

Learning by Fusing Heterogeneous Data

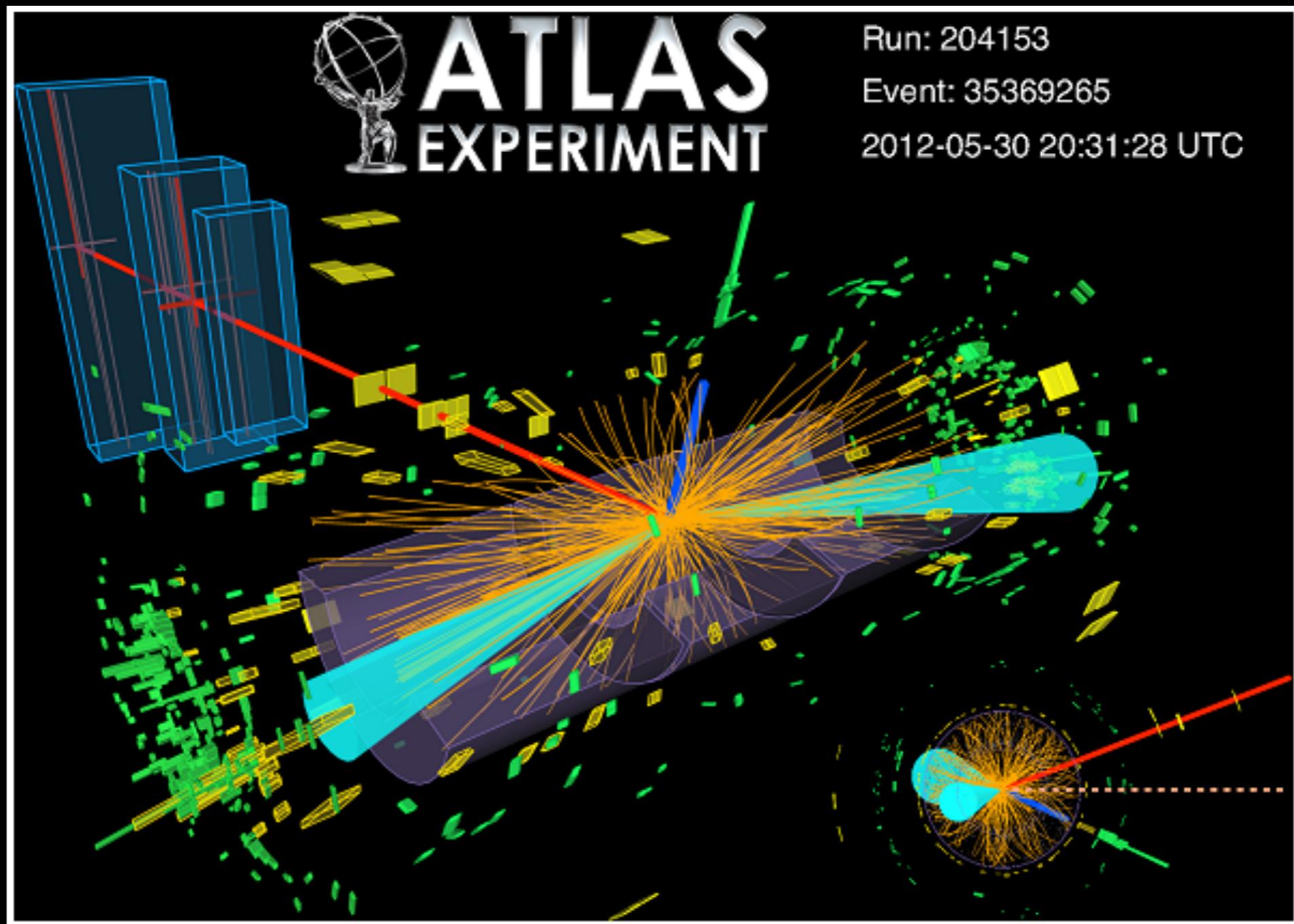
Marinka Zitnik

Thesis Defense, October 22 2015

Motivation

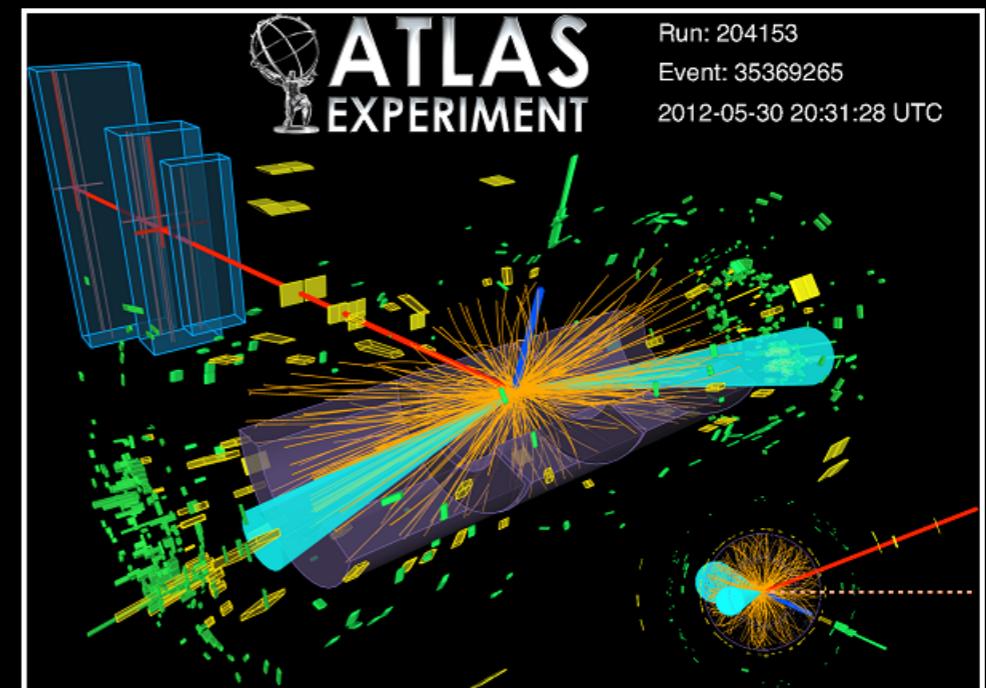
Large Heterogeneous Data Compendia

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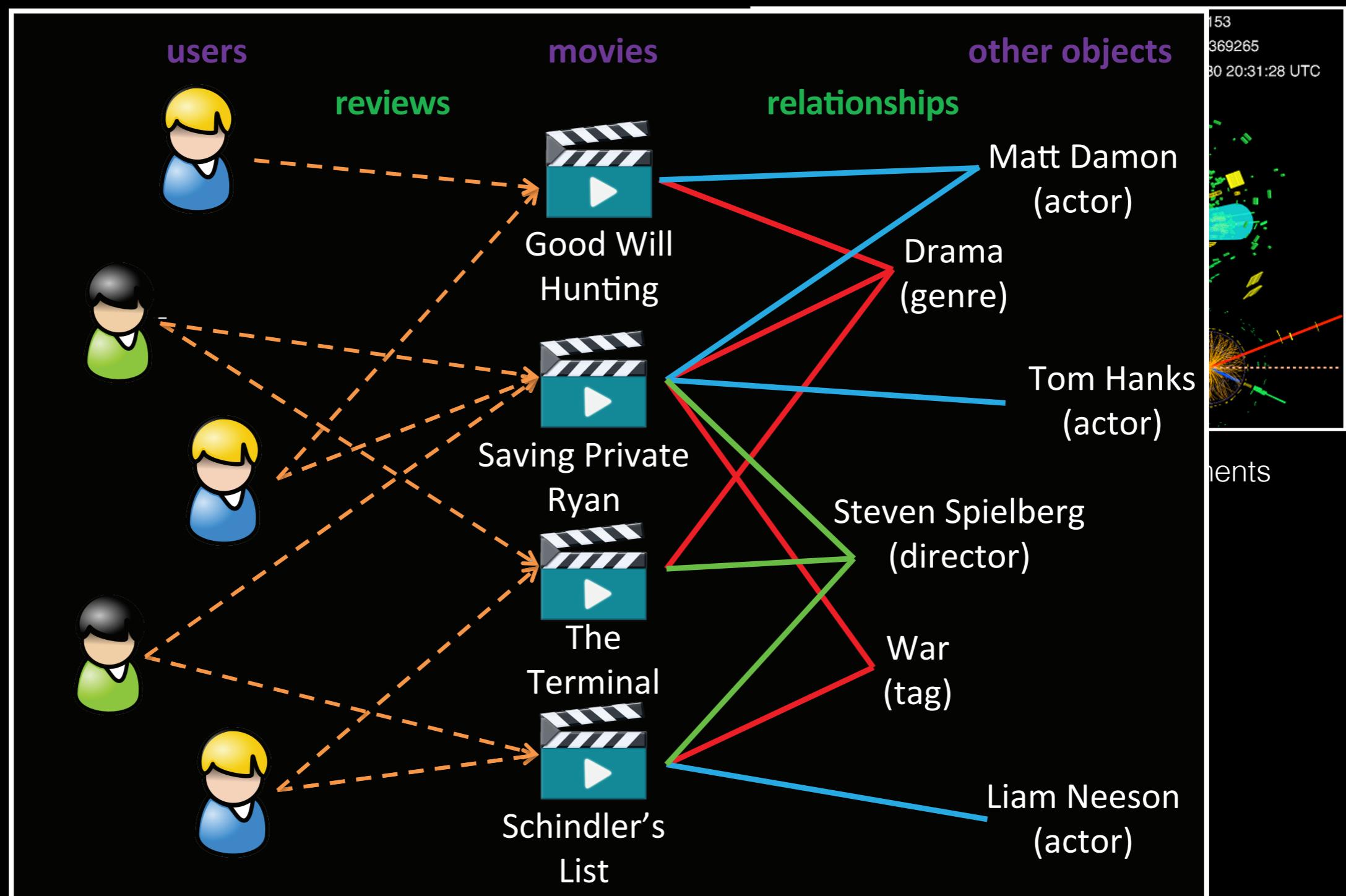
Large-scale physics experiments

