

symmetric
monoidal
(bi)categories
with feedback
and biological
networks

E Pareja-Tobes, M
Manrique, R
Tobes, E Pareja

symmetric monoidal (bi)categories with feedback and biological networks

E Pareja-Tobes M Manrique R Tobes E Pareja



Era7 bioinformatics

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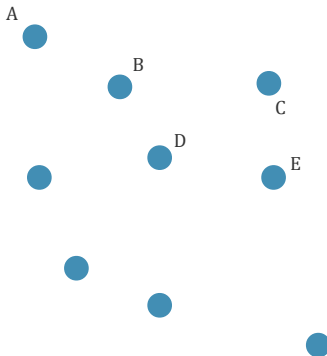
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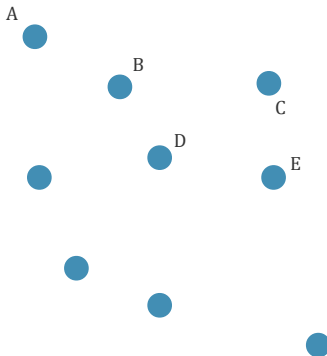
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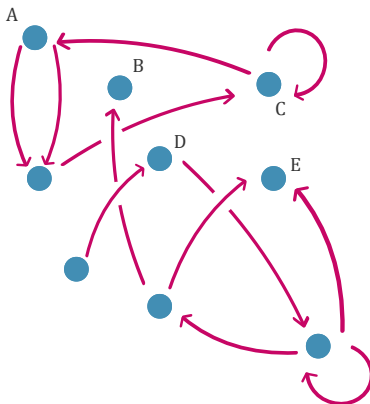
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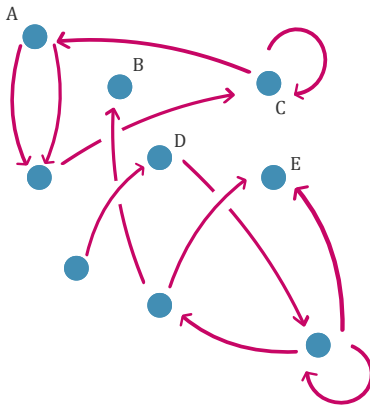
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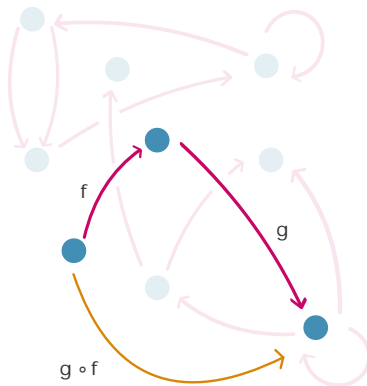
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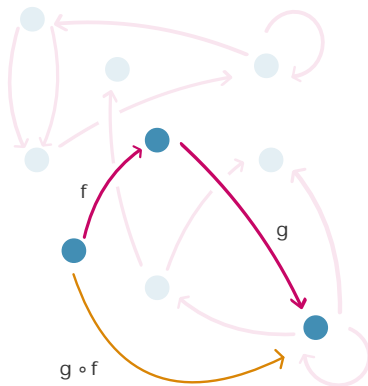
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- ▶ objects
- ▶ relations
- ▶ composition
- ▶ + some axioms



