Reversible Structures

Luca Cardelli   Cosimo Laneve

January 19, 2012

CMSB referee report #1

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One solutions would be to abandon the Bourbaki style in which the paper is written, and start by motivating the problem in terms of DNA computation and then show how it can be formalized in the framework presented.

There should be a section then summarizing all the results, how to interpret them and why the results do not completely correspond to the real physics, thermodynamics, etc. One technicals section should collect all the theorems and proofs.

... following CMSB's reviewer: plan

– (**motivations**) reversibility in nature: the instance of DNA circuits

– (**our solution**) the algebra of DNA circuits: *reversible structures*

– (**the appendix**) overview of the theory of reversible structures
  - reversibility/causality in reversible structures
  - causally equivalent computations (permutation equivalence) and the standardization theorem
  - modelling of asynchronous RCCS

motivations/reversibility

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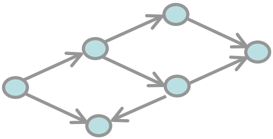
- implementations of these systems in physics or chemistry are usually reversible

- reversibility means undoing the computation *not in a deterministic way*:

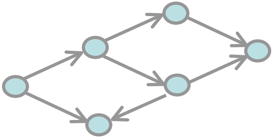
  > *states reached during a backward computation are states that could have been reached during the forward computation by just performing independent actions in a different order*

motivations/reversibility/example



transition system

motivations/reversibility/example



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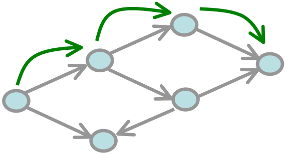
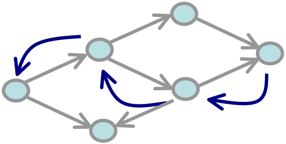
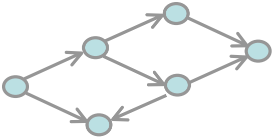


a computation



a reverted computation of its

motivations/reversibility/example



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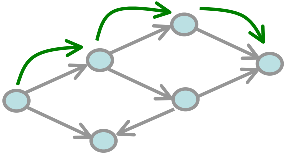
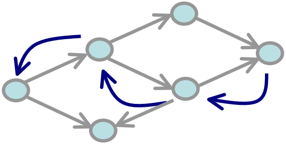


a computation



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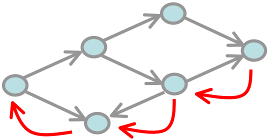

a different computation

motivations/the formalization of reversibility in nature

since parts of physics and chemistry are reversible,

what is the theory of reversibility underneath?

motivations/the formalization of reversibility in nature

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what is the theory of reversibility underneath?

said otherwise:

taking a reversible system in nature, what properties may we prove?

motivations/reversibility in DNA

- subsequences of a DNA strand are called domains

domains are independent of each other

- they cannot hybridize from any other domain except their complement

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- subsequences of a DNA strand are called domains

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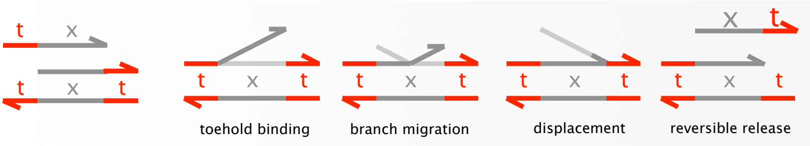
  - they cannot hybridize from any other domain except their complement

- there are very few short domains with reversible hybridizations

- and long domains with irreversible hybridizations

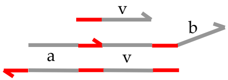
motivations/reversibility in DNA/branch migration

clever strand designs give reversible behaviours



.../reversibility in DNA/three-domains structures

– a three-domains transducer



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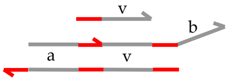
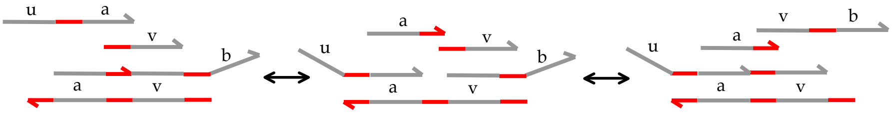


– its dynamics



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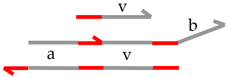