Large Heterogeneous Data Compendia



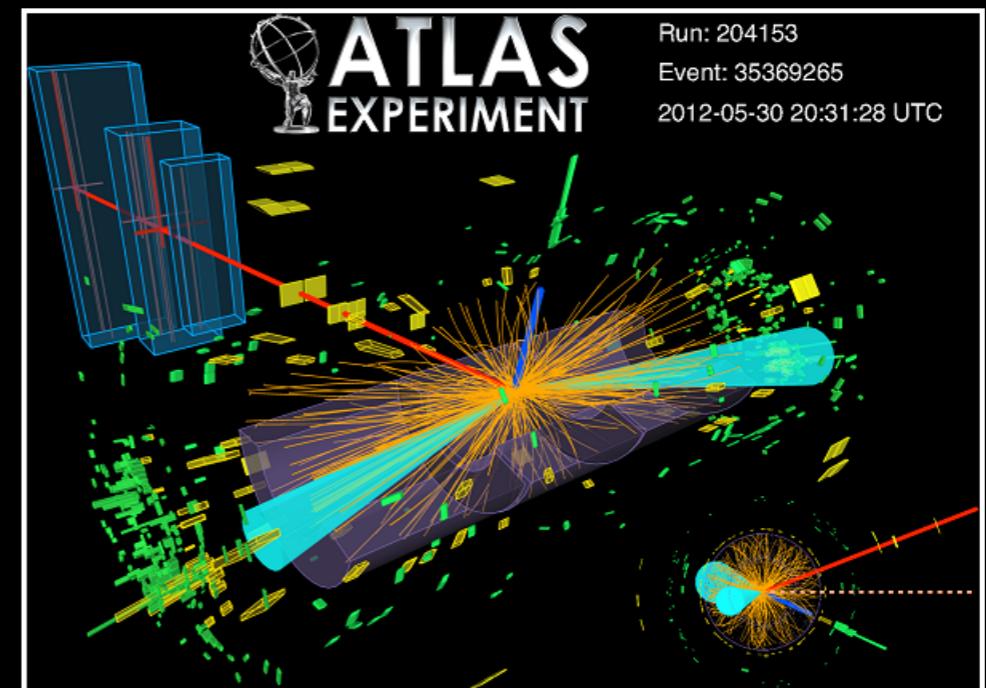
Large-scale physics experiments

Large Heterogeneous Data Compendia

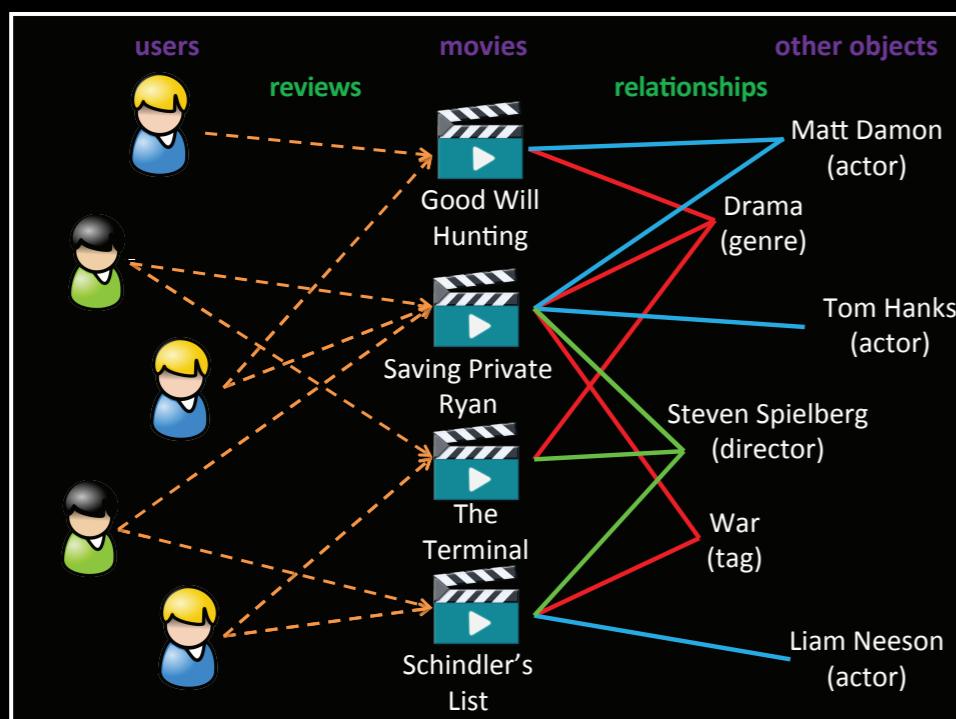


Social networks, recommender systems

Large Heterogeneous Data Compendia

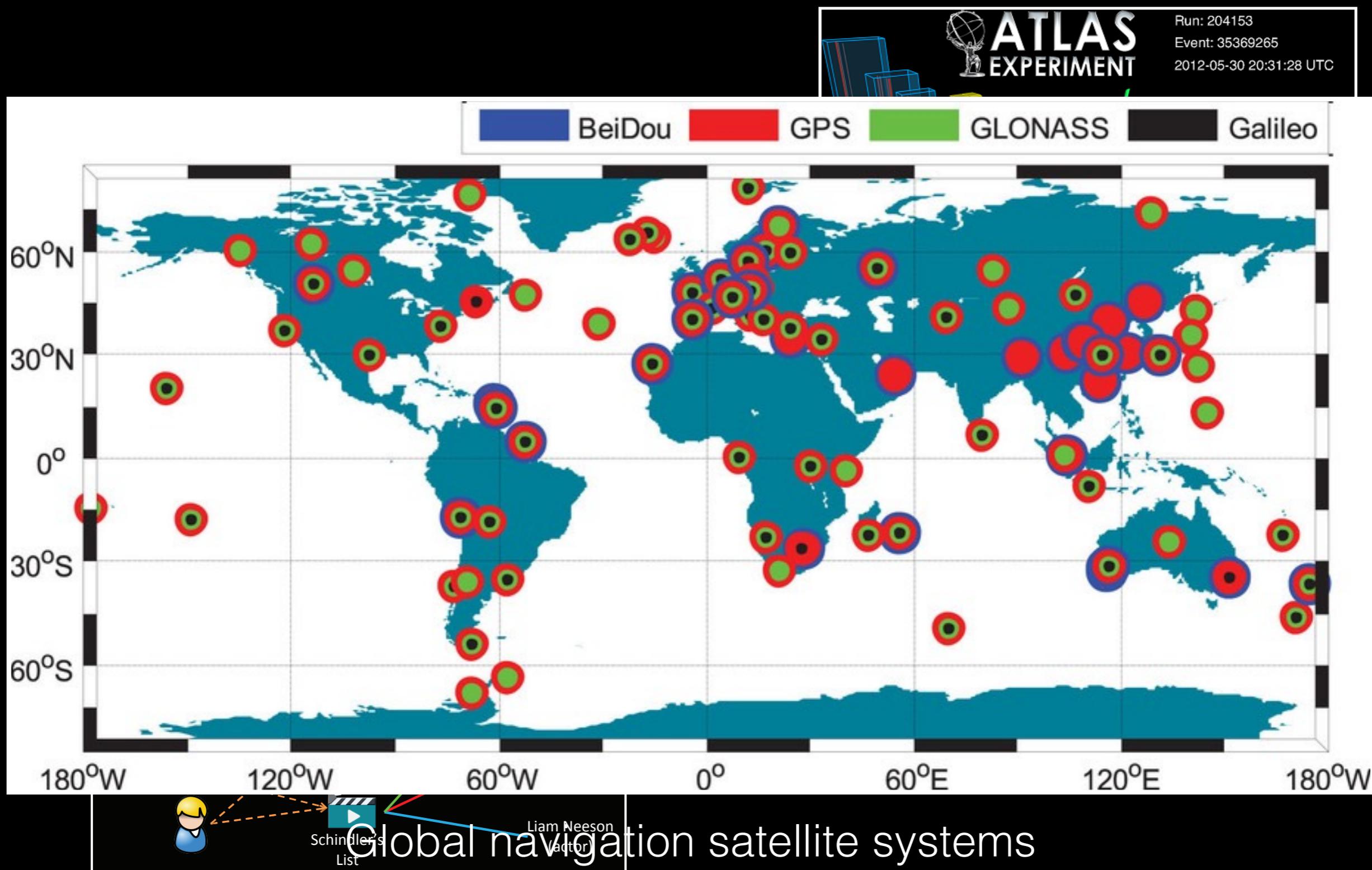


Large-scale physics experiments



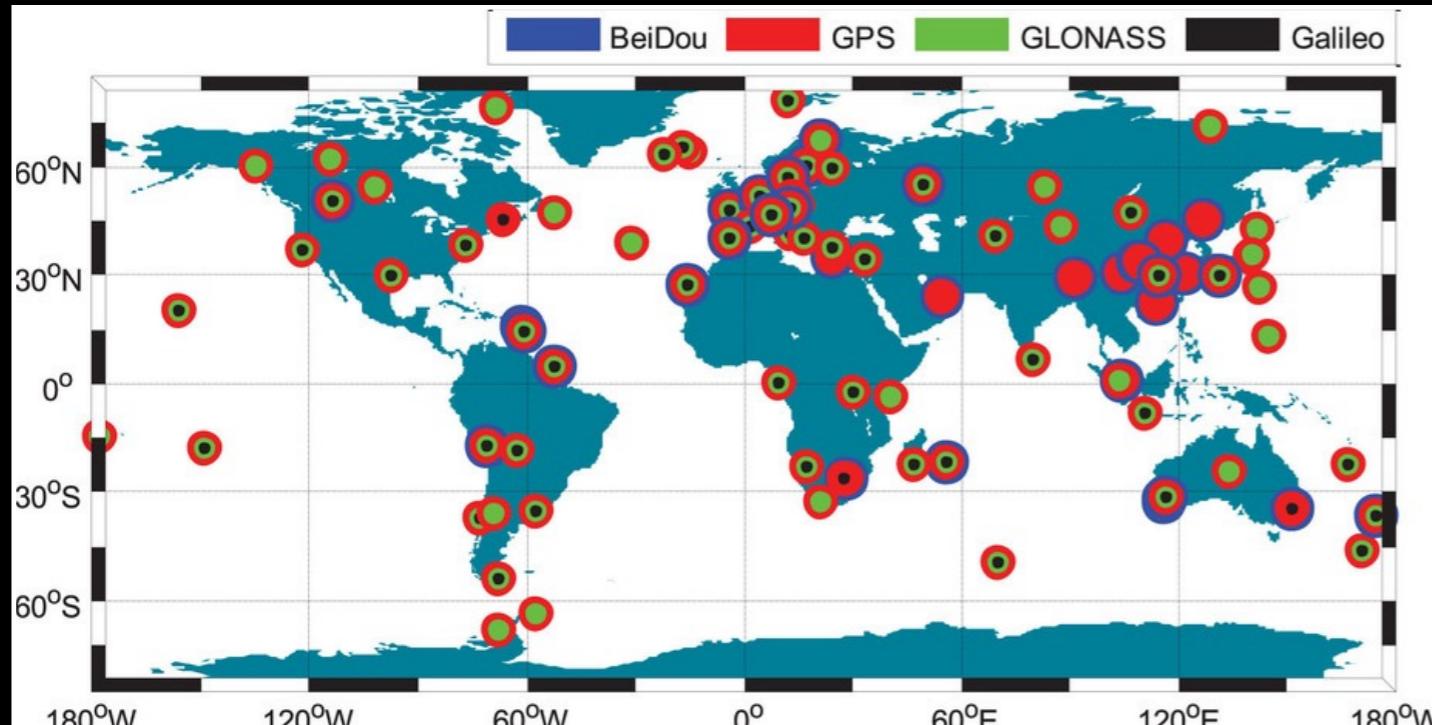
Social networks, recommender systems

Large Heterogeneous Data Compendia

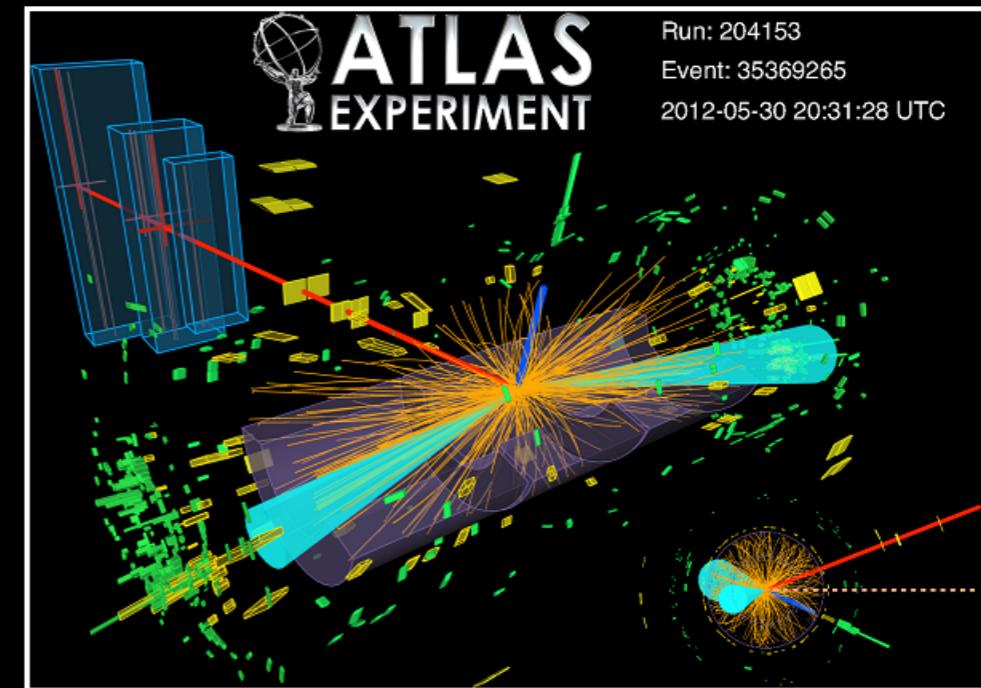


Social networks, recommender systems

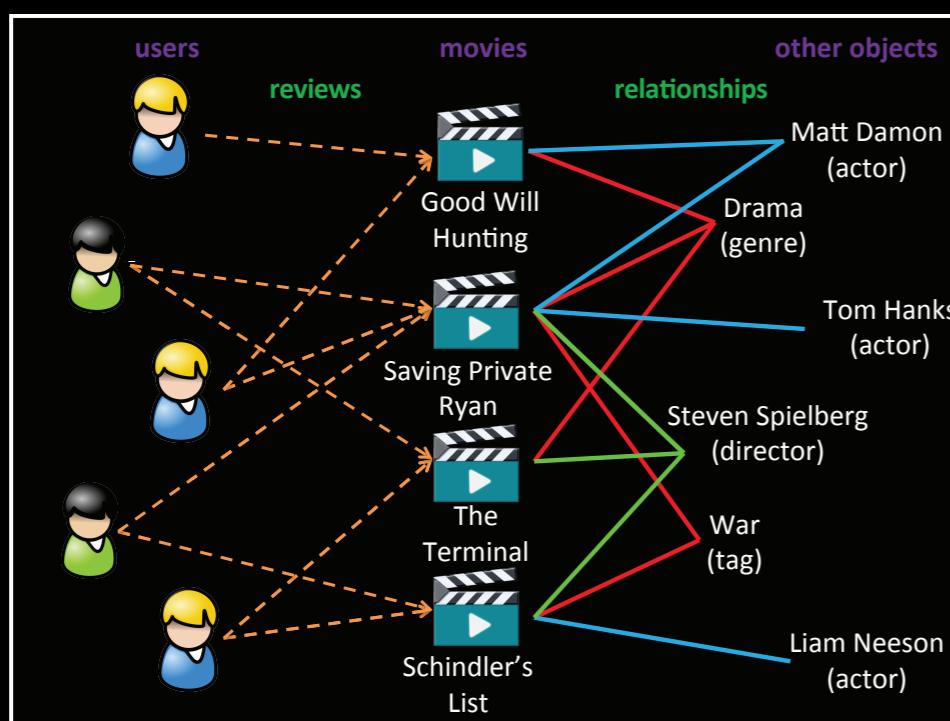
Large Heterogeneous Data Compendia



Global navigation satellite systems

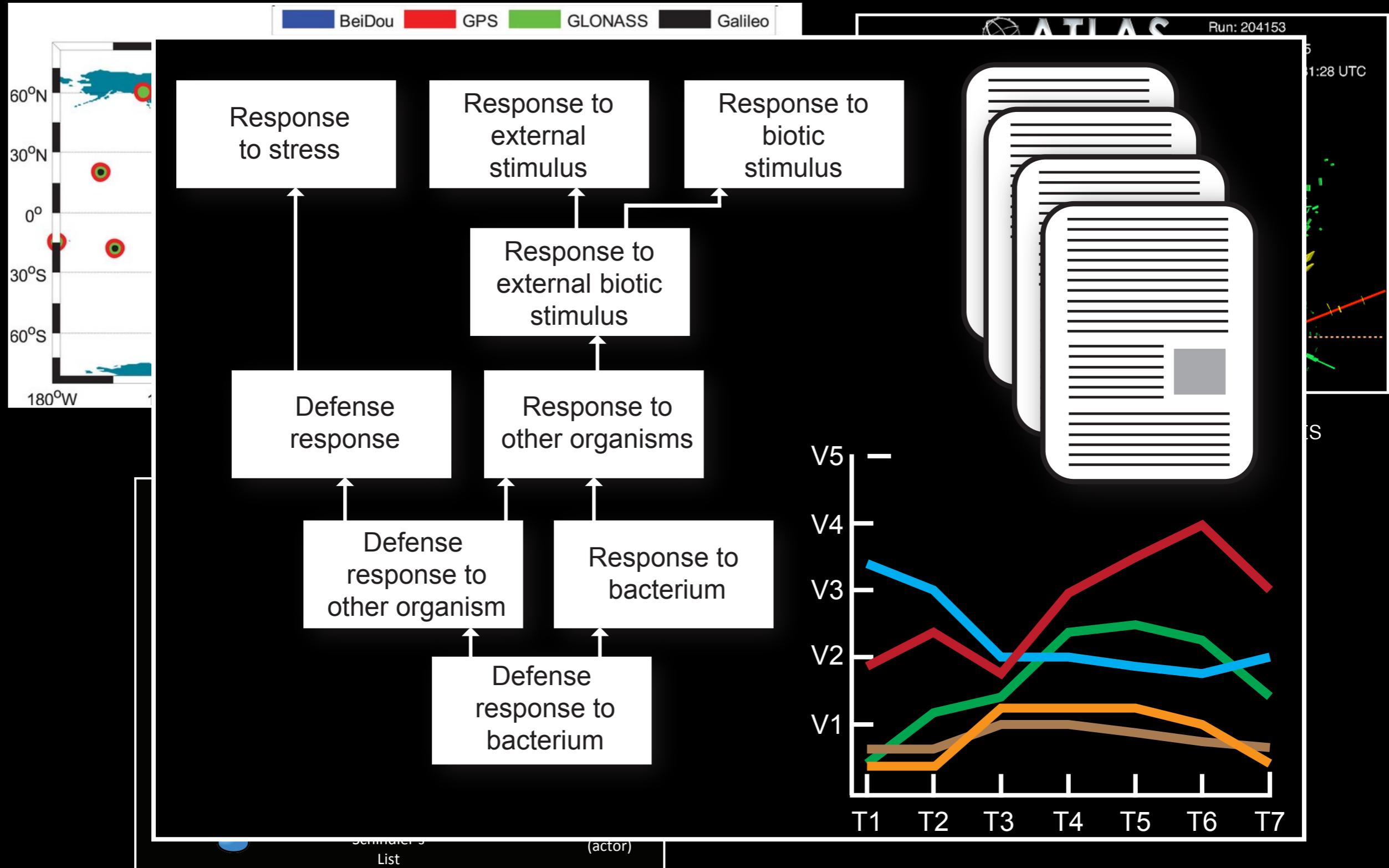


Large-scale physics experiments



Social networks, recommender systems

Large Heterogeneous Data Compendia

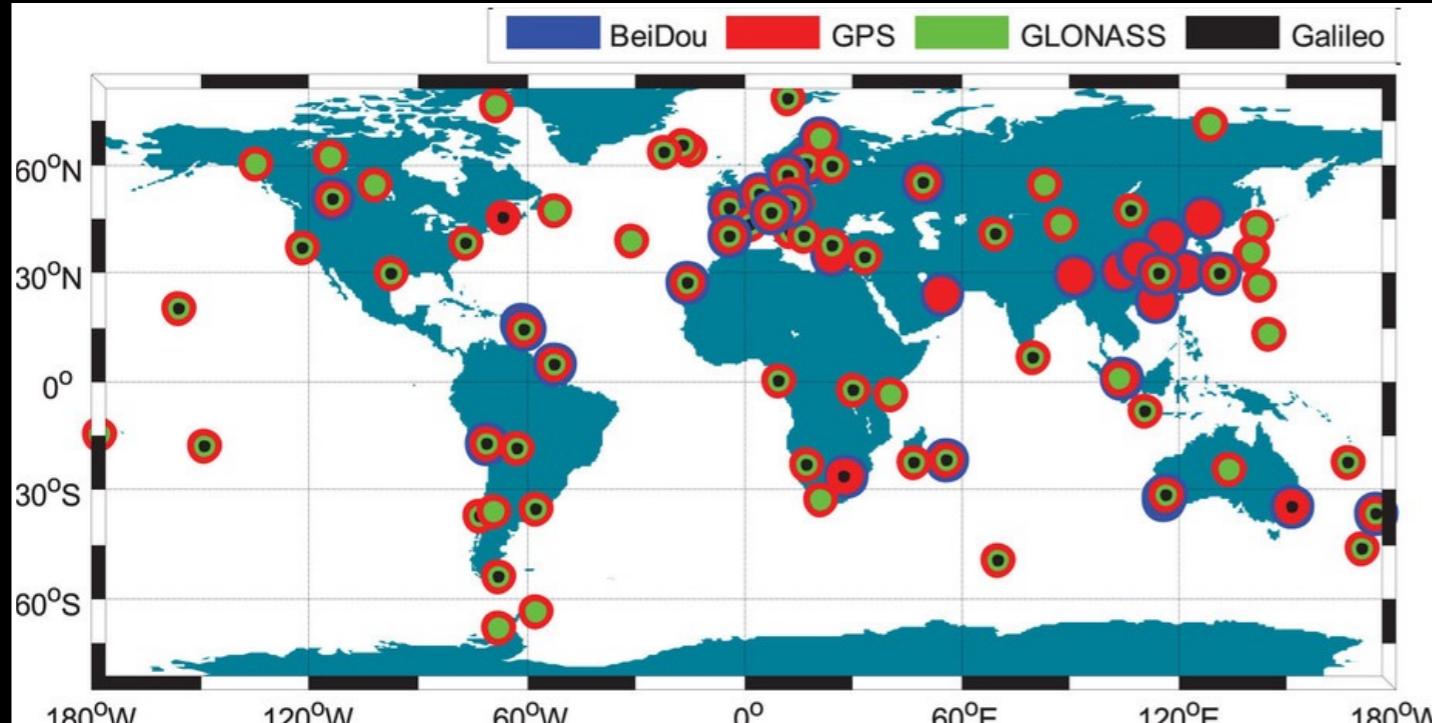


Social networks, recommender systems

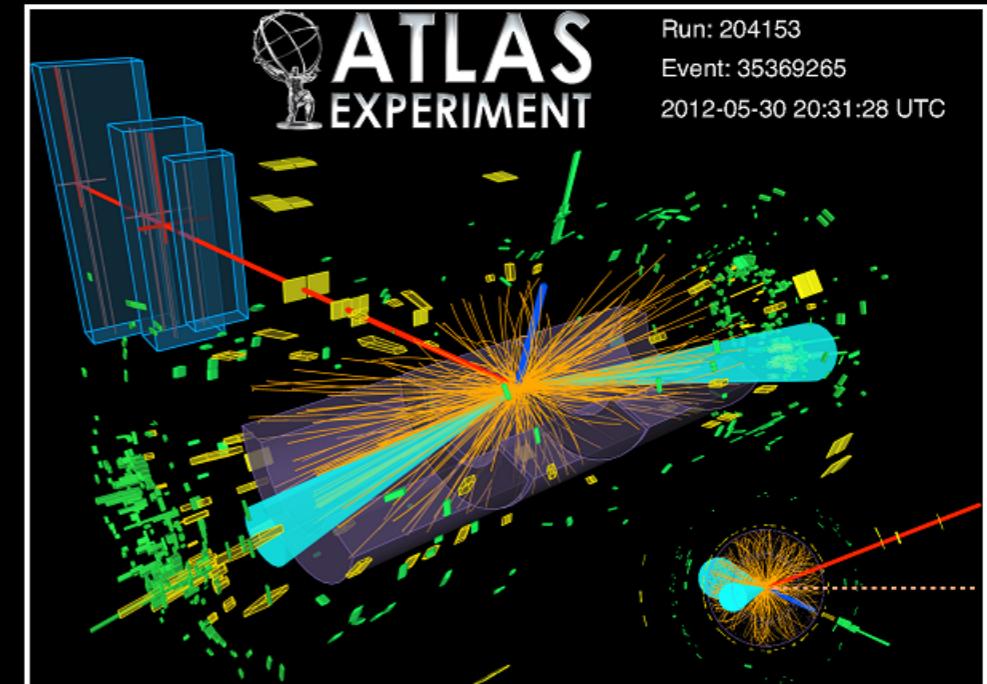
Molecular biology

