mathbf{Y_0},\mathbf{W}) < \epsilon \wedge \psi[\![\mathbf{Y},\mathbf{Y_0}]\!])$ does the same.

□

Since $\rangle\!\rangle\varphi\langle\!\langle_\epsilon$ is empty if and only if $\rangle\varphi\langle_\epsilon$ is empty too, we can use $\rangle\cdot\langle_\epsilon$ in place of $\rangle\!\rangle\cdot\langle\!\langle_\epsilon$ to evaluate Algorithm 1 and, in particular, the line 14 of it. This replacement does not affect the result of the computation, but decrease the complexity of the formulæ whose satisfiability should be tested by the algorithm.

5. Formulæ Simplifications

If the formalæ produced by the above described process assume a very specific, but quite frequent, form, then we can syntactically simplify them preserving their semantics. Such simplifications may decrease the complexity of decision procedures of the emptiness test on line 14 of Algorithm 1.

Lemma 2. *Let $\mathbb{S} \subseteq \mathbb{R}^n$ be a closed and convex set, $\epsilon \in \mathbb{R}_{>0}$, and $p \in \mathbb{R}^n$. If $\forall \mathbf{X_0}(\delta(p, \mathbf{X_0}) < \epsilon \rightarrow \exists \mathbf{X_1}(\mathbf{X_1} \in \mathbb{S} \wedge \delta(\mathbf{X_0}, \mathbf{X_1}) < \epsilon))$ holds, then $p \in \mathbb{S}$.*

Proof. The proof is given by contradiction. Let $p \in (\mathbb{R}^n \setminus \mathbb{S})$ satisfying the assumption of the lemma. By letting $\mathbf{X_0} = p$ we get $\exists \mathbf{X_1}(\mathbf{X_1} \in \mathbb{S} \wedge \delta(p, \mathbf{X_1}) < \epsilon)$, therefore $B(p, \epsilon) \cap \mathbb{S} \neq \varnothing$, and $\delta(p, \mathbb{S}) < \epsilon$.

Then the distance $\delta(p, conv(\mathbb{S}))$ is a nonzero number $d < \epsilon$, since $\mathbb{S} = conv(\mathbb{S})$ is closed. Let $q \in \mathbb{S}$ be such a point that $\delta(q, p) = d$. We can use the linear separability theorem: because $p = conv(p)$ and $\mathbb{S} = conv(\mathbb{S})$ are two disjoint convex sets, there exists a separating hyperplane perpendicular to the line through q and p.

Let us now consider a point $v \in B(p, \epsilon)$ on the line going through p and q such that $\delta(v, p) = \varepsilon - d/2$ and $\delta(v, q) = \varepsilon + d/2$. Then $\delta(v, \mathbb{S}) \geq \delta(v, q) > \varepsilon$, which is a contradiction with the assumption $\forall \mathbf{X_0}(\delta(p, \mathbf{X_0}) < \epsilon \rightarrow \exists \mathbf{X_1}(\mathbf{X_1} \in \mathbb{S} \wedge \delta(\mathbf{X_0}, \mathbf{X_1}) < \epsilon))$, if $d > 0$. Therefore $\delta(p, \mathbb{S}) = 0$, and because $\mathbb{S}$ is closed, $p \in \mathbb{S}$. □

Theorem 4. *Let $\mathcal{T}$ be a first-order theory over the reals, $\varphi_1[\mathbf{X}], \ldots, \varphi_k[\mathbf{X}]$ be k first-order formulæ $\mathcal{T}$-definable, such that sets $\{\!|\varphi_1|\!\}, \ldots, \{\!|\varphi_k|\!\} \subseteq \mathbb{R}^n$ are convex and closed, and let $\epsilon \in \mathbb{R}_{>0}$. Then the formula*

$$\psi[\mathbf{X}] \stackrel{def}{=} \exists \mathbf{X_0}(\forall \mathbf{X_1}(\delta(\mathbf{X_0}, \mathbf{X_1}) < \epsilon \rightarrow \bigwedge_{i=1}^{k} \exists \mathbf{X_{i+1}}(\varphi_i[\![\mathbf{X_{i+1}}]\!] \wedge \delta(\mathbf{X_{i+1}}, \mathbf{X_1}) < \epsilon)) \wedge \delta(\mathbf{X}, \mathbf{X_0}) < \epsilon)$$

is equivalent to the formula

$$\theta[\mathbf{X}] \stackrel{def}{=} \exists \mathbf{X_0}((\bigwedge_{i=1}^{k} \varphi_i[\![\mathbf{X_0}]\!]) \wedge \delta(\mathbf{X}, \mathbf{X_0}) < \epsilon).$$