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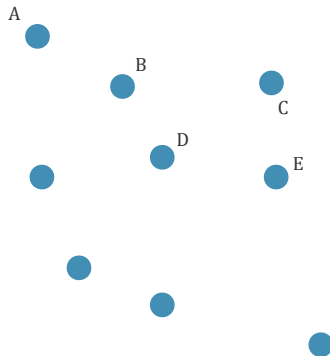
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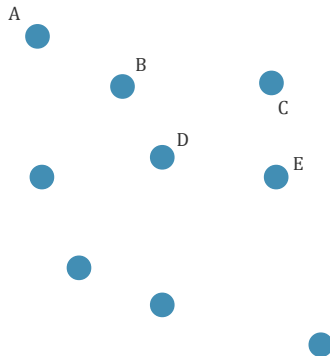
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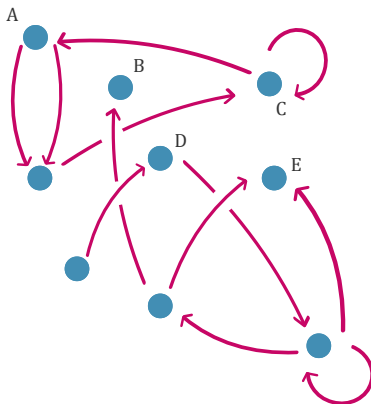
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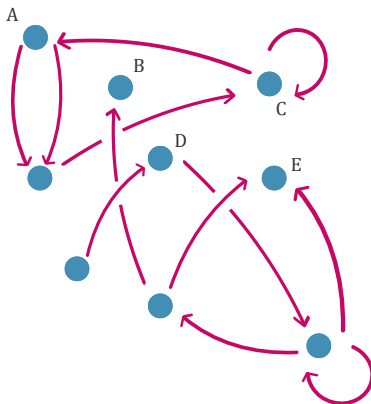
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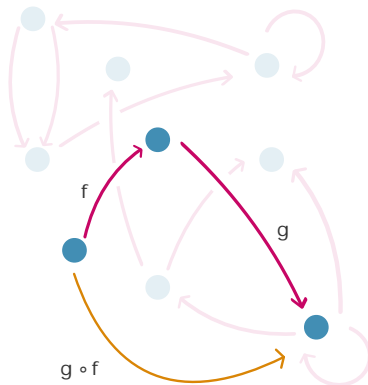
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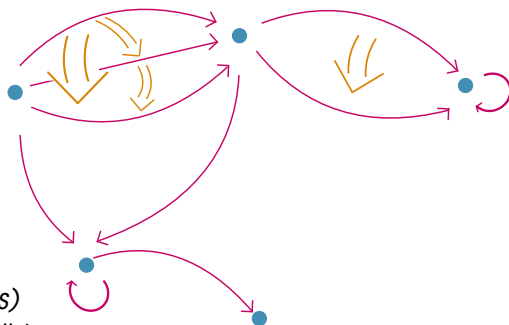
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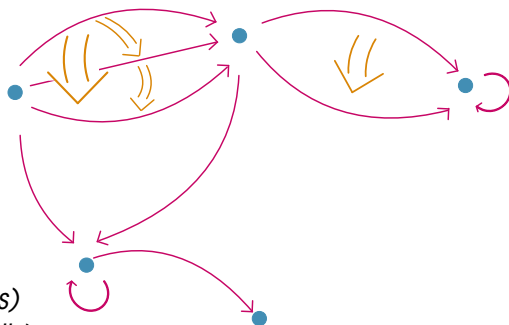
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- ▶ relations between relations (*2-cells*)
- ▶ 2 different compositions of 2-cells:

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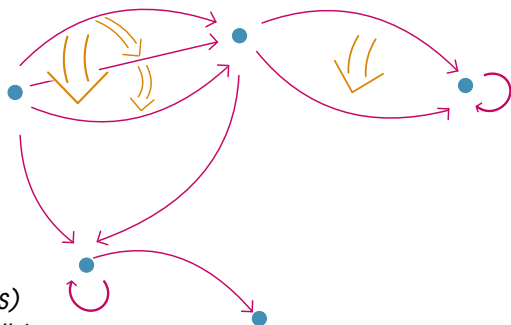
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- ▶ objects (*0-cells*)
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- ▶ 2 different compositions of 2-cells:
 - ▶ vertical \equiv *sequential*

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- ▶ 2 different compositions of 2-cells:
 - ▶ vertical \equiv *sequential*

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- ▶ objects (*0-cells*)
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- ▶ 2 different compositions of 2-cells:
 - ▶ vertical \equiv *sequential*
 - ▶ horizontal \equiv *parallel*

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- ▶ definition: *active area of research!*

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- ▶ definition: *active area of research!*

see for example

Higher-Dimensional Categories: an illustrated guide book Cheng, E. Lauda, A.

