π@: a π-based Process Calculus for the Implementation of Compartmentalised Bio-inspired Calculi

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Outline

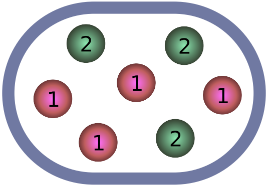
- Introduction
  - Biochemical modelling with the π-Calculus
  - Modelling compartments in π-Calculus
  - Two biologically inspired calculi: Bioambients, Brane
- π@: a core calculus
  - Encodings of bio-calculi into π@
- Conclusion

Biochemical modelling with the π-Calculus

Main ideas

- free floating biochemical elements (e.g. molecules) $m_1, m_2, \ldots$ $\Longrightarrow$ parallel processes $M_1, M_2, \ldots$;
- I/O channel $\Longrightarrow$ reaction capability;
- reaction $\Longrightarrow$ synchronisation/communication;

Example



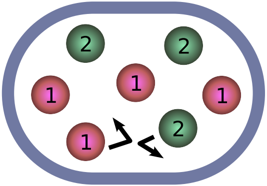
$$S \triangleq M_1 \mid M_1 \mid \cdots \mid M_2 \mid M_2 \mid \cdots$$

Biochemical modelling with the π-Calculus

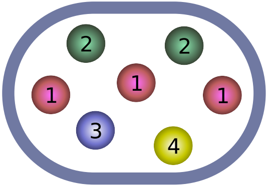
Binary reactions

Chemical reaction		π-Calculus system
		$M_1 \triangleq r.M_3 \qquad M_2 \triangleq \overline{r}.M_4$
$R: \quad m_1 + m_2 \rightarrow m_3 + m_4$	$\Longrightarrow$	
		$M_1 \vert M_2 \;\rightarrow\; M_3 \vert M_4$

Example



$\rightarrow$



$$M_1|M_1|\cdots|M_2|M_2|\cdots \qquad\qquad M_3|M_1|\cdots|M_4|M_2|\cdots$$

Biochemical modelling with the π-Calculus

Mutually exclusive reactions

Chemical reaction

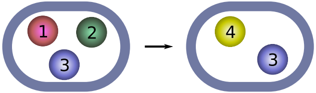
$$R_1 : \quad m_1 + m_2 \rightarrow m_4$$
$$R_2 : \quad m_1 + m_3 \rightarrow m_5$$

$\Longrightarrow$

π-Calculus system

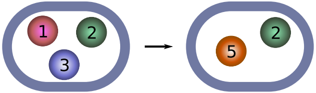
$$M_1 \triangleq r_1.M_4 + r_2.M_5$$
$$M_2 \triangleq \overline{r_1}.\mathbf{0}$$
$$M_3 \triangleq \overline{r_2}.\mathbf{0}$$

Example



$$M_1 | M_2 | M_3 \rightarrow M_4 \mid M_3$$

Example



$$M_1 | M_2 | M_3 \rightarrow M_5 \mid M_2$$

Biochemical modelling with the π-Calculus

Molecular binding

Chemical reaction

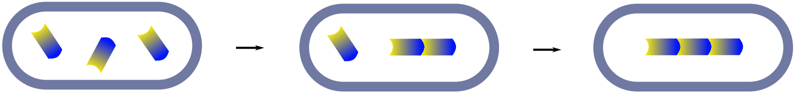
$$
\begin{aligned}
R_1 &: \quad m_1 + m_1 \rightarrow m_{11} \\
R_1^- &: \quad m_{11} \rightarrow m_1 + m_1 \\
R_{11} &: \quad m_{11} + m_1 \rightarrow m_{111} \\
R_{11}^- &: \quad m_{111} \rightarrow m_{11} + m_1 \\
&\ldots
\end{aligned}
$$

