HiPathia
Models of signaling pathway activity

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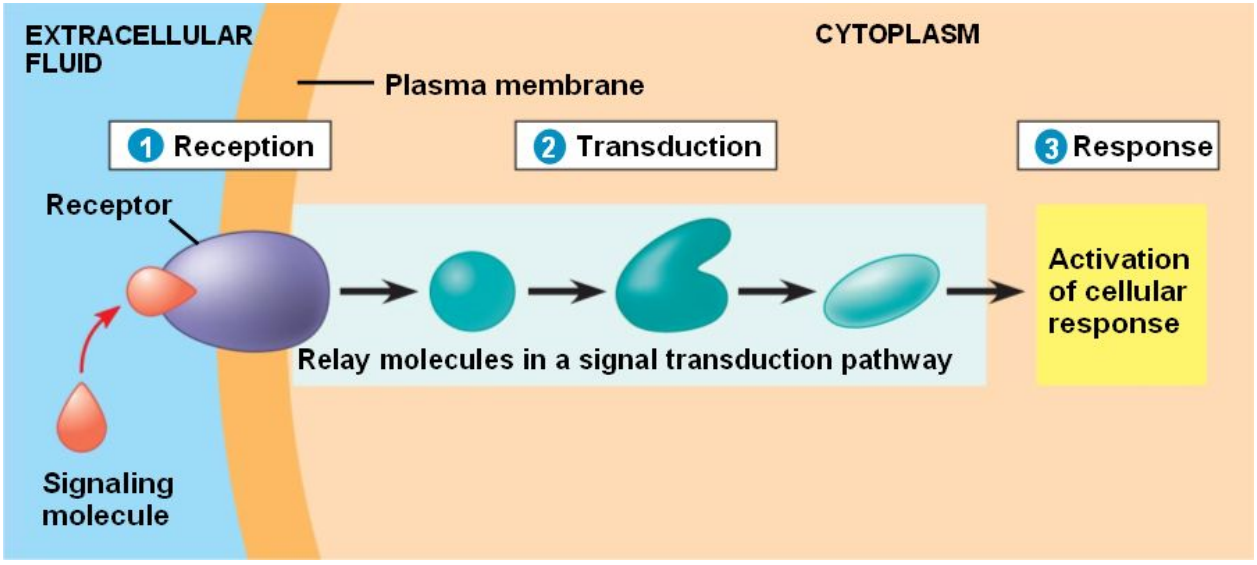
PRINCIPE FELIPE
CENTRO DE INVESTIGACION

Signaling pathways



Chemical signals

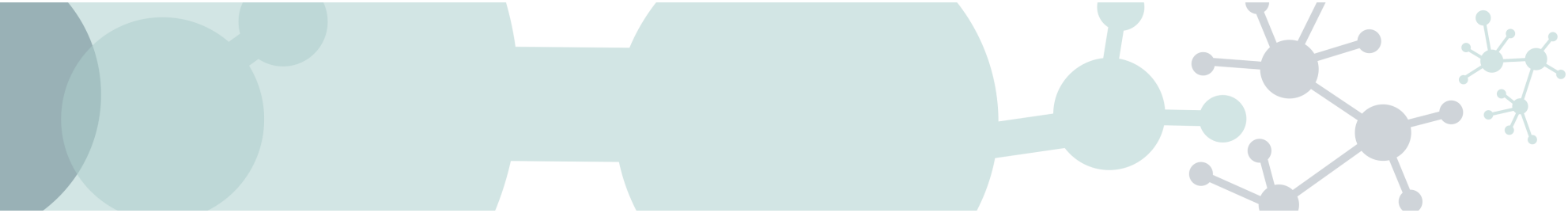
- Hormones
- Neurotransmiters
- Growth factors
- Cytokines
- Drugs

Activation & Inhibition

- Phosphorilation
- Dephosphorilation
- Glycosylation
- Ubiquitination
- Methylation

Cellular Function

- Apoptosis
- Survival
- Growth
- Migration
- Proliferation

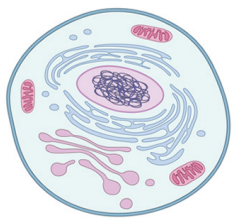


Pathway Analysis

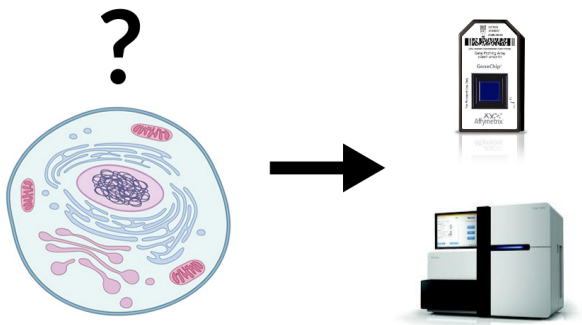
HiPathia

From cell to pathways

?