Proof. ($\Rightarrow$) Let $\psi[\![q]\!]$ hold for a point $q \in \mathbb{R}^n$. That is equivalent to the formula $\exists \mathbf{X_0}(\forall \mathbf{X_1}(\mathbf{X_1} \in B(\mathbf{X_0}, \epsilon) \rightarrow \bigwedge_{i=1}^{k} \exists \mathbf{X_{i+1}}(\mathbf{X_{i+1}} \in \{\!|\varphi_i|\!\} \cap B(\mathbf{X_1}, \epsilon))) \wedge \mathbf{X_0} \in B(q, \epsilon))$.

Now we can use Lemma 2, letting $p = \mathbf{X_0}, \mathbb{S} = \{\!|\varphi_i|\!\}$) and get for any choice of $i \in \{1, \ldots, k\}$ that $\mathbf{X_0} \in \{\!|\varphi_i|\!\}$. Then, $\theta[\![q]\!] = \exists \mathbf{X_0}(\mathbf{X_0} \in (\bigcap_{i=1}^{k} \{\!|\varphi_1|\!\}) \wedge \delta(q, \mathbf{X_0}) < \varepsilon)$ is true for the given point $q \in \mathbb{R}^n$.

($\Leftarrow$) Let $\theta[\![q]\!]$ hold for a point $q \in \mathbb{R}^n$. That means the same as the formula $\exists \mathbf{X_0}(\mathbf{X_0} \in (\bigcap_{i=1}^{k} \{\!|\varphi_i|\!\}) \cap B\,(q,\epsilon))$, which implies $\exists \mathbf{X_0}(\forall \mathbf{X_1}(\delta(\mathbf{X_0},\mathbf{X_1}) < \varepsilon \rightarrow \mathbf{X_0} \in \bigcap_{i=1}^{k} \{\!|\varphi_i|\!\}) \wedge \delta(\mathbf{X_0},\mathbf{X_1}) < \varepsilon)$, that in turn implies $\exists \mathbf{X_0}(\forall \mathbf{X_1}(\delta(\mathbf{X_0},\mathbf{X_1}) < \epsilon \rightarrow \bigwedge_{i=1}^{k} \exists \mathbf{X_{i+1}}(\mathbf{X_{i+1}} \in \{\!|\varphi_i|\!\} \wedge \delta(\mathbf{X_{i+1}},\mathbf{X_1}) < \epsilon)))$, because from above there exists at least $\mathbf{X_2} = \mathbf{X_0}, \mathbf{X_3} = \mathbf{X_0}, \ldots \mathbf{X_{k+1}} = \mathbf{X_0}$ for every $\mathbf{X_1} \in B\,(\mathbf{X_0},\epsilon)$. Which means $\psi[\![q]\!]$ holds. □

Theorem 5. *Let $\mathcal{T}$ be a first-order theory over the reals, $\varphi_1[\mathbf{X}],\ldots,\varphi_k[\mathbf{X}]$ be k first-order formulæ $\mathcal{T}$-definable, such that the union of sets $\{\!|\varphi_1|\!\},\ldots,\{\!|\varphi_k|\!\} \subseteq \mathbb{R}^n$ is a convex and closed subset of $\mathbb{R}^n$, and let $\epsilon \in \mathbb{R}_{>0}$.*

Then the formula

$$\psi[\mathbf{X}] \stackrel{def}{=} \exists \mathbf{X_0}(\forall \mathbf{X_1}(\delta(\mathbf{X_0},\mathbf{X_1}) < \epsilon \rightarrow \bigvee_{i=1}^{k} \exists \mathbf{X_{i+1}}(\varphi_i[\![\mathbf{X_{i+1}}]\!] \wedge \delta(\mathbf{X_{i+1}},\mathbf{X_1}) < \epsilon)) \wedge \delta(\mathbf{X},\mathbf{X_0}) < \epsilon)$$

is equivalent to the formula

$$\theta[\mathbf{X}] \stackrel{def}{=} \exists \mathbf{X_0}((\bigvee_{i=1}^{k} \varphi_i[\![\mathbf{X_0}]\!]) \wedge \delta(\mathbf{X},\mathbf{X_0}) < \epsilon).$$