$\Longrightarrow$

π-Calculus system

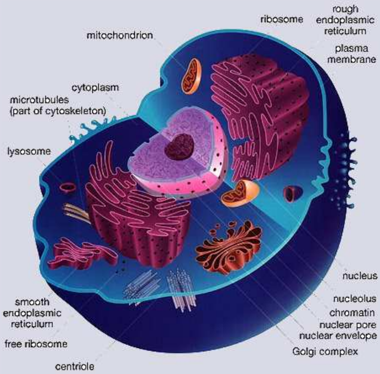
$$
\begin{aligned}
M(b_l) &\triangleq \overline{r}\langle b_l\rangle.M_l(b_l) + r(b_r).M_r(b_l, b_r) \\
M_l(b_l) &\triangleq r(b_r).M_{lr}(b_l, b_r) + \overline{b_l}.M \\
M_r(b_l, b_r) &\triangleq \overline{r}\langle b_l\rangle.M_{lr}(b_l, b_r) + b_l.M \\
M_{lr}(b_l, b_r) &\triangleq \overline{b_l}.M_r(b_r)
\end{aligned}
$$

Example



$$\nu a\ M(a) \mid \nu b\ M(b) \mid \nu c\ M(c) \ \rightarrow\ \cdots\ \rightarrow\ \nu abc\ (M_r | M_{lr} | M_l)$$

Compartments



Biological compartments

- systems organised into complex spatial and functional configurations (organelles, cells, tissues, organs, . . .)
- partial mobility of simple elements but also of whole structures (membrane channels, vesicular transport, . . .)

Static Compartment Modelling

Main ideas

- distinct names for same chemical species in different compartments
- transport as "renaming" reaction

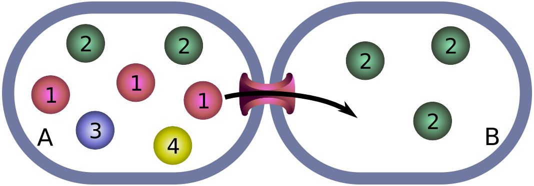
Example

Compartments A, B
$R: \quad m_1 + m_2 \rightarrow m_3 + m_4$

$\Longrightarrow$

$R_A: \quad m_1^a + m_2^a \rightarrow m_3^a + m_4^a$
$R_B: \quad m_1^b + m_2^b \rightarrow m_3^b + m_4^b$

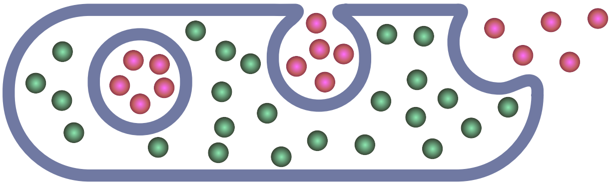
Inter-compartment transport: $T_{AB}: \quad m_1^a \rightarrow m_1^b$



Dynamic Compartment Modelling

Example

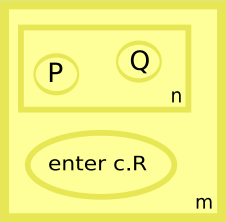
Exocytosis:



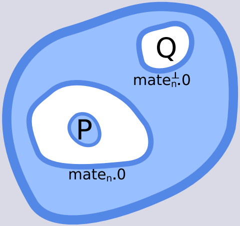
Problems

- how to grant that all processes are properly renamed?
- how to avoid overlapping of compartment operations?

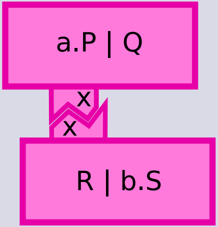
Bio-inspired Process Calculi with Compartments



BioAmbients



Brane Calculi



Beta-binders

Compartments

- explicitly formalised
- used at different levels of abstraction
- represented by ambients/membranes/boxes
- may be nested
- dynamical (created, merged/split, . . .)