From cell to pathways



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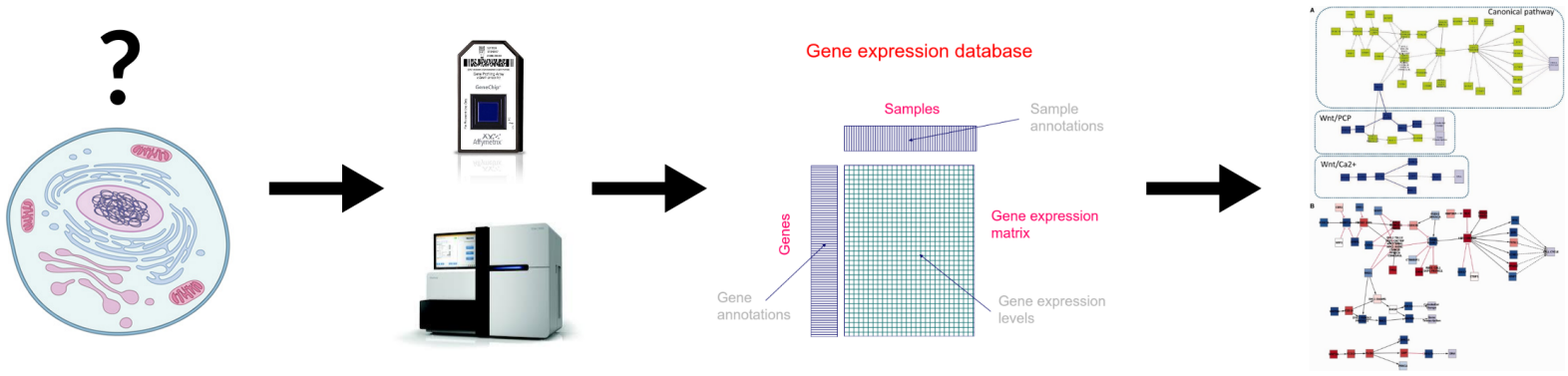
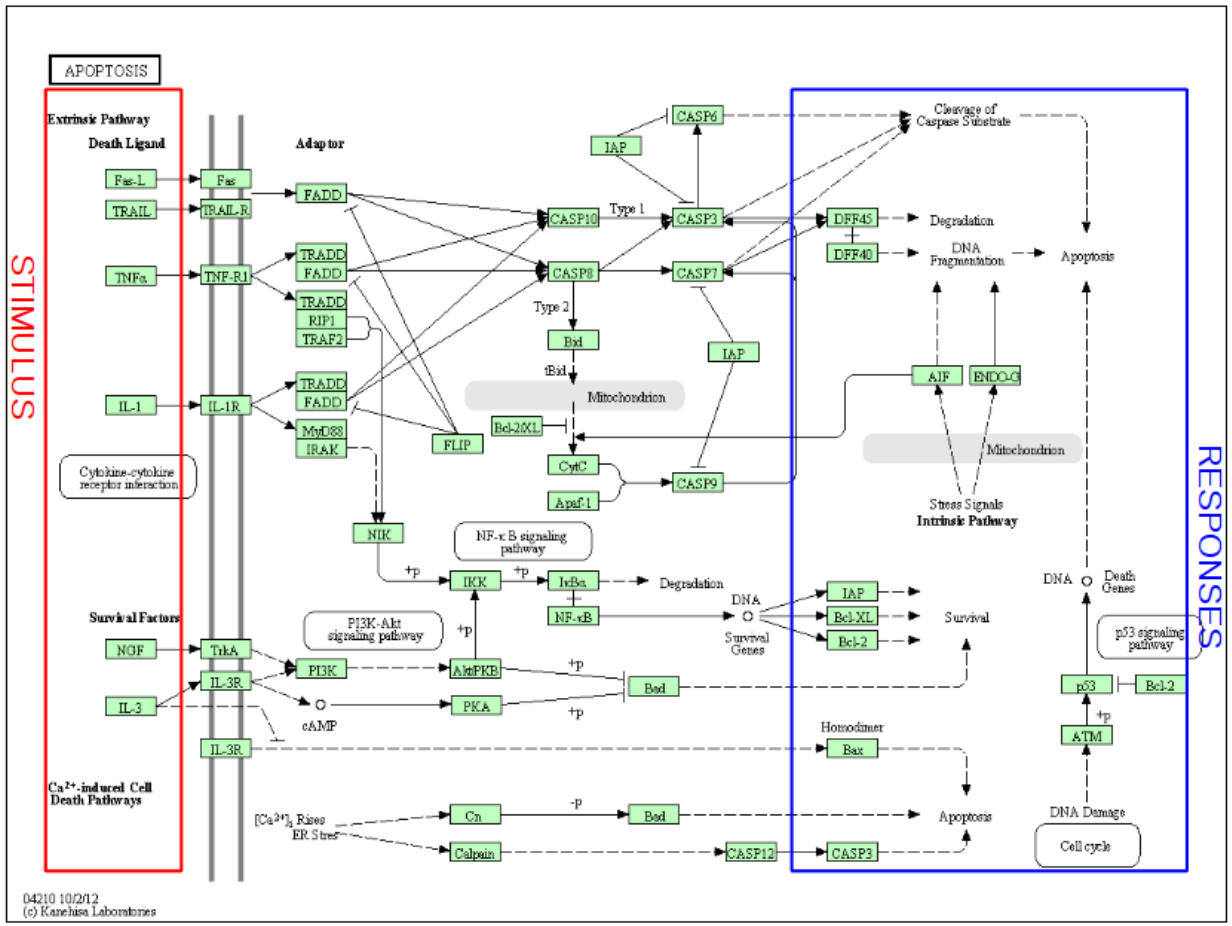