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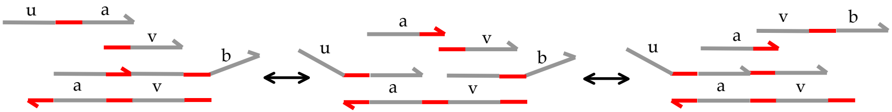
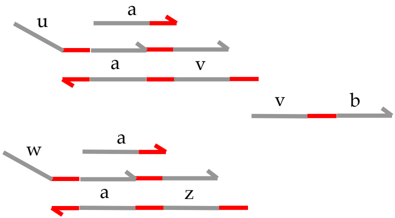


– and causalities



.../reversibility in DNA/massive concurrency

DNA circuits are *massively concurrent*:

- solutions consist of populations of species of strands and
- populations are not singletons

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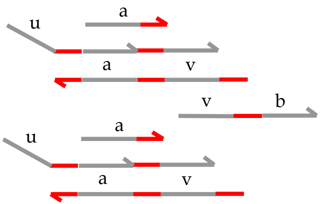
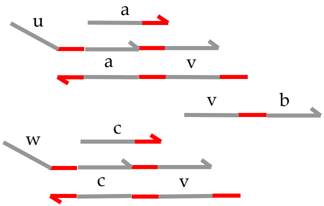
it is not possible to desynchronize processes that actually interacted in the past



.../reversibility in DNA/massive concurrency

the situation may be even worse due to bad designs



.../reversibility in DNA/issues

reversibility/causality in nature (massive concurrent systems) has not been studied

- theories have been defined for reversible calculi where processes retain unique ids (Danos-Krivine, Phillips-Ulidowski, Lanese-Mezzina-Stefani)

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question addressed by this talk:

what is the distance between current theories of reversible algebras and reversibility in nature?

our solution/the algebra of reversible structures

signals
gates

our solution/the algebra of reversible structures

signals : $u{:}\bar{a}$

gates

our solution/the algebra of reversible structures

signals : $u{:}\bar{a}$

gates : g *input part.output part* + ˆ

our solution/the algebra of reversible structures

signals : $u{:}\overline{a}$

gates : g $\quad$ *input part.output part* + ˆ

examples of gates:

$\hat{}a \centerdot a' \centerdot v{:}\overline{b}$ $\qquad$ $u{:}a \centerdot \hat{}a' \centerdot v{:}\overline{b}$

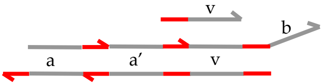
$$u{:}a \centerdot u'{:}a' \centerdot v{:}\overline{b}\hat{}$$

our solution/the algebra of reversible structures

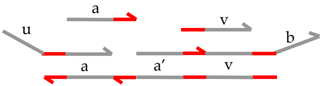
signals : $u{:}\overline{a}$

gates : g — *input part.output part* + ˆ

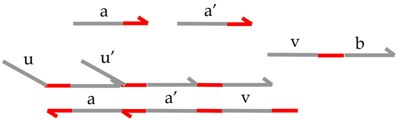
examples of gates:



$\hat{}a \bullet a' \bullet v{:}\overline{b}$



$u{:}a \bullet \hat{}a' \bullet v{:}\overline{b}$



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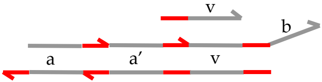

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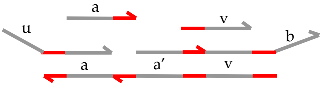

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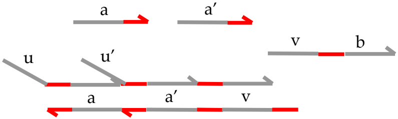

$u{:}a \bullet u'{:}a' \bullet v{:}\bar{b}\,\hat{}$

notation:

u, v, w:	ids	$a, \bar{a}, b, \bar{b}$:	names and conames
x, x':	ids, names and conames	A, B, C:	sequences of names;
$\bar{\mathtt{A}}, \bar{\mathtt{B}}, \bar{\mathtt{C}}$:	sequences of elements $u{:}\bar{a}$	$\mathtt{A}^{\perp}, \mathtt{B}^{\perp}, \mathtt{C}^{\perp}$:	sequences of elements $u{:}a$

our solution/the algebra of reversible structures/syntax

$$
\begin{array}{llllll}
\textit{structures}: & \mathtt{S} & ::= & & & \\
& & & \mathbf{0} & & \text{(null)} \\
& & | & u{:}\bar{a} & & \text{(signal)} \\
& & | & g & & \text{(gate)} \\
& & | & \mathtt{S} \mid \mathtt{S} & & \text{(parallel)} \\
& & | & (\mathtt{new}\ x)\mathtt{S} & & \text{(new)}
\end{array}
$$

