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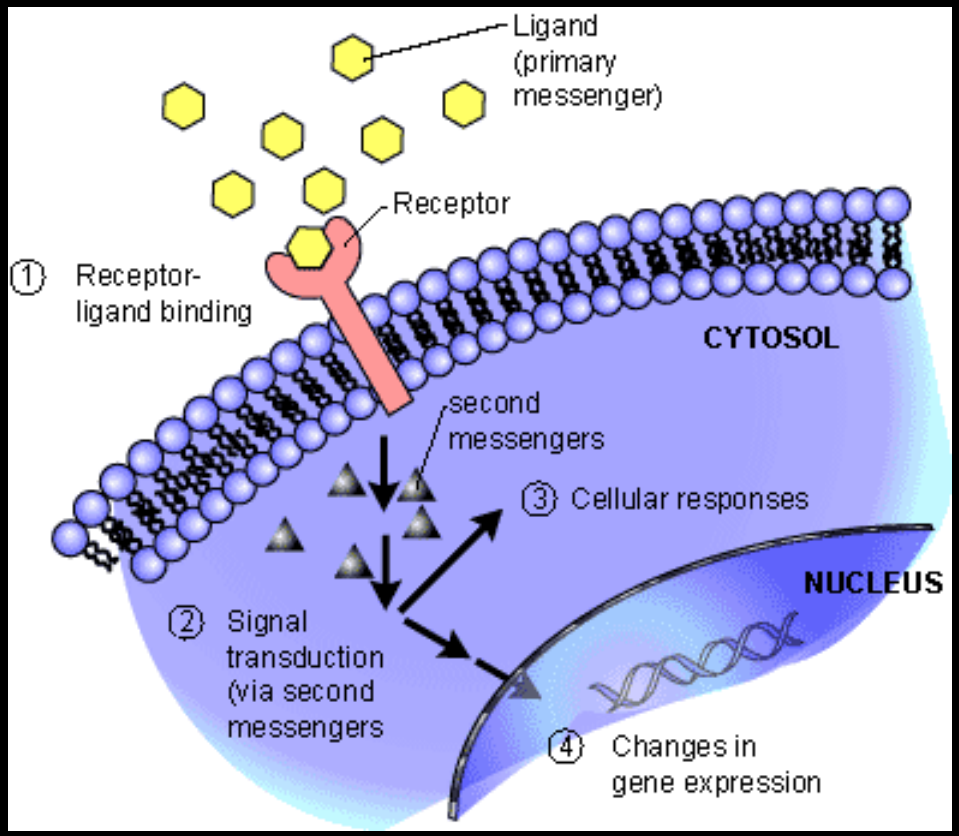
EPIGENETIC DEVELOPMENT IN NEURAL NETWORKS

Biology Background: the Ontogeny of a Multicellular Organism

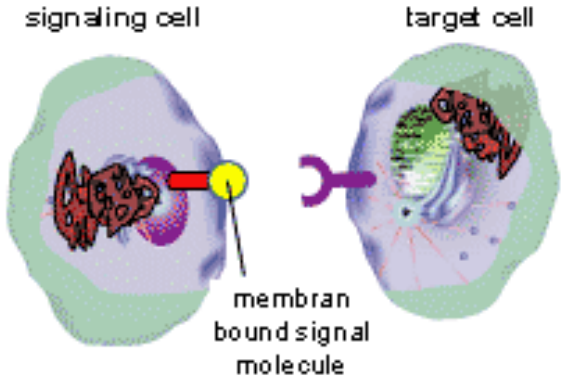
- A M-O starts out as a single cell, but during the course of it life ends up as a community of trillions of cells
- Cellular Differentiation is the mechanism for growth and development
- Intercellular signaling and response are responsible for regulating cellular morphogenesis



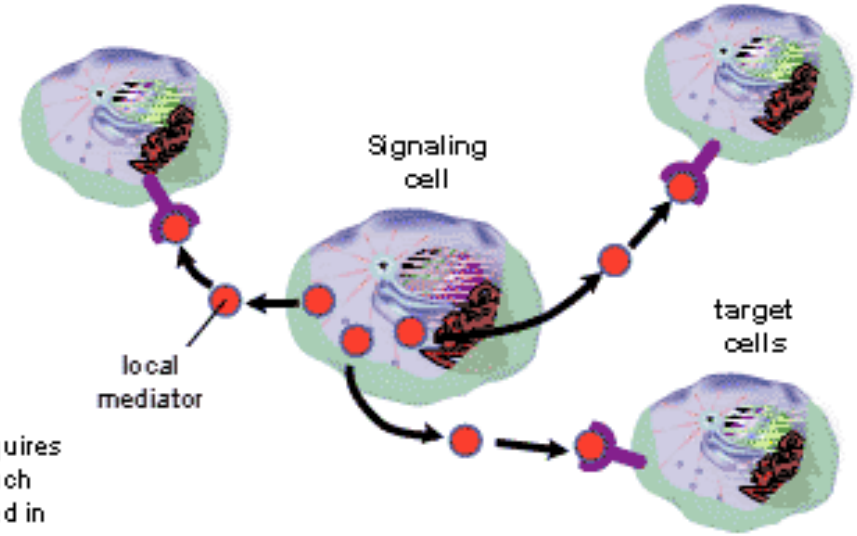
Cellular Communication: Signal Transduction

Possible behaviors:
- Secrete chemicals in response
- Chemotaxis
- Transcribe protein from RNA

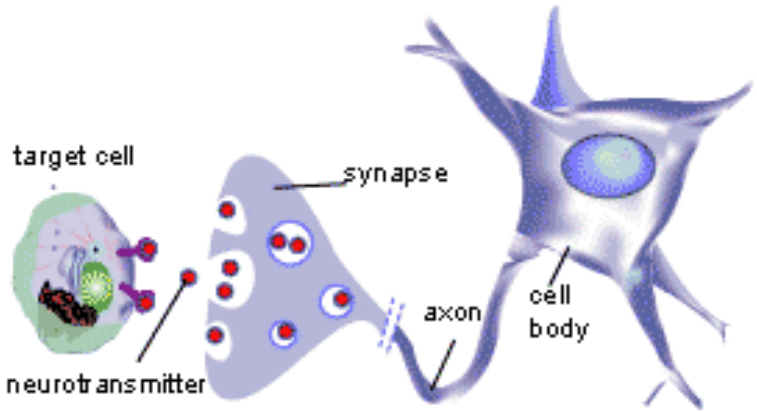
http://www.scq.ubc.ca/conversing-at-the-cellular-level-an-introduction-to-signal-transduction/