Marinka Zitnik - PhD Thesis

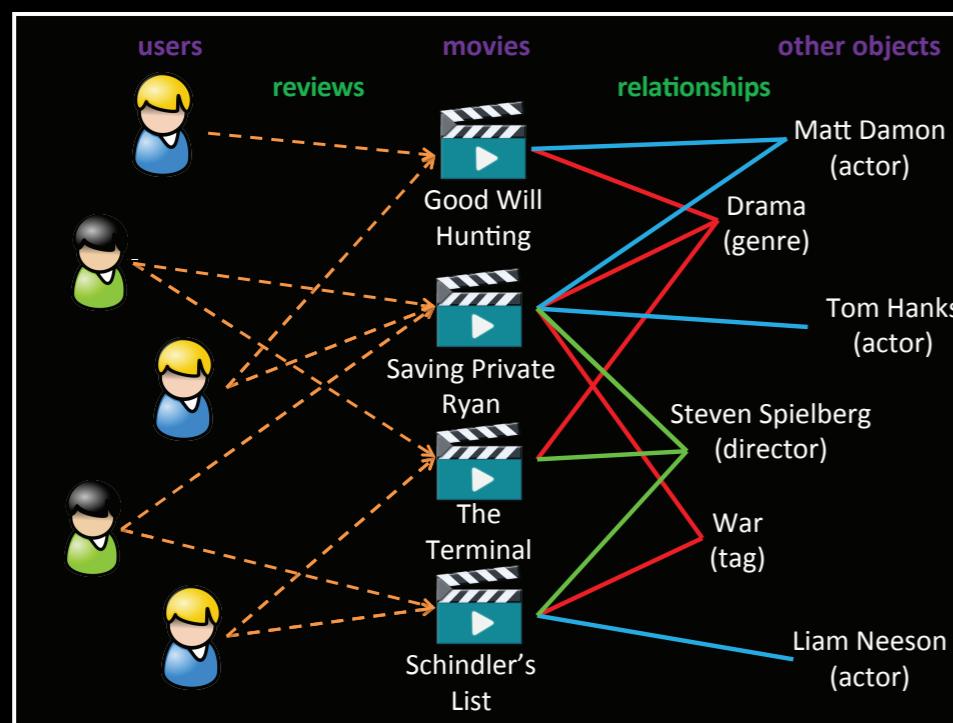
Large Heterogeneous Data Compendia



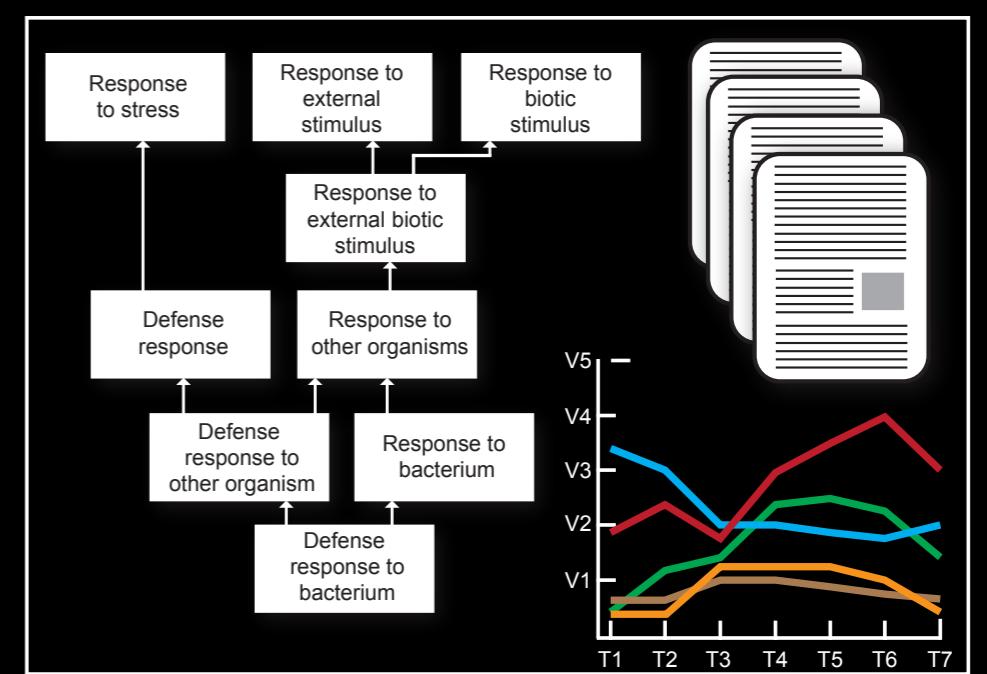
Global navigation satellite systems



Large-scale physics experiments



Social networks, recommender systems



Molecular biology

Complex relationships

Complex relationships

Objects of different types

Complex relationships

Objects of different types

Different points in time, space and scale

Complex relationships

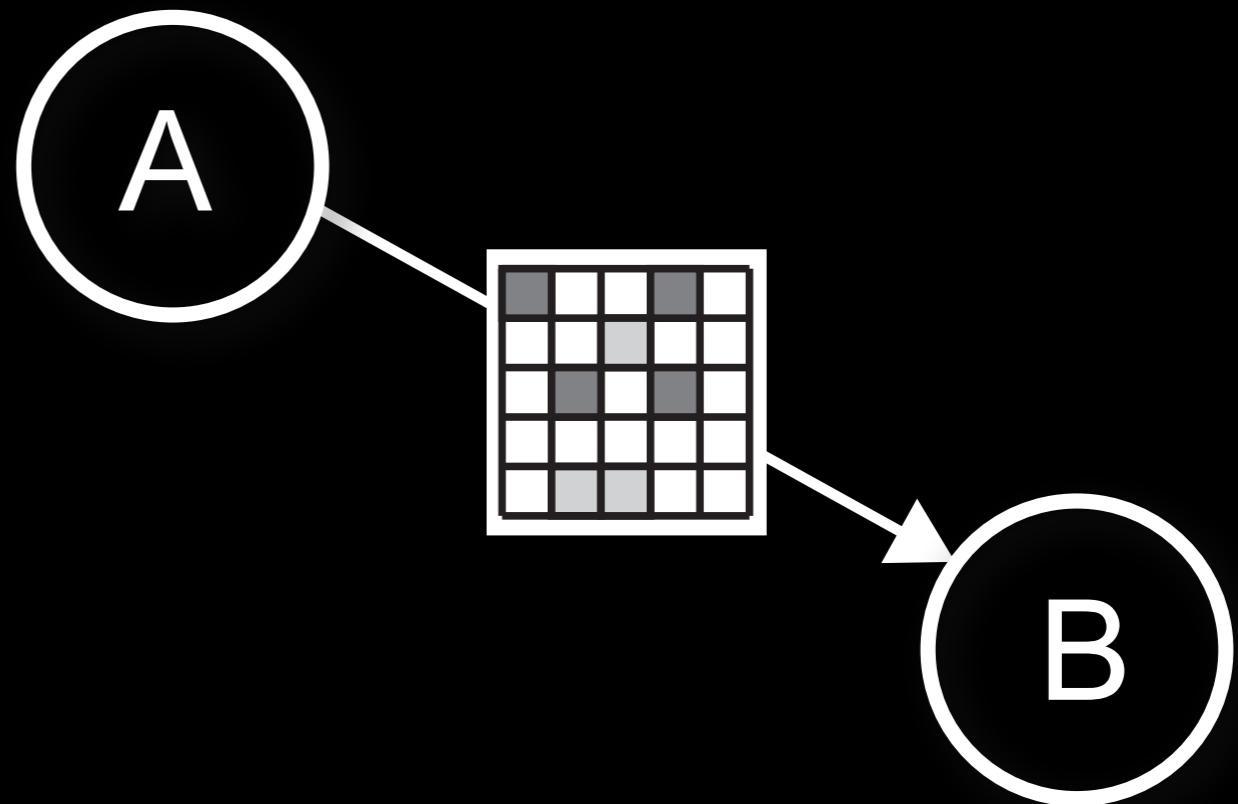
Objects of different types

Different points in time, space and scale

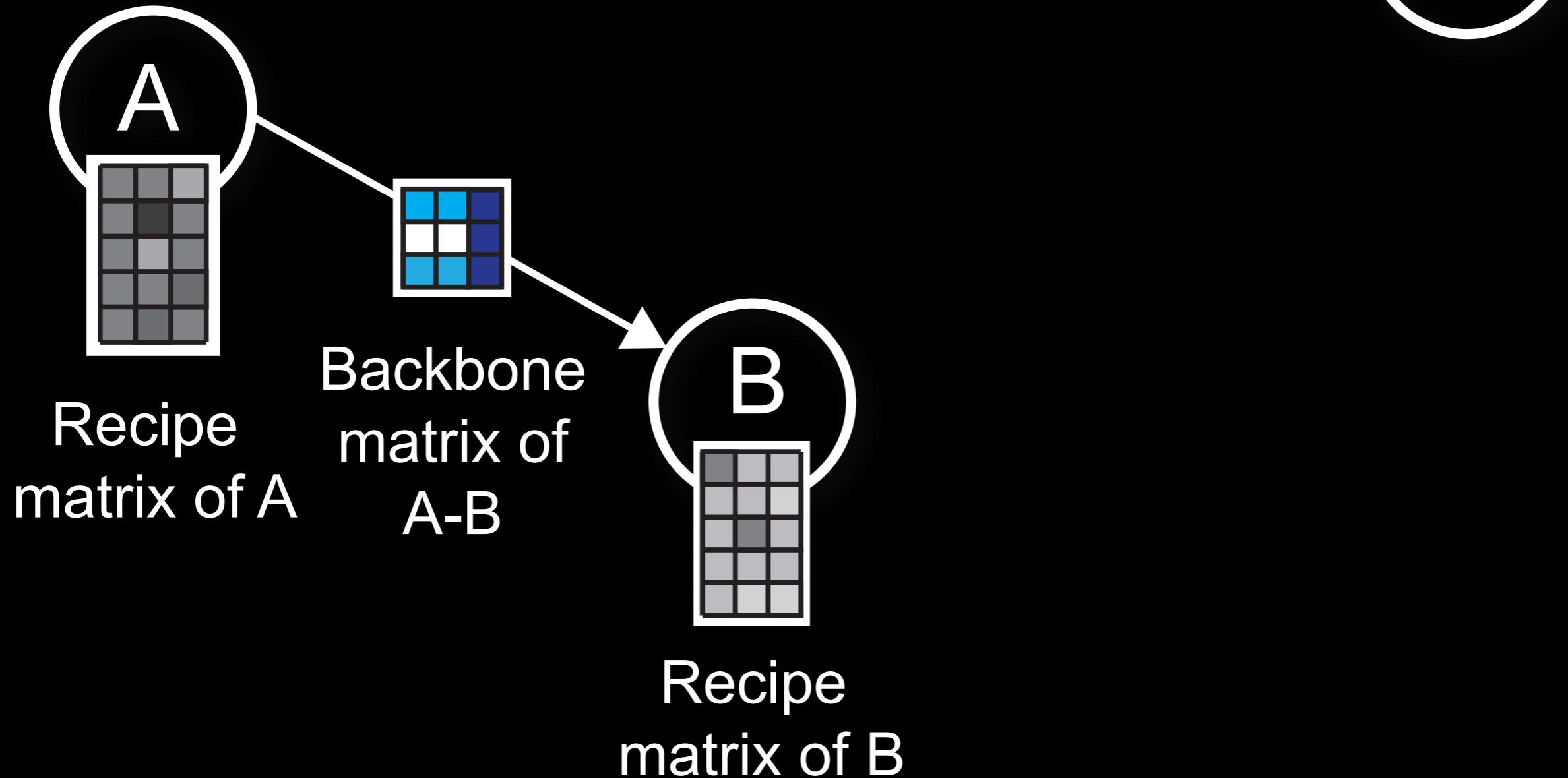
Different perspectives

Warming-Up

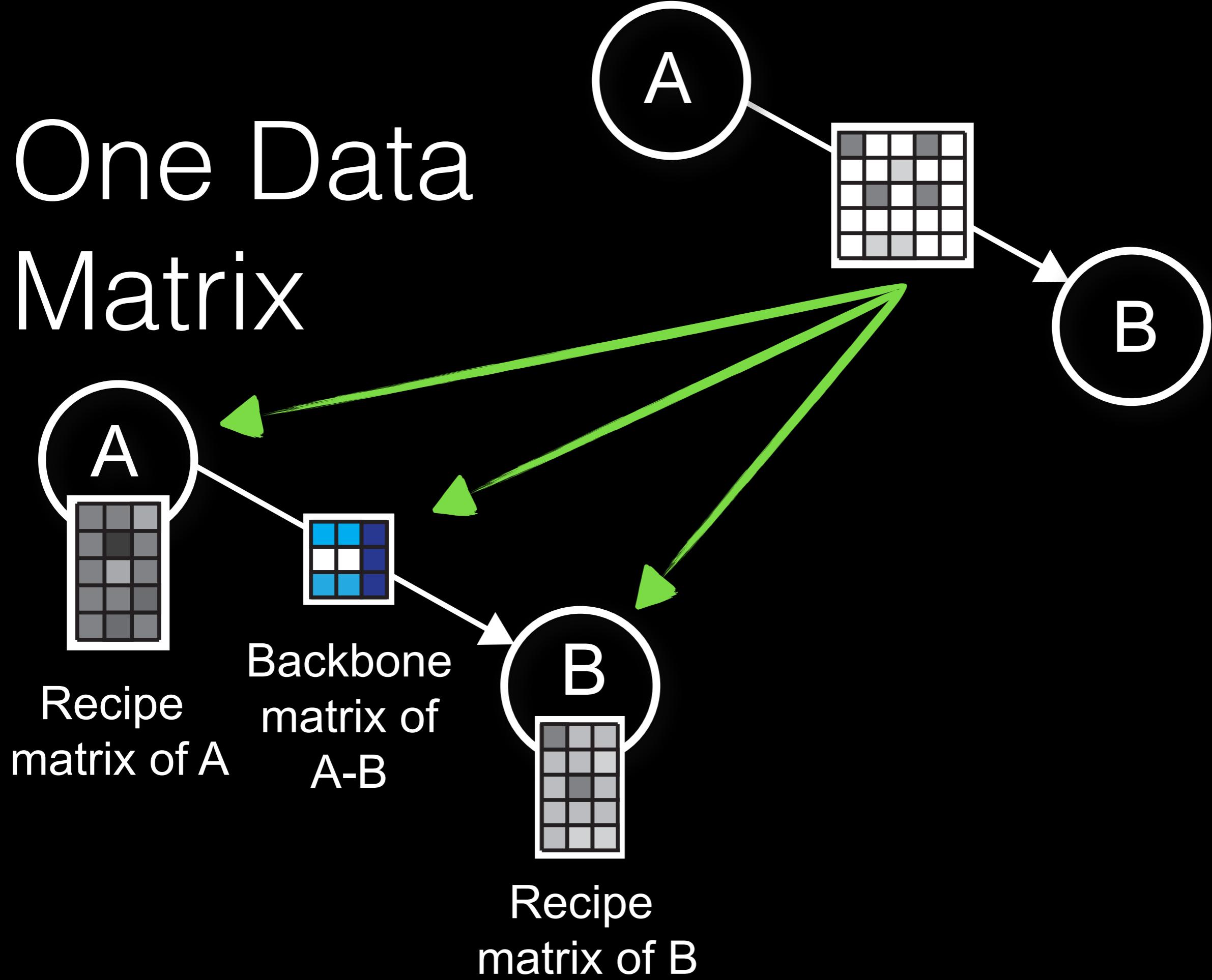
One Data Matrix



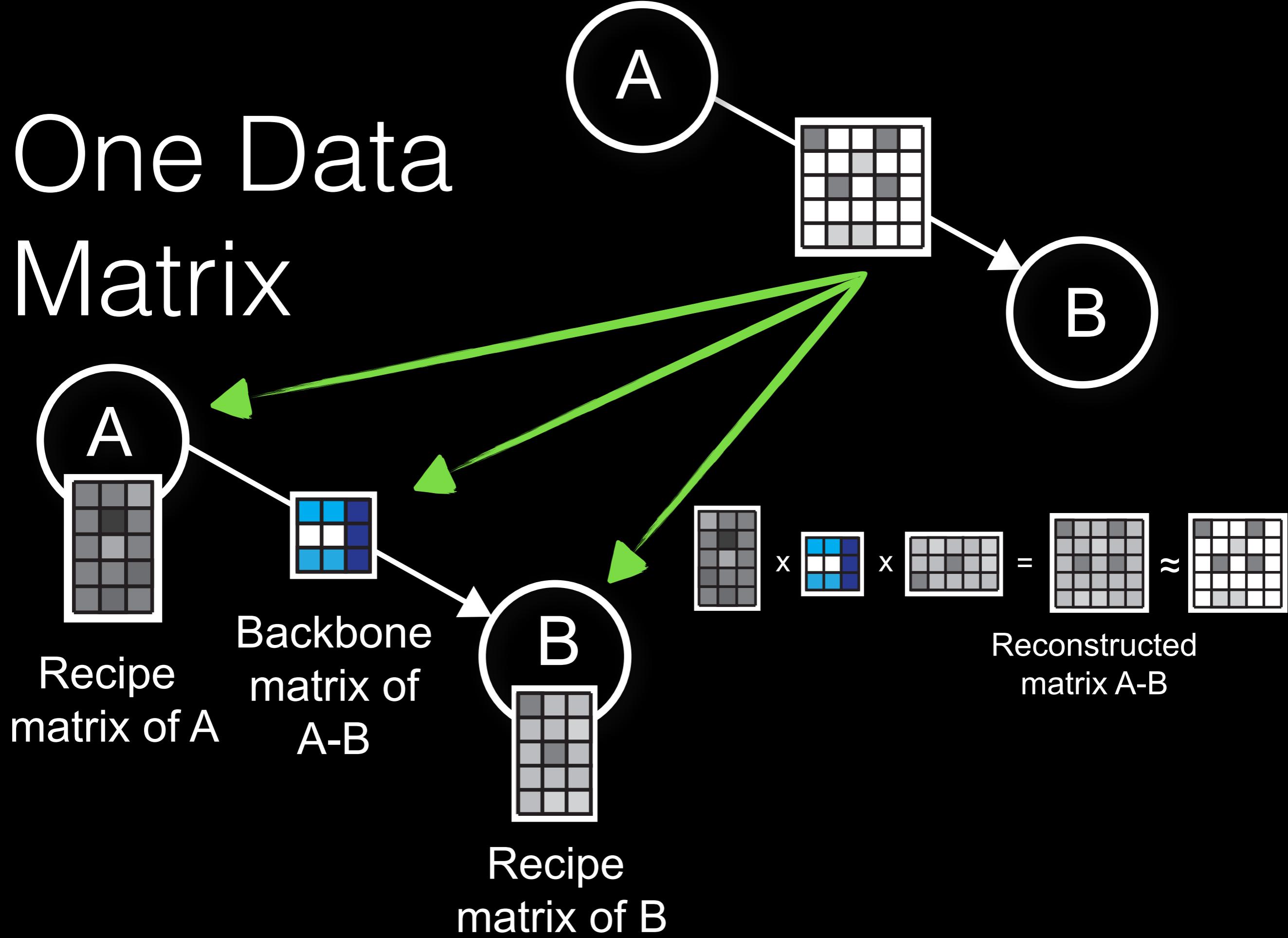
One Data Matrix



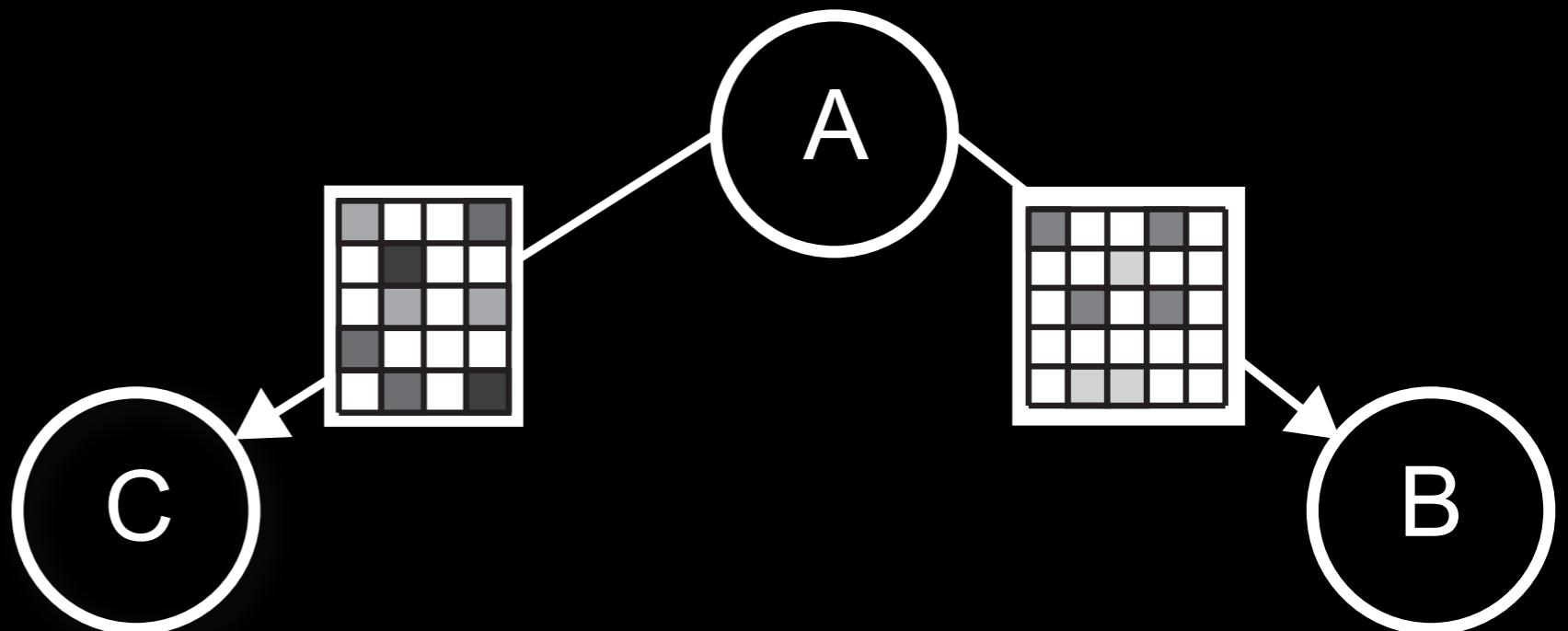
One Data Matrix



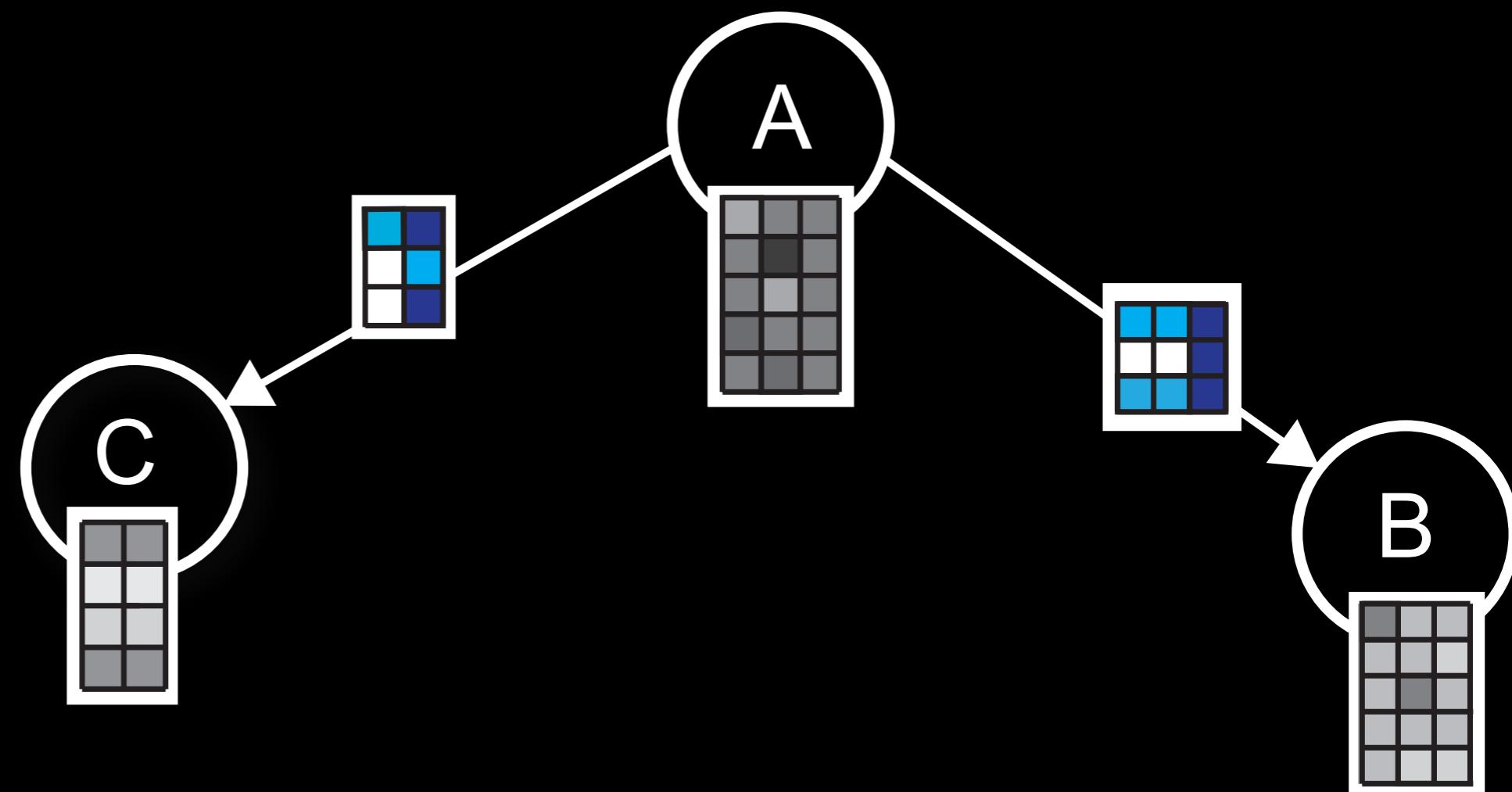
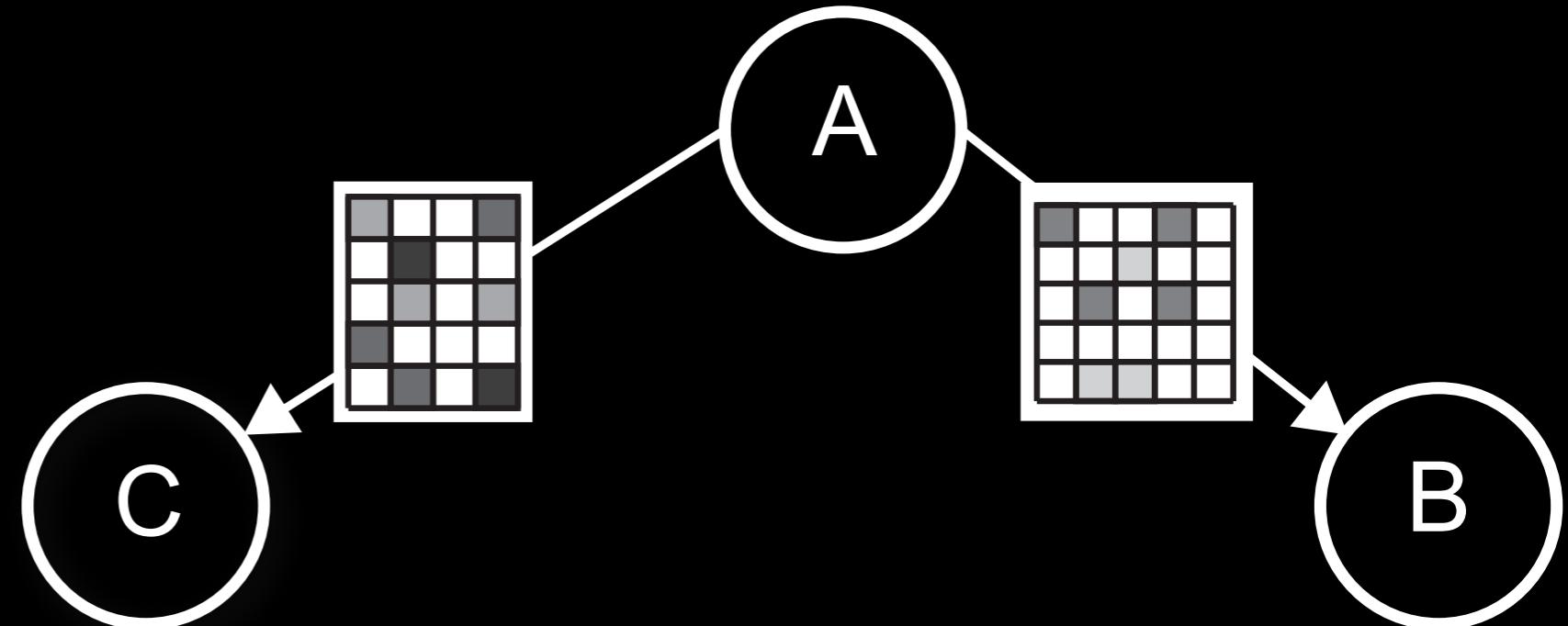
One Data Matrix