Pathways layout

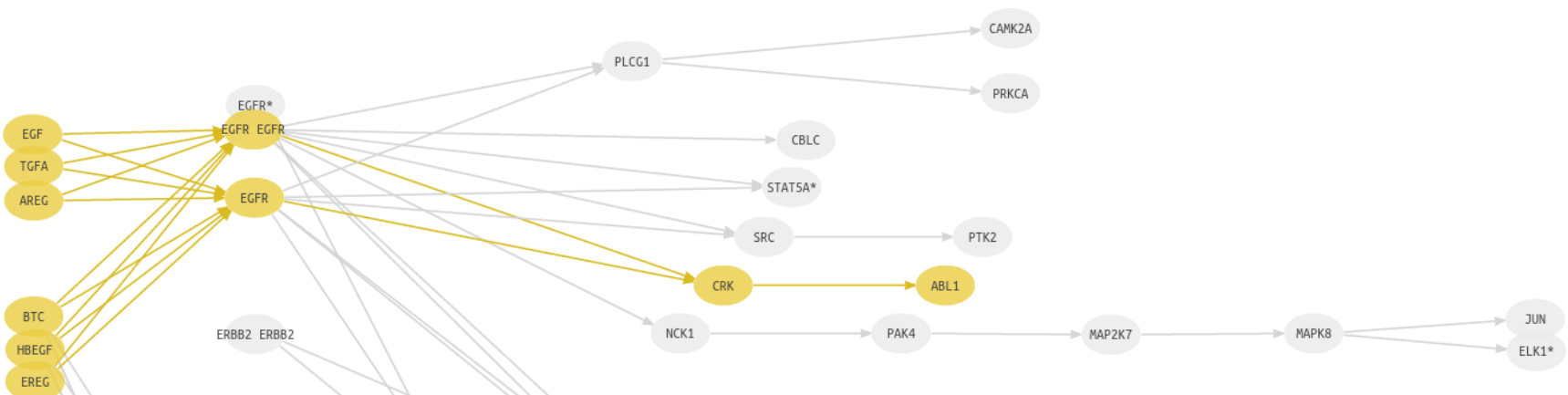
Take pathways information



Meaningful subpathways

Effector subpathway

Subpathway including any node from any receptor to one effector protein

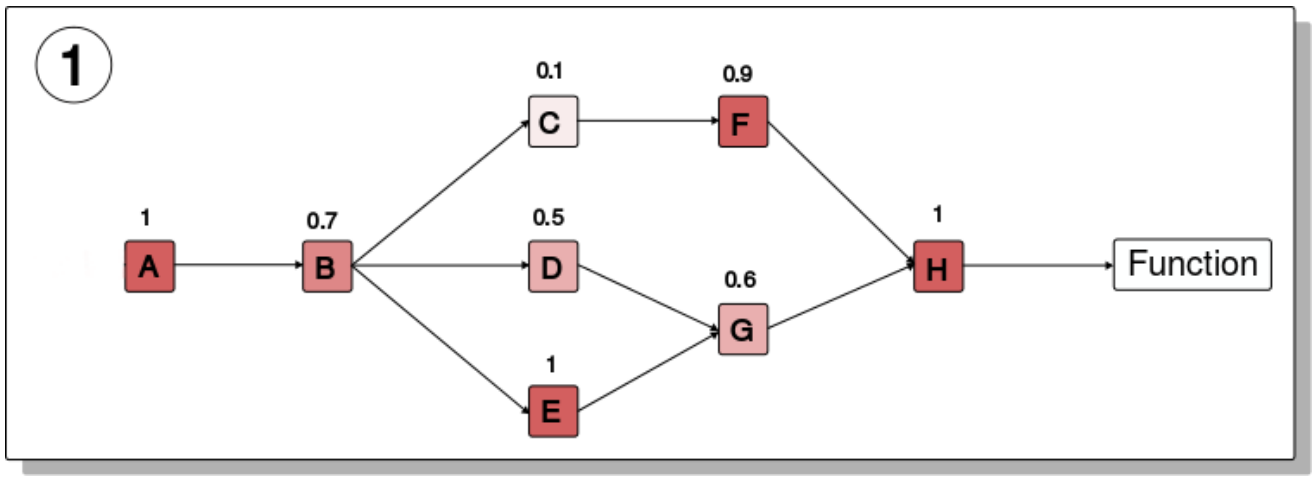


Computing the signal

1. Compute a node score based on the expression
2. Compute signal passing through each node n

$$S_n = v_n \cdot (1 - \prod_{s_i \in A} (1 - s_i)) \cdot \prod_{s_j \in I} (1 - s_j)$$

S_n: Signal value through n
v_n: Node value
A: Activation edges
I: Inhibition edges



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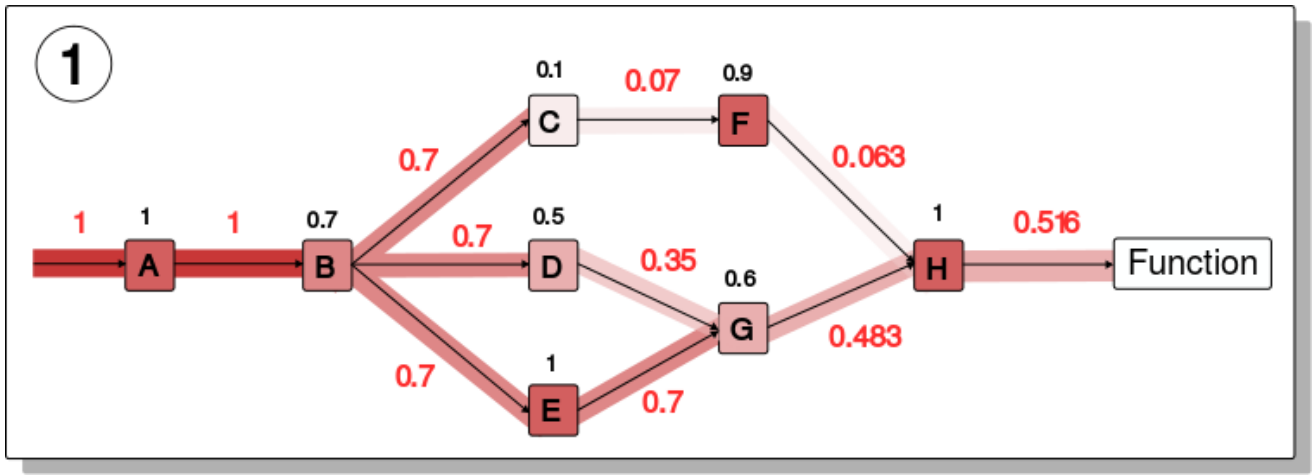

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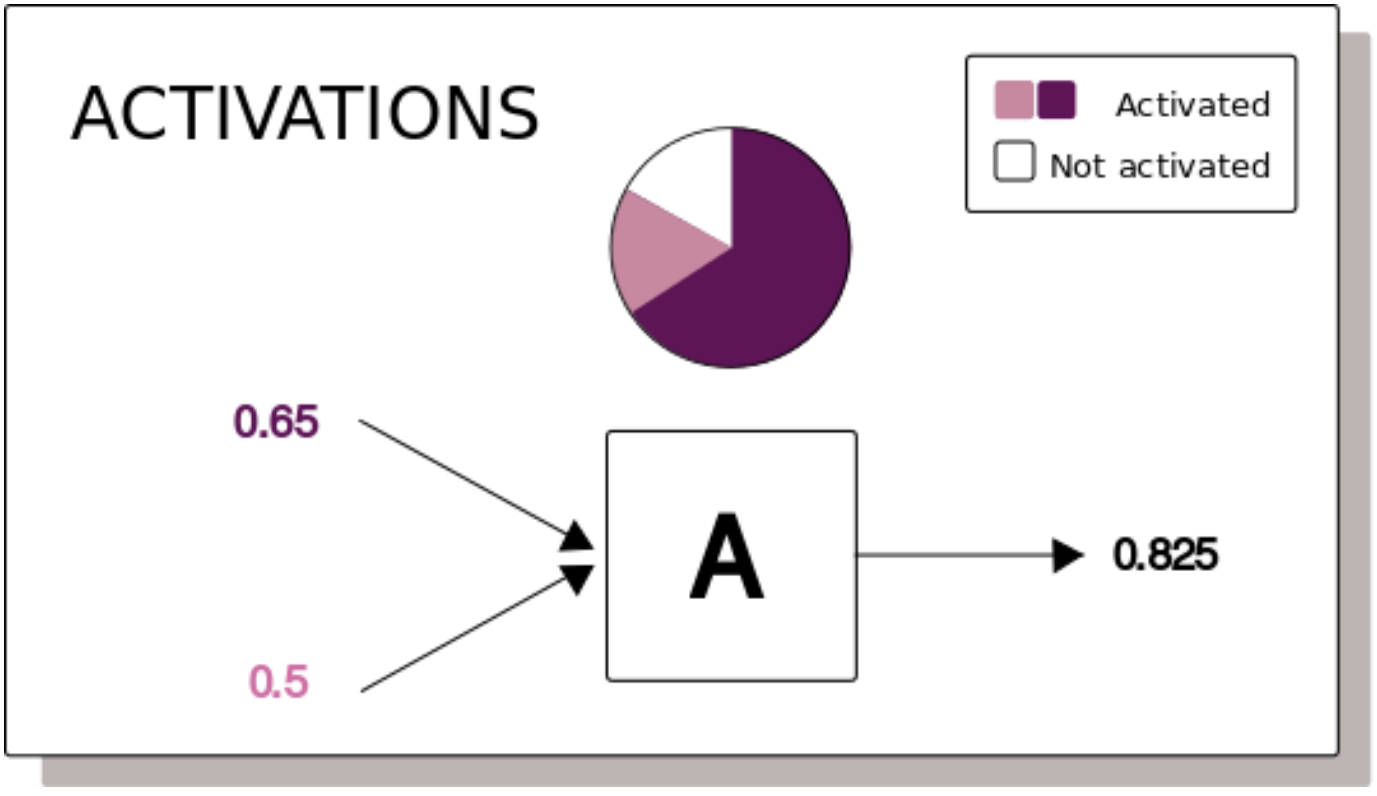