Proof. ($\Rightarrow$) Let $\psi[\![q]\!]$ hold for a point $q \in \mathbb{R}^n$. That is equivalent to the formula $\exists \mathbf{X_0}(\forall \mathbf{X_1}(\mathbf{X_1} \in B\,(\mathbf{X_0},\epsilon) \rightarrow \bigvee_{i=1}^{k} \exists \mathbf{X_{i+1}}(\mathbf{X_{i+1}} \in \{\!|\varphi_i|\!\} \cap B\,(\mathbf{X_1},\epsilon))) \wedge \mathbf{X_0} \in B\,(q,\epsilon))$, which is equivalent to $\exists \mathbf{X_0}(\forall \mathbf{X_1}(\mathbf{X_1} \in B\,(\mathbf{X_0},\epsilon) \rightarrow \exists \mathbf{X_2}(\mathbf{X_2} \in (\bigcup_{i=1}^{k} \{\!|\varphi_i|\!\}) \cap B\,(\mathbf{X_1},\epsilon))) \wedge \mathbf{X_0} \in B\,(q,\epsilon))$.

Now we can use Lemma 2, letting $p = \mathbf{X_0}, \mathbb{S} = \bigcup_{i=1}^{k} \{\!|\varphi_i|\!\}$, and get $\mathbf{X_0} \in \bigcup_{i=1}^{k} \{\!|\varphi_i[\mathbf{X}]|\!\} = \{\!|\bigvee_{i=1}^{k} \varphi_i[\mathbf{X}]|\!\}$. Then $\theta[\![q]\!] = \exists \mathbf{X_0}((\bigvee_{i=1}^{k} \varphi_i[\mathbf{X_0}]) \wedge \delta(q,\mathbf{X_0}) < \varepsilon)$ is true for the given point $q \in \mathbb{R}^n$.

($\Leftarrow$) Let $\theta[\![q]\!]$ hold for a point $q \in \mathbb{R}^n$. That means the same as the formula $\exists \mathbf{X_0}(\mathbf{X_0} \in (\bigcup_{i=1}^{k} \{\!|\varphi_i|\!\}) \cap B\,(q,\epsilon))$, which implies $\exists \mathbf{X_0}(\forall \mathbf{X_1}(\delta(\mathbf{X_0},\mathbf{X_1}) < \varepsilon \rightarrow \mathbf{X_0} \in \bigcup_{i=1}^{k} \{\!|\varphi_i|\!\}) \wedge \delta(\mathbf{X_0},\mathbf{X_1}) < \varepsilon)$, that in turn implies $\exists \mathbf{X_0}(\forall \mathbf{X_1}(\delta(\mathbf{X_0},\mathbf{X_1}) < \epsilon \rightarrow \bigvee_{i=1}^{k} \exists \mathbf{X_{i+1}}(\mathbf{X_{i+1}} \in \{\!|\varphi_i|\!\} \wedge \delta(\mathbf{X_{i+1}},\mathbf{X_1}) < \epsilon)))$, because from above, there exists $i \in \{1,2,\ldots,k\}$ satisfying $\mathbf{X_0} \in \{\!|\varphi_i|\!\}$, which means $\psi[\![q]\!]$ holds. □

Theorem 6. *If φ is a formula without free variables, then $\rangle\!\rangle\varphi\langle\!\langle_\epsilon = \rangle\varphi\langle_\epsilon = \{\!|\varphi|\!\}$.*

Proof. As first thing, let notice that the standard evaluation of a formula ψ without free variables is a truth value which can be true ($\top$) or false ($\bot$). Hence, the standard semantics of a formula without free variables is either $\{\!|\psi|\!\} = \mathbb{R}^*$ or $\{\!|\psi|\!\} = \varnothing$. Moreover, the ϵ-expansions of such kind of sets, correspond to the sets themselves, i.e., $B\,(\mathbb{R}^*,\epsilon) = \mathbb{R}^*$ and $B\,(\varnothing,\epsilon) = \varnothing$. Let first demonstrate by structural induction on a formula ψ without free variables that $\rangle\psi\langle_\epsilon = \{\!|\psi|\!\}$.