.../the algebra of reversible structures/reductions

$$\textit{input-capture}: \quad u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \hat{}\,a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}} \;\longrightarrow\; \mathtt{A}^{\perp} \,.\, u{:}a \,.\, \hat{}\,\mathtt{B} \,.\, \overline{\mathtt{C}}$$

$$\textit{input-release}: \quad \mathtt{A}^{\perp} \,.\, u{:}a \,.\, \hat{}\,\mathtt{B} \,.\, \overline{\mathtt{C}} \;\longrightarrow\; u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \hat{}\,a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}}$$

$$\textit{output-release}: \quad \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, \hat{}\,u{:}\overline{a} \,.\, \overline{\mathtt{C}} \;\longrightarrow\; u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, u{:}\overline{a} \,.\, \hat{}\,\overline{\mathtt{C}}$$

$$\textit{output-capture}: \quad u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, u{:}\overline{a} \,.\, \hat{}\,\overline{\mathtt{C}} \;\longrightarrow\; \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, \hat{}\,u{:}\overline{a} \,.\, \overline{\mathtt{C}}$$

.../the algebra of reversible structures/reductions

input-capture: $u{:}\overline{a} \mid \mathtt{A}^{\perp} \centerdot \hat{\ } a \centerdot \mathtt{B} \centerdot \overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} \centerdot u{:}a \centerdot \hat{\ }\mathtt{B} \centerdot \overline{\mathtt{C}}$

input-release: $\mathtt{A}^{\perp} \centerdot u{:}a \centerdot \hat{\ }\mathtt{B} \centerdot \overline{\mathtt{C}} \longrightarrow u{:}\overline{a} \mid \mathtt{A}^{\perp} \centerdot \hat{\ } a \centerdot \mathtt{B} \centerdot \overline{\mathtt{C}}$

output-release: $\mathtt{A}^{\perp} \centerdot \overline{\mathtt{B}} \centerdot \hat{\ } u{:}\overline{a} \centerdot \overline{\mathtt{C}} \longrightarrow u{:}\overline{a} \mid \mathtt{A}^{\perp} \centerdot \overline{\mathtt{B}} \centerdot u{:}\overline{a} \centerdot \hat{\ }\overline{\mathtt{C}}$

output-capture: $u{:}\overline{a} \mid \mathtt{A}^{\perp} \centerdot \overline{\mathtt{B}} \centerdot u{:}\overline{a} \centerdot \hat{\ }\overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} \centerdot \overline{\mathtt{B}} \centerdot \hat{\ } u{:}\overline{a} \centerdot \overline{\mathtt{C}}$

EXAMPLE:

$v{:}\overline{a} \mid w{:}\overline{a} \mid \hat{\ } a \centerdot u{:}\overline{b}$

.../the algebra of reversible structures/reductions

input-capture: $$u{:}\overline{a} \mid \mathtt{A}^{\perp} . \hat{\ }a . \mathtt{B} . \overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} . u{:}a . \hat{\ }\mathtt{B} . \overline{\mathtt{C}}$$

input-release: $$\mathtt{A}^{\perp} . u{:}a . \hat{\ }\mathtt{B} . \overline{\mathtt{C}} \longrightarrow u{:}\overline{a} \mid \mathtt{A}^{\perp} . \hat{\ }a . \mathtt{B} . \overline{\mathtt{C}}$$

output-release: $$\mathtt{A}^{\perp} . \overline{\mathtt{B}} . \hat{\ }u{:}\overline{a} . \overline{\mathtt{C}} \longrightarrow u{:}\overline{a} \mid \mathtt{A}^{\perp} . \overline{\mathtt{B}} . u{:}\overline{a} . \hat{\ }\overline{\mathtt{C}}$$

output-capture: $$u{:}\overline{a} \mid \mathtt{A}^{\perp} . \overline{\mathtt{B}} . u{:}\overline{a} . \hat{\ }\overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} . \overline{\mathtt{B}} . \hat{\ }u{:}\overline{a} . \overline{\mathtt{C}}$$