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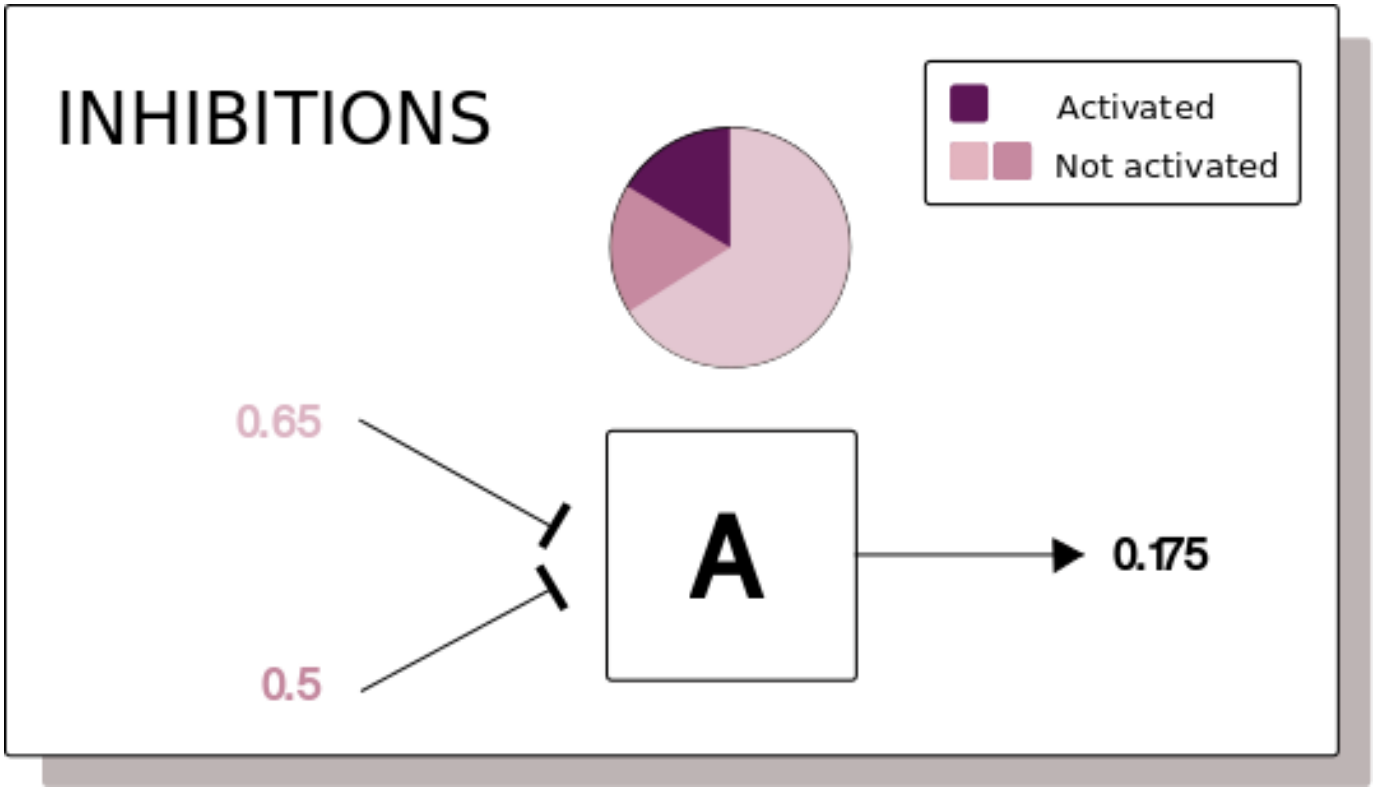