$t_1 \circ t_2$, for $\circ \in \{=, <\}$. $\rangle t_1 \circ t_2 \langle_\epsilon$ is defined as the union of all the centers of the ϵ-spheres entirely included into $\{\!| t_1 \circ t_2 |\!\}$. Since $(t_1 \circ t_2)$ is without free variables, either $\{\!| t_1 \circ t_2 |\!\} = \mathbb{R}^*$ or $\{\!| t_1 \circ t_2 |\!\} = \emptyset$. Let notice that both $\bigcup_{B(p,\epsilon)\subseteq\mathbb{R}^*}\{p\} = \mathbb{R}^*$ and $\bigcup_{B(p,\epsilon)\subseteq\emptyset}\{p\} = \emptyset$ hold. But this means that if $(t_1 \circ t_2)$ is true, then $\{\!| t_1 \circ t_2 |\!\} = \mathbb{R}^* = \rangle t_1 \circ t_2 \langle_\epsilon$, while if $(t_1 \circ t_2)$ is false, then $\{\!| t_1 \circ t_2 |\!\} = \emptyset = \rangle t_1 \circ t_2 \langle_\epsilon$. Then we can state that $\{\!| t_1 \circ t_2 |\!\} = \rangle t_1 \circ t_2 \langle_\epsilon$.

$\psi_1 \wedge \psi_2$. By the definition of erosion semantics $\rangle \psi_1 \wedge \psi_2 \langle_\epsilon \stackrel{def}{=} \rangle \psi_1 \langle_\epsilon \cap \rangle \psi_2 \langle_\epsilon$. Moreover, by inductive hypothesis we know that $\rangle \psi_1 \langle_\epsilon = \{\!| \psi_1 |\!\}$ and $\rangle \psi_2 \langle_\epsilon = \{\!| \psi_2 |\!\}$. Hence, $\{\!| \psi_1 \wedge \psi_2 |\!\} = \{\!| \psi_1 |\!\} \cap \{\!| \psi_2 |\!\} = \rangle \psi_1 \langle_\epsilon \cap \rangle \psi_2 \langle_\epsilon = \rangle \psi_1 \wedge \psi_2 \langle_\epsilon$ holds.

$\psi_1 \vee \psi_2$. Similarly to the previous case, exploiting the erosion semantics' definition and the inductive hypothesis, we have that the equalities $\{\!| \psi_1 \vee \psi_2 |\!\} = \{\!| \psi_1 |\!\} \cup \{\!| \psi_2 |\!\} = \rangle \psi_1 \langle_\epsilon \cup \rangle \psi_2 \langle_\epsilon = \rangle \psi_1 \vee \psi_2 \langle_\epsilon$ hold.

$\forall W \psi[W]$. In this case, $\rangle \forall W \psi[W] \langle_\epsilon \stackrel{def}{=} \bigcap_{r\in\mathbb{R}} \rangle \psi[\![r]\!] \langle_\epsilon$. By inductive hypothesis it holds that $\rangle \psi[r] \langle_\epsilon = \{\!| \psi[r] |\!\}$. Thus, by the standard semantics it follows that $\rangle \forall W \psi[W] \langle_\epsilon = \bigcap_{r\in\mathbb{R}} \rangle \psi[\![r]\!] \langle_\epsilon = \bigcap_{r\in\mathbb{R}} \{\!| \psi[\![r]\!] |\!\} = \{\!| \forall W \psi[W] |\!\}$.

$\exists W \psi[W]$. Similarly to the previous case, exploiting the erosion semantics' definition and the inductive hypothesis, we have that the equalities $\rangle \exists W \psi[W] \langle_\epsilon = \bigcup_{r\in\mathbb{R}} \rangle \psi[\![r]\!] \langle_\epsilon = \bigcup_{r\in\mathbb{R}} \{\!| \psi[\![r]\!] |\!\} = \{\!| \exists W \psi[W] |\!\}$ hold.

$\neg\psi$. By the definition of erosion semantics $\rangle \neg\psi \langle_\epsilon = \bigcup_{B(p,\epsilon)\cap\{\!|\psi|\!\}=\emptyset}\{p\}$. Note that if ψ is true, then $\rangle \neg\psi \langle_\epsilon = \bigcup_{B(p,\epsilon)\cap\mathbb{R}^*=\emptyset}\{p\} = \emptyset = \{\!| \neg\psi |\!\}$, while if ψ is false, then $\rangle \neg\psi \langle_\epsilon = \bigcup_{B(p,\epsilon)\cap\emptyset=\emptyset}\{p\} = \mathbb{R}^* = \{\!| \neg\psi |\!\}$, which means that $\rangle \neg\psi \langle_\epsilon = \{\!| \neg\psi |\!\}$.