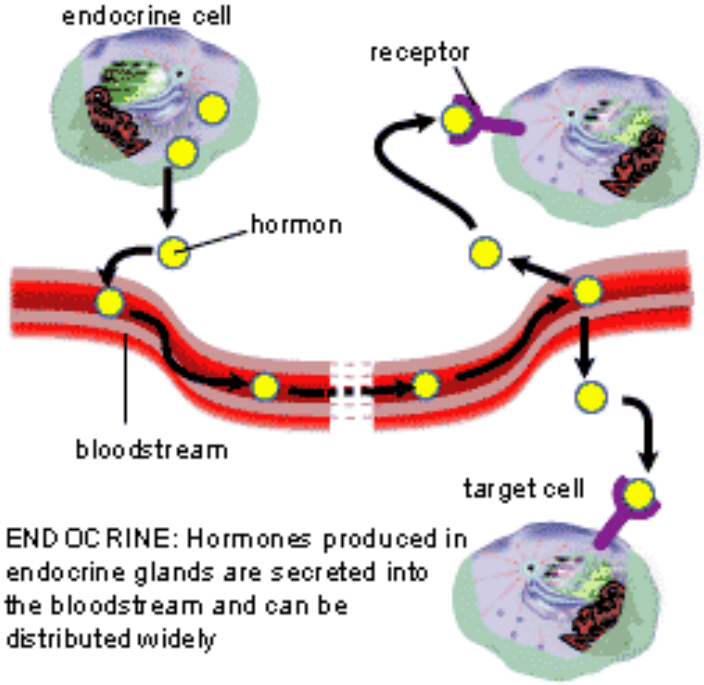
CONTACT-DEPENDENT: Contact-dependent signaling requires cell to be in direct membrane-to-membrane contact with each other. Many of the same types of signa l molecules are used in endocrine, paracrine, and neuronal signaling. The crucial differences lie in the speed and selectivity with which the signals are delivered to their targets.



PARACRINE: Paracrine signals are released by cells into the extracellular medium in their neighborhood and act locally.



NEURONAL: Neuronal signals are transmitted along axons to remote target cells.

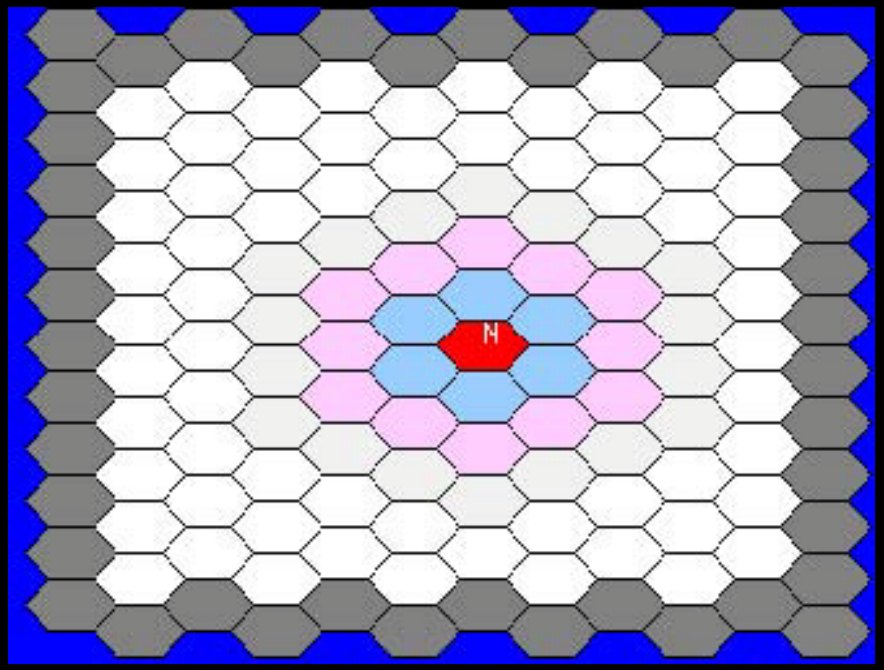


END OC RINE: Hormones produced in endocrine glands are secreted into the bloodstream and can be distributed widely

Astor & Adami:
A Developmental Model for the Evolution of Artificial Neural Networks

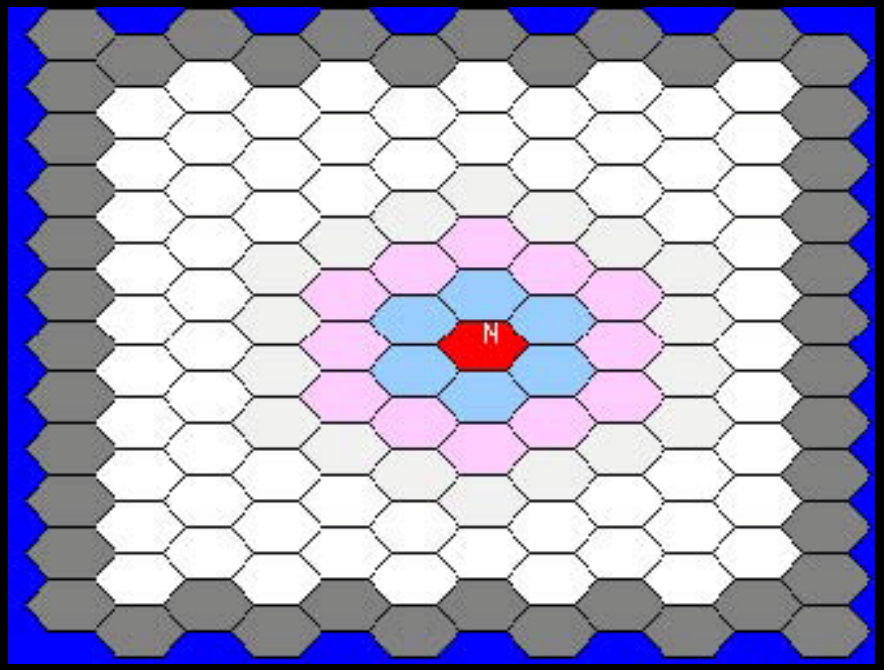
- Why a developmental model?
- Classical ANNs are fabricated to solve classification problems
- Apply biological realism towards scientific explanation, rather than simply using ANNs as an engineering tool

