Type Inference for Ratio Control Multiset-Based Systems

Bogdan Aman Gabriel Ciobanu

Romanian Academy, Institute of Computer Science
Bld. Carol I, no.8, 700505, Iași, România

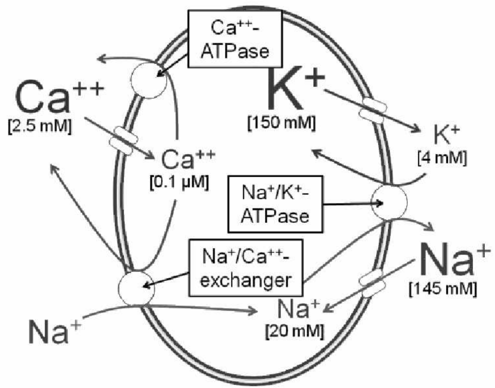
TYPES 2016
26th May 2016

Outline

Introduction

- All known producer-consumer models are extensions of the standard theory of predator-prey interactions described by Lotka and Volterra.
- Recently, in order to model more faithfully the interactions in such systems, the Lotka-Volterra model was extended with ratio-dependent interactions.
- However, these models are usually described by differential equations and do not explicitly track the quantities neither in the producer/consumer nor in the environment.

- Multiset-based formalisms are motivated by quantitative evolutions of various systems.
- In many biological systems a reaction takes place only if certain ratios between given thresholds are fulfilled (e.g, in sodium/potassium pump and ratio-dependent predator-prey systems).



- The sodium-potassium exchange pump that is a transmembrane transport protein that establishes and maintains the appropriate internal concentrations of sodium and potassium ions in cells.
- Under certain conditions, Na^{+} and Ca^{++} ions enter the cells because of the higher concentration outside the cell, while K^{+} ions exit the cell due to the higher concentration inside the cell.
- Several multiset rewriting systems are used to describe the dynamics of such systems which involve parallelism and concurrent access to resources.
- Petri nets and membrane systems represent good examples of multiset-based formalisms.

Introduction

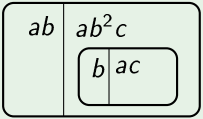
- Inspired by the functioning of these systems, we provide a discrete approach and a quantitative (multiset-based) type system involving a ratio control of the resources.
- The type checking and type inference algorithms basically will browse the systems and rules, and check or collect the type information for each rule independently.
- The membrane systems represent a formalism that has compartments enclosed by membranes, floating objects, proteins associated with the internal and external surfaces of the membranes, and built-in proteins (the pump) that transport and process chemical substances.
- The intent is to avoid errors in the definition of the formal model used to model biologic processes.

- We work with terms built by means of a membrane constructor $\langle - \mid - \rangle$, using a set O of objects. The syntax of terms $st \in ST$ is
$$st ::= u \mid \langle v \mid st \rangle \mid st\ st$$
- A pattern P is a term that may include variables from a set V:
$$P ::= st \mid \langle v\ y \mid P\ X \rangle \mid P\ P.$$
- A rewriting rule r is a pair of patterns (P_1, P_2), denoted by
$$P_1 \rightarrow P_2,$$
where $P_1 \neq \epsilon$ and $Var(P_1) \subseteq Var(P_2)$. A rewriting rule $P_1 \rightarrow P_2$ states that a term $P_1\sigma$ can be transformed into the term $P_2\sigma$, for some instantiation function σ.

A Multiset Model of Membranes

Example

Consider the depicted hierarchical nested system $\langle ab \mid ab^2c\ \langle b \mid ac\rangle\rangle$ with two levels having two evolution rewriting rules r_1 and r_2. Some examples of the notions defined above are given on the right part of the picture.



$r_1 : aX \to acX$

$r_2 : aX \to ab^2X$

Terms: $\langle ab \mid ab^2c\ \langle b \mid ac\rangle\rangle$ and ab^2c

Patterns: $\langle y \mid a\ X\ \langle b \mid ac\rangle\rangle$ and $a\ X$

Instantiation: $\sigma(X) = b^2c$, $\sigma(y) = ab$

Rewriting rule r_1: $aX \to acX$

Rewriting rule r_2: $aX \to ab^2X$

- The infinite set $\mathcal{C}$ of contexts (ranged over by C) is given by:
$$C ::= \Box \mid C\ st \mid \langle v \mid C \rangle.$$
- $C_1[\ st\ ]$ denotes the term obtained by replacing $\Box$ with st in C_1.
- Given a membrane system with integral proteins and a set of rewriting rules R, the reduction semantics of the system is the least transition relation $\rightarrow$ satisfying the following rule:
$$\frac{P_1 \rightarrow P_2 \in R \quad P_1\sigma \neq \epsilon \quad \sigma \in \Sigma \quad C \in \mathcal{C}}{C[P_1\sigma] \rightarrow C[P_2\sigma]}\ .$$
$\rightarrow^*$ denotes the reflexive and transitive closure of $\rightarrow$.