Finally, the DE semantics $\rangle\!\rangle \cdot \langle\!\langle_\epsilon$ of a formula ψ is defined as $B(\rangle \psi \langle_\epsilon, \epsilon)$. If ψ is without free variables, we know that $B(\rangle \psi \langle_\epsilon, \epsilon) = B(\{\!| \psi |\!\}, \epsilon)$. Moreover, since in this case $\{\!| \psi |\!\}$ is either $\mathbb{R}^*$ or $\emptyset$, it holds that $B(\{\!| \psi |\!\}, \epsilon) = \{\!| \psi |\!\}$, which in turn means that $\rangle\!\rangle \psi \langle\!\langle_\epsilon = B(\{\!| \psi |\!\}, \epsilon) = \{\!| \psi |\!\}$. In conclusion we can state that if a formula ψ is without free variables, then $\rangle\!\rangle \psi \langle\!\langle_\epsilon = \rangle \psi \langle_\epsilon = \{\!| \psi |\!\}$. □

6. Analysis of Two Biological Hybrid Models

Oscillatory electrical stimuli have been considered central for the activities of several brain regions since the '80s. It was shown that they play an important role in the olfactory information processing [10] and they were observed in the hippocampus [11], in the thalamus [12], and in the cortex [13]. Many studies suggested that, in the mammalian visual system, neurons signals may be group together through in-phase oscillations [14]. Hence, the development and analysis of models representing oscillatory phenomena assume a great importance in understanding the neurophysiological activities.

A simple continuous model of a single oscillator has been proposed in [15]. The model describes the evolutions of one excitatory neuron (N_e) and one inhibitory neuron (N_i) by mean of the ordinary differential system.

$$f(\tau,\lambda):\begin{cases}\dot{X}_e = -\frac{X_e}{\tau} + \tanh(\lambda * X_e) - \tanh(\lambda * X_e)\\ \dot{X}_i = -\frac{X_i}{\tau} + \tanh(\lambda * X_i) + \tanh(\lambda * X_i)\end{cases}, \tag{1}$$

where X_e and X_i are the output of N_e and N_i, respectively, τ is a characteristic time constant, and $\lambda > 0$ is the amplification gain.

We approximated the not linear part of the System (1) (i.e., $\tanh(\lambda * X)$) by the piecewise function $h_{\lambda,\alpha}(z)$ defined as follow:

$$h_{\lambda,\alpha}(z) \stackrel{\text{def}}{=} \begin{cases} -1 & \text{if } z < -\frac{\alpha}{\lambda}\\ \frac{\lambda}{\alpha} * z & \text{if } -\frac{\alpha}{\lambda} \le z < \frac{\alpha}{\lambda}\\ 1 & \text{if } z \ge \frac{\alpha}{\lambda}\end{cases}, \tag{2}$$

where α is the approximation coefficient which determines the slope of the central segment (see Figure 1). This leads to the hybrid automaton $H_{\tilde{f}}$ is depicted in Figure 2.

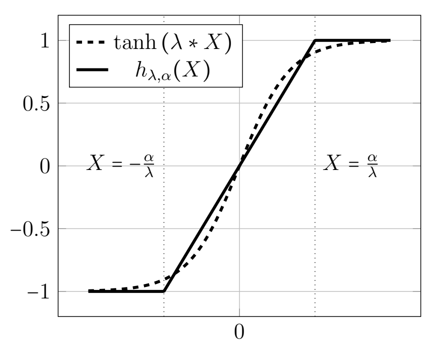

Figure 1: $h_{\lambda,\alpha}(X)$ approximating $\tanh(\lambda * X)$

We intend to study $H_{\tilde{f}}$ behavior through sphere semantics, exploiting cylindrical algebraic decomposition tools to automatically compute it. In particular, we want to prove that each point in the space reaches a bounded