Simulation of the “organism” occurs in a 2-D lattice



Each hexagonal “common” cell contains a concentration of various proteins, and may or may not contain a neuron. Gray cells are the boundary “skin.”

Four Protein Types



External: diffusive
Internal: non-diffusive
Cell-type: emitted by a cell and diffused
Neurotransmitters: direct cell-cell communication (non-diffusive)

Laws of the Universe

- Diffusion occurs discretely across the cells, and discretely across increments of time
- Through diffusion, a gradient can be set for communication
- The placement of sensors and actuators is hard-coded into the genome

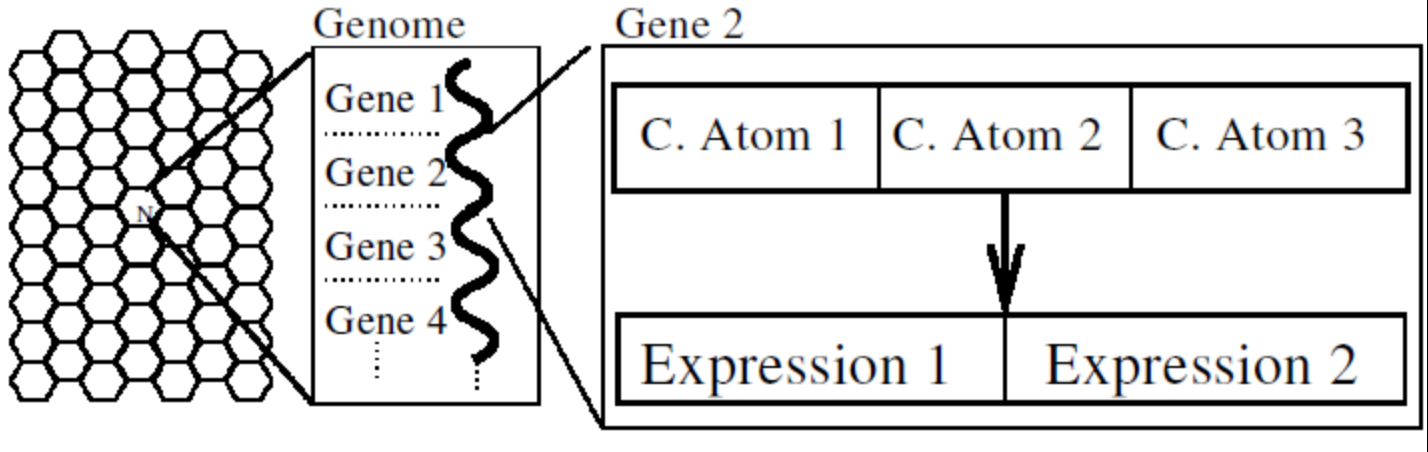
The Genome

- The genome determines the behavior of the cells in response to its environment (local concentrations of proteins)
- This is in contrast to the genome of classical evolutionary ANNs, where it explicitly encodes the connection weights and/or learning rule of the system

The Genome

- Cell behavior is governed by gene regulation and gene expression
- Gene regulation (in this simulation) is equivalent to cell type, which is determined by the presence or absence of cell-type protein
- Gene expression is computed by the input of the protein make-up of the cell's substrate

Genetic Structure



Each gene is composed of a string of condition atoms—Each of which is a function taking the value of a protein concentration in the cell's local substrate and returning the *evaluated condition* of the cell.

Condition atoms

Repressive

Type	Represses its gene if ...
SUP{CTPx}	cell is not of type CTPx
NSUP{CTPx}	cell is of type CTPx
ANY{PTx}	{PTx} = 0
NNY{PTx}	{PTx} ≠ 0