EXAMPLE:

$$w{:}\overline{a} \mid v{:}a . \hat{\ }u{:}\overline{b}$$

$$\nearrow$$

$$v{:}\overline{a} \mid w{:}\overline{a} \mid \hat{\ }a . u{:}\overline{b}$$

.../the algebra of reversible structures/reductions

input-capture: $u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \hat{}\,a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} \,.\, u{:}a \,.\, \hat{}\,\mathtt{B} \,.\, \overline{\mathtt{C}}$

input-release: $\mathtt{A}^{\perp} \,.\, u{:}a \,.\, \hat{}\,\mathtt{B} \,.\, \overline{\mathtt{C}} \longrightarrow u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \hat{}\,a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}}$

output-release: $\mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, \hat{}\,u{:}\overline{a} \,.\, \overline{\mathtt{C}} \longrightarrow u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, u{:}\overline{a} \,.\, \hat{}\,\overline{\mathtt{C}}$

output-capture: $u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, u{:}\overline{a} \,.\, \hat{}\,\overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, \hat{}\,u{:}\overline{a} \,.\, \overline{\mathtt{C}}$

EXAMPLE:

$$v{:}\overline{a} \mid w{:}\overline{a} \mid \hat{}\,a \,.\, u{:}\overline{b}$$

$$\searrow$$

$$v{:}\overline{a} \mid w{:}a \,.\, \hat{}\,u{:}\overline{b}$$

.../the algebra of reversible structures/reductions

input-capture: $u{:}\bar{a} \mid \mathtt{A}^{\perp} \,.\, {}^{\wedge}a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}} \quad \longrightarrow \quad \mathtt{A}^{\perp} \,.\, u{:}a \,.\, {}^{\wedge}\mathtt{B} \,.\, \overline{\mathtt{C}}$

input-release: $\mathtt{A}^{\perp} \,.\, u{:}a \,.\, {}^{\wedge}\mathtt{B} \,.\, \overline{\mathtt{C}} \quad \longrightarrow \quad u{:}\bar{a} \mid \mathtt{A}^{\perp} \,.\, {}^{\wedge}a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}}$

output-release: $\mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, {}^{\wedge}u{:}\bar{a} \,.\, \overline{\mathtt{C}} \quad \longrightarrow \quad u{:}\bar{a} \mid \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, u{:}\bar{a} \,.\, {}^{\wedge}\overline{\mathtt{C}}$

output-capture: $u{:}\bar{a} \mid \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, u{:}\bar{a} \,.\, {}^{\wedge}\overline{\mathtt{C}} \quad \longrightarrow \quad \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, {}^{\wedge}u{:}\bar{a} \,.\, \overline{\mathtt{C}}$

EXAMPLE:

$$v{:}\bar{a} \mid w{:}\bar{a} \mid {}^{\wedge}a \,.\, u{:}\bar{b} \quad \nearrow \quad w{:}\bar{a} \mid v{:}a \,.\, {}^{\wedge}u{:}\bar{b}$$

.../the algebra of reversible structures/reductions

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EXAMPLE:

$$w{:}\overline{a} \mid v{:}a \,.\, \hat{}\,u{:}\overline{b} \rightarrow w{:}\overline{a} \mid v{:}a \,.\, u{:}\overline{b}\,\hat{} \mid u{:}b$$

$$\nearrow$$

$$v{:}\overline{a} \mid w{:}\overline{a} \mid \hat{}\,a \,.\, u{:}\overline{b}$$

.../the algebra of reversible structures/reductions

input-capture: $u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \hat{\ } a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} \,.\, u{:}a \,.\, \hat{\ }\mathtt{B} \,.\, \overline{\mathtt{C}}$

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EXAMPLE:

$$v{:}\overline{a} \mid w{:}\overline{a} \mid \hat{\ } a \,.\, u{:}\overline{b} \nearrow w{:}\overline{a} \mid v{:}a \,.\, \hat{\ } u{:}\overline{b} \rightarrow w{:}\overline{a} \mid v{:}a \,.\, u{:}\overline{b}\hat{\ } \mid u{:}\overline{b}$$

$$v{:}\overline{a} \mid w{:}\overline{a} \mid \hat{\ } a \,.\, u{:}\overline{b} \searrow v{:}\overline{a} \mid w{:}a \,.\, \hat{\ } u{:}\overline{b}$$