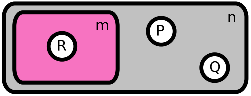
Overview of BioAmbients

BioAmbients: Mobile Ambients added with communication primitives

- compartments are represented by ambients
- ambients contain processes or nested ambients $\Longrightarrow$ *tree structure*
- special primitives allow π-Calculus-like name communication
- ambients may exit from, move inside, or merge with other ambients

Example

$$n[\ P \mid Q \mid m[\ R\ ]\ ]$$

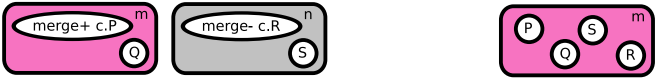


Ambient capabilities

Example

Merge:

$$m[merge+\ c.P|Q]\ \big|\ n[merge-\ c.R|S]\ \rightarrow\ m[P|Q|R|S]$$

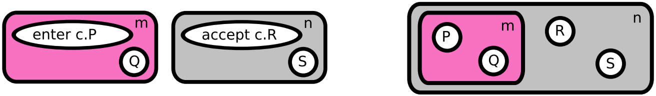


Ambient capabilities

Example

Enter/accept:

$$m[enter\ c.P|Q] \mid n[accept\ c.R|S] \ \rightarrow\ n[\ R \mid S \mid m[P|Q]\ ]$$



Exit/expel:

$$n[m[exit\ c.P|Q] \mid expel\ c.R|S] \ \rightarrow\ m[P|Q] \mid n[R|S]$$

Ambient communications

Example

Local (intra-ambient):

$$m[local\ c!\{a\}.P|local\ c?\{x\}.Q] \rightarrow m[P|Q\{a/x\}]$$

Sibling-to-sibling (inter-ambient):

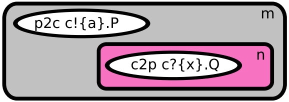
$$m[s2s\ c!\{a\}.P] \mid n[s2s\ c?\{x\}.Q] \rightarrow m[P] \mid n[Q\{a/x\}]$$

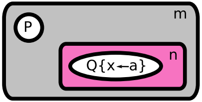
Ambient communications

Example

Parent-to-child/child-to-parent (inter-ambient, between nested ambients):

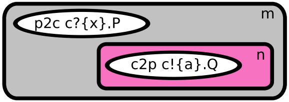
$$m[p2c\ c!\{a\}.P \mid n[c2p\ c?\{x\}.Q]\ ] \rightarrow m[P \mid n[Q\{a/x\}]\ ]$$

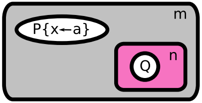




Child-to-parent/parent-to-child (inter-ambient, between nested ambients):

$$m[p2c\ c?\{x\}.P \mid n[c2p\ c!\{a\}.Q]\ ] \rightarrow m[P\{a/x\} \mid n[Q]\ ]$$





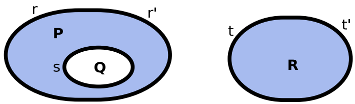
Overview of Brane Calculi

Brane Calculi: membranes as active sites of computation

- compartments are represented by membranes
- membranes may contain other membranes in a *tree structure*
- processes are located on membranes
- membranes transformations preserve *bitonality*

Example

$$r|r'(\!|\ P \circ s(\!|\ Q\ |\!)\ |\!) \circ t|t'(\!|\ R\ |\!)$$

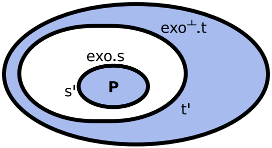


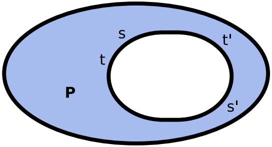
Bitonal operations

Example

Exocytosis:

$$(\!|\ exo^{\perp}.t \mid t'(\!| exo.s \mid s'(\!| P |\!) \circ Q |\!)\ |\!) \quad \rightarrow \quad (\!|\ P \circ s \mid s' \mid t \mid t'(\!| Q |\!)\ |\!)$$





Bitonal operations

Example

Phagocytosis:

$$phago.s|s'(\!|P|\!) \circ phago^{\perp}(r).t|t'(\!|Q|\!) \quad \rightarrow \quad t|t_0(\!|r(\!|s|s'(\!|P|\!)|\!) \circ Q|\!)$$

Motivation

Bio-inspired process calculi:

Pros

- faithful modelling
- easy to use (hopefully...)