Silences the entire gene if condition is met

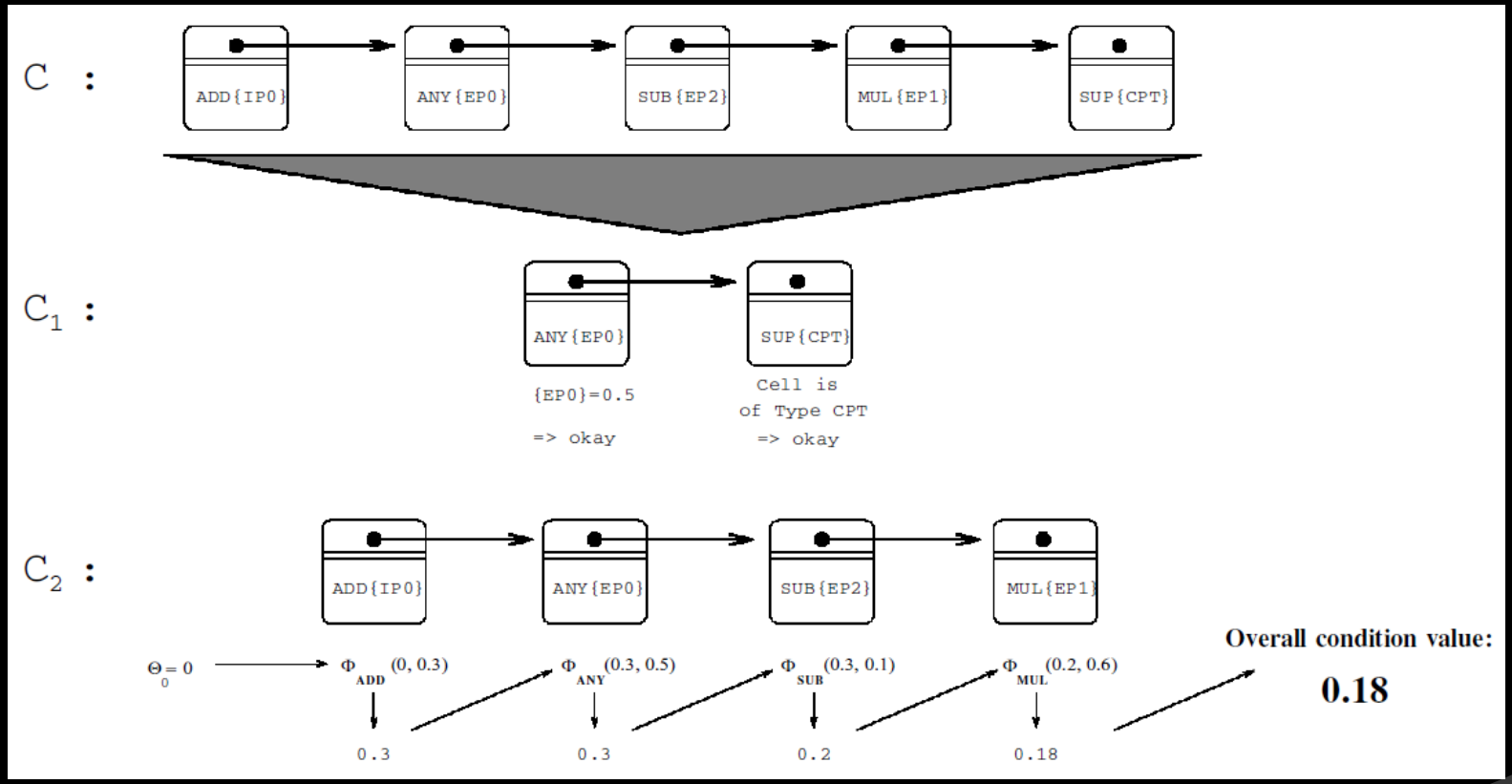
Evaluative

Type	Evaluation value Φ	
SUB{PTx}	$\Phi(\Theta, \text{SUB}[\text{PTx}])$	$= R_0^1(\Theta - \{\text{PTx}\})$
ADD{PTx}	$\Phi(\Theta, \text{ADD}[\text{PTx}])$	$= R_0^1(\Theta + \{\text{PTx}\})$
MUL{PTx}	$\Phi(\Theta, \text{MUL}[\text{PTx}])$	$= \Theta * \{\text{PTx}\}$
AND{PTx}	$\Phi(\Theta, \text{AND}[\text{PTx}])$	$= \min(\Theta, \{\text{PTx}\})$
NAND{PTx}	$\Phi(\Theta, \text{NAND}[\text{PTx}])$	$= 1 - \min(\Theta, \{\text{PTx}\})$
OR{PTx}	$\Phi(\Theta, \text{OR}[\text{PTx}])$	$= \max(\Theta, \{\text{PTx}\})$
NOR{PTx}	$\Phi(\Theta, \text{NOR}[\text{PTx}])$	$= 1 - \max(\Theta, \{\text{PTx}\})$
NOC	$\Phi(\Theta, \text{NOC})$	$= \Theta$; the neutral condition
NNY{PTx}	$\Phi(\Theta, \text{NNY}[\text{PTx}])$	$= \Theta$, if $\{\text{PTx}\} = 0$
ANY{PTx}	$\Phi(\Theta, \text{ANY}[\text{PTx}])$	$= \Theta$, if $\{\text{PTx}\} \neq 0$

Gene Evaluation:

- The final evaluated condition of the cell is determined via a recursive function:
- $$\Phi_C = \Phi(\ldots\Phi(\Phi(\Theta_0, b_1), b_2), \ldots, b_m),$$
- where each Φ in the nest is a condition atom, and Θ_0 is the initial evaluated condition of the cell, given by:
- $$\Theta_0 = \begin{cases} 1, & \text{if } b_1 \text{ is of type } \texttt{MUL, AND, NAND, SUB, ANY, NNY} \\ 0, & \text{if } b_1 \text{ is of type } \texttt{ADD, OR, NOR} \end{cases}$$

Gene Expression:



C is the complete gene, C1 is the sub-condition comprising the repressive atoms, C2 comprises the evaluative condition atoms.

Morphogenesis & communication

- The expression of each gene results in a “developmental command,” influenced by the overall condition value of the cell after the evaluated condition is computed and expressed

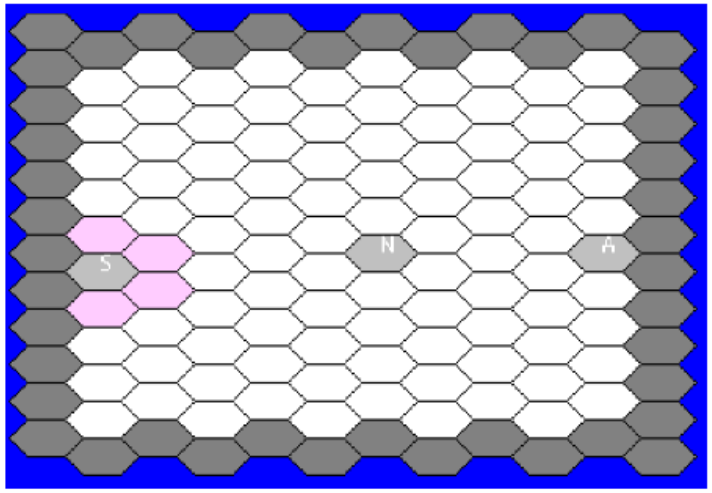
Morphogenesis & communication

Expression	Command description	Influence of condition value
PRD{XY}	produce substrate XY	production quantity
GDR{XY}	grow dendrite following gradient of XY	probability to grow
GRA{XY}	grow axon following gradient of XY	probability to grow
SPL{CTPx}	divide. Offspring is of type CTPx	probability to split
EXT	excitatory stimulus	increase rate
INH	inhibitory stimulus	decrease rate
MOD+{NTx}	increase connection weights	strengthening factor
MOD-{NTx}	decrease connection weights	weakening factor
RLX{NTx}	relax weights slightly	multiplier
DFN{NTx}	define the type of neurotransmitter	none
NOP	null action, neutrality	