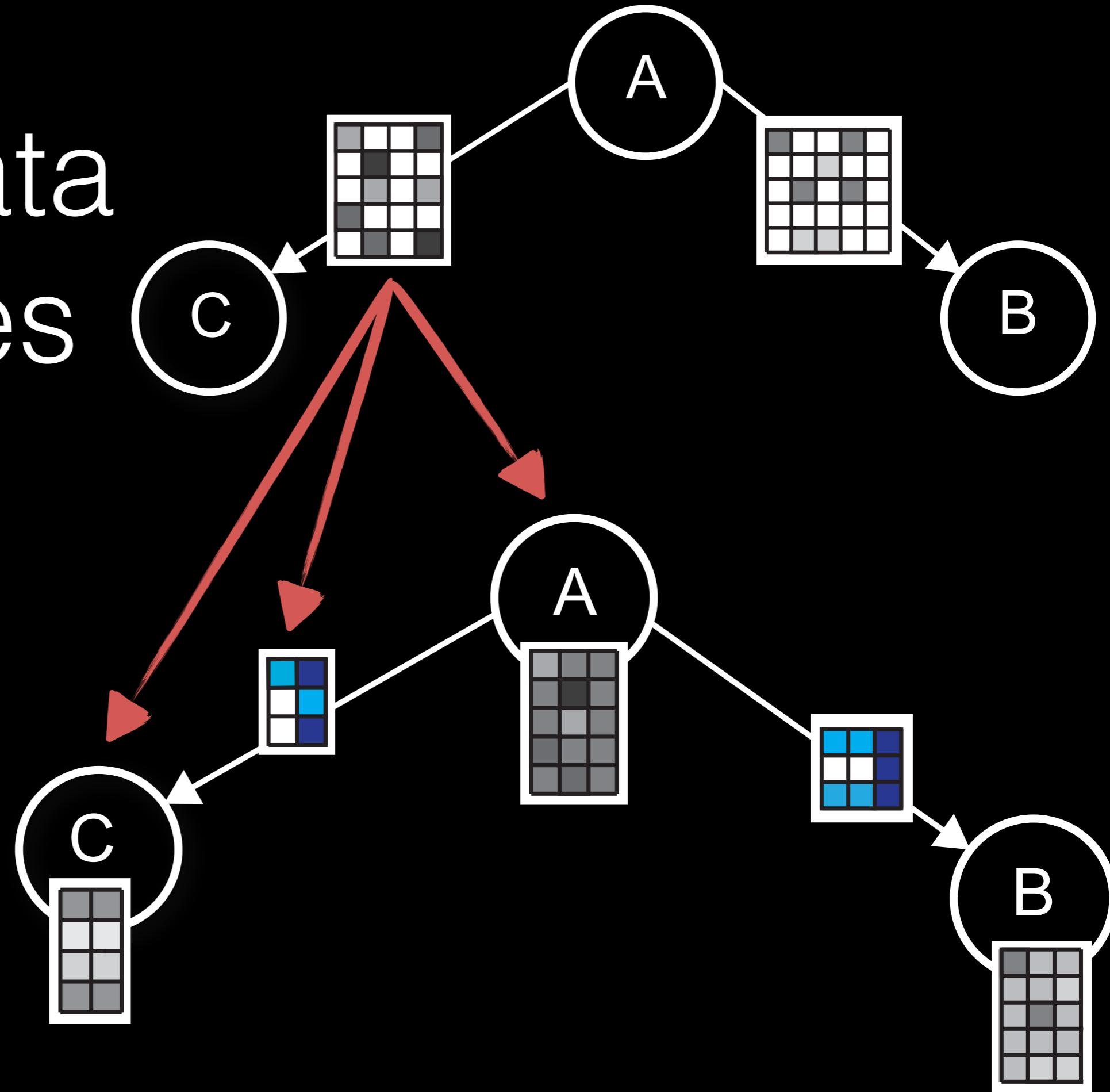
Two Data Matrices



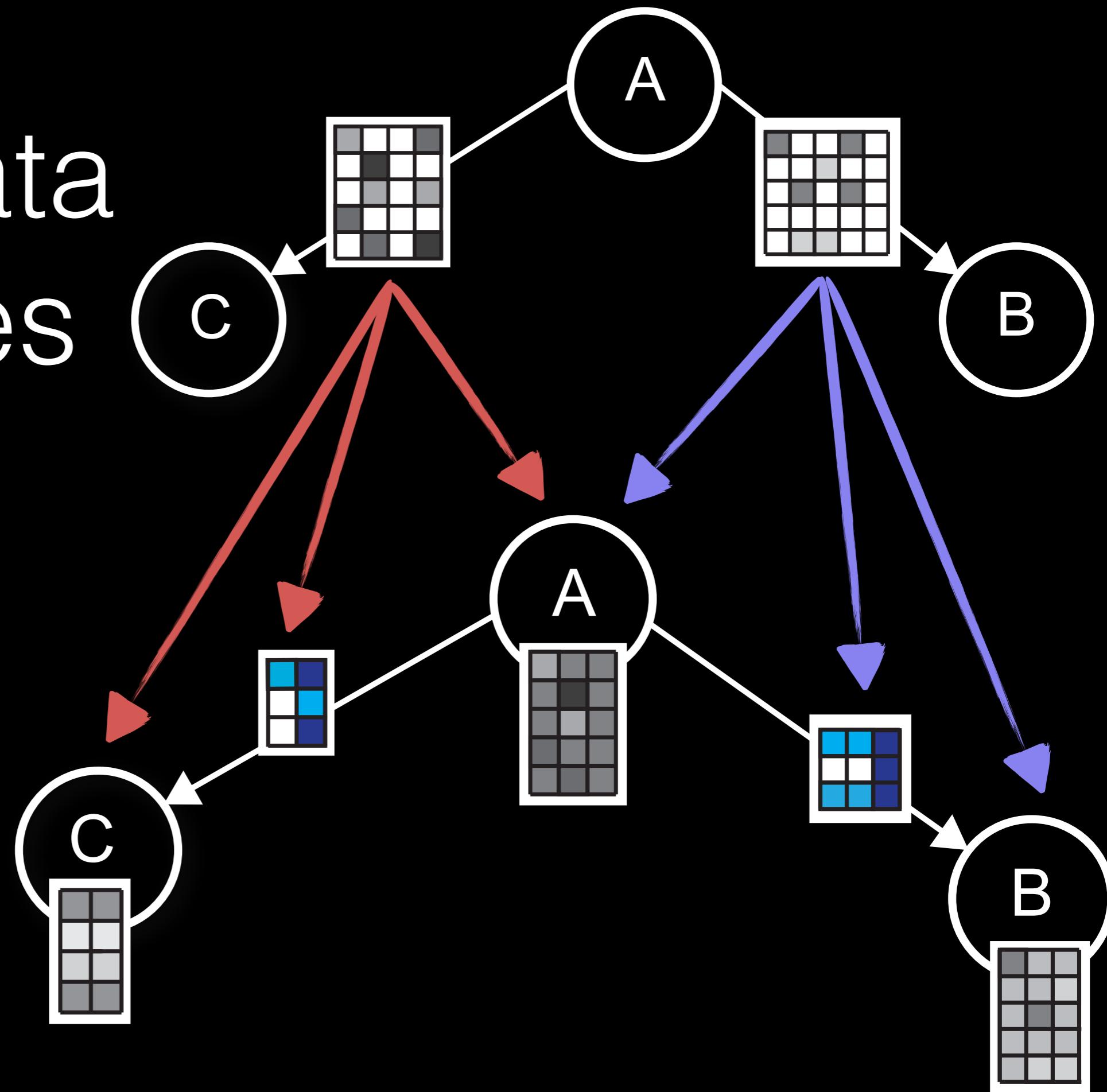
Two Data Matrices



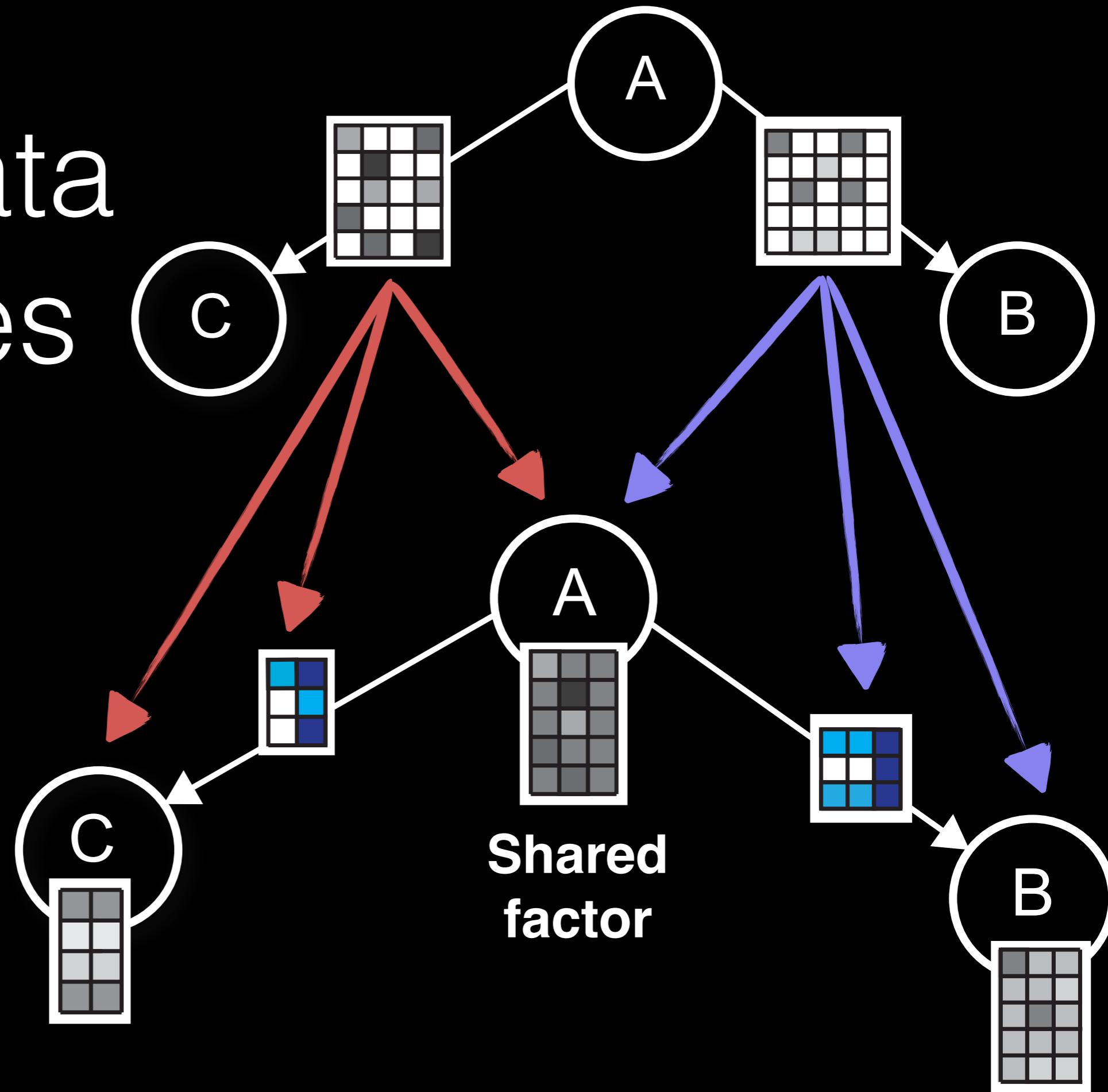
Two Data Matrices



Two Data Matrices

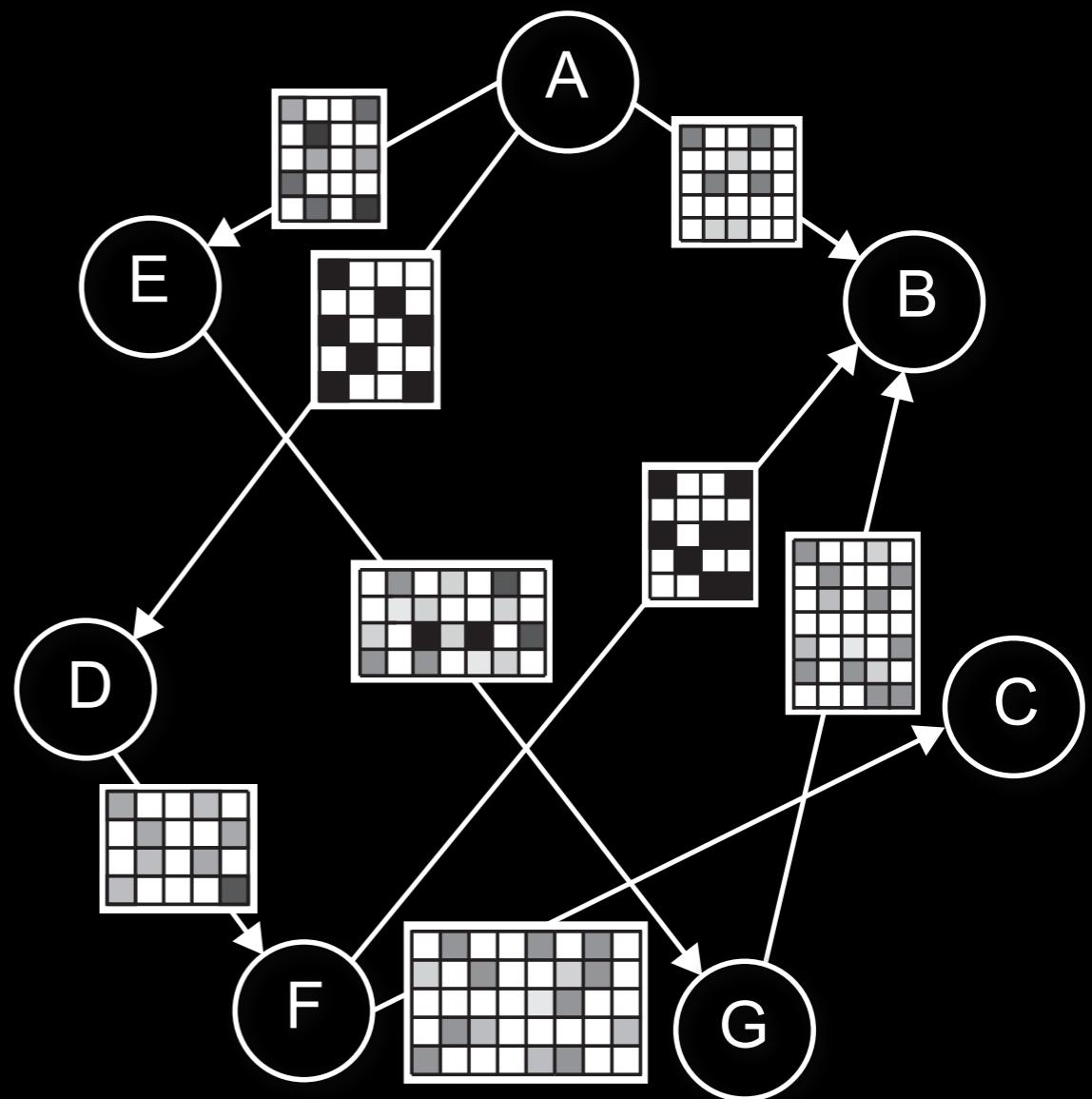


Two Data Matrices

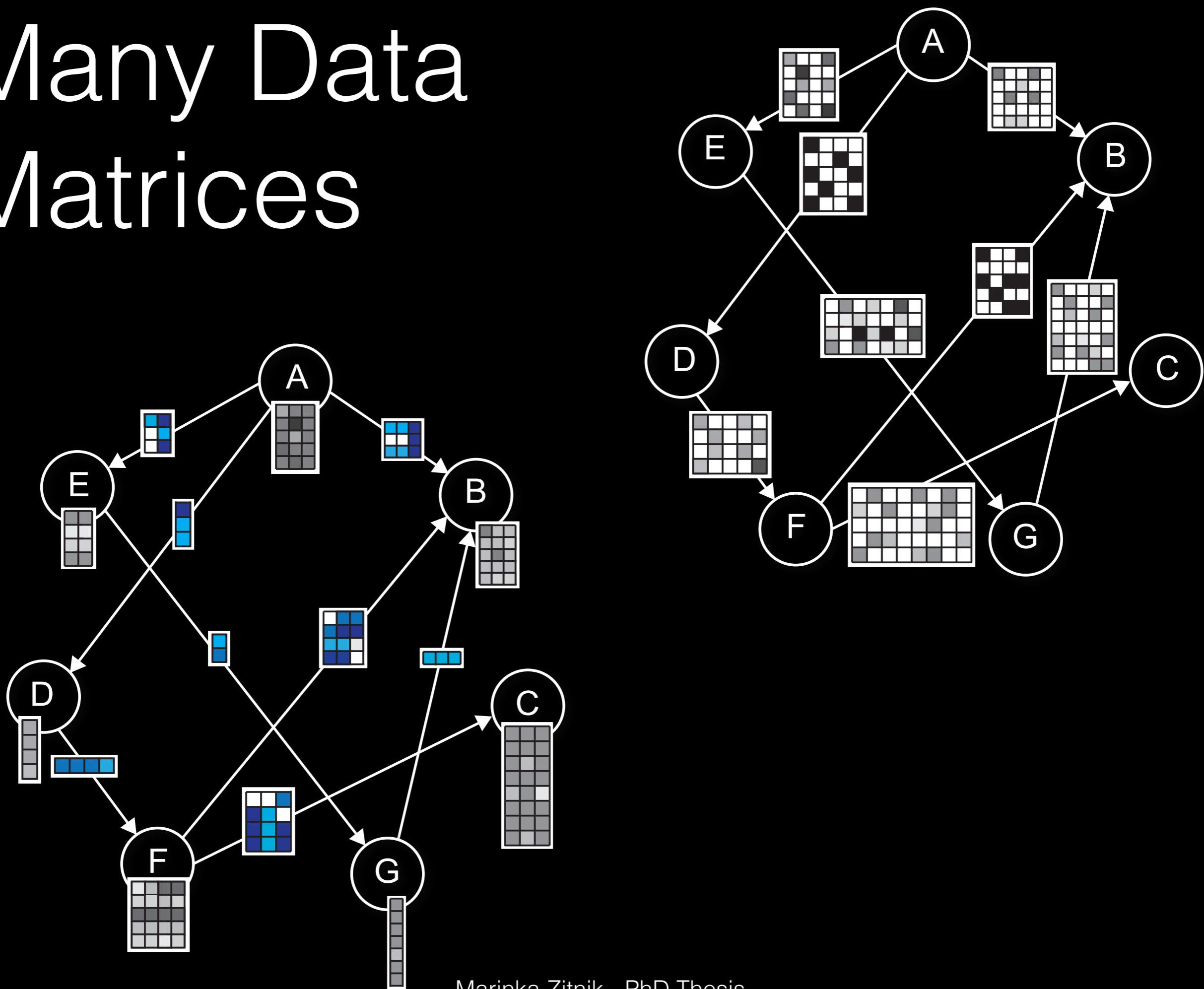


Data Fusion by Collective Matrix Factorization

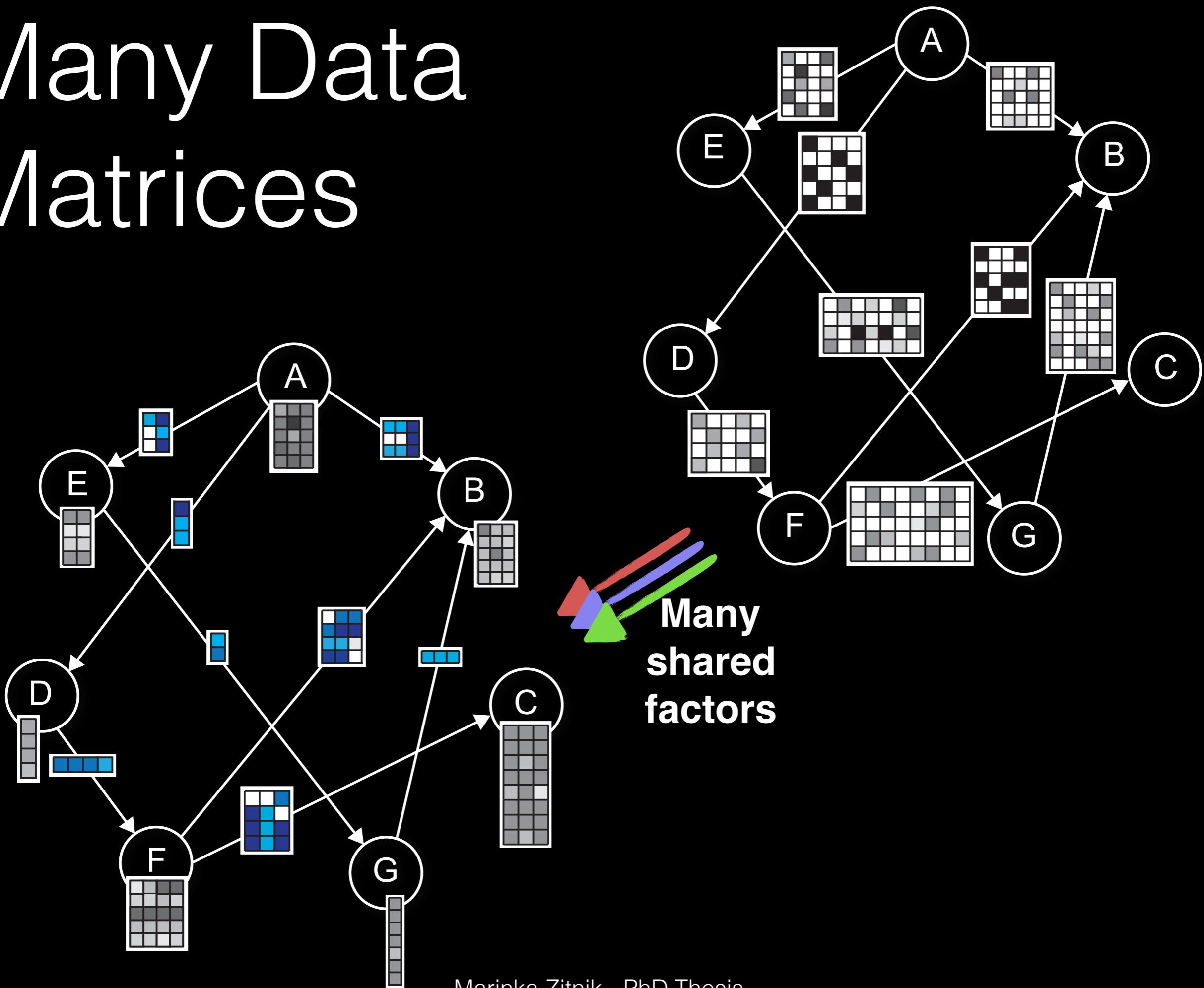
Many Data Matrices



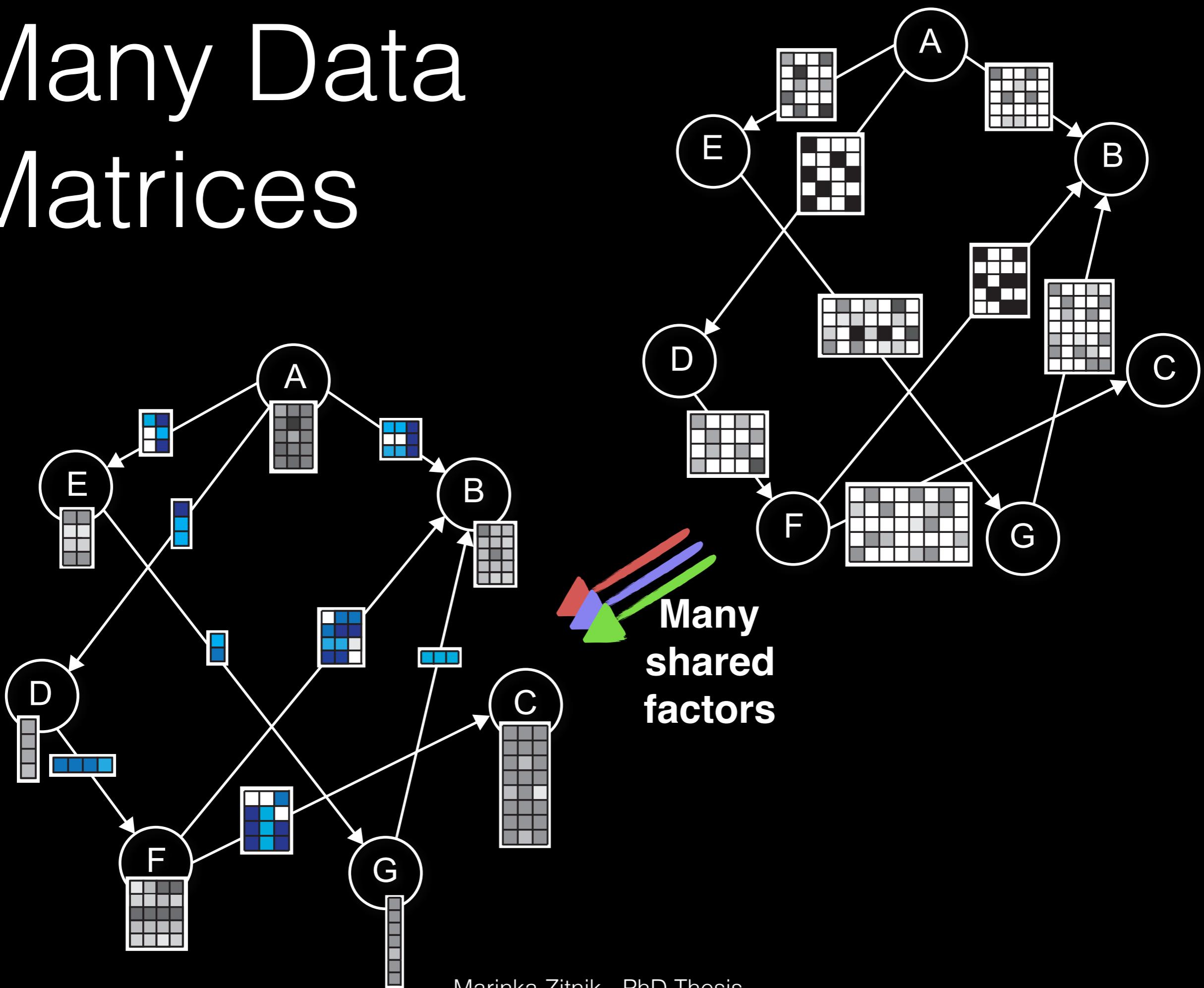
Many Data Matrices



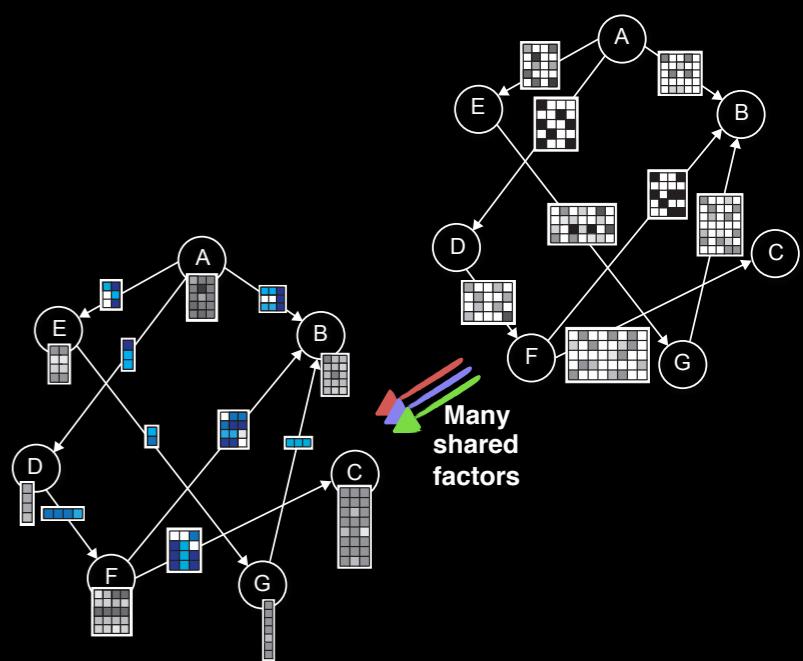
Many Data Matrices



Many Data Matrices

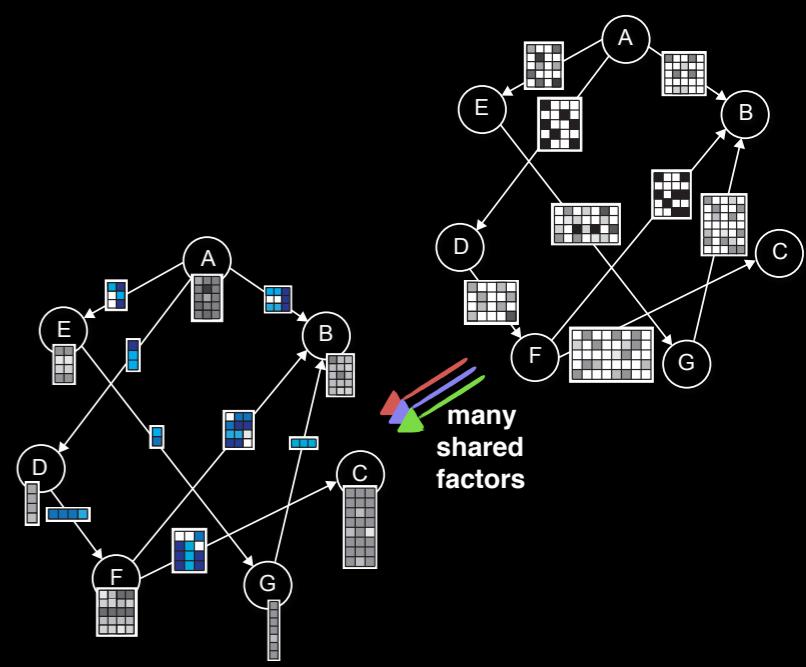


Many Data Matrices



Many Data Matrices

Optimization Problem

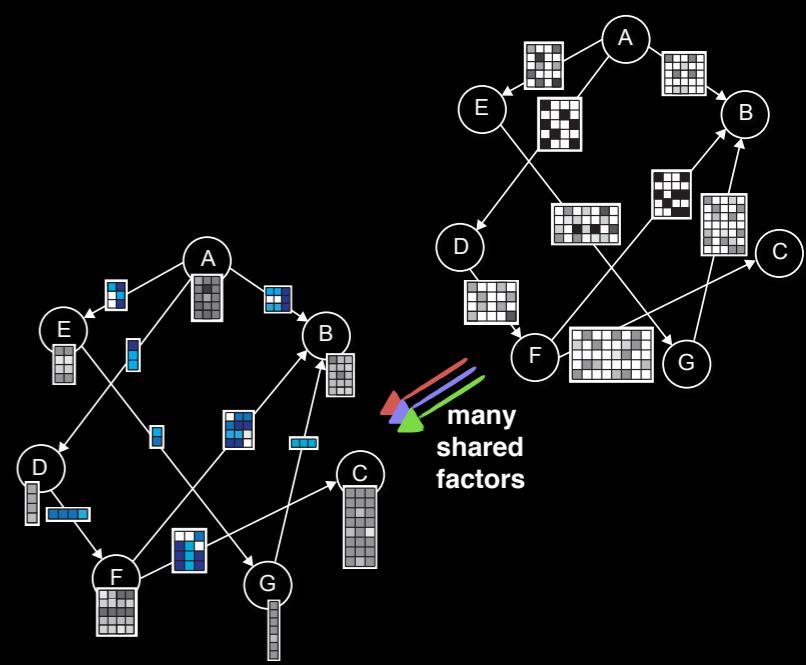


Many Data Matrices Optimization Problem

Given

$$\mathcal{R} = \{\mathbf{R}_{ij}; i \text{ and } j \text{ are object types}\}$$

$$\mathcal{C} = \{\Theta_i^l; l = 1, 2, \dots, l_i, i \text{ is an object type}\}$$



Many Data Matrices Optimization Problem

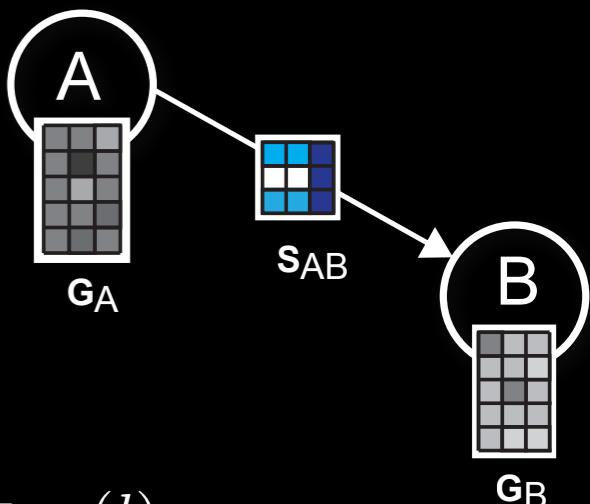
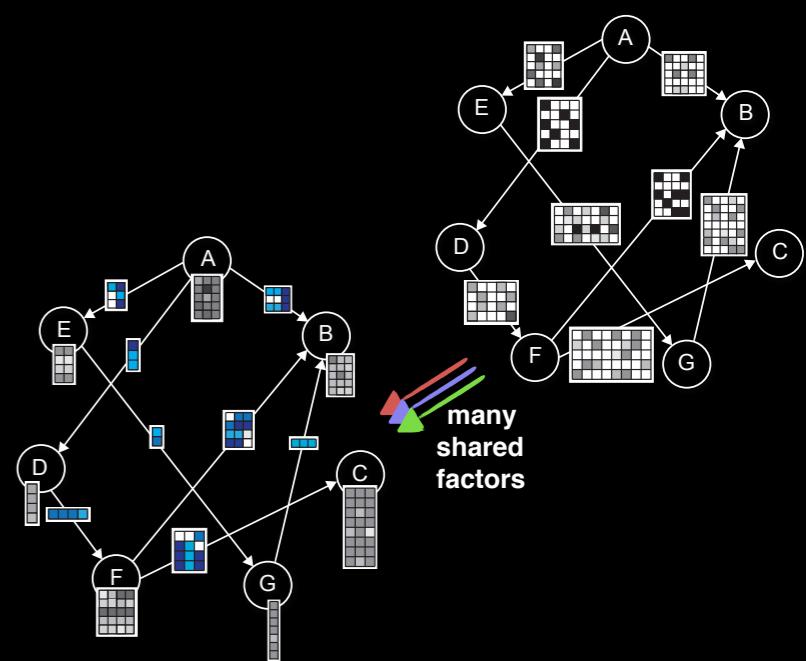
Given

$$\mathcal{R} = \{\mathbf{R}_{ij}; i \text{ and } j \text{ are object types}\}$$

$$\mathcal{C} = \{\Theta_i^l; l = 1, 2, \dots, l_i, i \text{ is an object type}\}$$

Find latent matrices \mathbf{G}_i and \mathbf{S}_{ij} that minimize

$$\min_{\mathbf{G}_i \geq 0, \mathbf{S}_{ij}} \sum_{\mathbf{R}_{ij} \in \mathcal{R}} \|\mathbf{R}_{ij} - \mathbf{G}_i \mathbf{S}_{ij} \mathbf{G}_j^T\|_{\text{Fro}}^2 + \sum_{\Theta_i \in \mathcal{C}} \sum_{l=1}^{l_i} \text{tr}(\mathbf{G}_i^T \Theta_i^{(l)} \mathbf{G}_i)$$