Cons

- specialised
- no easy cross coding
- need to develop new
  - theoretical analyses
  - software tools

Motivation

- what common compartment-related features?
- what the simplest/minimal language primitives to express all of (most of) them?

π@ (paillette): a Conservative Core Calculus

Aim

To provide a *core* calculus

- simple, general purpose
- embedding the key features of bio-inspired calculi

The π@ Calculus [Versari, ESOP'07]

π@ ::= π-Calculus + polyadic synchronisation + priority

π@ features

- conservative π-Calculus extension
- polyadic synchronisation for modeling compartment scoping
- priority for gaining atomicity of sequences of operations

Localisation by means of Polyadic Synchronisation

Polyadic synchronisation: channels are identified by one *or more* names

π-Calculus

$$P \equiv \overline{c}.P'$$

π@

$$P \equiv \overline{c_1 @ c_2}.P'$$

Compartments may be represented by one of the names of each channel:

$$P \equiv \overline{c@compartment_P}.P' \qquad Q \equiv c@compartment_Q.Q'$$

- P and Q may share free names
- P and Q may interact iff $compartment_P = compartment_Q$

Atomicity by means of Priority

Priority: high-priority reactions happen *before* lower-priority ones

Example

$$S \equiv \overline{l}.P_1 \mid l.P_2 \mid \overline{h}.Q_1 \mid h.Q_2 \quad \not\to \quad T \equiv P_1 \mid P_2 \mid \overline{h}.Q_1 \mid h.Q_2$$

$$S \equiv \overline{l}.P_1 \mid l.P_2 \mid \overline{h}.Q_1 \mid h.Q_2 \quad \to \quad S_2 \equiv \overline{l}.P_1 \mid l.P_2 \mid Q_1 \mid Q_2$$

$$\to \quad S_3 \equiv P_1 \mid P_2 \mid Q_1 \mid Q_2$$

Each atomic sequence of operations may be encoded as *a low priority reaction followed by an unlimited number of high priority reactions*:

$$P_1 \equiv \overline{seq_1}.\underline{op_{11}}.\underline{op_{12}}.\underline{op_{13}} \qquad P_2 \equiv \overline{seq_2}.\underline{op_{21}}.\underline{op_{22}}.\underline{op_{23}}$$

The executions of P_1 and P_2 never overlap

π@ Syntax

π@ syntax

$$P \;::=\; \sum_{i\in I} \pi_i.P_i \;\;\Big|\;\; P \mid Q \;\;\Big|\;\; !P \;\;\Big|\;\; (\nu\, x)P$$

$$\pi \;::=\; \tau \;\;\Big|\;\; \mu_1@\cdots@\mu_n : k(x) \;\;\Big|\;\; \overline{\mu_1@\cdots@\mu_n : k}\langle x\rangle$$

- each channel is represented by a vector of one or more names $\mu_1, \ldots, \mu_n$
- each input or output action has a priority k
- higher priority actions are executed first
- priority is static

π@ Semantics

π@ reduction semantics

π@ semantics

$$\frac{\tau \notin \bigcup_{i<k} I^i(M)}{\tau : k.P + M \ \rightarrow_k \ P} \qquad \frac{P \ \rightarrow_k \ P'}{(\nu\ x)P \ \rightarrow_k \ (\nu\ x)P'}$$

