Information processing in living cells: mapping a logic gate to a gene regulation event

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Intracellular signal chains connect signal reception with memory usage (gene regulation). Many signal chains influence one another. Therefore, it has been proposed that the assembly represents a network of molecular switches that perform signal processing. In order to strengthen this idea, the logical AND gate is associated with a gene regulation event.

In mammalian pre-implantation embryos, the first cell differentiation concerns the decision of morula cells to enter the trophectoderm (TE) line or the inner cell mass (ICM) line. TE cells develop into placental tissue, and ICM cells become the embryo proper. Gene CDX2 is expressed only in TE cells; its gene product regulates other genes. Expression of CDX2 is triggered by two signals: First, cell position – cells at the outer part of the morula express CDX2, those in the interior do not; second, cell polarization – cells in which part of the surface has no contacts to other cells express CDX2, cells having neighbors all around do not. Cell position is sensed and mediated by the NOTCH pathway, polarization by HIPPO signaling.

A model is presented, where the two signals are inputs into a logic gate. The physical manifestation of the gate is the trophectoderm enhancer of the CDX2 gene, which contains specific targets for both signals. The model needs to satisfy available experimental evidence:

1. Experimental elimination of either enhancer target allows CDX2 expression. These results alone suggest that the signals function as an OR gate.
2. Sparse individual cells at the embryo surface that are non-polarized develop into ICM cells. This indicates that the two signals are not redundant but cooperate (AND).

The AND gate model gives an explanation for both results, provided that the elimination of either one enhancer target (experiment 1) converts the AND gate to a buffer gate.