Many Data Matrices Optimization Problem

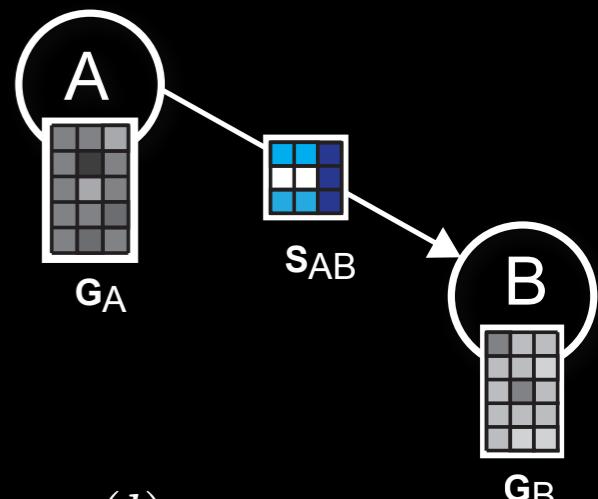
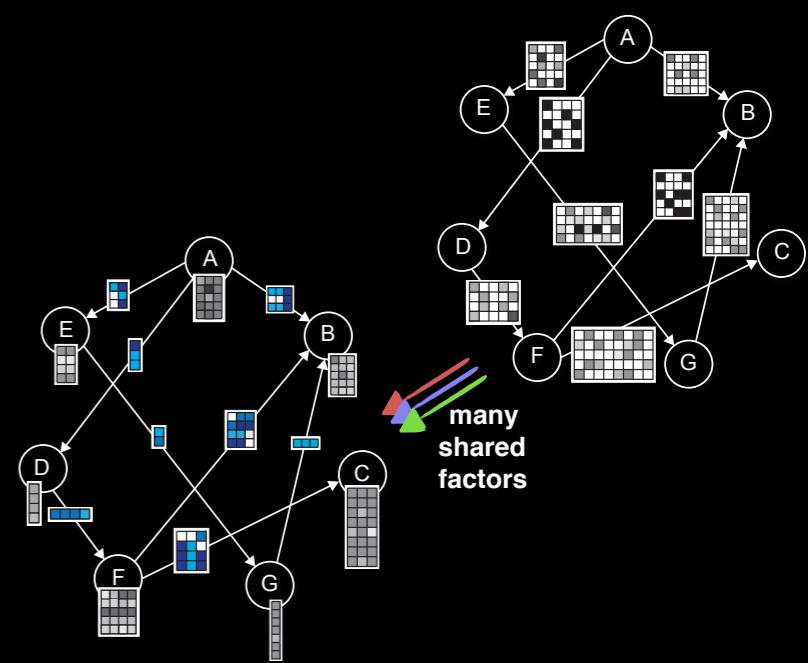
Given

$$\mathcal{R} = \{\mathbf{R}_{ij}; i \text{ and } j \text{ are object types}\}$$

$$\mathcal{C} = \{\Theta_i^l; l = 1, 2, \dots, l_i, i \text{ is an object type}\}$$

Find latent matrices \mathbf{G}_i and \mathbf{S}_{ij} that minimize

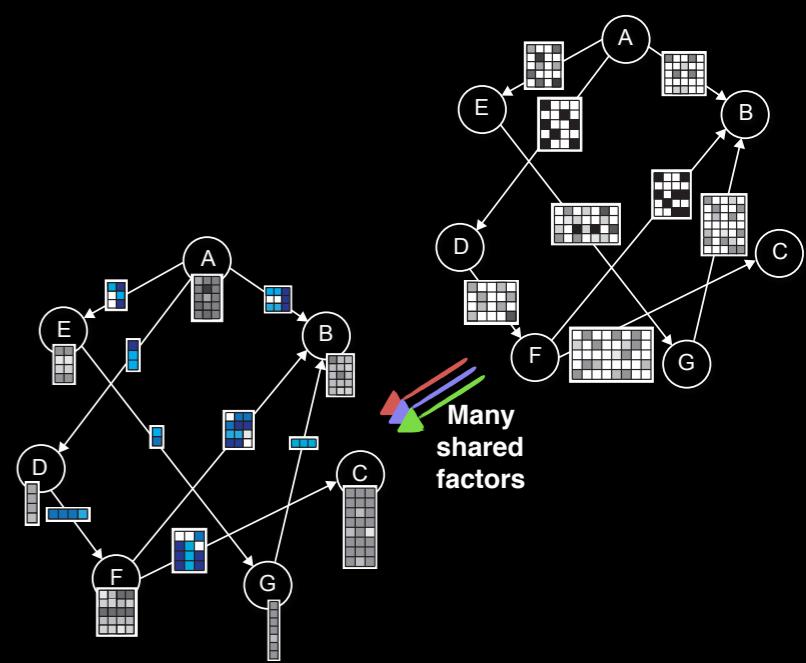
$$\min_{\mathbf{G}_i \geq 0, \mathbf{S}_{ij}} \sum_{\mathbf{R}_{ij} \in \mathcal{R}} \|\mathbf{R}_{ij} - \mathbf{G}_i \mathbf{S}_{ij} \mathbf{G}_j^T\|_{\text{Fro}}^2 + \sum_{\Theta_i \in \mathcal{C}} \sum_{l=1}^{l_i} \text{tr}(\mathbf{G}_i^T \Theta_i^{(l)} \mathbf{G}_i)$$



The problem is non-convex. The global optimum is unknown

Many Data Matrices

Solution: DFMF Algorithm



Many Matrix Solution: DF

Input: A set \mathcal{R} of relation matrices \mathbf{R}_{ij} ; constraint matrices $\Theta^{(t)}$ for $t \in \{1, 2, \dots, \max_i t_i\}$; ranks k_1, k_2, \dots, k_r ($i, j \in [r]$).
Output: Matrix factors \mathbf{S} and \mathbf{G} .

- 1) Initialize \mathbf{G}_i for $i = 1, 2, \dots, r$.
- 2) Repeat until convergence:
 - Construct \mathbf{R} and \mathbf{G} using their definitions in Eq. (1) and Eq. (3).
 - Update \mathbf{S} using:

$$\mathbf{S} \leftarrow (\mathbf{G}^T \mathbf{G})^{-1} \mathbf{G}^T \mathbf{R} \mathbf{G} (\mathbf{G}^T \mathbf{G})^{-1}.$$

- Set $\mathbf{G}_i^{(e)} \leftarrow \mathbf{0}$ for $i = 1, 2, \dots, r$.
- Set $\mathbf{G}_i^{(d)} \leftarrow \mathbf{0}$ for $i = 1, 2, \dots, r$.
- For $\mathbf{R}_{ij} \in \mathcal{R}$:

$$\begin{aligned} \mathbf{G}_i^{(e)} &+= (\mathbf{R}_{ij} \mathbf{G}_j \mathbf{S}_{ij}^T)^+ + \mathbf{G}_i (\mathbf{S}_{ij} \mathbf{G}_j^T \mathbf{G}_j \mathbf{S}_{ij}^T)^- \\ \mathbf{G}_i^{(d)} &+= (\mathbf{R}_{ij} \mathbf{G}_j \mathbf{S}_{ij}^T)^- + \mathbf{G}_i (\mathbf{S}_{ij} \mathbf{G}_j^T \mathbf{G}_j \mathbf{S}_{ij}^T)^+ \\ \mathbf{G}_j^{(e)} &+= (\mathbf{R}_{ij}^T \mathbf{G}_i \mathbf{S}_{ij})^+ + \mathbf{G}_j (\mathbf{S}_{ij}^T \mathbf{G}_i^T \mathbf{G}_i \mathbf{S}_{ij})^- \\ \mathbf{G}_j^{(d)} &+= (\mathbf{R}_{ij}^T \mathbf{G}_i \mathbf{S}_{ij})^- + \mathbf{G}_j (\mathbf{S}_{ij}^T \mathbf{G}_i^T \mathbf{G}_i \mathbf{S}_{ij})^+ \end{aligned} \quad (10)$$

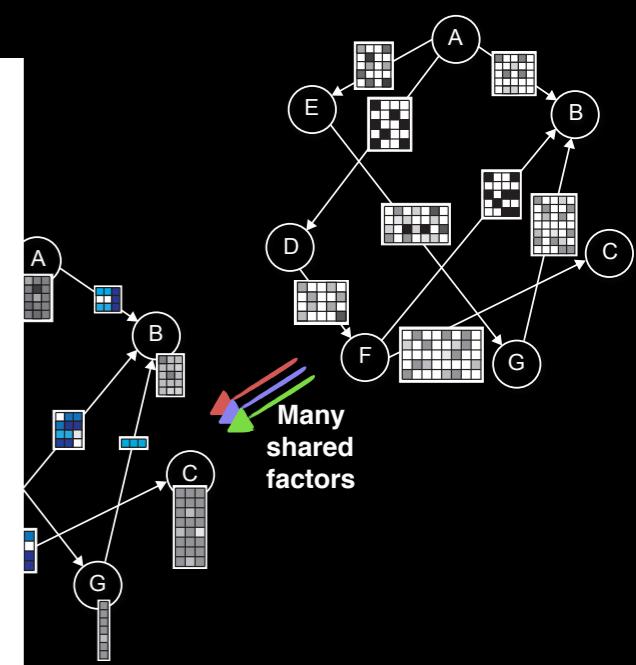
- For $t = 1, 2, \dots, \max_i t_i$:

$$\begin{aligned} \mathbf{G}_i^{(e)} &+= [\Theta_i^{(t)}]^- \mathbf{G}_i \quad \text{for } i = 1, 2, \dots, r \\ \mathbf{G}_i^{(d)} &+= [\Theta_i^{(t)}]^+ \mathbf{G}_i \quad \text{for } i = 1, 2, \dots, r \end{aligned} \quad (11)$$

- Construct \mathbf{G} as:

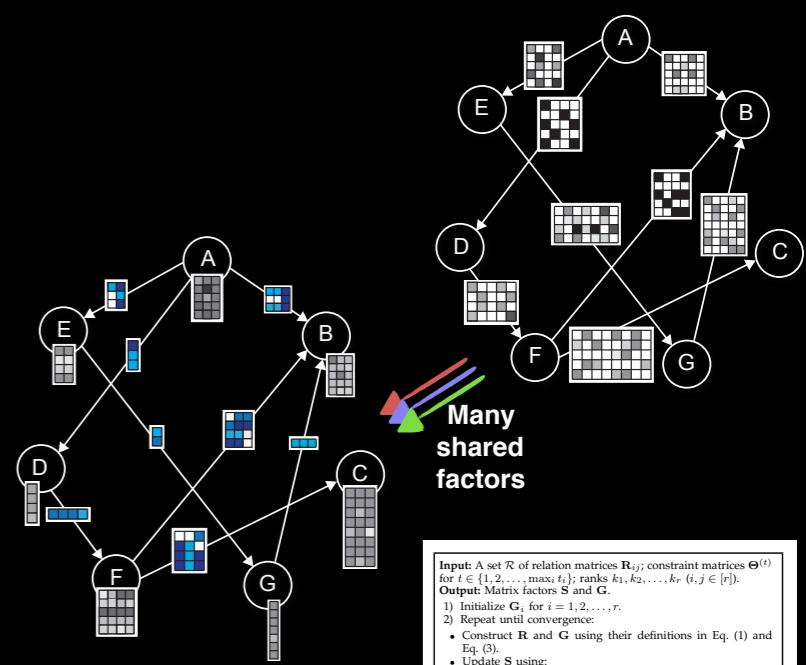
$$\mathbf{G} \leftarrow \mathbf{G} \circ \text{Diag}\left(\sqrt{\frac{\mathbf{G}_1^{(e)}}{\mathbf{G}_1^{(d)}}}, \sqrt{\frac{\mathbf{G}_2^{(e)}}{\mathbf{G}_2^{(d)}}}, \dots, \sqrt{\frac{\mathbf{G}_r^{(e)}}{\mathbf{G}_r^{(d)}}}\right), \quad (12)$$

where \circ denotes the Hadamard product. The $\sqrt{\cdot}$ and \div are entry-wise operations.



Many Data Matrices

Solution: DFMF Algorithm



Input: A set \mathcal{R} of relation matrices R_{ij} ; constraint matrices $\Theta^{(t)}$ for $t \in \{1, 2, \dots, \max_i t_i\}$; ranks k_1, k_2, \dots, k_r ($i, j \in [r]$).
Output: Matrix factors \mathbf{S} and \mathbf{G} .

- 1) Initialize \mathbf{G}_i for $i = 1, 2, \dots, r$.
- 2) Repeat until convergence:
 - Construct \mathbf{R} and \mathbf{G} using their definitions in Eq. (1) and Eq. (3).
 - Update \mathbf{S} using:

$$\mathbf{S} \leftarrow (\mathbf{G}^T \mathbf{G})^{-1} \mathbf{G}^T \mathbf{R} \mathbf{G} (\mathbf{G}^T \mathbf{G})^{-1}.$$
 - Set $\mathbf{G}_i^{(e)} \leftarrow \mathbf{0}$ for $i = 1, 2, \dots, r$.
 - Set $\mathbf{G}_i^{(d)} \leftarrow \mathbf{0}$ for $i = 1, 2, \dots, r$.
 - For $\mathbf{R}_{ij} \in \mathcal{R}$:
 - $\mathbf{G}_i^{(e)} \quad + = \quad (\mathbf{R}_{ij} \mathbf{G}_j \mathbf{S}_{ij}^T)^+ + \mathbf{G}_i (\mathbf{S}_{ij} \mathbf{G}_j^T \mathbf{G}_j \mathbf{S}_{ij}^T)^-$
 - $\mathbf{G}_i^{(d)} \quad + = \quad (\mathbf{R}_{ij} \mathbf{G}_j \mathbf{S}_{ij}^T)^- + \mathbf{G}_i (\mathbf{S}_{ij} \mathbf{G}_j^T \mathbf{G}_j \mathbf{S}_{ij}^T)^+$
 - $\mathbf{G}_j^{(e)} \quad + = \quad (\mathbf{R}_i^T \mathbf{G}_i \mathbf{S}_{ij})^+ + \mathbf{G}_j (\mathbf{S}_i^T \mathbf{G}_i^T \mathbf{G}_i \mathbf{S}_{ij})^-$
 - $\mathbf{G}_j^{(d)} \quad + = \quad (\mathbf{R}_i^T \mathbf{G}_i \mathbf{S}_{ij})^- + \mathbf{G}_j (\mathbf{S}_i^T \mathbf{G}_i^T \mathbf{G}_i \mathbf{S}_{ij})^+$ (10)
- For $t = 1, 2, \dots, \max_i t_i$:

 - $\mathbf{G}_i^{(e)} \quad + = \quad [\Theta_i^{(t)}]^- \mathbf{G}_i \quad \text{for } i = 1, 2, \dots, r$
 - $\mathbf{G}_i^{(d)} \quad + = \quad [\Theta_i^{(t)}]^+ \mathbf{G}_i \quad \text{for } i = 1, 2, \dots, r$ (11)

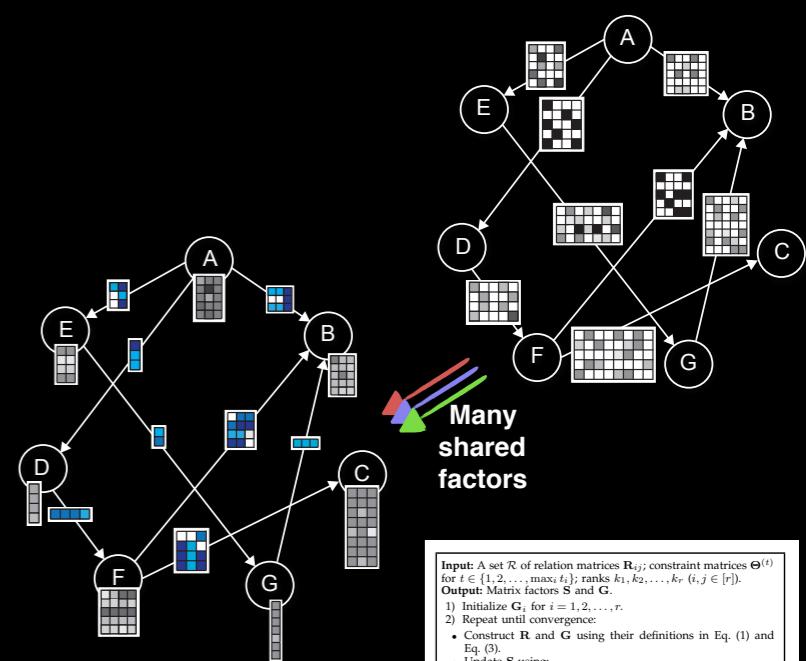
- Construct \mathbf{G} as:

$$\mathbf{G} \leftarrow \mathbf{G} \circ \text{Diag}\left(\sqrt{\frac{\mathbf{G}_1^{(e)}}{\mathbf{G}_1^{(d)}}}, \sqrt{\frac{\mathbf{G}_2^{(e)}}{\mathbf{G}_2^{(d)}}}, \dots, \sqrt{\frac{\mathbf{G}_r^{(e)}}{\mathbf{G}_r^{(d)}}}\right), \quad (12)$$

where \circ denotes the Hadamard product. The $\sqrt{\cdot}$ and $\frac{\cdot}{\cdot}$ are entry-wise operations.

Many Data Matrices

Solution: DFMF Algorithm



Input: A set \mathcal{R} of relation matrices \mathbf{R}_{ij} ; constraint matrices $\Theta^{(t)}$ for $t \in \{1, 2, \dots, \max_i t_i\}$; ranks k_1, k_2, \dots, k_r ($i, j \in [r]$).
 Output: Matrix factors \mathbf{S} and \mathbf{G} .

- 1) Initialize \mathbf{G}_i for $i = 1, 2, \dots, r$.
- 2) Repeat until convergence:
 - Construct \mathbf{R} and \mathbf{G} using their definitions in Eq. (I) and Eq. (3).
 - Update \mathbf{S} using:

$$\mathbf{S} \leftarrow (\mathbf{G}^T \mathbf{G})^{-1} \mathbf{G}^T \mathbf{R} \mathbf{G} (\mathbf{G}^T \mathbf{G})^{-1}.$$
 - Set $\mathbf{G}_i^{(e)} \leftarrow \mathbf{0}$ for $i = 1, 2, \dots, r$.
 - Set $\mathbf{G}_i^{(d)} \leftarrow \mathbf{0}$ for $i = 1, 2, \dots, r$.
 - For $\mathbf{R}_{ij} \in \mathcal{R}$:
 - $\mathbf{G}_i^{(e)} \quad + = \quad (\mathbf{R}_{ij} \mathbf{G}_j \mathbf{S}_{ij}^T)^+ + \mathbf{G}_i (\mathbf{S}_{ij} \mathbf{G}_j^T \mathbf{G}_j \mathbf{S}_{ij}^T)^-$
 - $\mathbf{G}_i^{(d)} \quad + = \quad (\mathbf{R}_{ij} \mathbf{G}_j \mathbf{S}_{ij}^T)^- + \mathbf{G}_i (\mathbf{S}_{ij} \mathbf{G}_j^T \mathbf{G}_j \mathbf{S}_{ij}^T)^+$
 - $\mathbf{G}_j^{(e)} \quad + = \quad (\mathbf{R}_{ij}^T \mathbf{G}_i \mathbf{S}_{ij})^+ + \mathbf{G}_j (\mathbf{S}_{ij}^T \mathbf{G}_i^T \mathbf{G}_i \mathbf{S}_{ij})^-$
 - $\mathbf{G}_j^{(d)} \quad + = \quad (\mathbf{R}_{ij}^T \mathbf{G}_i \mathbf{S}_{ij})^- + \mathbf{G}_j (\mathbf{S}_{ij}^T \mathbf{G}_i^T \mathbf{G}_i \mathbf{S}_{ij})^+$ (10)
- For $t = 1, 2, \dots, \max_i t_i$:
 - $\mathbf{G}_i^{(e)} \quad + = \quad [\Theta_i^{(t)}]^- \mathbf{G}_i \quad \text{for } i = 1, 2, \dots, r$
 - $\mathbf{G}_i^{(d)} \quad + = \quad [\Theta_i^{(t)}]^+ \mathbf{G}_i \quad \text{for } i = 1, 2, \dots, r$ (11)
- Construct \mathbf{G} as:

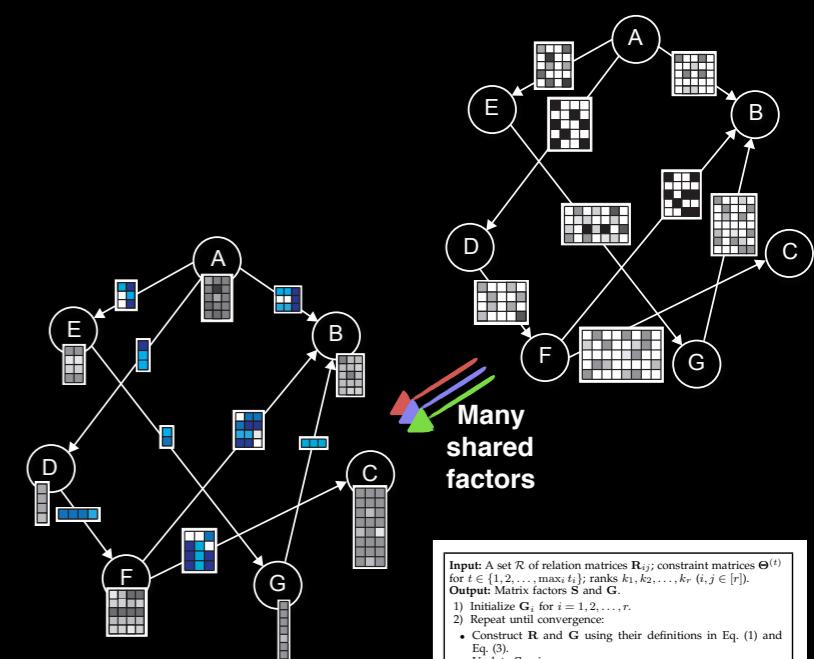
$$\mathbf{G} \leftarrow \mathbf{G} \circ \text{Diag}\left(\sqrt{\frac{\mathbf{G}_1^{(e)}}{\mathbf{G}_1^{(d)}}}, \sqrt{\frac{\mathbf{G}_2^{(e)}}{\mathbf{G}_2^{(d)}}}, \dots, \sqrt{\frac{\mathbf{G}_r^{(e)}}{\mathbf{G}_r^{(d)}}}\right), \quad (12)$$

where \circ denotes the Hadamard product. The $\sqrt{\cdot}$ and $\frac{\cdot}{\cdot}$ are entry-wise operations.

Theorem 1 (Correctness of DFMF algorithm): If the update rules for matrix factors \mathbf{G}_i and \mathbf{S}_{ij} from the DFMF algorithm converge, then the final solution satisfies the Karush-Kuhn-Tucker conditions of optimality.

Many Data Matrices

Solution: DFMF Algorithm



Input: A set \mathcal{R} of relation matrices \mathbf{R}_{ij} ; constraint matrices $\Theta^{(t)}$ for $t \in \{1, 2, \dots, \max_i t_i\}$; ranks k_1, k_2, \dots, k_r ($i, j \in [r]$).
Output: Matrix factors \mathbf{S} and \mathbf{G} .

- 1) Initialize \mathbf{G}_i for $i = 1, 2, \dots, r$.
- 2) Repeat until convergence:
 - Construct \mathbf{R} and \mathbf{G} using their definitions in Eq. (1) and Eq. (3).
 - Update \mathbf{S} using:
$$\mathbf{S} \leftarrow (\mathbf{G}^T \mathbf{G})^{-1} \mathbf{G}^T \mathbf{R} \mathbf{G} (\mathbf{G}^T \mathbf{G})^{-1}.$$
 - Set $\mathbf{G}_i^{(e)} \leftarrow \mathbf{0}$ for $i = 1, 2, \dots, r$.
 - Set $\mathbf{G}_i^{(d)} \leftarrow \mathbf{0}$ for $i = 1, 2, \dots, r$.
 - For $\mathbf{R}_{ij} \in \mathcal{R}$:
 - $\mathbf{G}_i^{(e)} \quad + = \quad (\mathbf{R}_{ij} \mathbf{G}_j \mathbf{S}_{ij}^T)^+ + \mathbf{G}_i (\mathbf{S}_{ij} \mathbf{G}_j^T \mathbf{G}_j \mathbf{S}_{ij}^T)^-$
 - $\mathbf{G}_i^{(d)} \quad + = \quad (\mathbf{R}_{ij} \mathbf{G}_j \mathbf{S}_{ij}^T)^- + \mathbf{G}_i (\mathbf{S}_{ij} \mathbf{G}_j^T \mathbf{G}_j \mathbf{S}_{ij}^T)^+$
 - $\mathbf{G}_j^{(e)} \quad + = \quad (\mathbf{R}_i^T \mathbf{G}_i \mathbf{S}_{ij})^+ + \mathbf{G}_j (\mathbf{S}_i^T \mathbf{G}_i^T \mathbf{G}_i \mathbf{S}_{ij})^-$
 - $\mathbf{G}_j^{(d)} \quad + = \quad (\mathbf{R}_i^T \mathbf{G}_i \mathbf{S}_{ij})^- + \mathbf{G}_j (\mathbf{S}_i^T \mathbf{G}_i^T \mathbf{G}_i \mathbf{S}_{ij})^+$ (10)
- For $t = 1, 2, \dots, \max_i t_i$:

 - $\mathbf{G}_i^{(e)} \quad + = \quad [\Theta_i^{(t)}]^- \mathbf{G}_i \quad \text{for } i = 1, 2, \dots, r$
 - $\mathbf{G}_i^{(d)} \quad + = \quad [\Theta_i^{(t)}]^+ \mathbf{G}_i \quad \text{for } i = 1, 2, \dots, r$ (11)

- Construct \mathbf{G} as:

$$\mathbf{G} \leftarrow \mathbf{G} \circ \text{Diag}\left(\sqrt{\frac{\mathbf{G}_1^{(e)}}{\mathbf{G}_1^{(d)}}}, \sqrt{\frac{\mathbf{G}_2^{(e)}}{\mathbf{G}_2^{(d)}}}, \dots, \sqrt{\frac{\mathbf{G}_r^{(e)}}{\mathbf{G}_r^{(d)}}}\right), \quad (12)$$

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Theorem 1 (Correctness of DFMF algorithm): If the update rules for matrix factors \mathbf{G}_i and \mathbf{S}_{ij} from the DFMF algorithm converge, then the final solution satisfies the Karush-Kuhn-Tucker conditions of optimality.