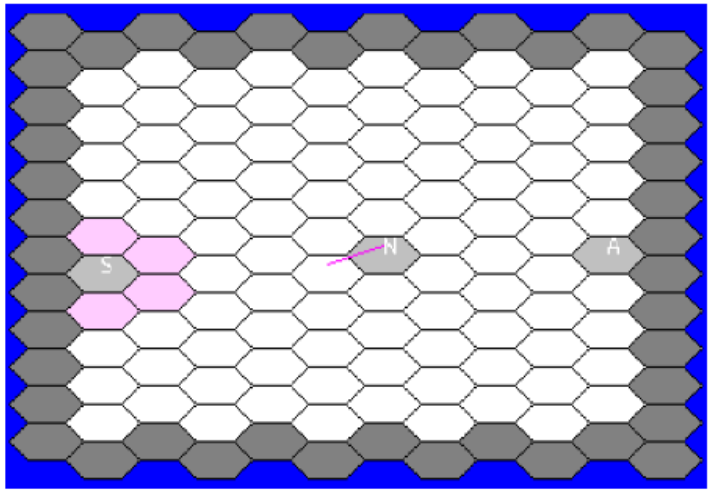
Morphogenesis & communication

- The commands are functions taking as input the overall condition value
- Growth commands take a directional value as additional input (the direction of a gradient)
- Neural modulation commands take a neurotransmitter type as additional input

Dendritic Growth

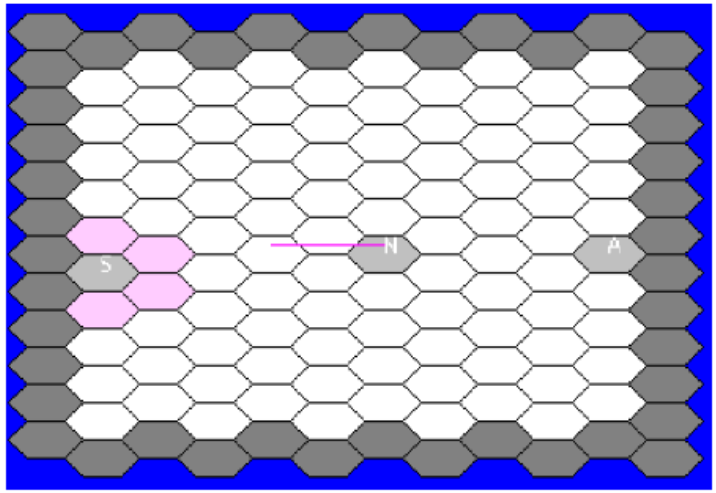


a) t=4. The sensor cell just started to produce SPT0.

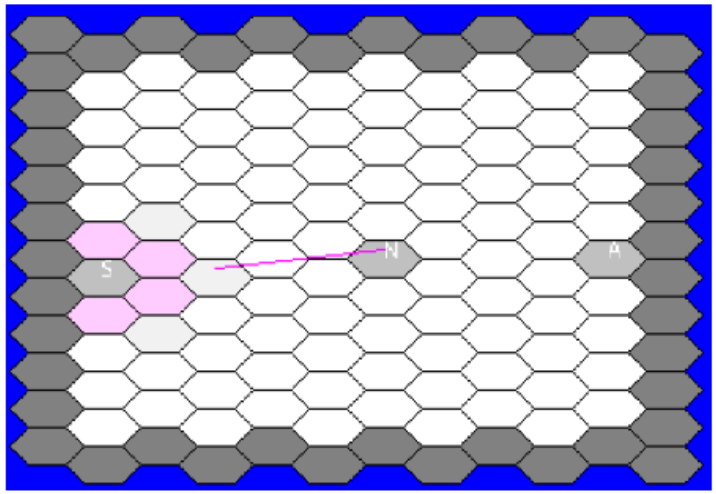


b) t=5. Once the neuron cell has detected non-zero concentrations of SPT0, it starts to grow a dendritic connection.

Dendritic Growth

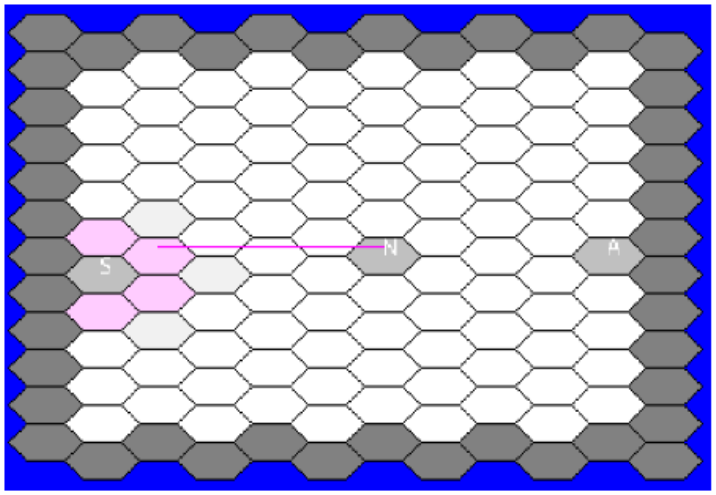


c) t=6. The growing dendrite follows the gradient of SPT0, ...