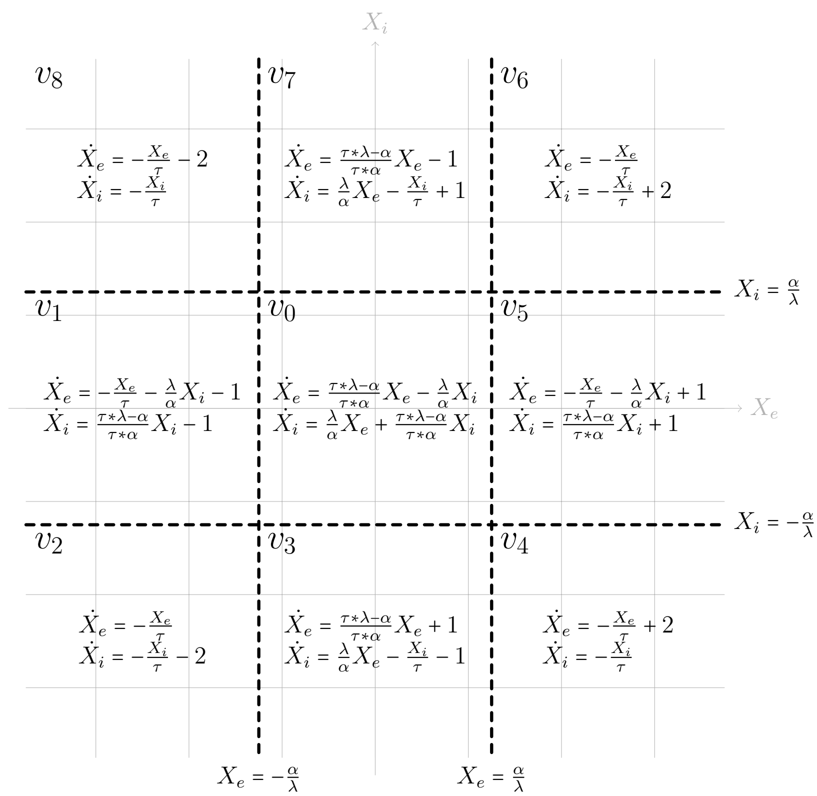

Figure 2: A graphical representation of the hybrid automaton $H_{\tilde{f}}$ associated to the function $\tilde{f}_\alpha(\tau, \lambda)$

region which includes the limit cycle. Notice that in this example our automata have unbounded invariants, hence the termination of sphere semantics reachability algorithm is not guaranteed.

First of all, we replace the differential equations with the corresponding first-degree Taylor polynomials. In order to keep the presentation simple, in this section we fix the parameters as follows $\tau = 3$, $\lambda = 1$, $\alpha = 2$. Hence, the activations correspond to the axis $X_i = \pm 2$ and $X_e = \pm 2$.

We start computing the intersections of the limit cycle with the activation regions. Consider for instance the intersection $Q_0 = \langle x_{Q_0}, 2 \rangle$ of the limit cycle with $X_i = 2$ and $X_e > 0$. We have that x_{Q_0} is the unique solution of the equation which describes the intersection of the diamond-like limit cycle with $X_i = 2$. Similarly, consider point $Q_1 = \langle 2, y_{Q_1} \rangle$ that in turn corresponds to the intersection of the limit cycle with $X_e = 2$ and $X_i > 0$. Let us now consider a point P_0 located on $X_i = 2$ such that its distance d_0 from Q_0 is at least 2ϵ, i.e., $P_0 = \langle x_{P_0}, 2\rangle$ and $\delta(Q_0, P_0) = d_0 > 2\epsilon$. Consider now any point P_1 on $X_e = 2$ resulting from the sphere semantics evaluation of the continuous evolution which starts in P_0 inside location v_6. Thus, let denote with d_1 the distance between such P_1 and Q_1, i.e., $\delta(Q_1, P_1) = d_1$. If we could prove that d_1 is always smaller than d_0, then we would be able to conclude that all the points which start from a distance of at least 2ϵ from the limit cycle converge to a flow tube having diameter 2ϵ that includes the limit cycle. Of course, to obtain such conclusion, we need to prove this property on all locations.

We can formalize this concept through a first-order formula. We denote with r and s the straight lines $X_i = 2$ and $X_e = 2$, respectively, and with the notation $Q_0 \in r \cap C \cap X_e > 0$ the membership of Q_0 to the intersection of straight line r with limit cycle C and positive X_e semi-plane. Moreover, with the notation $(\!| P_0 \to_C P_1 |\!)_\epsilon$ we denote the continuous transition from point P_0 to point P_1 performed exploiting sphere semantics. Thus, our desired property can be expressed as:

$$\forall Q_0 Q_1 \forall P_0 P_1 \big((Q_0 \in r \cap C \cap X_e > 0 \wedge Q_1 \in s \cap C \cap X_i > 0 \wedge P_0 \in r \cap X_e > 0 \wedge \\ P_1 \in s \cap X_e > 0 \wedge \delta(Q_0, P_0) > 2\epsilon \wedge (\!| P_0 \to_C P_1 |\!)_\epsilon) \to \delta(Q_1, P_1) < \delta(Q_0, P_0) \big) \quad (3)$$

stating the convergence to the limit flow tube in location v_6. Such property can be easily rewritten for each location of the hybrid automaton, changing the roles of activation border lines r and s.