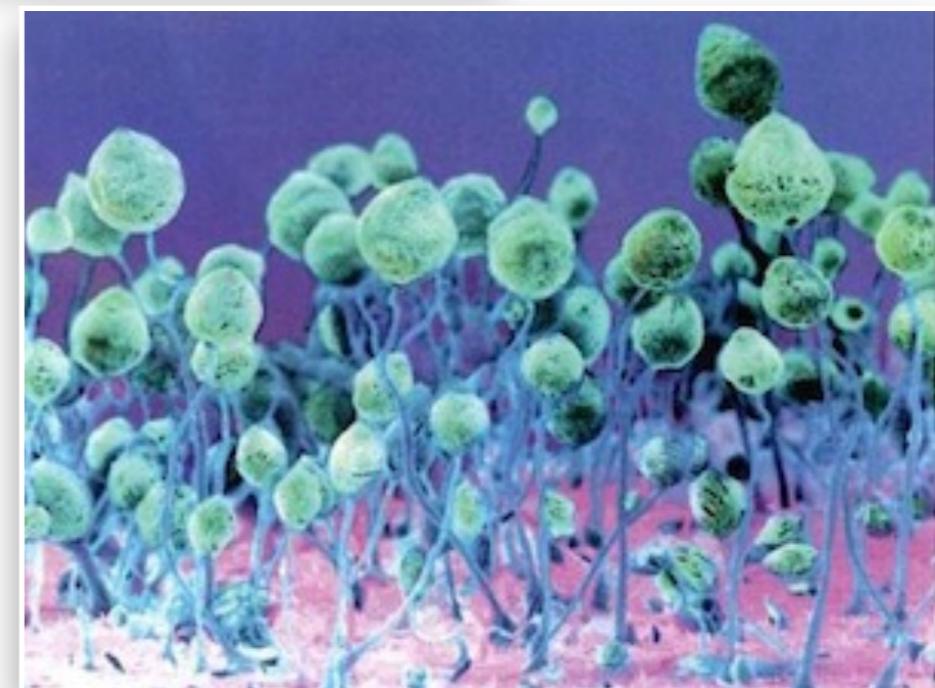
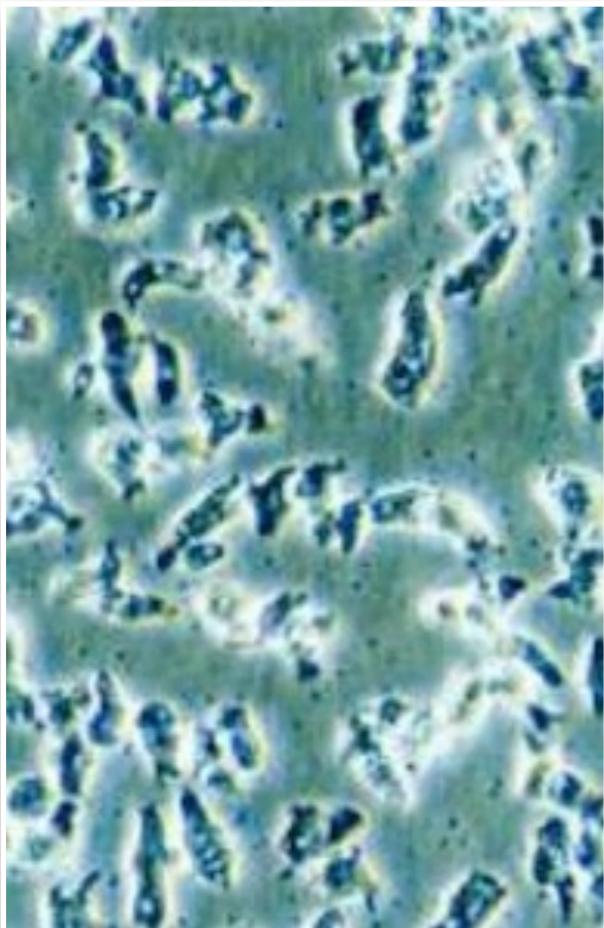
Theorem 2 (Convergence of DFMF algorithm): The objective function:

$$\min_{\mathbf{G}_i \geq 0, \mathbf{S}_{ij}} \sum_{\mathbf{R}_{ij} \in \mathcal{R}} \|\mathbf{R}_{ij} - \mathbf{G}_i \mathbf{S}_{ij} \mathbf{G}_j^T\|_{\text{Fro}}^2 + \sum_{\Theta_i \in \mathcal{C}} \sum_{l=1}^{l_i} \text{tr}(\mathbf{G}_i^T \Theta_i^{(l)} \mathbf{G}_i)$$

is nonincreasing under the updating rules for matrix factors \mathbf{G}_i and \mathbf{S}_{ij} given by DFMF algorithm.

Two Case Studies of Collective Matrix Factorization

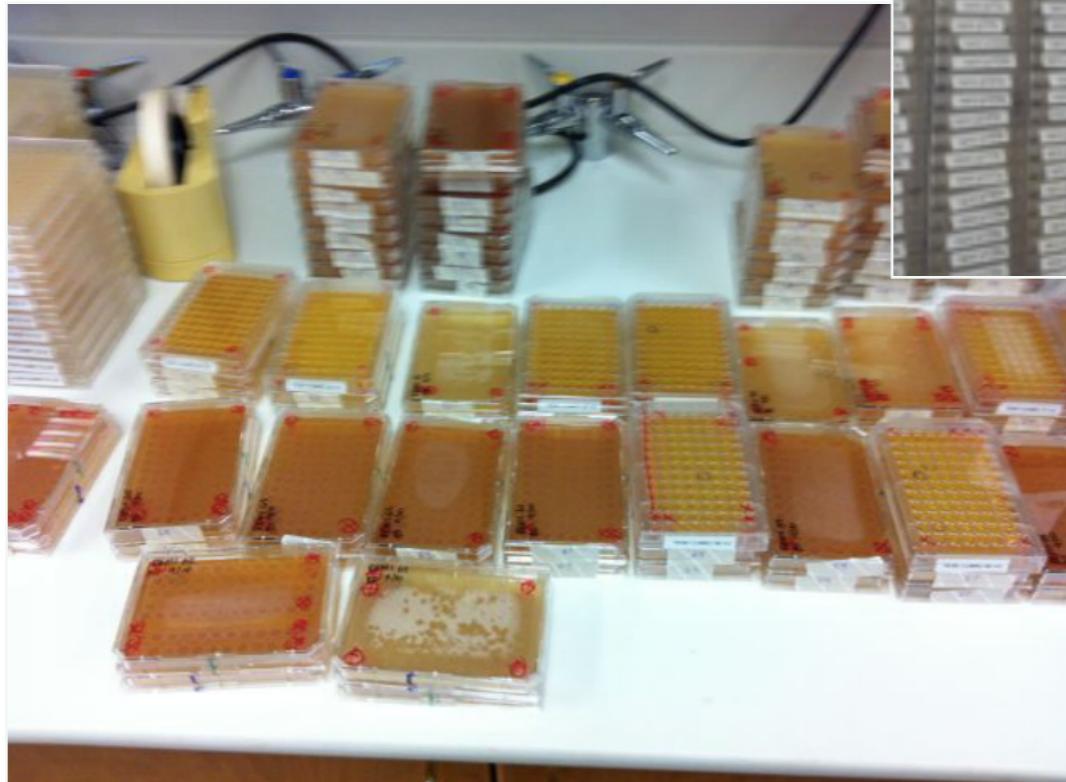
#1: Amoeba



Search for Bacterial Response Genes

50,000 clonal mutants

genetic screen



genome 12,000 genes
found 7 genes
workload 5 years
estimated ~200 genes

Gram+ defective:
swp1, gpi, nagB1

Gram- defective:
clkB, spc3, alyL, nip7

Dictyostelium Bacterial Gene Hunt

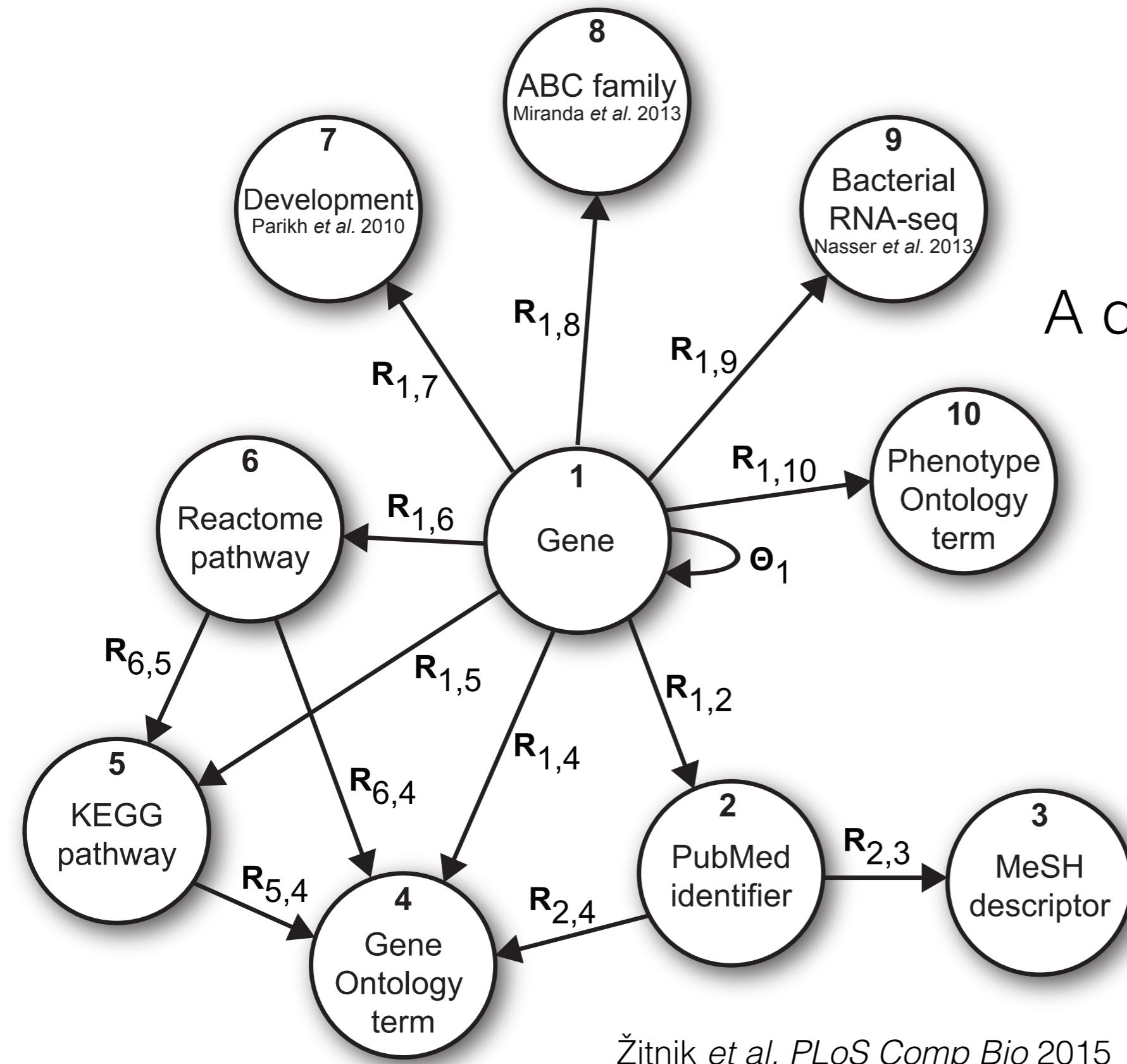
A data-driven approach

14 data sources
4 Gram- seed genes
9 candidate genes

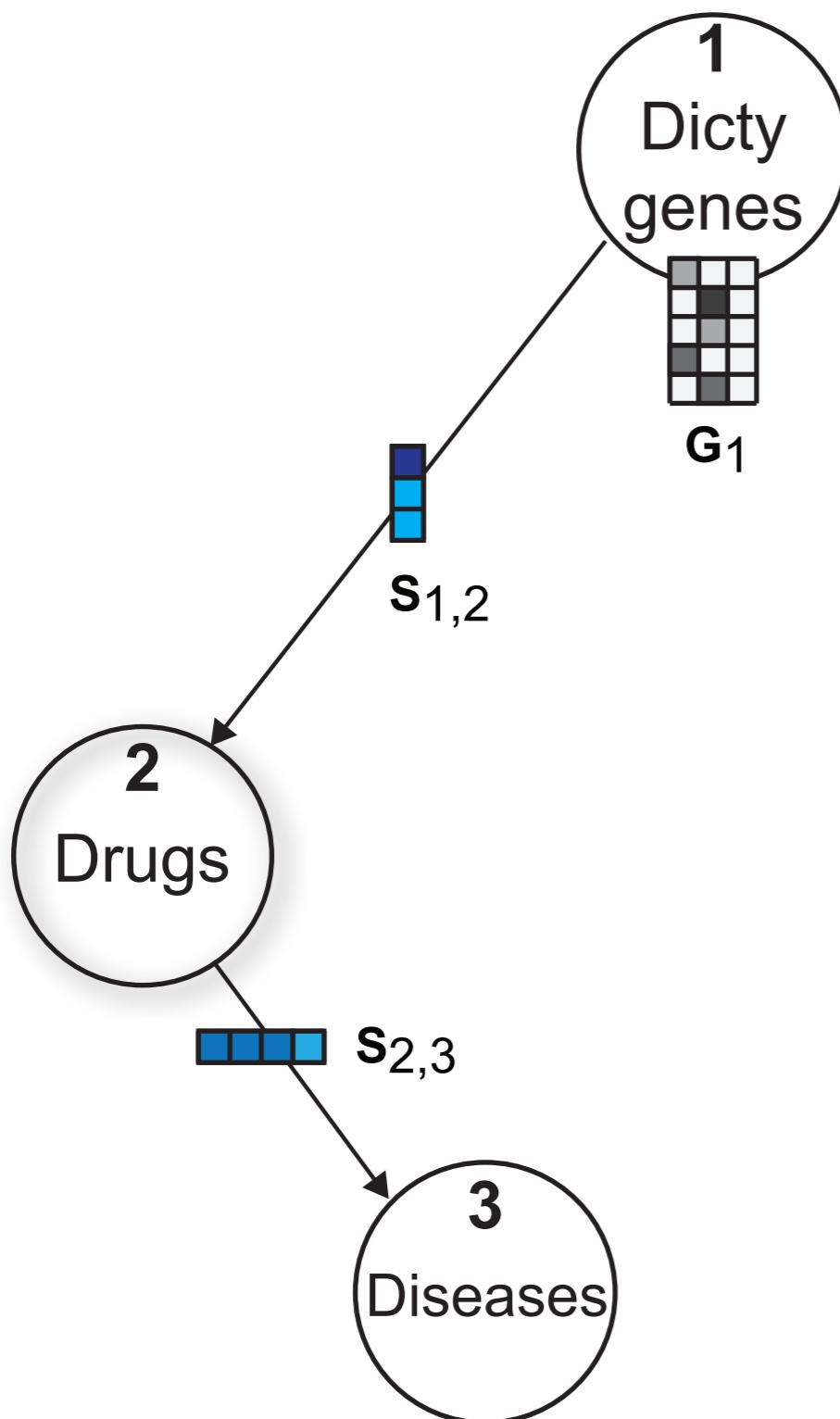
Dictyostelium Bacterial Gene Hunt

A data-driven approach

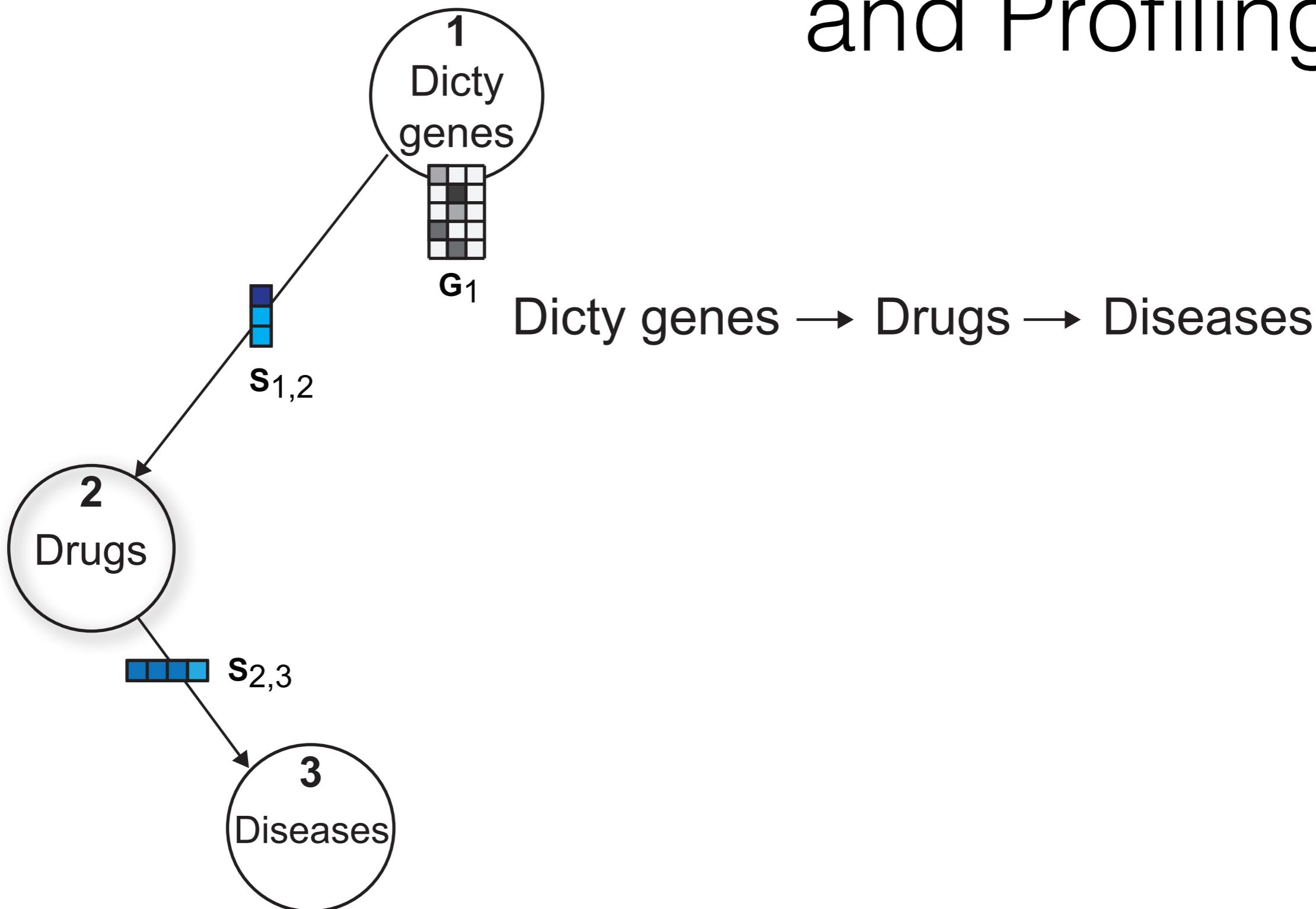
14 data sources
4 Gram- seed genes
9 candidate genes



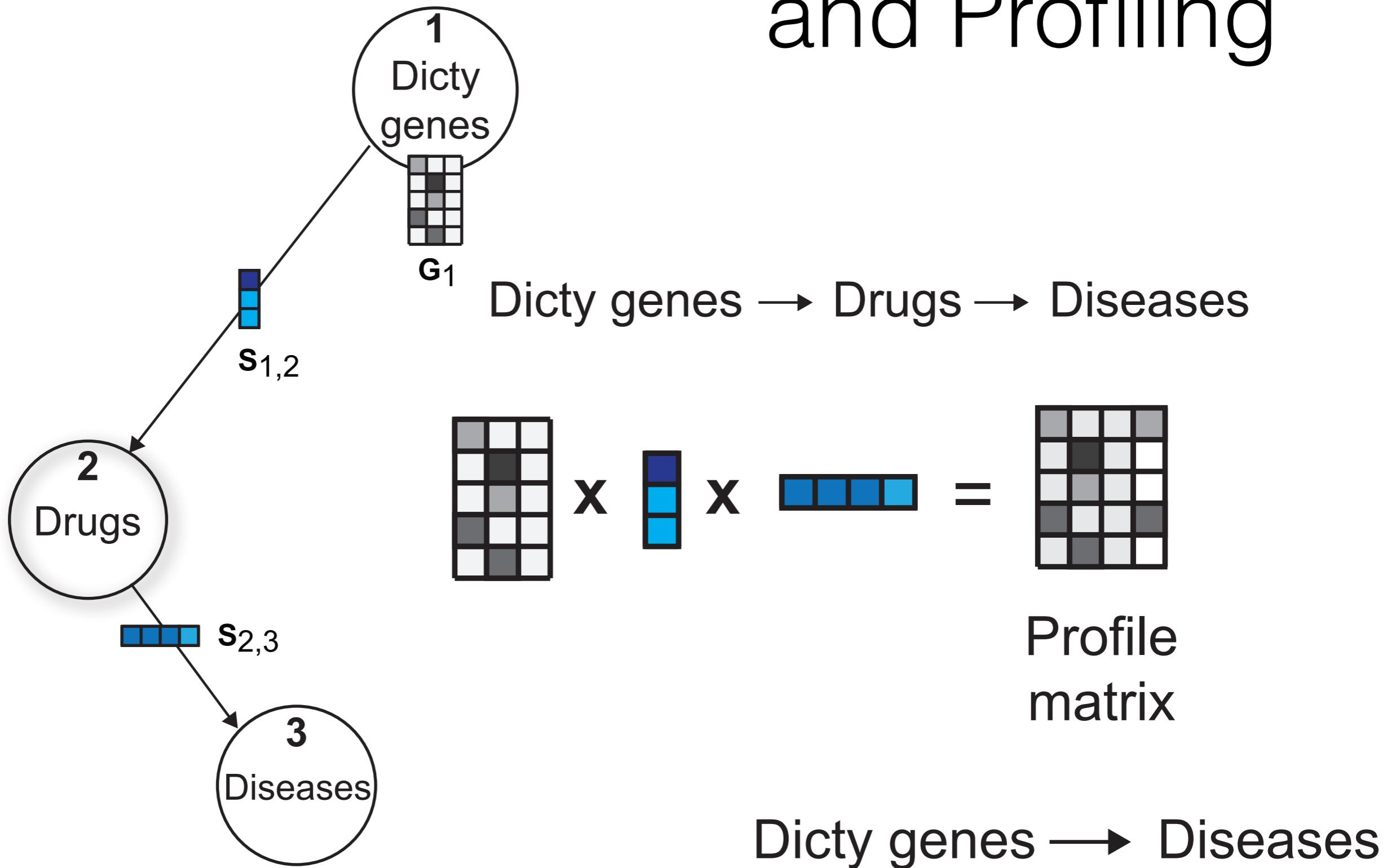
Latent Chaining and Profiling

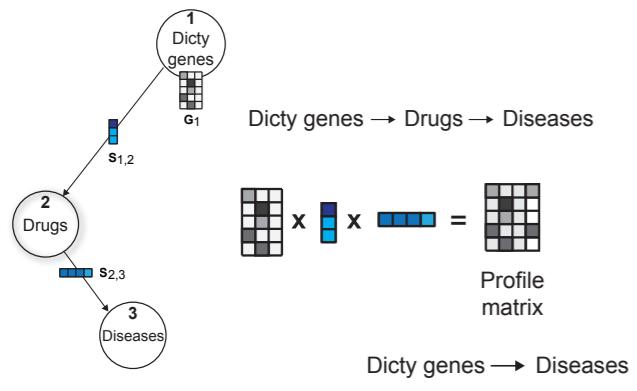


Latent Chaining and Profiling



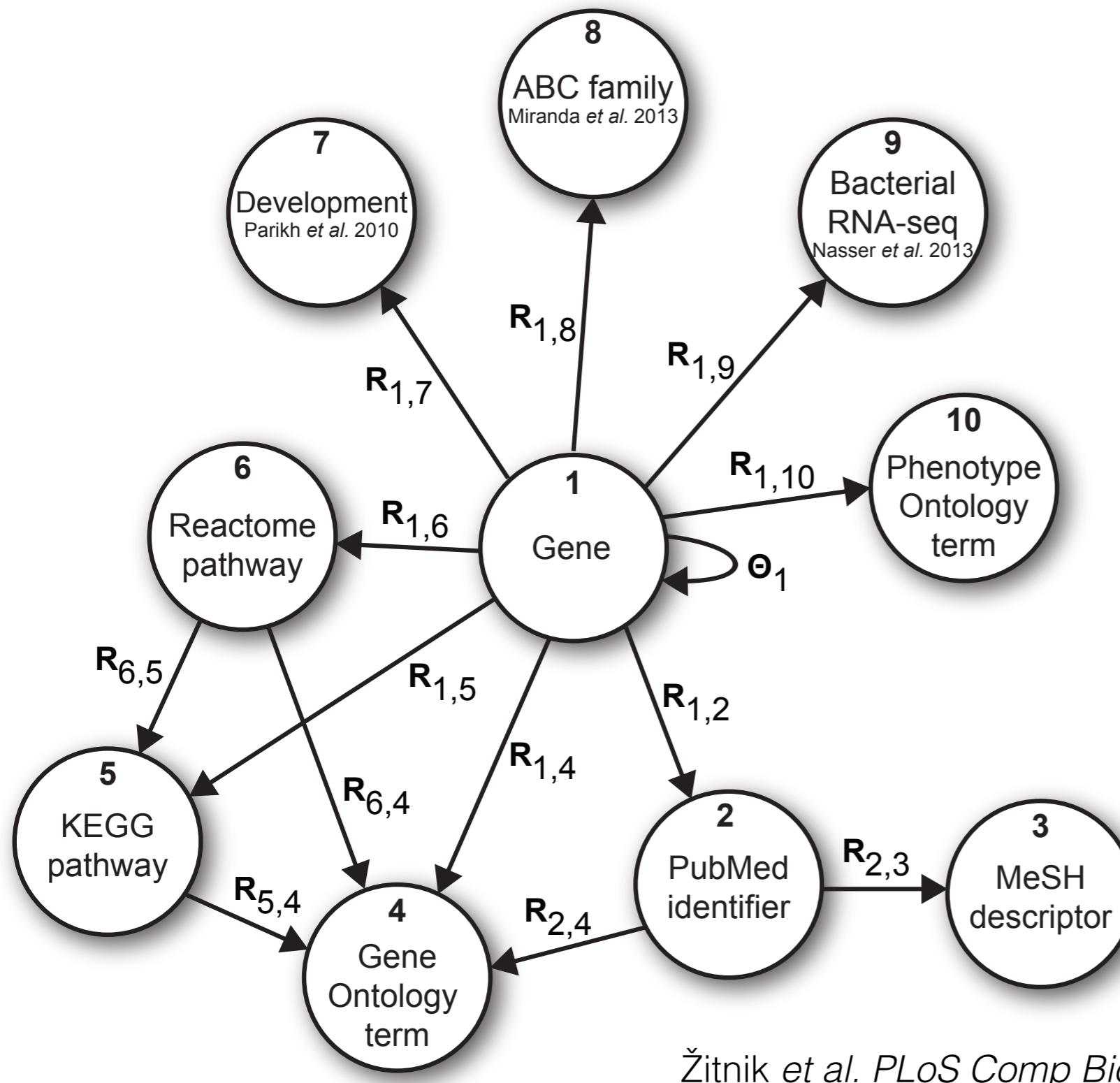
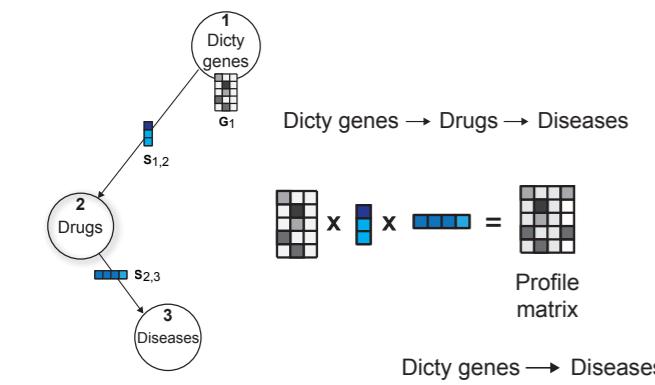
Latent Chaining and Profiling