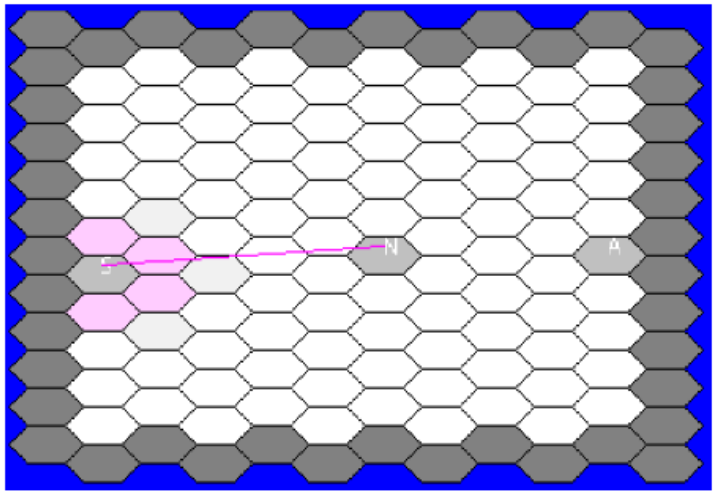


d) t=7 ... while the sensor cell-type protein keeps on diffusing.

Dendritic Growth



e) t=8. Finally, the growing dendrite approaches the sensor cell ...

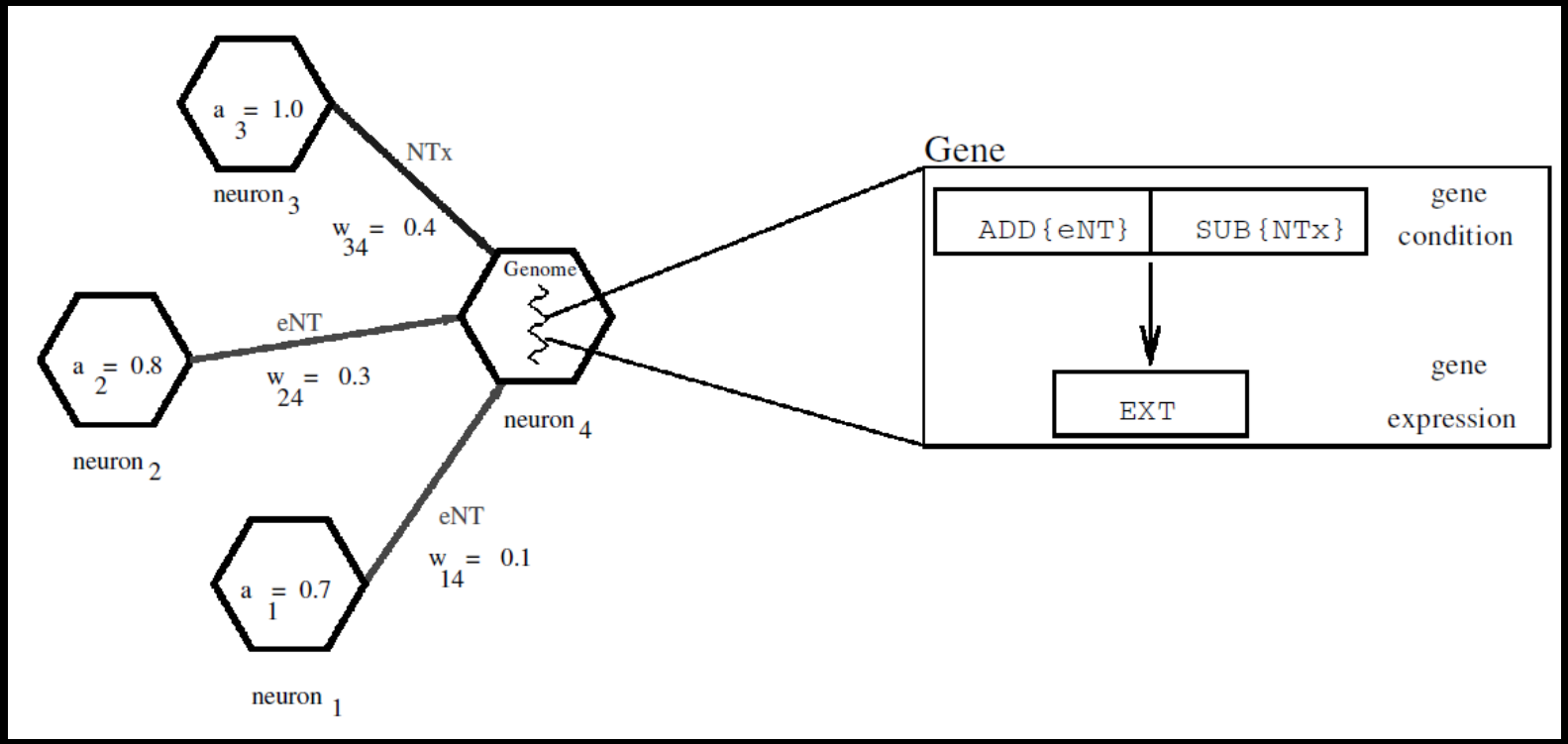


f) t=9 ... and establishes the dendritic connection.

Learning(!)

- Neural networks are established through growth factors – signals sent from neighboring cells encouraging the development of axons and dendrites
- Learning rules are not explicitly programmed in
- Rather, they are the product of genetic expression
- Good learning rules are adaptive

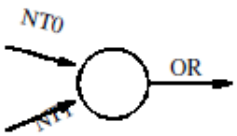
Learning(!)



Neuron 4 is inhibited because this gene lowers the cell's evaluated condition according to the NTx neurotransmitter. More importantly, a weighted sum is implemented in the expression of the genome.