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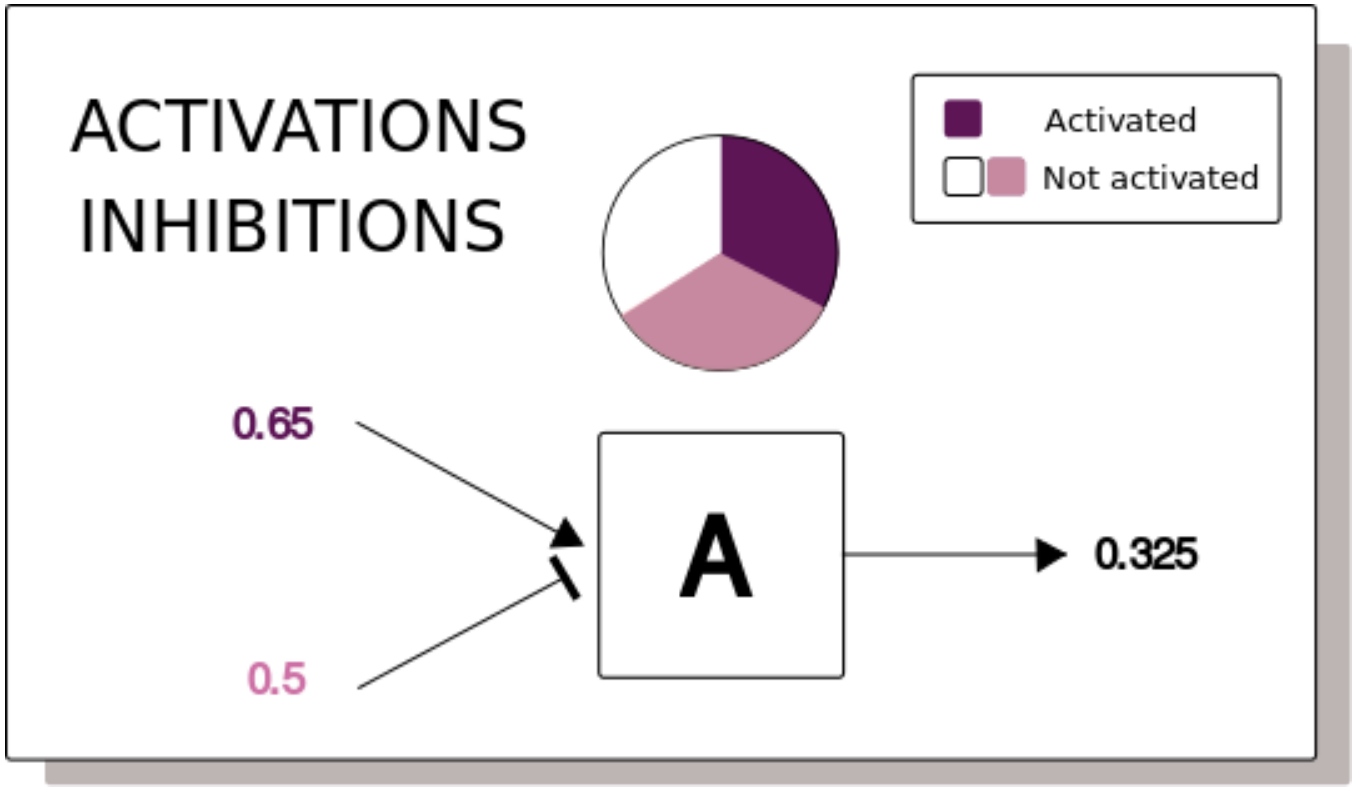
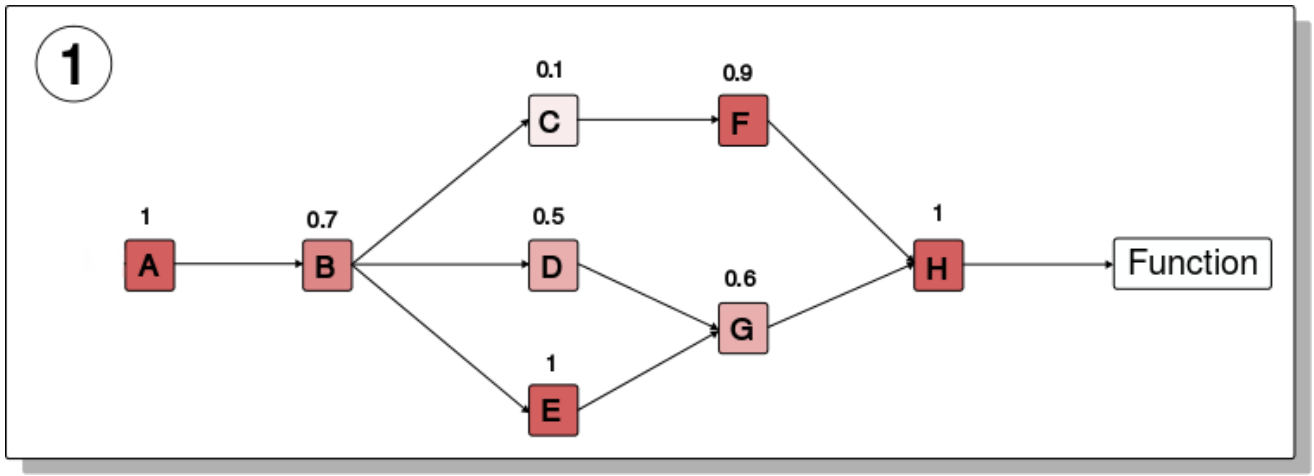


Signal values

- Input signal 1 in any input node
- Compute the signal through each node iteratively
- Loops can be processed
- Subpathway signal: last node signal



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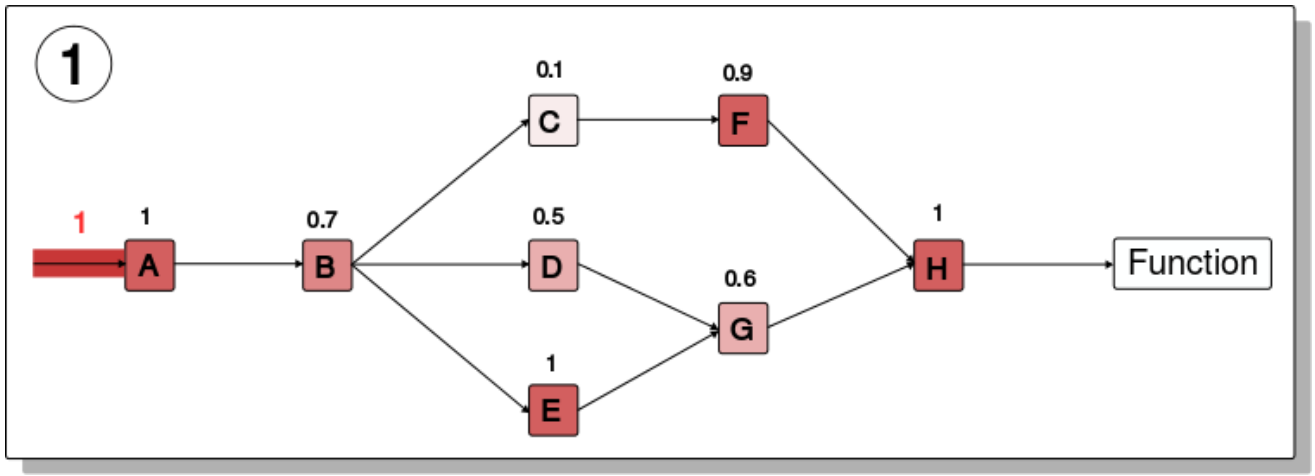