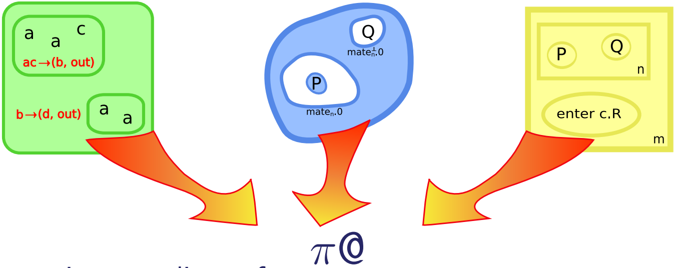
$$\frac{\tau \notin \bigcup_{i<k} I^i(M \mid N)}{(\mu : k(y).P + M) \mid (\overline{\mu} : k\langle z\rangle.Q + N) \ \rightarrow_k \ P\{z/y\} \mid Q}$$

$$\frac{P \ \rightarrow_k \ P' \qquad \tau \notin \bigcup_{i<k} I^i(P \mid Q)}{P \mid Q \ \rightarrow_k \ P' \mid Q} \qquad \frac{P \equiv Q \quad P \ \rightarrow_k \ P' \quad P' \equiv Q'}{Q \ \rightarrow_k \ Q'}$$

- the only difference from π-Calculus semantics is the side condition in red: no additional rules required;
- the $I^k(P)$ function represents the set of actions of priority k ready to be executed by the process P.

Encodings into π@

Encodings



Parallel-preserving encodings of

- BioAmbients, Brane Calculi [Versari, ESOP'07]
- some P systems (with maximal parallelism!) [Versari, MECBIC'07]
- Beta-binders [Cappello, Quaglia, to appear]

into π@ have been provided.

Encoding requirements

Definition

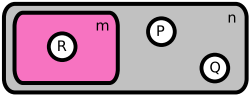
Reasonable encoding:

- parallel-preserving $[\![P_1 \mid P_2]\!] = [\![P_1]\!] \mid [\![P_2]\!]$
- renaming preserving: σ permutation of names, $[\![\sigma(P)]\!] = \theta([\![P]\!])$;
- termination invariance: $P \Downarrow$ iff $[\![P]\!] \Downarrow$, $P \Uparrow$ iff $[\![P]\!] \Uparrow$;
- operational correspondence:
  - if $P \rightarrow P'$ then $[\![P]\!] \rightarrow^* [\![P']\!]$,
  - if $[\![P]\!] \rightarrow^* Q$ then $\exists P' : P \rightarrow^* P' \wedge Q \rightarrow^* [\![P']\!]$.

Encoding Bioambients

Example

$n[\ P \mid Q \mid m[\ R\ ]\ ]$



Encoding specifies compartment and parent compartment names:

$$[\![P]\!] \equiv [\![P]\!]_{c,pc}$$

Basic operators are homomorphically coded

$$[\![P \mid Q]\!]_{c,pc} \equiv [\![P]\!]_{c,pc} \mid [\![Q]\!]_{c,pc}$$

$$[\![(new\ x)P]\!]_{c,pc} \equiv (\nu\ x)[\![P]\!]_{c,pc}$$

Nested compartments are represented by private names

$$[\![[\ P\ ]]\!]_{c,pc} \equiv (\nu\ \ cmp)[\![P]\!]_{cmp,c}$$

Encoding Bioambients Communications

Local communication:

$$[\![\ local\ c!\{a\}.P\ ]\!]_{m,pm} \triangleq \overline{local@c@m}\langle a\rangle.[\![\ P\ ]\!]_{m,pm}$$

$$[\![\ local\ c?\{x\}.Q\ ]\!]_{m,pm} \triangleq local@c@m(x).[\![\ Q\ ]\!]_{m,pm}$$

Example

$$m[local\ c!\{a\}.P|local\ c?\{x\}.Q] \rightarrow m[P|Q\{a/x\}]$$

Encoding Bioambients Communications

Sibling-to-sibling communication:

$$[\![\ s2s\ c!\{a\}.P\ ]\!]_{m,pm} \triangleq \overline{s2s@c@pm}\langle a\rangle.[\![\ P\ ]\!]_{m,pm}$$

$$[\![\ s2s\ c?\{x\}.Q\ ]\!]_{n,pn} \triangleq s2s@c@pn(x).[\![\ Q\ ]\!]_{n,pn}$$