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- ▶ *Bicategories of processes* Katis P. Sabadini N. Walters R. 1997
- ▶ *On the algebra of systems with feedback and boundary* Katis P. Sabadini N. Walters R. 2000

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There is an operation, \otimes , which acts on

objects:

$$A, B \mapsto A \otimes B$$

and 1-cells:

$$(A \xrightarrow{f} B, C \xrightarrow{g} D) \mapsto A \otimes C \xrightarrow{f \otimes g} B \otimes D$$

\equiv *parallel composition*

+ *associativity, unit, and symmetry*

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symmetric monoidal

There is an operation, \otimes , which acts on

objects:

$$A, B \mapsto A \otimes B$$

and 1-cells:

$$(A \xrightarrow{f} B, C \xrightarrow{g} D) \mapsto A \otimes C \xrightarrow{f \otimes g} B \otimes D$$

\equiv *parallel composition*

+ *associativity, unit, and symmetry*

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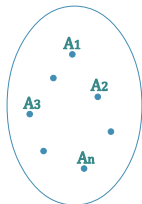
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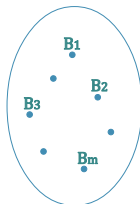
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interpretation

input



output



source

$$A_1 \otimes \dots \otimes A_n$$

target

$$B_1 \otimes \dots \otimes B_m$$

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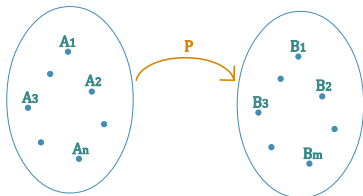
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interpretation

process



1-cell

$$A_1 \otimes \dots \otimes A_n \xrightarrow{p} B_1 \otimes \dots \otimes B_m$$

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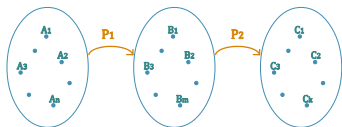
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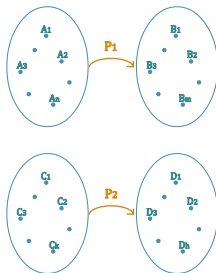
sequential composition



composition of 1-cells

$$\begin{array}{ccc} A_1 \otimes \dots \otimes A_n & \xrightarrow{p_1} & B_1 \otimes \dots \otimes B_m \\ & \searrow p_2 \circ p_1 & \downarrow p_2 \\ & & C_1 \otimes \dots \otimes C_k \end{array}$$

parallel composition



tensor

$$\begin{array}{c} (A_1 \otimes \dots \otimes A_n) \otimes (C_1 \otimes \dots \otimes C_k) \\ \downarrow p_1 \otimes p_2 \\ (B_1 \otimes \dots \otimes B_m) \otimes (D_1 \otimes \dots \otimes D_j) \end{array}$$

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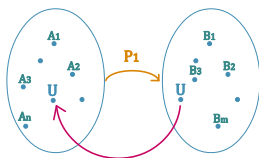
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feedback



feedback

$$\begin{array}{ccc} A \otimes U & \xrightarrow{p} & B \otimes U \\ & \Downarrow & \\ A & \xrightarrow{\text{fb}_U(f)} & B \end{array}$$

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why?

- ▶ metabolic, transcriptional and signaling phenomena involved
- ▶ data available
- ▶ enough complexity as a test for this kind of approach

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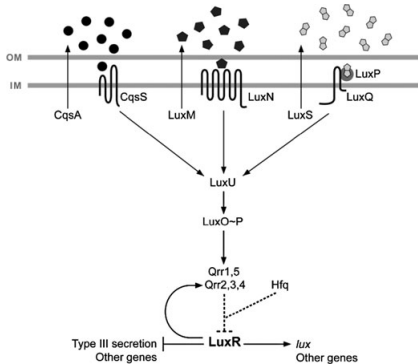