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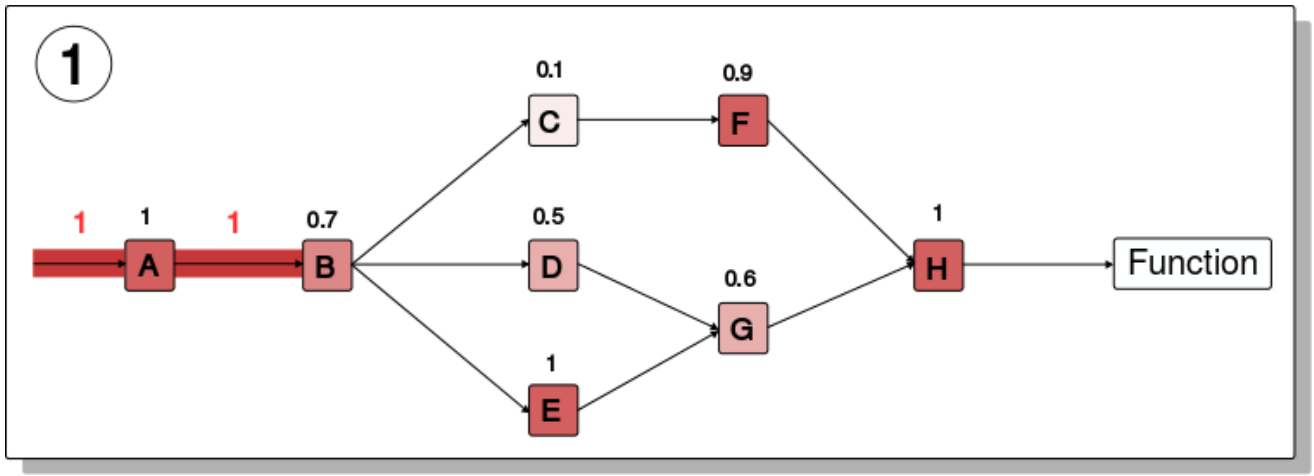

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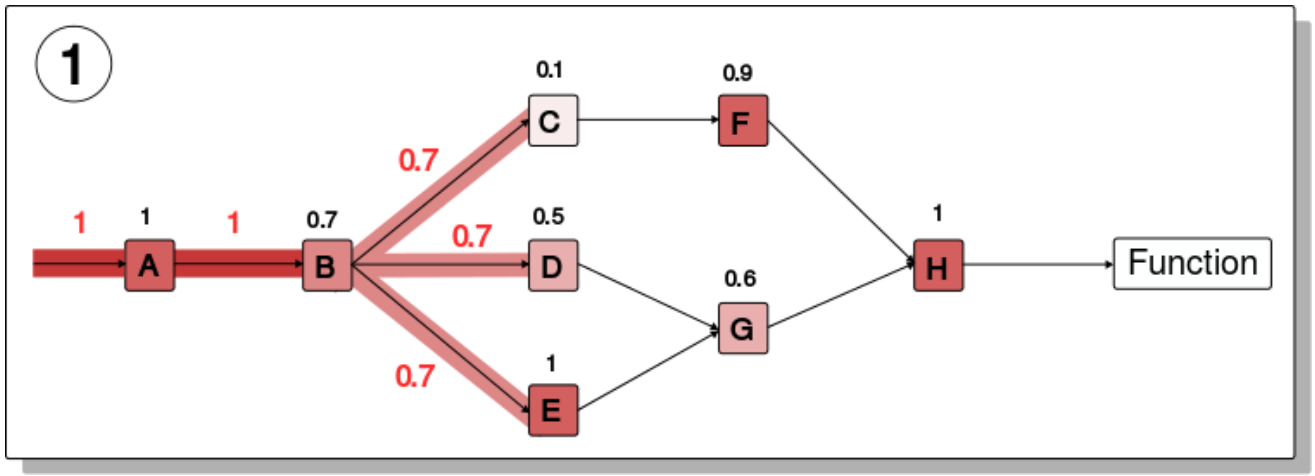

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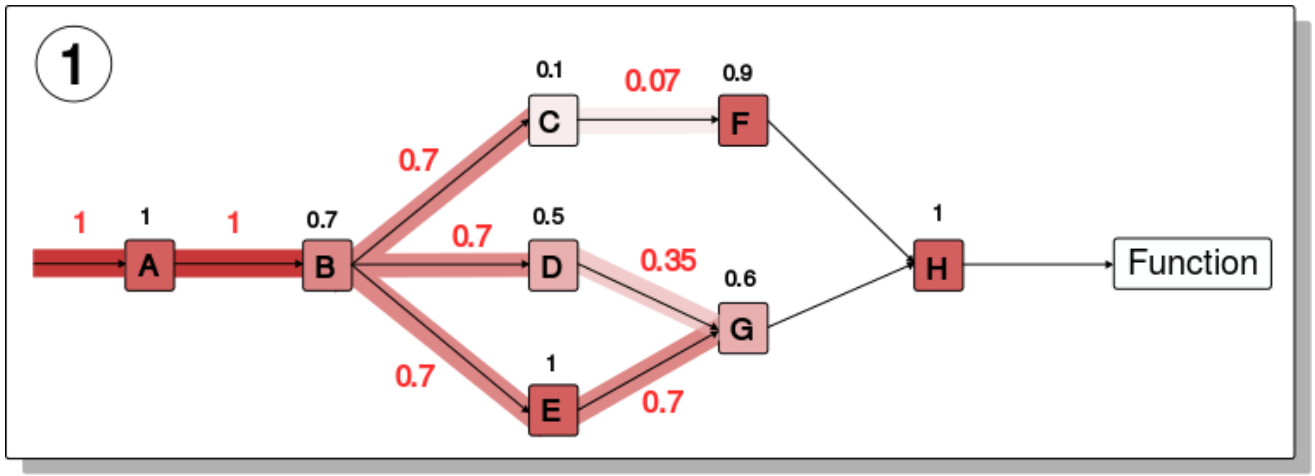