Example

$$m[s2s\ c!\{a\}.P] \mid n[s2s\ c?\{x\}.Q] \ \rightarrow\ m[P] \mid n[Q\{a/x\}]$$

Encoding Bioambients Communications

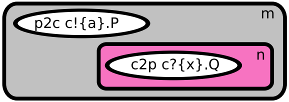
Parent-to-child communication:

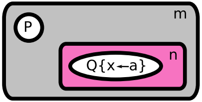
$$\llbracket\, p2c\ c!\{a\}.P \,\rrbracket_{m,pm} \triangleq \overline{p2c@c@m}\langle a\rangle.\llbracket\, P \,\rrbracket_{m,pm}$$

$$\llbracket\, c2p\ c?\{x\}.P \,\rrbracket_{n,pn} \triangleq p2c@c@pn(x).\llbracket\, P \,\rrbracket_{n,pn}$$

Example

$$m[p2c\ c!\{a\}.P \mid n[c2p\ c?\{x\}.Q]\,] \rightarrow m[P \mid n[Q\{a/x\}]\,]$$





Encoding Bioambients Capabilities

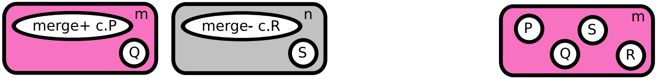
Merge:

$$[\![\ merge+\ \ c.P\ ]\!]_{m,pm} \triangleq \overline{merge@c@pm}\langle m\rangle.[\![\ P\ ]\!]_{m,pm}$$

$$[\![\ merge-\ \ c.P\ ]\!]_{n,pn} \triangleq merge@c@pn(x).\overline{bcast}\langle merge, n, x\rangle.[\![\ P\ ]\!]_{x,pn}$$

Example

$$m[merge+\ c.P|Q]\ \big|\ n[merge-\ c.R|S]\ \rightarrow\ m[P|Q|R|S]$$



Encoding Bioambients Capabilities

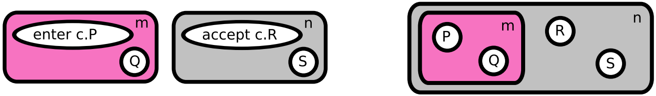
Enter/accept:

$$[\![\ accept\ c.R\ ]\!]_{n,pn} \triangleq \overline{enter@c@pn}\langle n\rangle.[\![\ R\ ]\!]_{n,pn}$$

$$[\![\ enter\ c.P\ ]\!]_{m,pm} \triangleq enter@c@pm(x).\overline{\underline{bcast}}\langle enter, m, x\rangle.[\![\ P\ ]\!]_{m,x}$$

Example

$$m[enter\ c.P|Q] \mid n[accept\ c.R|S] \rightarrow n[\ R \mid S \mid m[P|Q]\ ]$$



Encoding Bioambients Capabilities

Exit/expel:

$$[\![\ expel\ c.R\ ]\!]_{n,pn} \triangleq \overline{expel@c@n}\langle pn\rangle.[\![\ R\ ]\!]_{n,pn}$$

$$[\![\ exit\ c.P\ ]\!]_{m,pm} \triangleq expel@c@pm(x).\overline{\underline{bcast}}\langle exit, m, x\rangle.[\![\ P\ ]\!]_{m,x}$$

Example

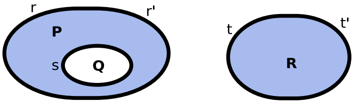
$$n[m[exit\ c.P|Q]\ |\ expel\ c.R|S] \ \rightarrow\ m[P|Q]\ |\ n[R|S]$$

