Termination Problems in Chemical Kinetics

Gianluigi Zavattaro
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Joint work with
Luca Cardelli
Termination Problems in Chemical Kinetics

A \xrightarrow{r} C_1 + \ldots + C_n \leftrightarrow A ::= \tau;r;C_1|\ldots|C_n + b@s;0
A+B \xrightarrow{s} D_1 + \ldots + D_m \leftrightarrow B ::= \overline{b}@s;D_1|\ldots|D_m

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A $\rightarrow^r C_1 + \ldots + C_n$  $\iff$  $A ::= \tau @ r; C_1 | \ldots | C_n + b @ s; 0$

A + B $\rightarrow^s D_1 + \ldots + D_m$  $\iff$  $B ::= \overline{b} @ s; D_1 | \ldots | D_m$

Chemical systems expressed as a set of mono- and bi-molecular reactions

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A \rightarrow^r C_1 + \ldots + C_n \iff A ::= \tau@r;C_1 | \ldots | C_n + b@s;0

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Chemical Ground Form (CGF): a process algebraic view of Chemical Kinetics [TCS08]

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A $\rightarrow^r C_1 + \ldots + C_n \iff A ::= \tau@r;C_1|\ldots|C_n + b@s;0$

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What is the computational power of Chemical Kinetics?

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A \xrightarrow{r} C_1 + \ldots + C_n \iff A ::= \tau \cdot r ; C_1 | \ldots | C_n + b \cdot s ; \emptyset

A + B \xrightarrow{s} D_1 + \ldots + D_m \iff B ::= \overline{b} \cdot s ; D_1 | \ldots | D_m

Is TERMINATION decidable in Chemical Kinetics?

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Plan of the talk

- Chemical Kinetics as a Computational Model
  - ... not a new issue
- Chemical Ground Form (CGF) [TCS08]
  - ... a new way to analyze chemical kinetics
- Considered TERMINATION problems:
  - Purely Nondeterministic semantics:
    - Existential termination (one computation terminates)
    - Universal termination (all computations terminate)
  - Stochastic semantics:
    - Existential termination (terminate with probability $p > 0$)
    - Probabilistic termination (terminate with probability $p > \varepsilon$ with $0 < \varepsilon < 1$)
    - Universal termination (terminate with probability $p = 1$)
- Concluding remarks
Plan of the talk

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- **Concluding remarks**
Is Chemical Kinetics Turing powerful?

  - Answer: **YES**... but justification not convincing (only Digital Computers with bounded memory are considered)

  - Answer: **YES**... but justification not convincing (only Minsky Machines with bounded computation are considered)

  - Answer: **NO**... but all Minsky and Turing Machines can be at least approximated with any given degree of precision
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Chemical Ground Forms

- Stochastic variant of Milner’s CCS, with an equivalent graphical notation (Stochastic Collective Automata)

![Diagram of Chemical Ground Forms]

Termination Problems in Chemical Kinetics
Stochastic semantics

- Actions take (an exponentially distributed amount of) time
  - Internal delay: \( \tau \)
    - \( \Pr(\text{internal delay} < t) = 1 - e^{-rt} \)
  - Synchronization between complementary actions: ?a@r, !a@r
    - \( \Pr(\text{synchronization time} < t) = 1 - e^{-rt} \)
Example

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Example

Starting process: $A | A'$
Example

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Termination Problems in Chemical Kinetics
Example

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Example

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Example

Starting process: $A | A'$
Example

Starting process: $A | A'$

$\tau, a, a, \ldots, \tau, b, \ldots, \tau$

Termination Problems in Chemical Kinetics
Example

Starting process: A | A'

a, a, ..., τ, b, ..., τ
Example

Starting process: \( \text{A} | \text{A'} \)
CGF = Chemical Kinetics

Continuous-State Semantics = Continuous Chemistry

CGF = CK

Discrete-State Semantics = Discrete Chemistry
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- **Concluding remarks**
Example: does it terminate?

but what you mean by “terminate”?