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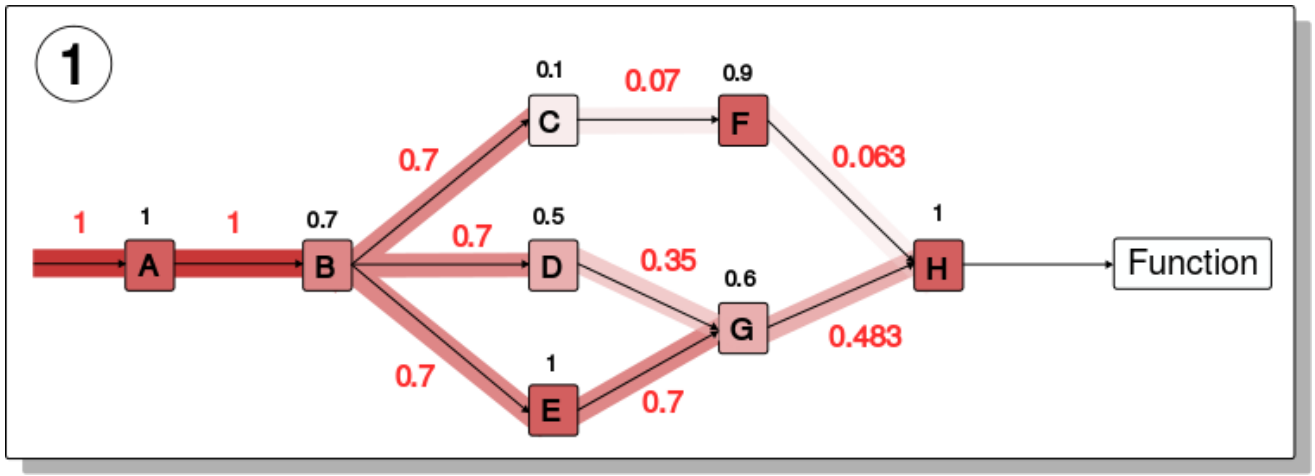

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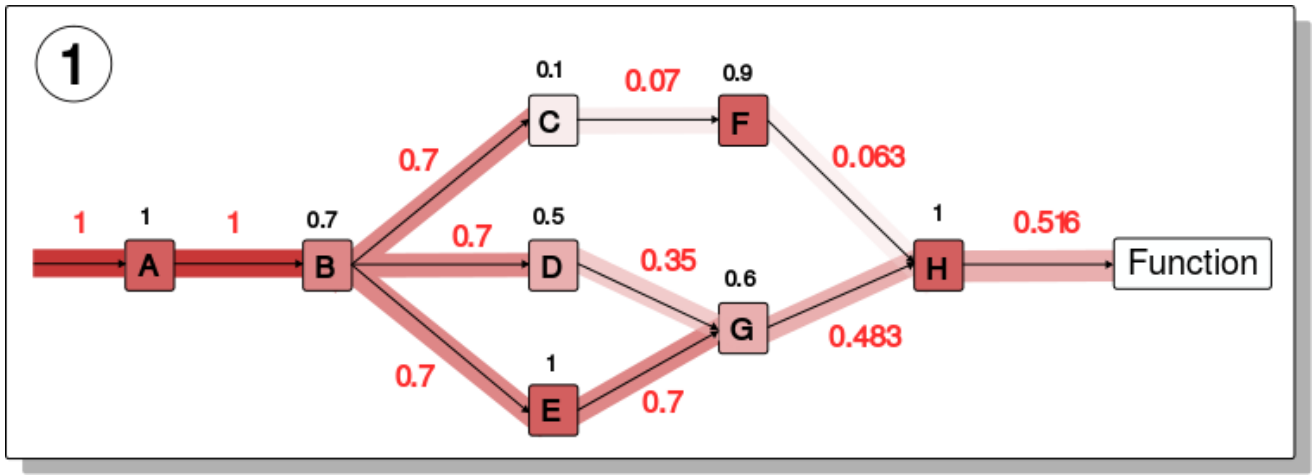
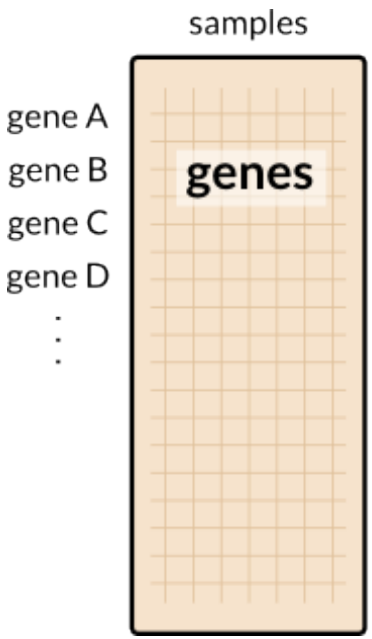


Functional annotation

1. Estimate effector proteins activation
2. Annotate effector proteins functions
   - Uniprot keywords
   - GO annotation



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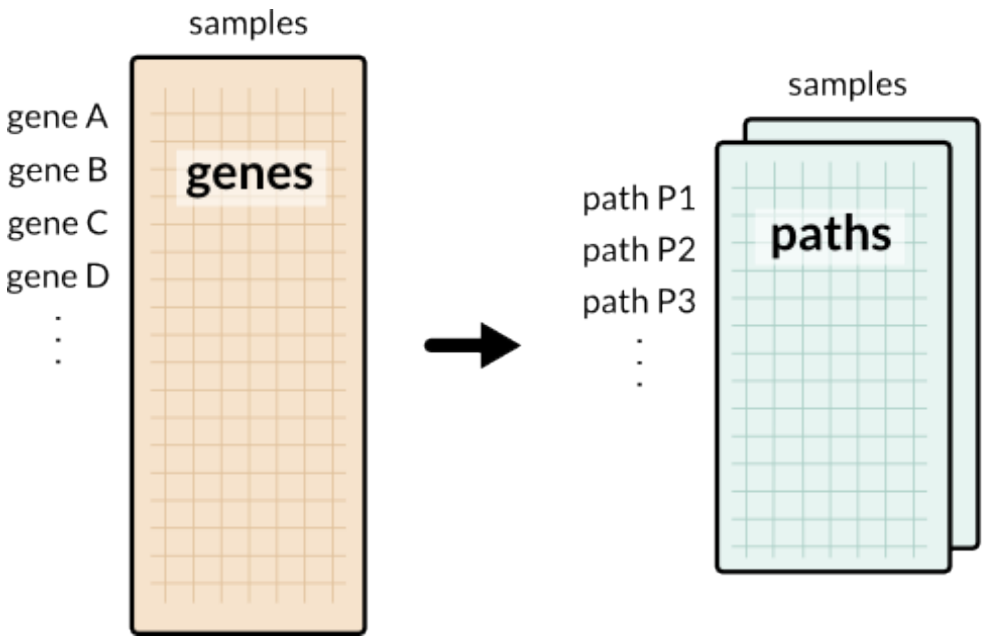