Example

- Given all these definitions, the functioning of the Na/K pump can be now described by means of the following rules:

$$r_1 : \langle E_1\ x \mid\ Na^3\ X\ \rangle \to \langle E_1\ Na^3\ x \mid\ X\ \rangle$$
$$r_2 : \langle E_1\ Na^3\ x \mid\ ATP\ X\ \rangle \to \langle E_1^P\ Na^3\ x \mid ADP\ X\ \rangle$$
$$r_3 : \langle E_1^P\ Na^3\ x \mid\ X\ \rangle \to \langle E_2^P\ x \mid\ X\ \rangle\ Na^3$$
$$r_4 : \langle E_2^P\ x \mid ; X\ \rangle\ K^2 \to \langle E_2^P\ K^2\ x \mid\ X\ \rangle$$
$$r_5 : \langle E_2^P\ K^2\ x \mid\ X\ \rangle \to \langle E_1\ K^2\ x \mid\ P_i\ X\ \rangle$$
$$r_6 : \langle E_1\ K^2\ x \mid\ X\ \rangle \to \langle E_1\ x \mid\ K^2\ X\ \rangle$$

- if we have an initial membrane $\langle E_1 \mid ATP^3\ Na^8\ K^2\rangle Na^9\ K^5$ by applying twice the above rules we reach a system $\langle E_1 \mid ATP\ ADP^2\ P_i^2\ Na^2\ K^6\rangle Na^{15}\ K^1$.
- So the system keeps sending Na outside the cell and K inside regardless of any known ratio thresholds (by lab experiments).
- But this is not how a biological cell works!

Ratio-based Type System Over Multisets

- Type theory has been used in biological formalisms in order to transfer the complexity of biological properties from evolution rules to types (e.g., CLS by Dezani).
- The syntax of types is simple, easy to understand and use, and these aspects make types ideal for expressing general constraints.
- The behaviour of typed terms can be controlled by a type system in order to avoid unwanted behaviours.
- According to [Kennedy,1986], the evolution of a healthy cell ensures that the ratio between objects (e.g., Na^{+}/K^{+}) of a cell is kept between certain values.
- We investigate the application of type systems to the previously defined model.

Ratio-based Type System Over Multisets

- Each object a in O is classified with an element of T (set of basic types); Γ denotes this classification.
- For each ordered pair of basic types (t_1, t_2), the existence of one function is assumed: $min : T \times T \to (0, \infty) \cup \{\diamond\}$.
- We consider that the maximum ratio between t_1 and t_2, denoted by $max(t_1, t_2)$ could be determined using the relation $min(t_1, t_2) \cdot max(t_2, t_1) = 1$. Giving this relation in what follows we use only the min function.
- $min(t_1, t_2) = \diamond$ means that this function is undefined for the pair of types (t_1, t_2). Biologically speaking, the ratio between the types t_1 and t_2 is either unknown, or can be ignored.

Ratio-based Type System Over Multisets

We consider only local properties: the objects influence each other only if

- they are present inside the same membrane;
- they are on sibling membranes;
- one is present inside and the other is on the membrane;
- one is present outside and the other is on the membrane.

Definition (Consistent Basic Types)

A system using a set of basic types T and the function *min* is consistent if:

1. $\forall t_1, t_2 \in T$, $min(t_1, t_2) \neq \diamond$ iff $min(t_2, t_1) \neq \diamond$;
2. $\forall t_1, t_2 \in T$ if $min(t_1, t_2) \neq \diamond$, then $min(t_1, t_2) \leq 1/min(t_2, t_1)$.

Ratio-based Type System Over Multisets

Example

- Let us assume a consistent system, the function:

$$min(t_1, t_2) = \begin{cases} 0.6 & \text{if } t_1 = t_{Na} \text{ and } t_2 = t_K \\ 0.25 & \text{if } t_1 = t_K \text{ and } t_2 = t_{Na} \,. \\ \diamond & \text{otherwise} \end{cases}$$

  and the previous set of rules, the well-formed term

$$[ATP^3\ Na^8\ K^2]_{E_1} Na^9\ K^5$$

  is rewritten in a well-formed term

  $[ATP^3\ Na^8\ K^2]_{E_1} Na^9\ K^5 \Rightarrow^* [ATP^2\ ADP\ P_i\ Na^5\ K^4]_{E_1} Na^{12}\ K^3$.
- Another rule cannot be applied because we would obtain terms that are not well-formed.

- In order to model more faithfully the interactions in producer-consumer systems, the Lotka-Volterra model was extended with ratio-dependent interactions.
- In particular the sodium/potassium pump extrudes sodium ions in exchange for potassium ions only if the ratios of these elements are between certain lower and upper bounds.
- To properly cope with such constraints, we introduce a ratio-based type system over multisets.
- We proved that if a system is well-typed and an evolution rule is applied, then the obtained system is also well-typed.
- We provided a type inference algorithm for deducing the type of each term in the multiset framework, and prove the soundness and completeness results for this type inference.

Thank you!