Fig. 1. Model of the *V. harveyi* Quorum-Sensing Circuit. *V. harveyi* produces and detects three AIs and through modulation of the levels of the master transcriptional regulator, LuxR, controls downstream QS-target genes. The three AIs are: CAI-1 (circles) which binds to CqsS, HAI-1 (pentagons) which binds to LuxN and AI-2 (double pentagons) which binds to LuxPQ. At LCD, when LuxO is phosphorylated (LuxO-P), it activates transcription of the genes encoding the five Qrr sRNAs which work in conjunction with Hfq to destabilize the mRNA of *luxR*. At HCD, when LuxO is not phosphorylated, *qrr* transcription ceases, *luxR* mRNA is stabilized and LuxR protein is produced. In a feedback loop, LuxR activates expression of *qrr2*, *qrr3* and *qrr4*, which affects the timing of the QS transitions. OM, outer membrane; IM, inner membrane.

A small-RNA-mediated negative feedback loop controls quorum-sensing dynamics in Vibrio harveyi. Tu KC,

Waters CM, Svenningsen SL, Bassler BL. *Mol Microbiol.* 2008. 70, 896-907

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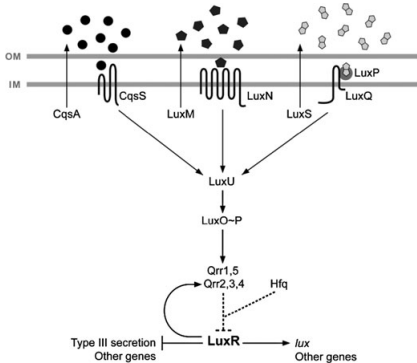
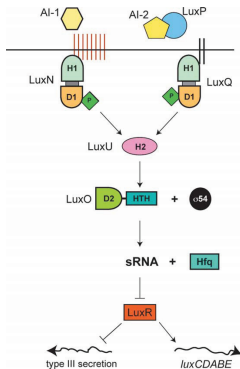


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Scheme 1. Representation of the known quorum-sensing pathway in *V. harveyi*. Autoinducers AI-1 and AI-2 are shown as a hexagon and pentagon, respectively. Phosphorylation sites are identified by H or D representing histidine or aspartic acid residues. As shown, the aspartic acid residues of LuxQ and LuxN are phosphorylated (P). LuxO is shown with the consensus helix-turn-helix (HTH) motif.

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Solution structure and dynamics of LuxU from Vibrio harveyi, a phosphotransferase protein involved in bacterial quorum sensing. Ulrich DL, Kojetin D, Bassler BL, Cavanagh J, Loria JP *J Mol Biol.* 2005. 347, 297-307.

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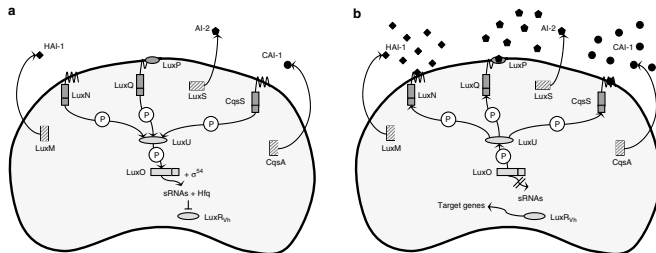


Figure 1 Quorum sensing in *Vibrio harveyi*. The LuxM, LuxS and CqsA enzymes synthesize the autoinducers harveyi autoinducer 1 (HAI-1), autoinducer 2 (AI-2) and cholerae autoinducer 1 (CAI-1), respectively. These autoinducers are detected at the cell surface by the LuxN, LuxQ and CqsS two-component receptor proteins, respectively. Detection of AI-2 by LuxQ requires the periplasmic protein LuxP. (a) In the absence of autoinducers, the receptors autophosphorylate and transfer phosphate to LuxO via LuxU. Phosphorylation activates LuxO, which together with σ^{54} activates the production of five small regulatory RNAs (sRNAs). These sRNAs, together with the chaperone Hfq, destabilize the mRNA encoding the transcriptional regulator LuxR_{vh}. Therefore, in the absence of autoinducers, the LuxR_{vh} protein is not produced. (b) In the presence of high concentrations of the autoinducers, the receptor proteins switch from kinases to phosphatases, which result in dephosphorylation of LuxO. Dephosphorylated LuxO is inactive and therefore, the sRNAs are not formed and the transcriptional regulator LuxR_{vh} is produced. See text for more details. © denotes phosphotransfer.