Starting process: $A | A'$

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Several notions of terminations

- **Nondeterministic semantics**
  - **Existential termination**: there exists one terminating computation
  - **Universal termination**: all computations terminate

- **Stochastic semantics**
  - **Existential termination**: the process terminates with prob. > 0
  - **Probabilistic termination**: the process terminates with prob. > \(\varepsilon\) (with \(0 < \varepsilon < 1\))
  - **Universal termination**: the process terminates with prob. = 1
Example: does it “existentially” terminate?

Starting process: $A | A'$
Example: does it “existentially” terminate?

Starting process: $A | A'$
Example: does it “universally” terminate?

Starting process: $A | A'$
Example: does it "universally" terminate?

NO

Starting process: $A | A'$
Several notions of terminations

- **Nondeterministic semantics**
  - *Existential termination*: there exists one terminating computation
  - *Universal termination*: all computations terminate

- **Stochastic semantics**
  - *Existential termination*: the process terminates with prob. $> 0$
  - *Probabilistic termination*: the process terminates with prob. $> \varepsilon$ (with $0 < \varepsilon < 1$)
  - *Universal termination*: the process terminates with prob. $= 1$
Example: does it “existentially” terminate?

Starting process: $A | A'$
Example: does it "existentially" terminate?

Starting process: $A|A'$
Example: does it "universally" terminate?

Starting process: A | A'
Example: does it “universally” terminate?

Starting process: A | A’
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- Concluding remarks
Both terminations decidable under nondeterministic semantics

- We reduce **existential** and **universal** termination for CGF to termination for **Petri Nets**
  - In Petri Nets several properties such as reachability, coverability, termination, divergence,... are decidable
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- Concluding remarks
Existential termination (decidable)

- Proof by reduction to existential termination under the nondeterministic semantics
  - a CGF process terminates with prob. \( > 0 \) iff it existentially terminates under the nondeterministic semantics
Probabilistic termination (undecidable)

- Proof by reduction to Random Access Machine (RAM) termination

- RAMs [Min67]:
  - **Registers**: \( r_1 \ldots r_n \) hold natural numbers
  - **Program**: sequence of indexed instructions
    - \( i: \text{Inc}(r_j) \): add 1 to the content of \( r_j \) and go to the next instruction
    - \( i: \text{DecJump}(r_j,s) \): if the content of \( r_j \) is not 0 then decrease by 1 and go to the next instruction; otherwise jump to instruction \( s \)
RAM encoding

- **RAMs cannot** be faithfully modeled by a CGF process
  - otherwise (by decidability of existential term. in CGF) RAM termination is decidable

- **RAMs can** be modeled by a CGF process that includes also wrong computations, but the prob. a wrong computation is scheduled is smaller than any given $\varepsilon > 0$
Approximate RAM modeling

i: Inc(r_j)

I_i

I_{i+1} \quad R_j

\tau

k: DecJump(r_j, s)

I_k

I_{k+1} \quad I_s

\tau

\text{Problem:}
\text{wrong jump!}

r_j with content n_j:

R_j \ldots \quad R_j

n_j instances
Approximate RAM modeling

\[ i: \text{Inc}(r_j) \]
\[ \tau \]
\[ I_i \]
\[ I_{i+1} \]
\[ R_j \]

\[ k: \text{DecJump}(r_j,s) \]
\[ \tau \]
\[ !\text{dec}_j \]
\[ \tau \]
\[ !\text{inh} \]
\[ I_k \]
\[ I_{k+1} \]
\[ I_s \]