Encoding Brane

Basic Encodings

Example

$$r|r'\llparenthesis\ P \circ s\llparenthesis\ Q\ \rrparenthesis\ \rrparenthesis \circ t|t'\llparenthesis\ R\ \rrparenthesis$$



$$\begin{aligned}
\llbracket\, P \,\rrbracket &\triangleq \llbracket\, P \,\rrbracket_{pc} \\
\llbracket\, P \circ Q \,\rrbracket_{pc} &\triangleq \llbracket\, P \,\rrbracket_{pc} \mid \llbracket\, Q \,\rrbracket_{pc} \\
\llbracket\, s\llparenthesis P \rrparenthesis \,\rrbracket_{pc} &\triangleq (\nu\ c)(\llbracket\, s \,\rrbracket_{c,pc} \mid \llbracket\, P \,\rrbracket_{c}) \\
\llbracket\, s \mid r \,\rrbracket_{c,pc} &\triangleq \llbracket\, s \,\rrbracket_{c,pc} \mid \llbracket\, r \,\rrbracket_{c,pc}
\end{aligned}$$

Encoding Brane Actions

Exocytosis

$$[\![\ exo_n^{\perp}.t\ ]\!]_{c,pc} \triangleq \overline{exo@n@c}\langle pc\rangle.[\![\ t\ ]\!]_{c,pc}$$

$$[\![\ exo_n.s\ ]\!]_{c',pc'} \triangleq exo@n@pc'(x).\underline{\overline{bcast}}\langle exo, c', x\rangle.[\![\ s\ ]\!]_{pc',x}$$

Example

$$(\!|\ exo^{\perp}.t \mid t'(\!| exo.s \mid s'(\!|P|\!) \circ Q |\!)\ |\!) \quad \rightarrow \quad (\!|\ P \circ s \mid s' \mid t \mid t'(\!|Q|\!)\ |\!)$$

Encoding Brane Actions

Phagocytosis

$$[\![\ phago_n^{\perp}(r).t\ ]\!]_{c,pc} \triangleq (\nu\ x)(\overline{phago@n@pc}\langle x\rangle.([\![\ t\ ]\!]_{c,pc} \mid [\![\ r\ ]\!]_{x,c}))$$

$$[\![\ phago_n.s\ ]\!]_{c',pc'} \triangleq phago@n@pc'(x).\overline{\underline{bcast}}\langle phago, c', x\rangle.[\![\ s\ ]\!]_{c',x}$$

Example

$$phago.s|s'(\!|P|\!) \circ phago^{\perp}(r).t|t'(\!|Q|\!) \quad \rightarrow \quad t|t_0(\!|r(\!|s|s'(\!|P|\!)|\!) \circ Q|\!)$$

Encoding Comparison

Example

$$\llbracket\ exit\ c.P\ \rrbracket_{m,pm} \triangleq \quad expel@c@pm(x).\overline{\underline{bcast}}\langle exit, m, x\rangle.\llbracket\ P\ \rrbracket_{m,x}$$

$$\llbracket\ exo_n.s\ \rrbracket_{c',pc'} \triangleq \quad exo@n@pc'(x).\overline{\underline{bcast}}\langle exo, c', x\rangle.\llbracket\ s\ \rrbracket_{pc',x}$$

The encodings of BioAmbients and Brane Calculi

- reflect the similar tree structure of compartments: the difference is *the scope of the name of compartments*
- reflect the atonality/bitonality of operations: the difference is *the name broadcasted to the involved processes*
- show that the key mechanisms for handling the compartment structure are the same (scoping of communication, broadcast-like messages to notify changes in the structure)

Conclusion

π@ Features

- simple (very close to π-Calculus syntax)
- conservative (almost same π-Calculus semantics)
- concise (reactions are specified once, additional information on compartments and volumes are specified only if required)
- little implementation effort as extension of current implementations of the π-Calculus
- compartments with dynamical structure
- cross-compartment elements are straightforwardly and consistently specified
- almost unlimited compartment semantics (able to encode BioAmbients, Brane Calculi, Projective Brane, . . .)

Future Work

Future work

- further encodings of bio-inspired calculi into π@
  - or in stochastic π@ by preserving stochastic semantics
- further investigation on the expressiveness of priority
- non-interleaving semantics for π@

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