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Sorgeloos P, Verstraete W, Bossier P *ISME J.* 2008. 2, 19-26.

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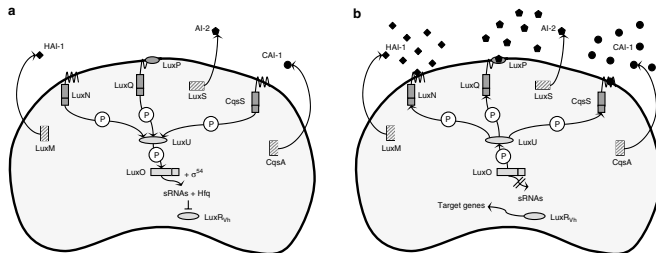


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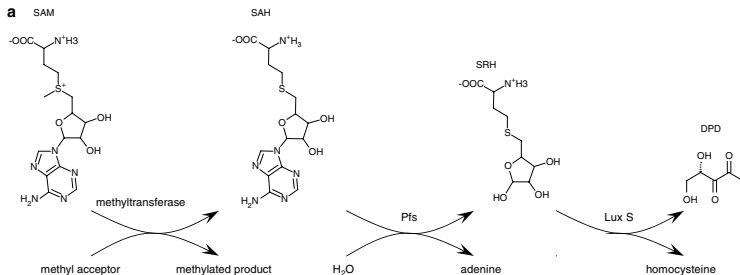
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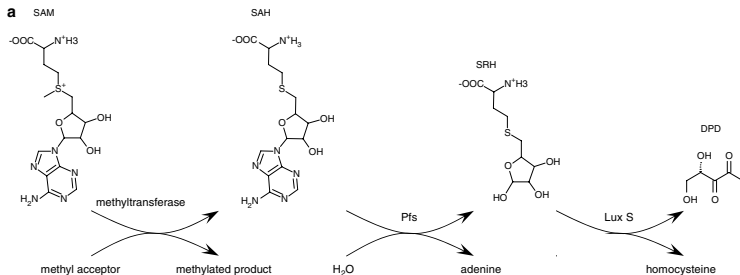
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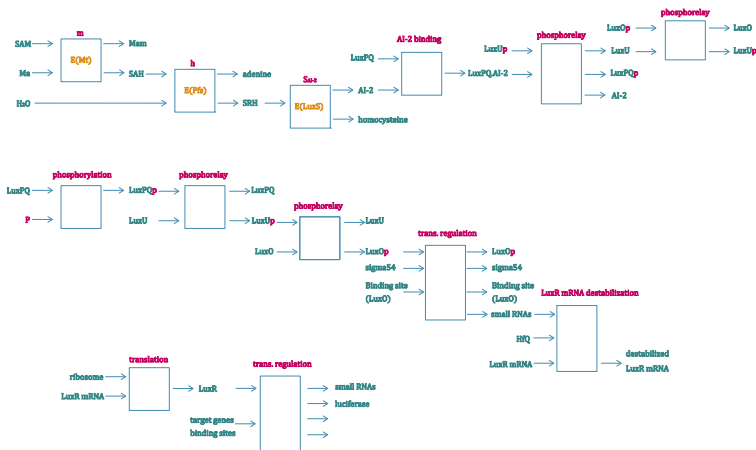
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Representing place/transition nets in Span (Graph) Katis, P. and Sabadini, N. and

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objects and relations

objects, relations,
relations between
relations ...

symmetric
monoidal
categories with
feedback

example model: Quorum
sensing

Relationship with other
approaches

the future

Work in progress

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