But in an unbounded computation, with infinitely many DecJump, the prob. of a wrong jump is 1

\[ p < 1/h^2 \]
Approximate RAM modeling

\[ i: \text{Inc}(r_j) \]

\[ \tau \]

\[ I_i \quad I_{i+1} \quad R_j \]

\[ k: \text{DecJump}(r_j, s) \]

\[ \tau \quad \tau \quad \tau \]

\[ !\text{inh} \quad !\text{inh} \quad !\text{inh} \]

\[ I_k \quad I_{k+1} \quad I_s \]

\[ !\text{dec}_j \]

\[ R_j \quad \ldots \quad R_j \]

\[ n_j \text{ instances} \]

\[ R_j \quad ?\text{dec}_j \]

\[ h \text{ instances} \]

\[ \text{Inh} \quad \ldots \quad \text{Inh} \]

\[ ?\text{inh} \]

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Approximate RAM modeling

\( i: \text{Inc}(r_j) \)

\( k: \text{DecJump}(r_j, s) \)

\( r_j \text{ with content } n_j: \)

\( \text{Rj} \ldots \text{Rj} \)

\( n_j \text{ instances} \)

\( \text{Rj} \quad \text{Dec}_j \quad \text{Rj} \)

\( \text{Inh} \ldots \text{Inh} \)

\( h \text{ instances} \)

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Approximate RAM modeling

\[ k: \text{DecJump}(r_j, s) \]

\[ \tau \]

\[ !\text{dec}_j \]

\[ \tau \]

\[ !\text{inh} \]

\[ \tau \]

\[ !\text{inh} \]

Incrementing the occurrences of \( \text{Inh} \) the prob. of a wrong jump is

\[ p < \sum_{i=\text{inth}}^{\infty} \frac{1}{i^2} \]

Termination Problems in Chemical Kinetics
Universal termination (undecidable)

Proof by reduction in two steps:

- **(step 1)** Reduction of RAM termination to FinitelyFaultyRAM (FFRAM) divergence
  - FFRAMs are nondeterministic RAMs that, in case of DecJump with nonempty register, can jump (but only finitely many times!)

- **(step 2)** Reduction of FFRAM divergence to --the complement of-- universal termination in CGF
First reduction

- Given a RAM consider the following FFRAM algorithm:
  1. “Randomly” generate a value $k$ (possible thanks to FFRAM nondeterminism)
  2. Simulate at most $k$ steps of the RAM
  3. If the simulation reached a terminated state return to step 2.
- This algorithm has an infinite computation (i.e. diverges) iff the given RAM terminates
Second Reduction

i: Inc($r_j$)

\[ I_i \xrightarrow{\tau} I_{i+1} \]

k: DecJump($r_j, s$)

\[ I_k \]

\[ \tau \]

\[ !dec_j \]

\[ !inh \]

\[ \tau \]

\[ I_{k+1} \]

\[ Inh \]

\[ I_s \]

$r_j$ with content $n_j$:

\[ R_j \ldots R_j \]

\[ n_j \text{ instances} \]

\[ ?dec_j \]

\[ \text{n instances} \]

\[ ?inh \]

\[ \text{h instances} \]

Termination Problems in Chemical Kinetics
Second Reduction

i: Inc(r_j)

k: DecJump(r_j, s)

r_j with content n_j:

n_j instances

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Conclusion

- Is Chemical Kinetics Turing powerful?
  - An additional proof that it is **NOT** but Turing complete formalisms can be **approximated** with any given degree of precision

- **“Perpetual”** and **“ephemeral”** chemical systems
  - Surely “perpetual”: **DECIDABLE**
  - Surely “ephemeral”: **UNDECIDABLE**
  - Possibly “perpetual”/“ephemeral”: **UNDECIDABLE**
Related work

- **Petri nets**
  - Universal termination is decidable but it is not in **fair** Petri nets [Car87]

- **Lossy channels**
  - Universal termination is decidable but it is not in **probabilistic** lossy channels [Abd. et al.00]

- **“Turifying” chemical kinetics**
  - CGF extended with a mechanism for molecule **association/dissociation** (inspired by biochemistry) is Turing powerful [AB08]