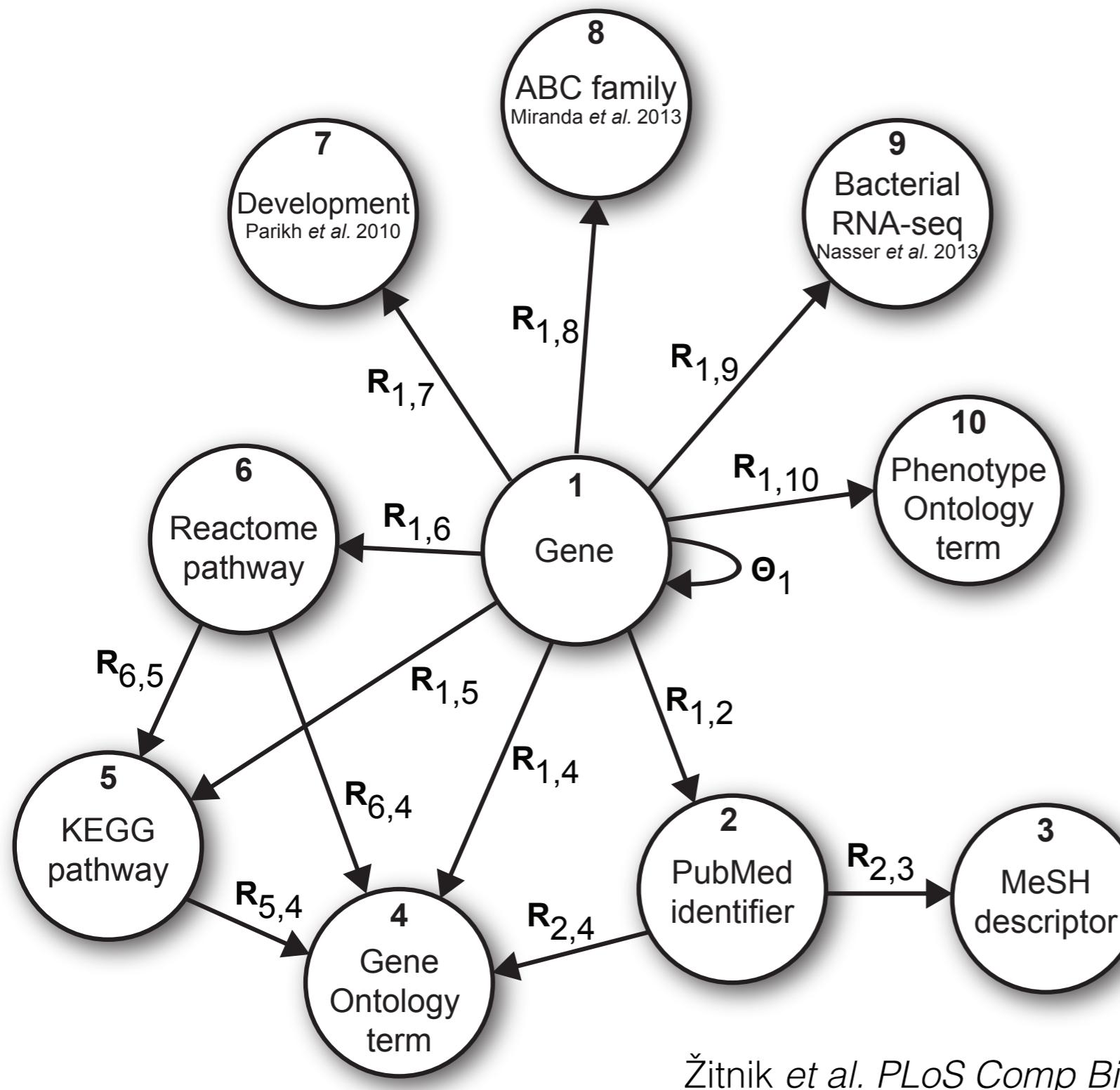
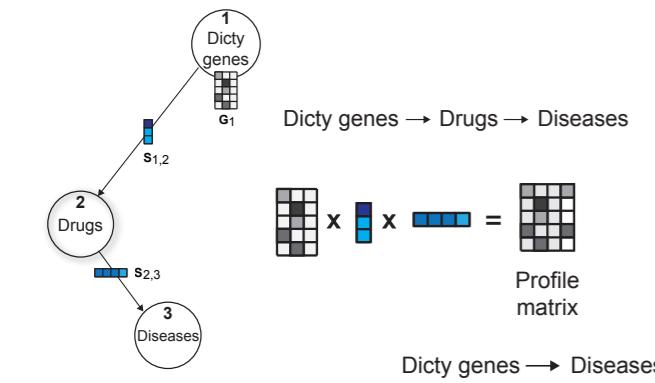


Latent Chaining and Profiling

Latent Chaining and Profiling



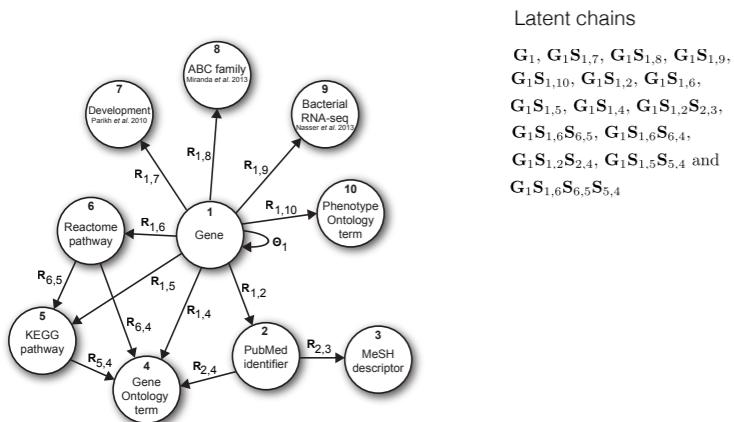
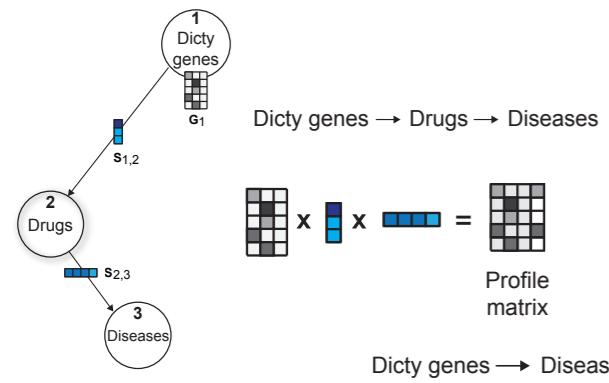
Latent Chaining and Profiling



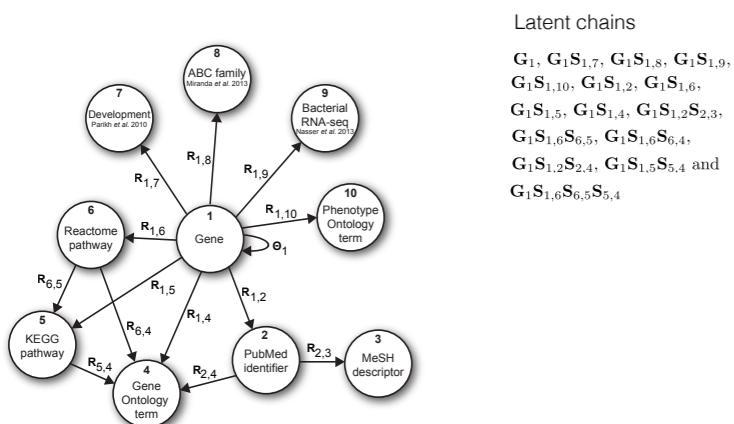
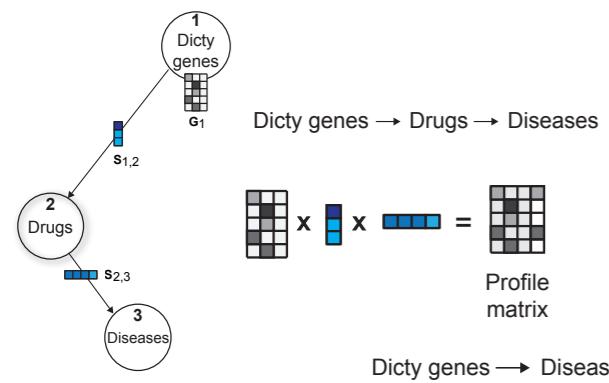
Latent chains

$G_1, G_1S_{1,7}, G_1S_{1,8}, G_1S_{1,9},$
 $G_1S_{1,10}, G_1S_{1,2}, G_1S_{1,6},$
 $G_1S_{1,5}, G_1S_{1,4}, G_1S_{1,2}S_{2,3},$
 $G_1S_{1,6}S_{6,5}, G_1S_{1,6}S_{6,4},$
 $G_1S_{1,2}S_{2,4}, G_1S_{1,5}S_{5,4}$ and
 $G_1S_{1,6}S_{6,5}S_{5,4}$

Latent Chaining and Profiling



Latent Chaining and Profiling



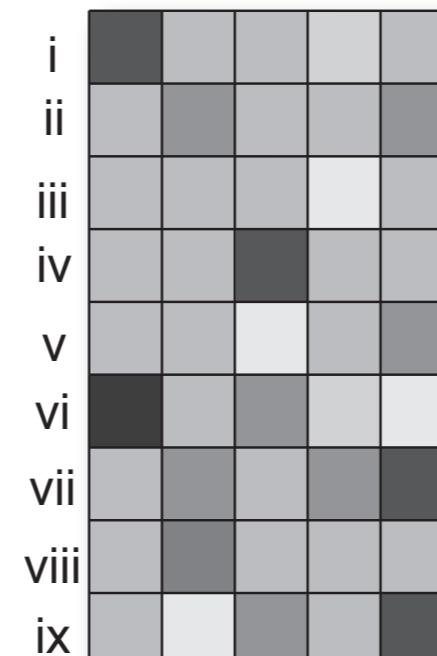
Candidate gene

Seed genes

Chains

Similarity scoring

Seed genes



Similarity score aggregation

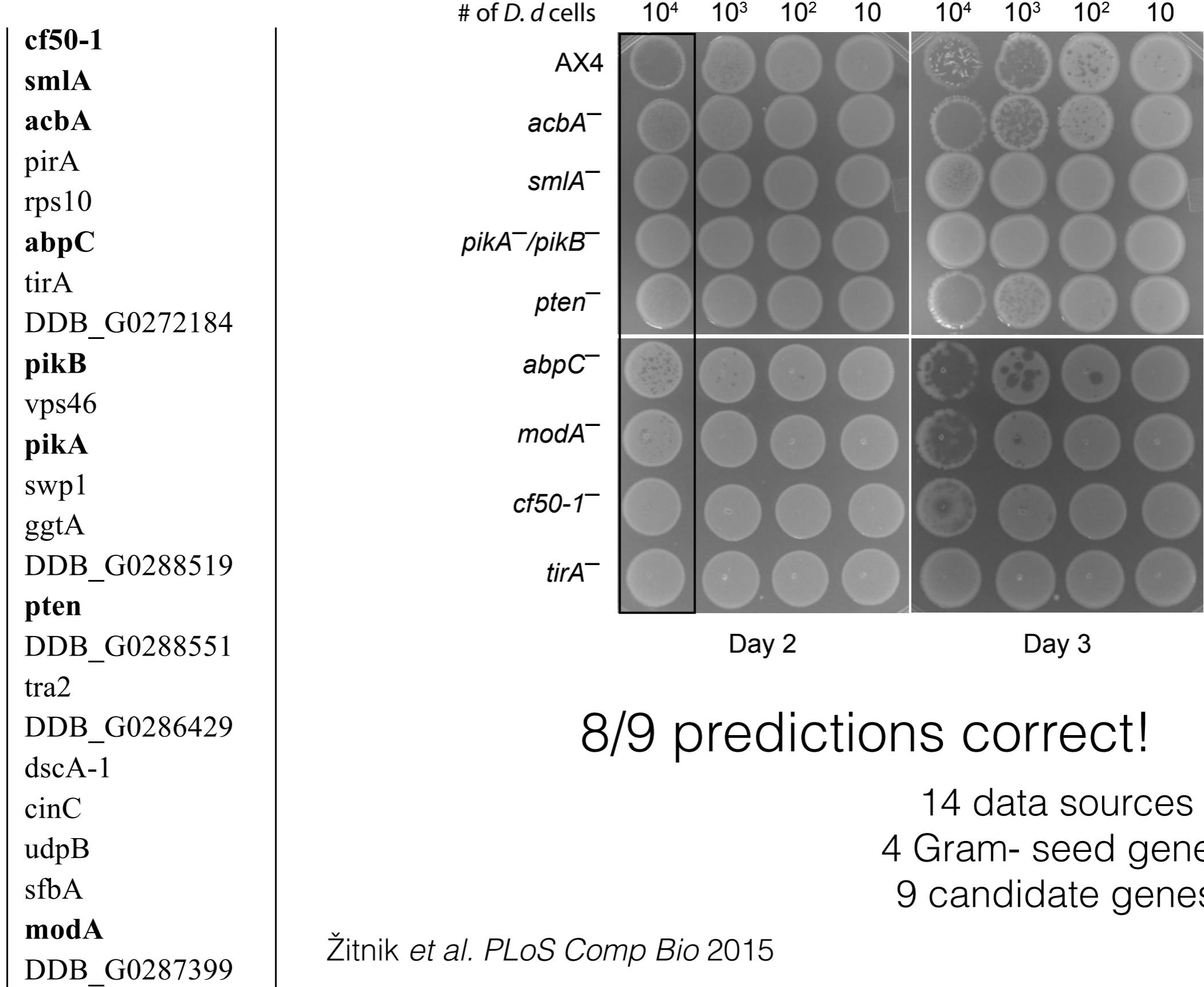
Scored candidate gene

Dictyostelium Bacterial Gene Hunt

Dictyostelium Bacterial Gene Hunt

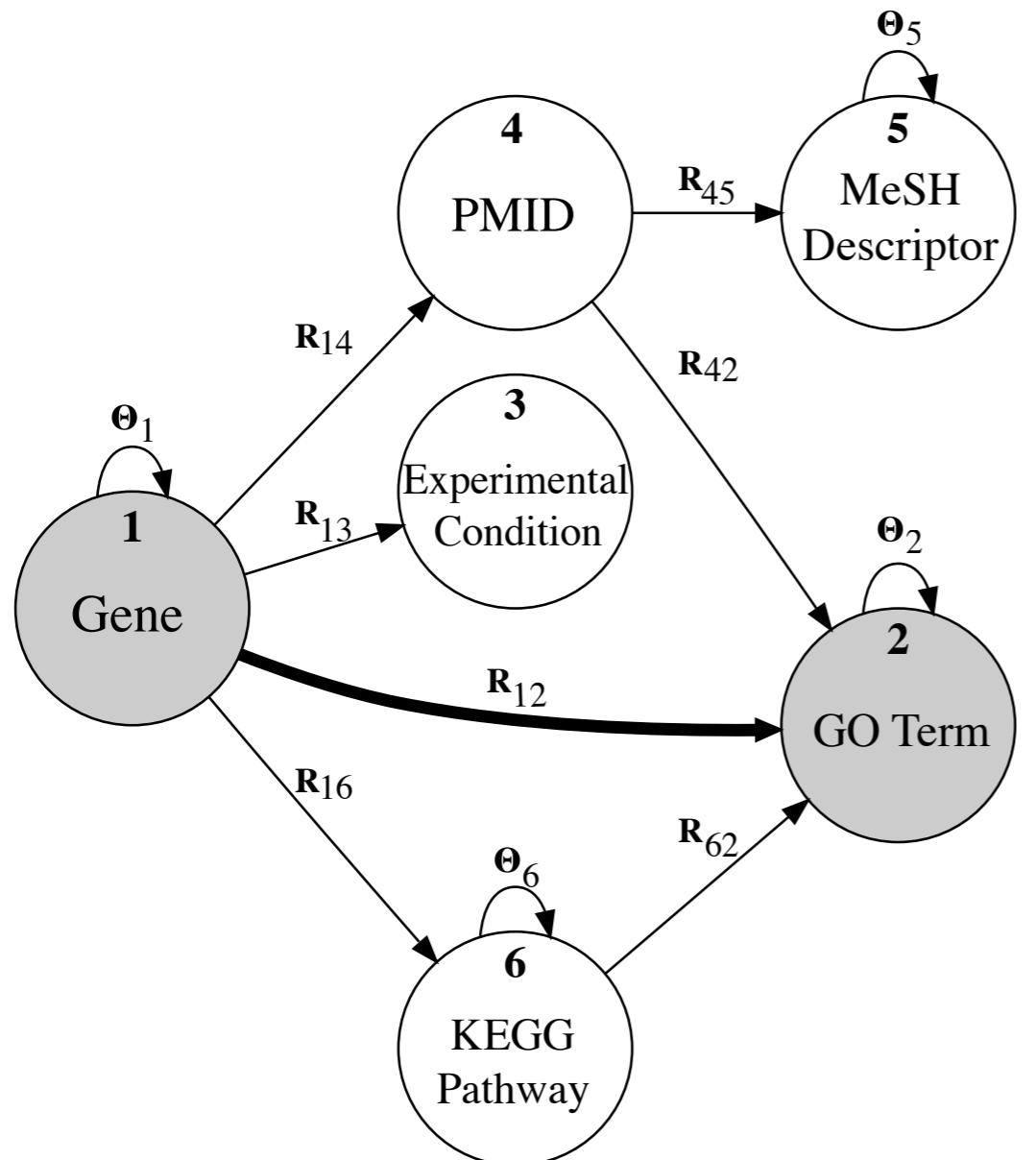
cf50-1
smlA
acbA
pirA
rps10
abpC
tirA
DDB_G0272184
pikB
vps46
pikA
swp1
ggtA
DDB_G0288519
pten
DDB_G0288551
tra2
DDB_G0286429
dscA-1
cinC
udpB
sfbA
modA
DDB_G0287399