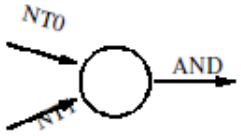
Implementing Logic Functions

Simple binary-logic gates:



Genes:

```
ANY{NT0}  ->  EXT
ANY{NT1}  ->  EXT
```



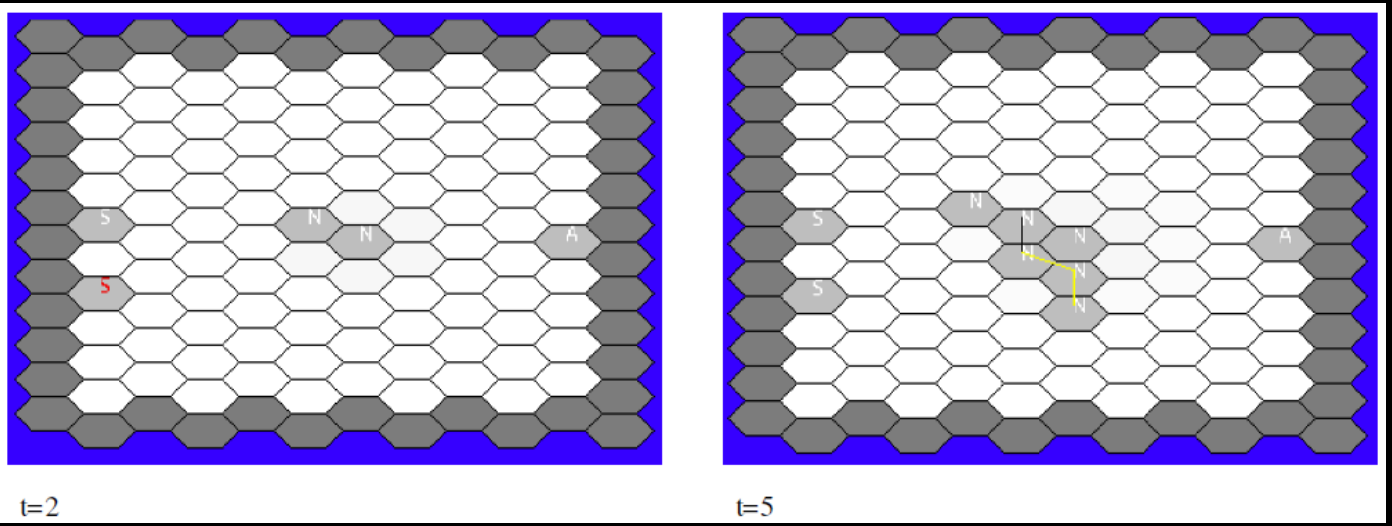
Gene:

```
ANY{NT0}  ANY{NT1}  ->  EXT
```