We implemented a Python package that encodes the ϵ-semantics framework together with the simplifications presented in Section 5. Moreover, this package provides easy-to-use interfaces to `REDLOG` and allow us to test the satisfiability of a formula. We used it to both evaluate $(\!| P_0 \to_C P_1 |\!)_\epsilon$ and prove our conjectures (the result is computed within few seconds).

As far as $\langle 0, 0\rangle$ is concerned, it is immediate to prove that it reaches points different from itself and, hence, it reaches the limit flow tube.

Other interesting properties that automatically verified express, for instance, the fact that applying the sphere semantics there are points that cross the limit cycle (in both directions). This is quite natural since points closer than ϵ to the limit cycle get expanded and cross it.

In order to investigate the effectiveness of our methods, we performed further analysis on a different biological system: the glycemic control in diabetic patients. Such control task consists in monitoring and correcting the blood glucose level of a patient affected by diabetes. Since it is well known that a good glycemic control plays an important role in the diabetes care, it is important to develop and study models that may result useful in the design of insulin infusion devices.

The investigated hybrid automaton is based on the continuos model presented in [16]. The overall system is depicted by the following system.

$$\begin{aligned}\frac{dG}{dt} &= -p_1 G - X(G + G_B) + g(t)\\ \frac{dX}{dt} &= -p_2 X + p_3 I\\ \frac{dI}{dt} &= -n(I + I_B) + \frac{1}{V_I} i(t)\end{aligned}$$

where the functions $g(t)$ and $i(t)$ directly depend on G and t, respectively, and are piecewise defined as:

$$i(t) = \begin{cases} \frac{25}{3} & G(t) \leq 4 \\ \frac{25}{3}(G(t) - 3) & G(t) \in [4, 8] \\ \frac{125}{3} & G(t) \geq 8 \end{cases} \qquad g(t) = \begin{cases} \frac{t}{60} & t \leq 30 \\ \frac{120-t}{180} & t \in [30, 120] \\ 0 & t \geq 120 \end{cases}.$$

The variable G characterizes the plasma glucose concentration, X the insulin concentration in the remote compartment, while I is the free plasma insulin concentration. The constants G_B and I_B represent the basal reference values of plasma glucose and insulin, respectively, while $i(t)$ and $g(t)$ describe the infusion evolution of glucose and insulin into the bloodstream of the patient.

First of all, we dived the space into nine different sectors, accordingly with the combination between the different evolutions of the functions $g(t)$ and $i(t)$. Since the phases of $g(t)$ directly depend on time, we added a further variable to our model: the time variable T that measure the time since the begin of the simulation. We approximate the differential equations with the corresponding first-degree Taylor polynomials. The resultant hybrid automaton is depicted in Figure 3, where all the activations are satisfied when the variables G and T assume the values that lie on the dashed straight lines, while the resets are simply identity functions.

Given our model, we may want to test whether the glucose concentration grows too fast or not. This behavior can be identified by testing the reachability of a half-space above a given line: the higher the slope of the line,