.../the algebra of reversible structures/reductions

input-capture: $u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \hat{\ } a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} \,.\, u{:}a \,.\, \hat{\ }\mathtt{B} \,.\, \overline{\mathtt{C}}$

input-release: $\mathtt{A}^{\perp} \,.\, u{:}a \,.\, \hat{\ }\mathtt{B} \,.\, \overline{\mathtt{C}} \longrightarrow u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \hat{\ } a \,.\, \mathtt{B} \,.\, \overline{\mathtt{C}}$

output-release: $\mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, \hat{\ } u{:}\overline{a} \,.\, \overline{\mathtt{C}} \longrightarrow u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, u{:}\overline{a} \,.\, \hat{\ }\overline{\mathtt{C}}$

output-capture: $u{:}\overline{a} \mid \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, u{:}\overline{a} \,.\, \hat{\ }\overline{\mathtt{C}} \longrightarrow \mathtt{A}^{\perp} \,.\, \overline{\mathtt{B}} \,.\, \hat{\ } u{:}\overline{a} \,.\, \overline{\mathtt{C}}$

reverse reductions:

input-capture/*input-release* and *output-release*/*output-capture*

.../modelling of concurrent operators (pearls)

join input ($a \mid b \triangleright \overline{c}$)

input-guarded choice ($a.\overline{b} + a'.\overline{c}$)

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$$(\texttt{new}\ v, e)(\ e.\ a.\ u{:}\overline{b} \quad | \quad e.\ a'.\ u'{:}\overline{c} \quad | \quad v{:}\overline{e}\ )$$

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– similarly for mixed-guarded choice

this is the basic scheme for implementing *asynchronous RCCS*

.../weak coherence and DNA realizability

a structure is weak coherent whenever ids are uniquely associated to names and co-names

- if $u{:}\alpha$ and $u{:}\alpha'$ occur in the structure then either $\alpha = \alpha'$ or $\alpha = \overline{\alpha'}$

STATEMENT: (weak coherent) reversible structures may be implemented into three domains DNA strands

.../causality in a nutshell

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1. reversibility is reduced to causal (in)dependencies

   two reductions are (causally) dependent if they have either the signal or the gate in common

   note: *two reductions may be dependent even if they concern different elements (of the same population)*

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3. define *permutation equivalence*, an equivalence on computations that is insensible

   (i) to swapping of consecutive independent reductions

   (ii) to the removal of consecutive reverse reductions

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4. a computation σ' is *the reverse of* σ if $\sigma;\sigma' \sim \varepsilon$

.../causality: diamond lemma and perm. equivalence

$$u{:}\overline{a} \mid \hat{}a \centerdot v{:}\overline{b} \mid u{:}a \centerdot \hat{}v{:}\overline{b}$$

$$u \mid \hat{}a \circ v \swarrow$$

$$u{:}a \centerdot \hat{}v{:}\overline{b} \mid u{:}a \centerdot \hat{}v{:}\overline{b}$$

$$u \circ \hat{}v \searrow$$

$$u{:}a \centerdot \hat{}v{:}\overline{b} \mid u{:}a \centerdot v{:}\overline{b}\hat{} \mid v{:}b$$

.../causality: diamond lemma and perm. equivalence

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$$u{:}a \centerdot \hat{}v{:}\overline{b} \mid u{:}a \centerdot v{:}\overline{b}\hat{} \mid v{:}\overline{b}$$

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$$u \circ \hat{}\,v \searrow$$

$$u{:}a \bullet \hat{}\,v{:}\bar{b} \mid u{:}a \bullet v{:}\bar{b}\,\hat{} \mid v{:}\bar{b}$$

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$$u{:}\bar{a} \mid \hat{\ }a \bullet v{:}\bar{b} \mid u{:}a \bullet \hat{\ }v{:}\bar{b}$$

$$\color{red}{u \mid \hat{\ }a \circ v} \swarrow \qquad\qquad \searrow \color{red}{u \circ \hat{\ }v}$$

$$u{:}a \bullet \hat{\ }v{:}\bar{b} \mid u{:}a \bullet \hat{\ }v{:}\bar{b} \qquad\qquad u{:}\bar{a} \mid \hat{\ }a \bullet v{:}\bar{b} \mid u{:}a \bullet v{:}\bar{b}\hat{\ } \mid v{:}\bar{b}$$

$$\color{red}{u \circ \hat{\ }v} \searrow \qquad\qquad \swarrow \color{red}{u \mid \hat{\ }a \circ v}$$

$$u{:}a \bullet \hat{\ }v{:}\bar{b} \mid u{:}a \bullet v{:}\bar{b}\hat{\ } \mid v{:}\bar{b}$$