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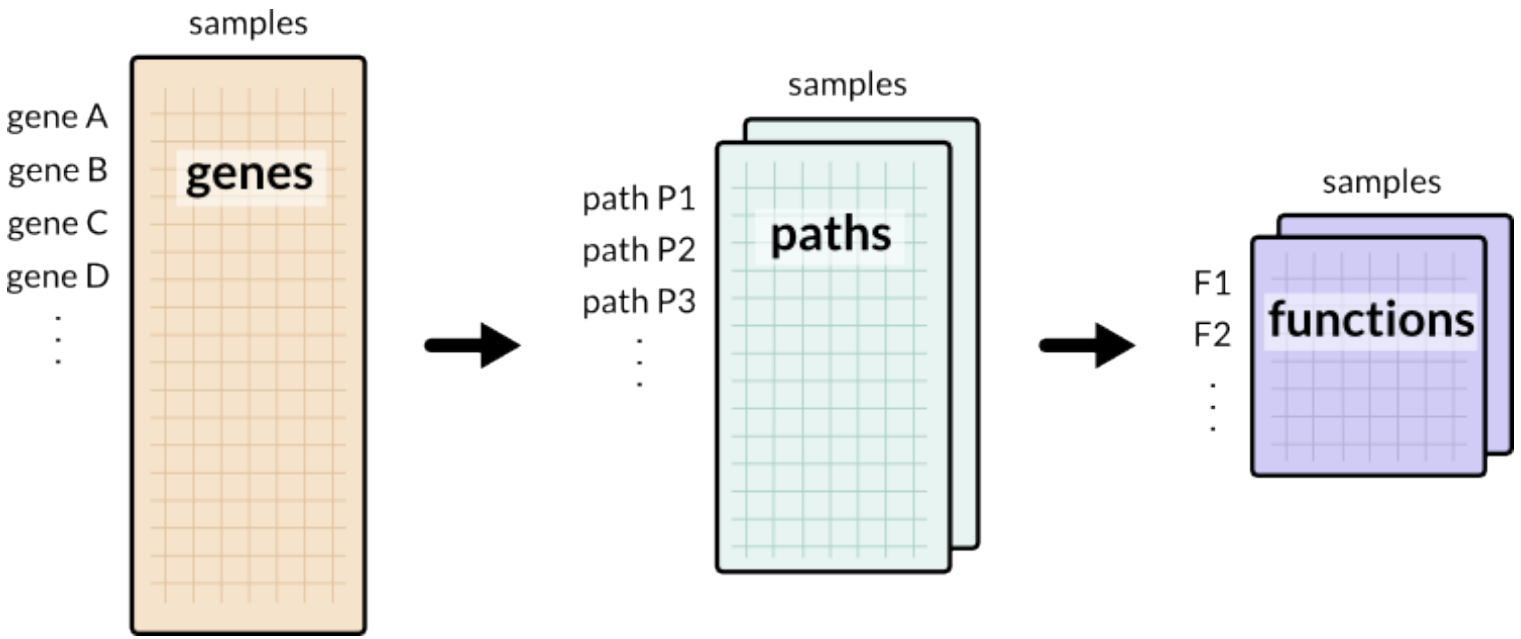

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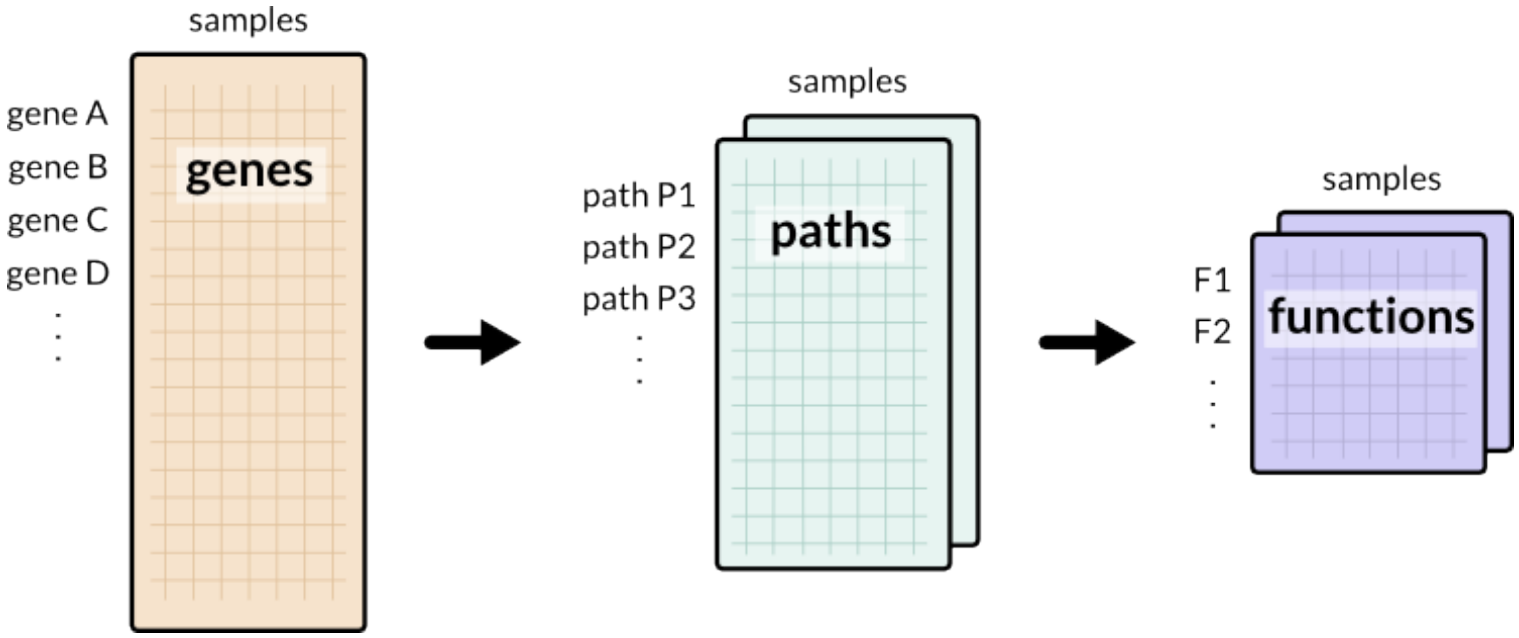

Method comparison