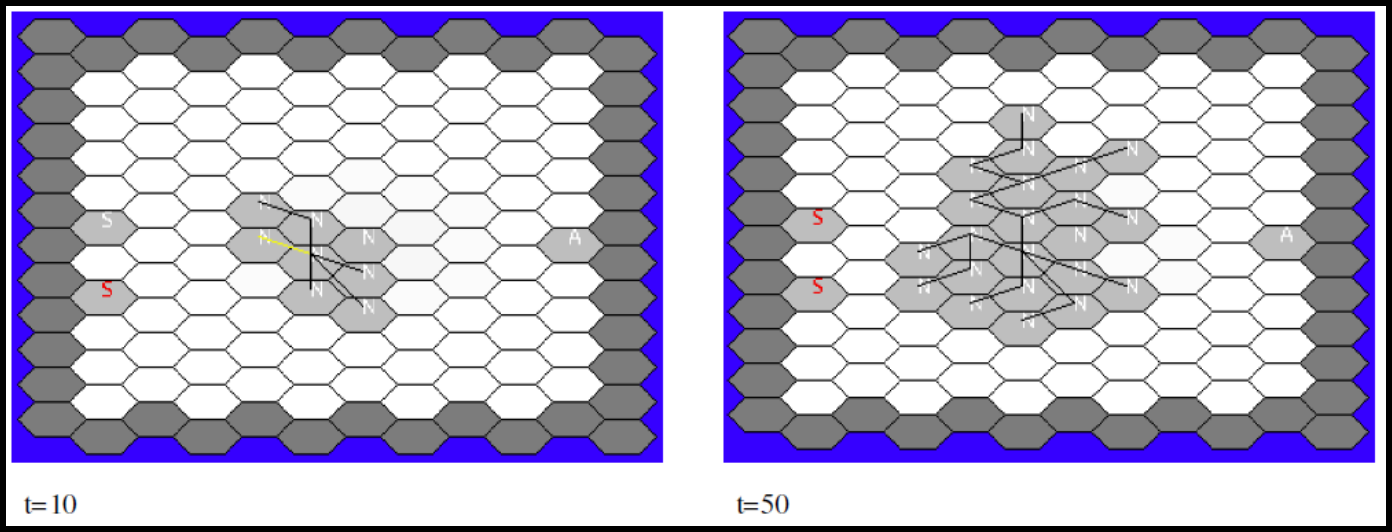
Gene:

```
NNY{NT0}  ->  EXT
```

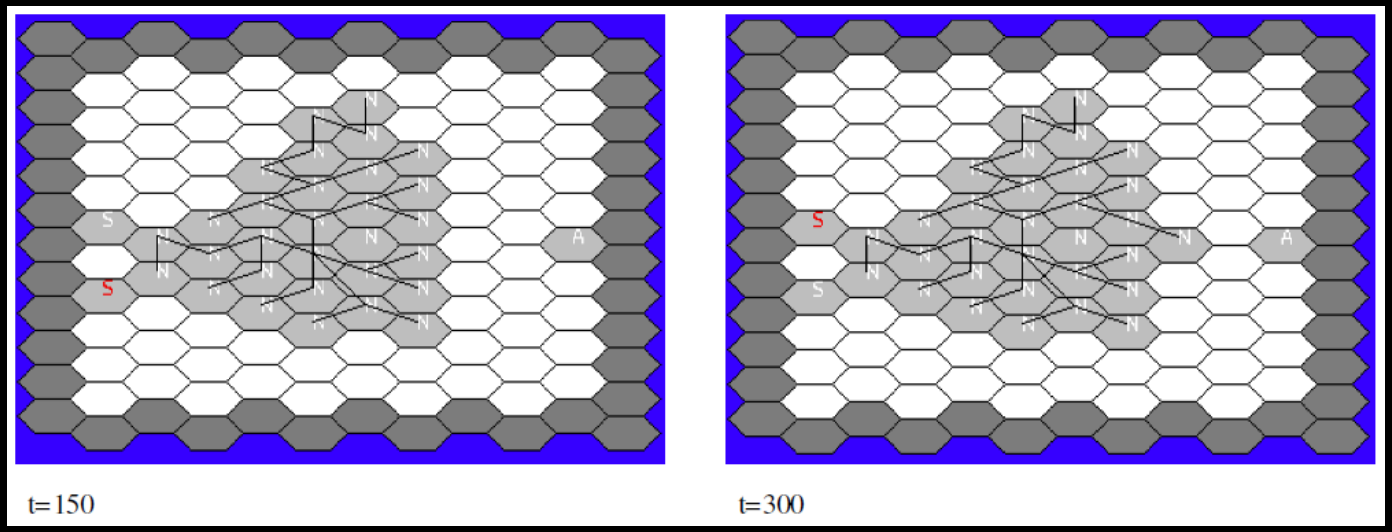
Growing a Network



Growing a Network



Growing a Network

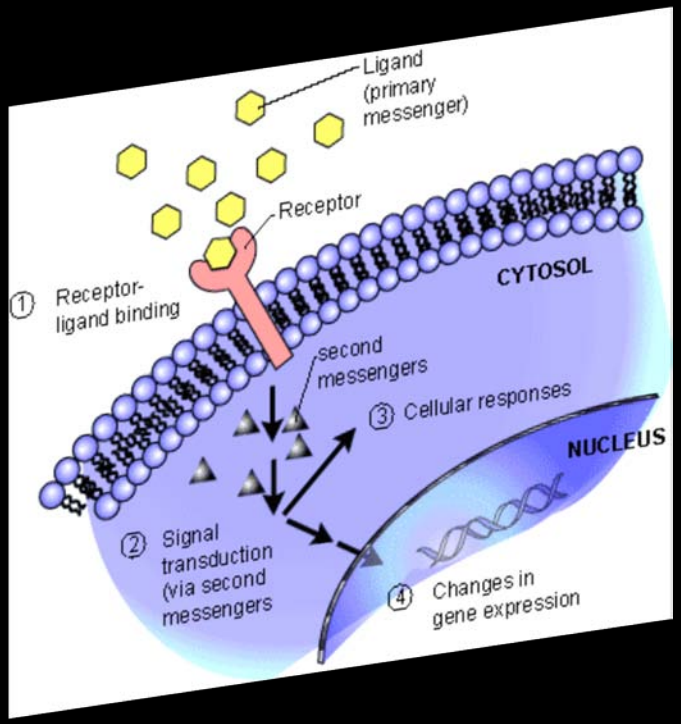


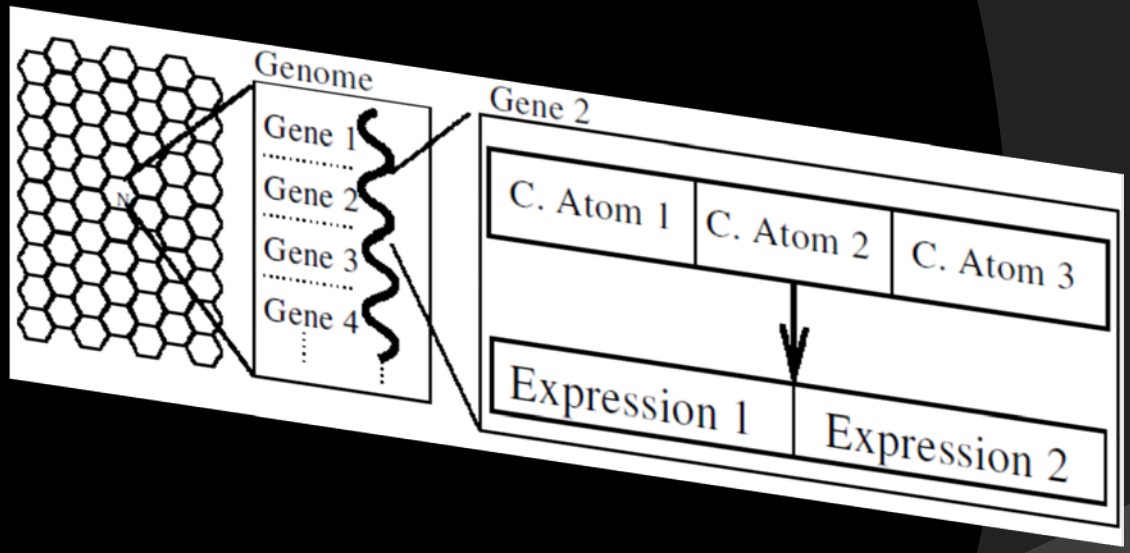
t=150 t=300

Evolution

- Genomes are never hand-coded, so connections and learning rules are not specified
- Moreover, they are both removed from direct selection
- Having a network capable of learning is adaptive (as selected for by the researcher), but the genome codes for various cell type behaviors

Biological Realism?





Biological Realism?

- The key to success in abstraction is implementing functions while implementing as little structure as possible
- In a real cell, the genome is not read off each time there is an input chemical
- Rather, input signal can be stored in the cytoplasm or organelles, or cause morphological changes without the production of new proteins

Biological Realism?

- Moreover, there are many cell behaviors that this simulation lacks:
  - Taxis – cell movement
  - Apoptosis – cell death
  - Rigid, invariant structure of the organism

Biological Realism?

- But there is a computational pressure for simplification of the model
- The larger the genome, the larger the search space
- Astor & Adami's solution is to put there systems up on the web, similar to Folding@Home

Resources

- J. C. Astor, C. Adami. A Developmental Model for the Evolution of Artificial Neural Networks. Artificial Life 2000 6:3, 189-218
- Jonathan Bard (2008) Morphogenesis. Scholarpedia, 3(6):2422
- Jamie Davies (2008) Cellular mechanisms of morphogenesis. Scholarpedia, 3(2):3615
- David Secko (2003) CONVERSING AT THE CELLULAR LEVEL: AN INTRODUCTION TO SIGNAL TRANSDUCTION. The Science Creative Quarterly. [http://www.scq.ubc.ca/conversing-at-the-cellular-level-an-introduction-to-signal-transduction/]