.../causality: issues

$$u{:}\overline{a} \mid u{:}\overline{a} \mid \hat{}a \centerdot v{:}\overline{b} \mid w{:}c \centerdot u{:}\overline{a}\hat{}$$

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$$u{:}\bar{a} \mid u{:}\bar{a} \mid \hat{}a \centerdot v{:}\bar{b} \mid w{:}c \centerdot u{:}\bar{a}\hat{} \quad \xrightarrow{u \mid \hat{}a \circ v} \quad u{:}\bar{a} \mid u{:}a \centerdot \hat{}v{:}\bar{b} \mid w{:}c \centerdot u{:}\bar{a}\hat{}$$

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$$u{:}\bar{a} \mid u{:}\bar{a} \mid {}^{\frown}a \,.\, v{:}\bar{b} \mid w{:}c \,.\, u{:}\bar{a}^{\frown} \xrightarrow{u \,|\, {}^{\frown}a \circ v} u{:}\bar{a} \mid u{:}a \,.\, {}^{\frown}v{:}\bar{b} \mid w{:}c \,.\, u{:}\bar{a}^{\frown}$$

$$\xrightarrow{u \,|\, w \circ u^{\frown}} u{:}a \,.\, {}^{\frown}v{:}\bar{b} \mid w{:}c \,.\, {}^{\frown}u{:}\bar{a}$$

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$$u{:}\bar{a} \mid u{:}\bar{a} \mid \hat{}\, a \,.\, v{:}\bar{b} \mid w{:}c \,.\, u{:}\bar{a}\,\hat{} \quad \xrightarrow{u \,\mid\, \hat{}\, a \circ v} \quad u{:}\bar{a} \mid u{:}a \,.\, \hat{}\, v{:}\bar{b} \mid w{:}c \,.\, u{:}\bar{a}\,\hat{}$$

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cannot be swapped because $u \mid \hat{}\, a \circ v$ and $u \mid w \circ u\,\hat{}$ have terms in common

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RATIONALE: in massive concurrent systems, different occurrences of a same molecule cannot be separated

- we do not catch *multiplicities*
- a similar anomaly is present in Petri nets (*cf.* Degano, Meseguer, Montanari)

the appendix/the standardization theorem

STATEMENT: let $\mu_1 ; \sigma ; \mu_n$ be a computation of a weak coherent structure such that μ_n is the reverse of μ_1

- *there is a shorter computation that is permutation equivalent to $\mu_1 ; \sigma ; \mu_n$*

the appendix/the standardization theorem

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- *there is a shorter computation that is permutation equivalent to $\mu_1 ; \sigma ; \mu_n$*

the evolution of a gate in a computation without reverse reductions (normal) is unidirectional

the appendix/coherence

a structure is coherent when it contains exactly one molecule of every species and different species have disjoint ids

EXAMPLES: $u{:}\bar{a} \mid \hat{}a \centerdot v{:}\bar{a}$ and $v{:}\bar{a} \mid u{:}a \centerdot v{:}\bar{a}\hat{}$ are coherent

$v{:}\bar{a} \mid \hat{}a \centerdot v{:}\bar{a}$ and $\hat{}b \centerdot v{:}\bar{a} \mid \hat{}b \centerdot v{:}\bar{a}$ are not

the appendix/consequences of coherence

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STATEMENT: *two coinitial computations of a coherent structure are permutation equivalent if and only if they are cofinal*

(false in weak-coherent structures)

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STATEMENT: *coherent structures encode in a causally consistent way asynchronous Reversible CCS*

STATEMENT: *the reachability problem in coherent structure has a computational complexity of $O(n^2)$, where n is the number of gates in the structure*

(in weak-coherent structures, reachability is EXPSPACE complete)

conclusions

research directions:

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- coherence is very hard to achieve in nature
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  + this makes possible to model standard irreversible operators of programming languages in DNA

conclusions

research directions:

- coherence is very hard to achieve in nature
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- reversible structures may be extended with irreversible combinators (that may be implemented in DNA)
  + this makes possible to model standard irreversible operators of programming languages in DNA
- studying biological relevant problems in reversible structures may be simpler
  + we already studied reachability; other issues are absence of molecules/processes, persistence of materials, $\cdots$