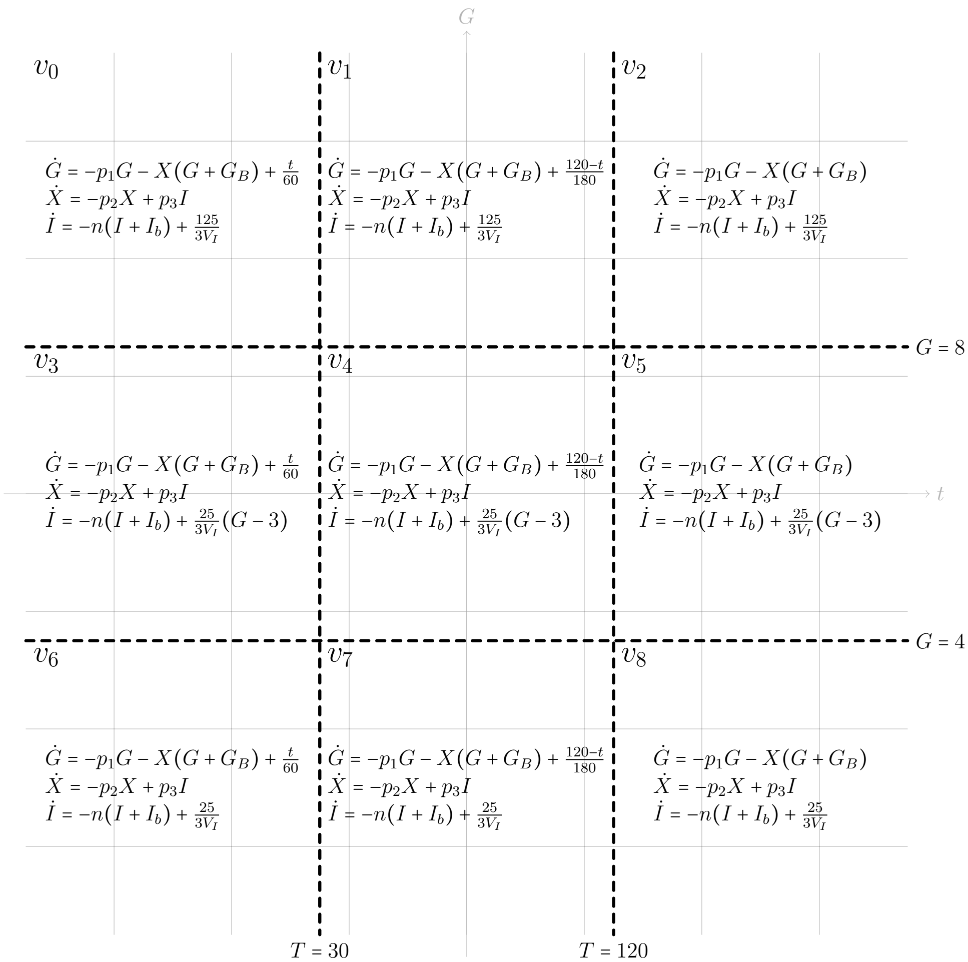

Figure 3: A graphical representation of the glycemic control hybrid automaton.

the greater the growth of the glucose concentration. We chose the half-space $6 * (t + 105) \leq 135G$ and we automatically checked that this region is not reachable from $G \in [-2, 2] \wedge X = 0 \wedge I \in [-0.1, 0.1] \wedge T = 0$. Such verification was performed exploiting both the ϵ-semantics presented in Section 3. The sphere semantics was used inside the Algorithm 1 in order to obtain a halting criterion that takes into account the indeterminism intrinsic in the nature of the system. We evaluated the formula returned by the algorithm in the dilated erosion semantics, with the purpose of establishing whether the states taken into account are robustly reachable. Note the using the dilated erosion semantics directly inside the Algorithm 1, the result of the computation would have been the formula characterizing the empty set. This is mainly due to the fact that activation formulæ, which regulate the discrete jumps between the locations, are defined to be satisfied just by a single point.

7. Conclusions

This work is ideally organized into two parts. The first part is theoretical: it recalls the notions of ϵ-semantics and hybrid automaton, it describes a new reachability algorithm based on ϵ-semantics and enables us to analyze any hybrid automaton in Michael's form, it introduces two ϵ-semantics whose evaluations can be reduced to the decidability of a first-order formula, and, finally, it shows how to simplify this formula. The second part deals with two biological applications: a neural oscillator whose components derive from the approximation of the continuous model presented in [15], and a glycemic control in diabetic patients based on the continuous model provided in [16].

After the formalization of the models through hybrid automata, we analyzed their behaviours considering the approach based on the ϵ-semantics.

In the neural oscillator, the simulation on the application of the ϵ-semantics has revealed the any point which begins its evolution from a distance of at least 2ϵ from the limit cycle, converges to a flow tube which possesses a diameter equal to 2ϵ and that includes the limit cycle. Due to size of the formulæ which compose the hybrid automaton and the growth of such formalæ introduced by the translation of the ϵ-semantics evaluations, a direct computation of the reachable set would have high complexity and eventually returns results of difficult interpretation. For this reason, we have reformulated the problem in form of a closed property which guarantees the convergence of any point towards the limit cycle of the modeled system.

In the study of the glycemic control we performed a decisional reachability test wondering whether a certain configuration of the system was reachable. A combination of two different ϵ-semantics was exploited in order to obtain both a valid halting criterion and an overview on the robustness of the system dynamics. The evaluation of the reachability formula, performed with an under-approximation ϵ-semantics, returns an empty set, it may the evidence of a slow growth of the glucose concentration under some specific parameters.

As future work, in order to analyze the behaviour of a group of neural oscillators, we plan to combine several hybrid automata and to study their evolutions always adopting the approximation approach based on the ϵ-semantics. Moreover, it is in our interest to extend the study of the glycemic control to the computation of the whole reachability set, eventually defining new ϵ-semantics and formulæ simplifications that make the computation of the reachability set more efficient.

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