Dictyostelium Bacterial Gene Hunt

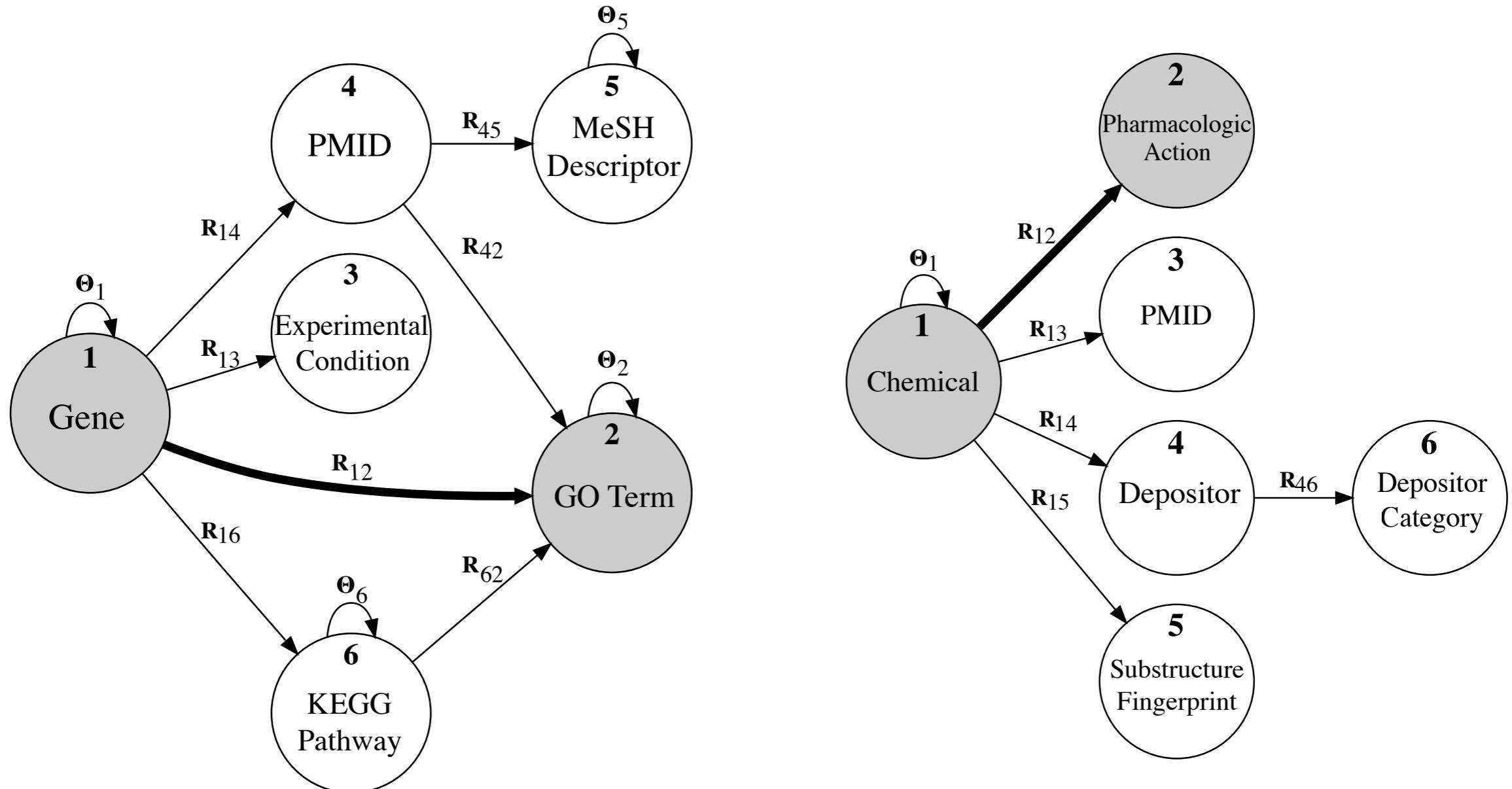


#2: Functional Genomics

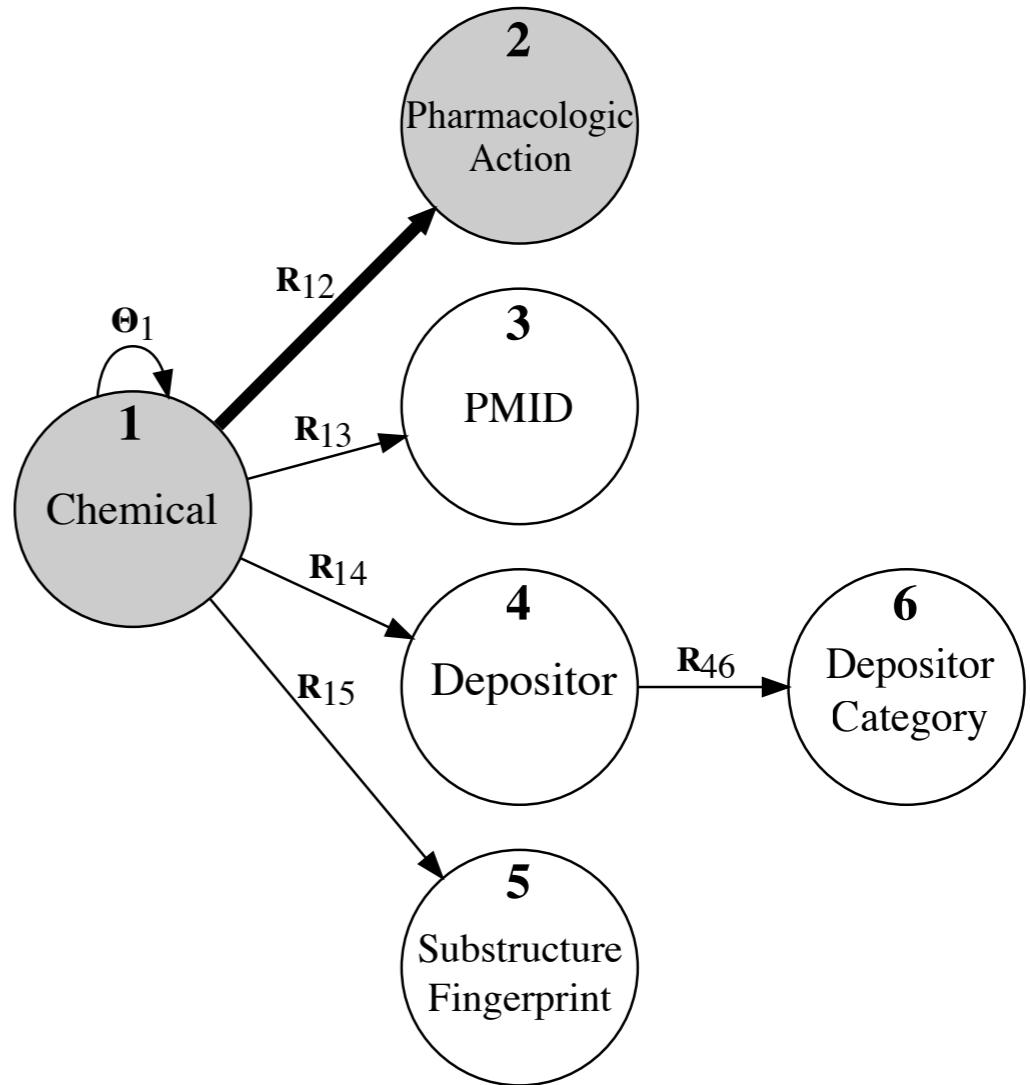
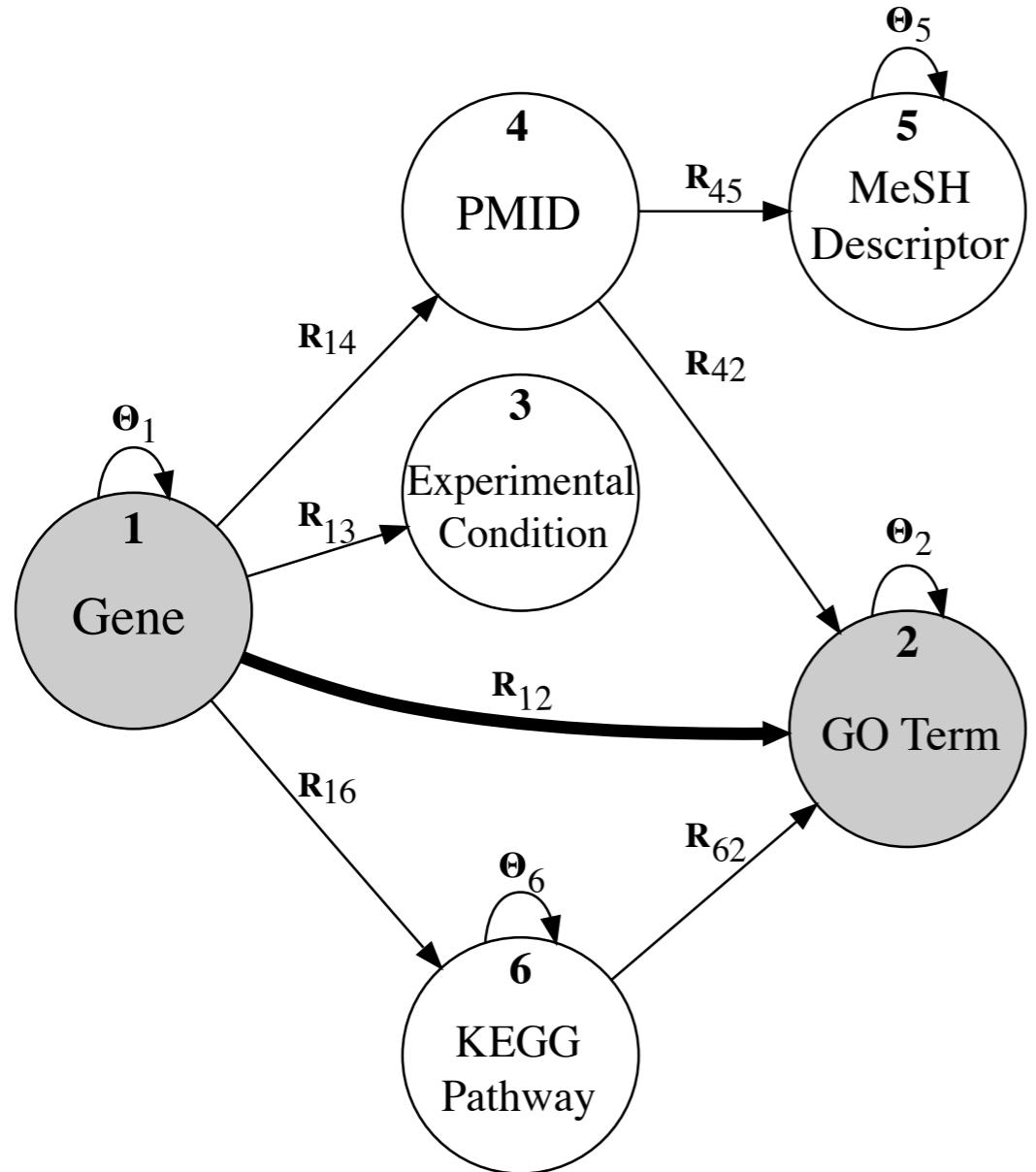
#2: Functional Genomics



#2: Functional Genomics

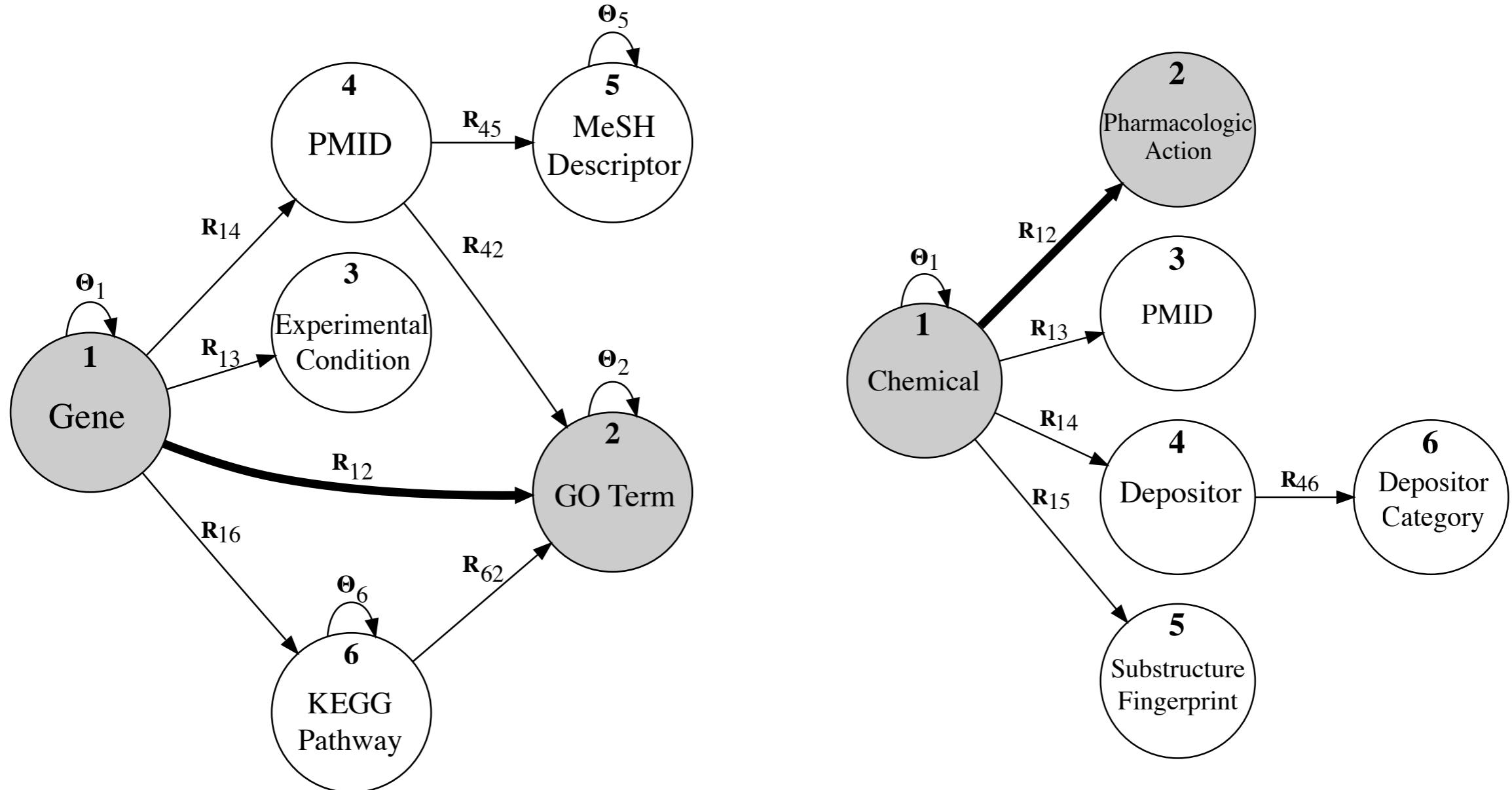


#2: Functional Genomics



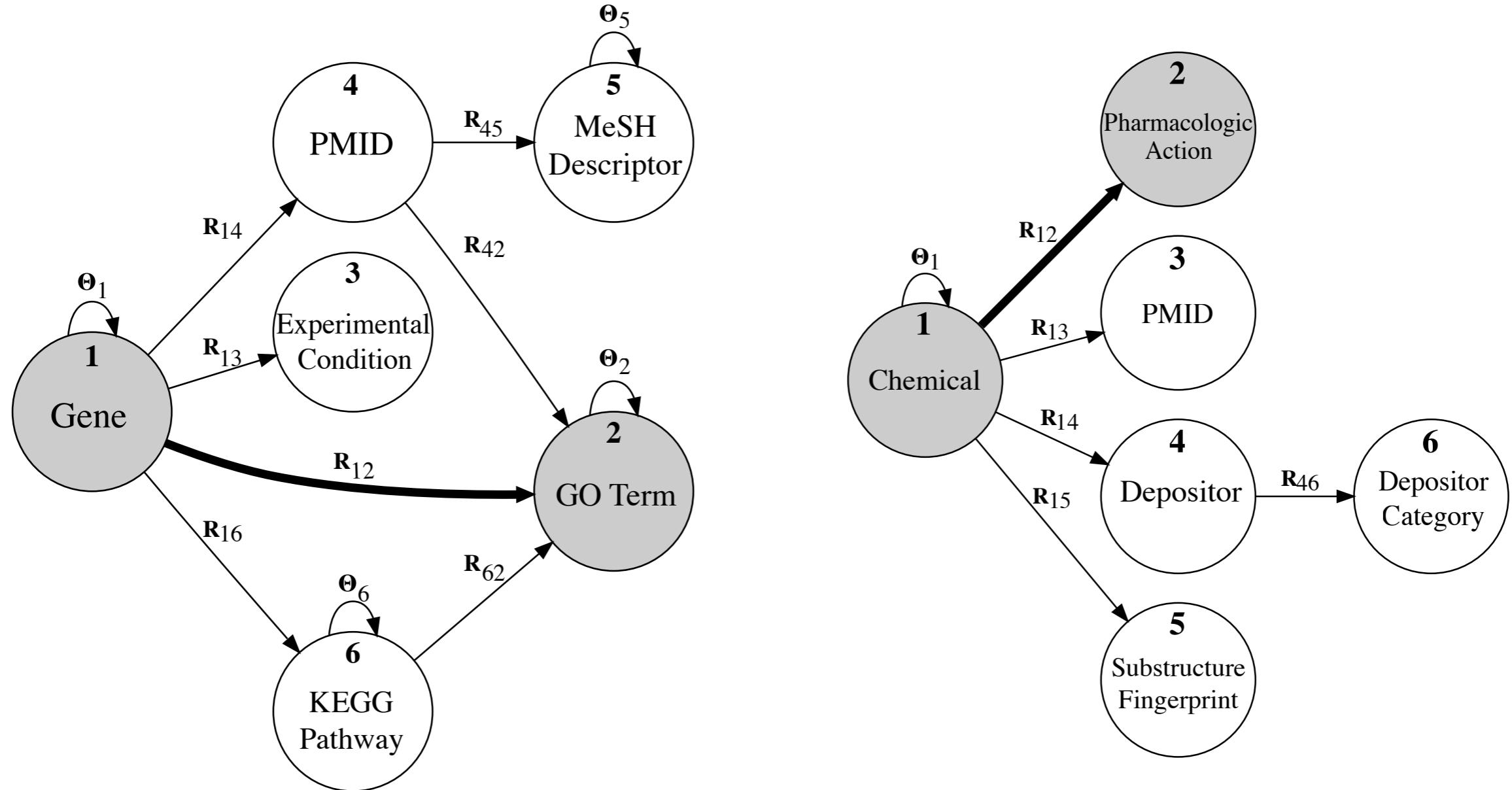
Prediction task	DFMF	
	F_1	AUC
100 <i>D. discoideum</i> genes	0.799	0.801
1000 <i>D. discoideum</i> genes	0.826	0.823
Whole <i>D. discoideum</i> genome	0.831	0.849
Pharmacologic actions	0.663	0.834

#2: Functional Genomics



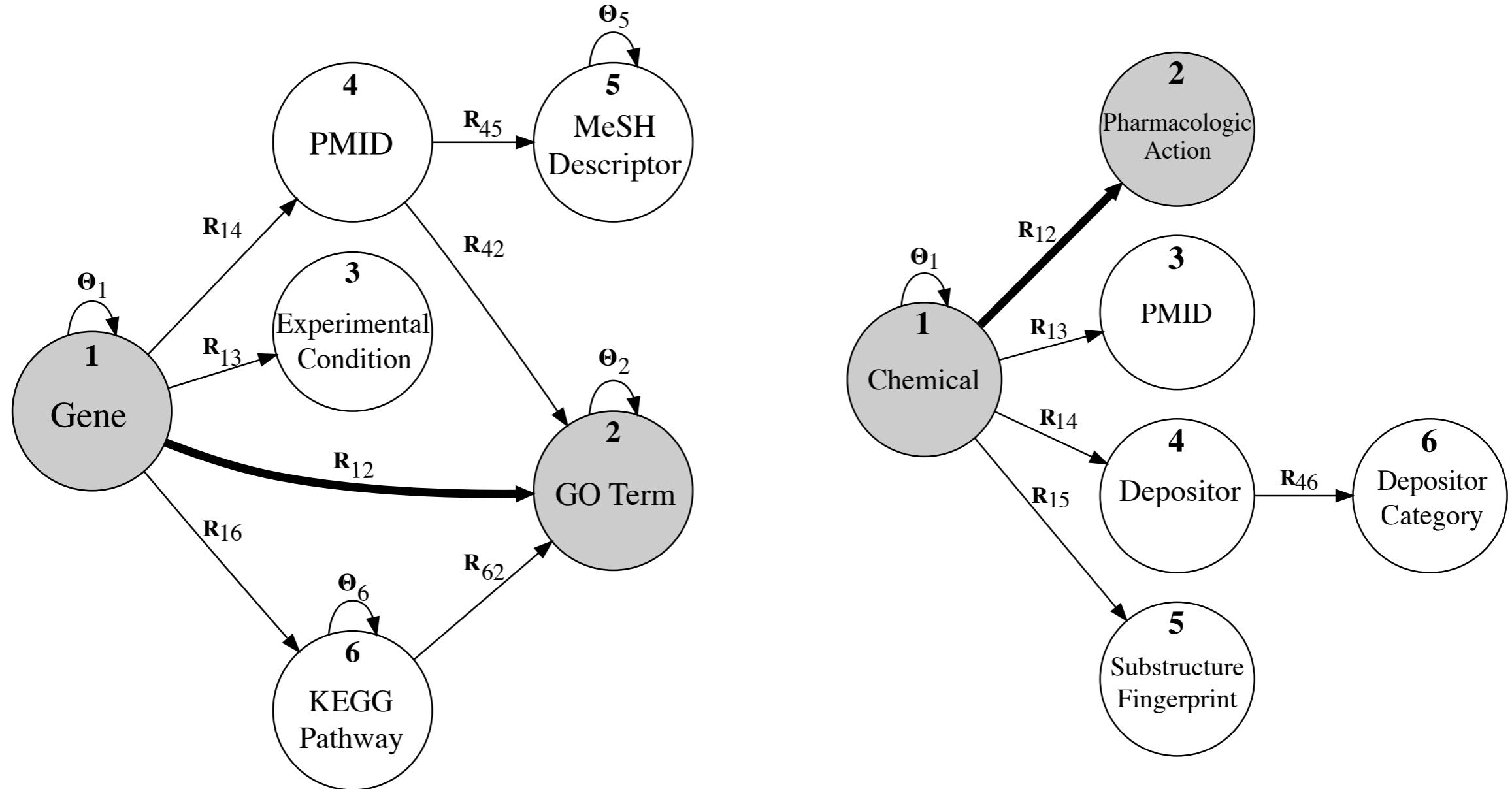
Prediction task	DFMF		MKL	
	F_1	AUC	F_1	AUC
100 <i>D. discoideum</i> genes	0.799	0.801	0.781	0.788
1000 <i>D. discoideum</i> genes	0.826	0.823	0.787	0.798
Whole <i>D. discoideum</i> genome	0.831	0.849	0.800	0.821
Pharmacologic actions	0.663	0.834	0.639	0.811

#2: Functional Genomics



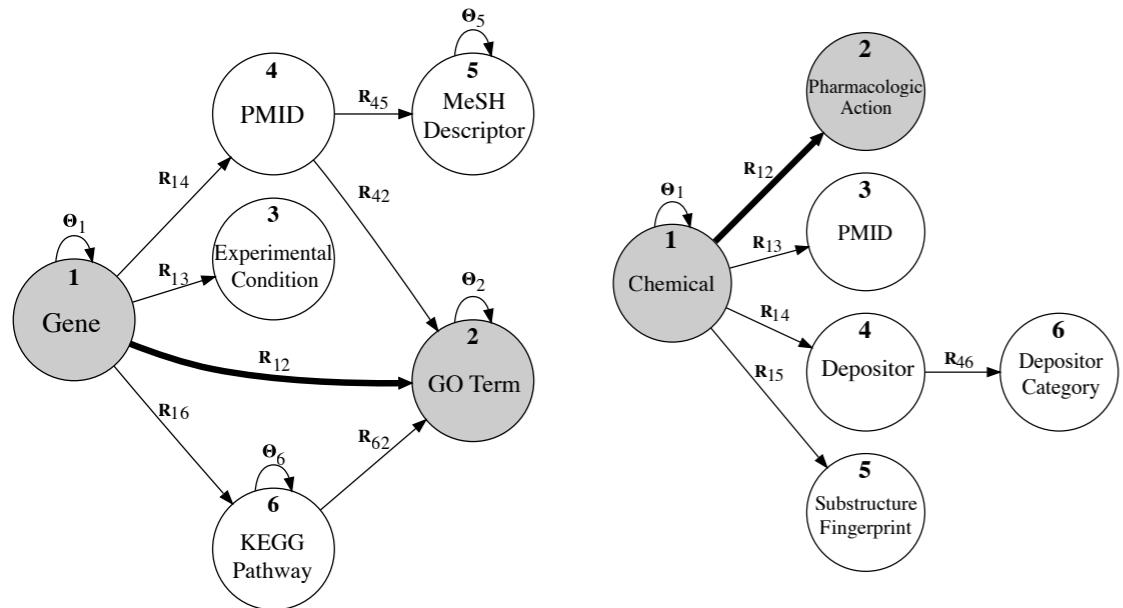
Prediction task	DFMF		MKL		RF	
	F_1	AUC	F_1	AUC	F_1	AUC
100 <i>D. discoideum</i> genes	0.799	0.801	0.781	0.788	0.761	0.785
1000 <i>D. discoideum</i> genes	0.826	0.823	0.787	0.798	0.767	0.788
Whole <i>D. discoideum</i> genome	0.831	0.849	0.800	0.821	0.782	0.801
Pharmacologic actions	0.663	0.834	0.639	0.811	0.643	0.819

#2: Functional Genomics



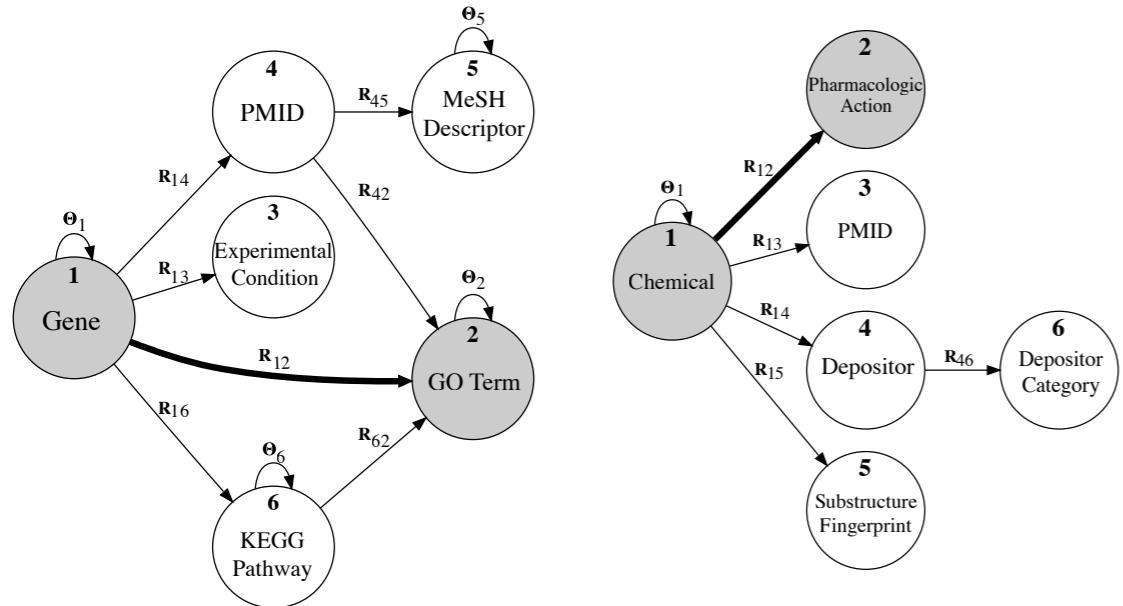
Prediction task	DFMF		MKL		RF		tri-SPMF	
	F_1	AUC	F_1	AUC	F_1	AUC	F_1	AUC
100 <i>D. discoideum</i> genes	0.799	0.801	0.781	0.788	0.761	0.785	0.731	0.724
1000 <i>D. discoideum</i> genes	0.826	0.823	0.787	0.798	0.767	0.788	0.756	0.741
Whole <i>D. discoideum</i> genome	0.831	0.849	0.800	0.821	0.782	0.801	0.778	0.787
Pharmacologic actions	0.663	0.834	0.639	0.811	0.643	0.819	0.641	0.810

#2: Functional Genomics



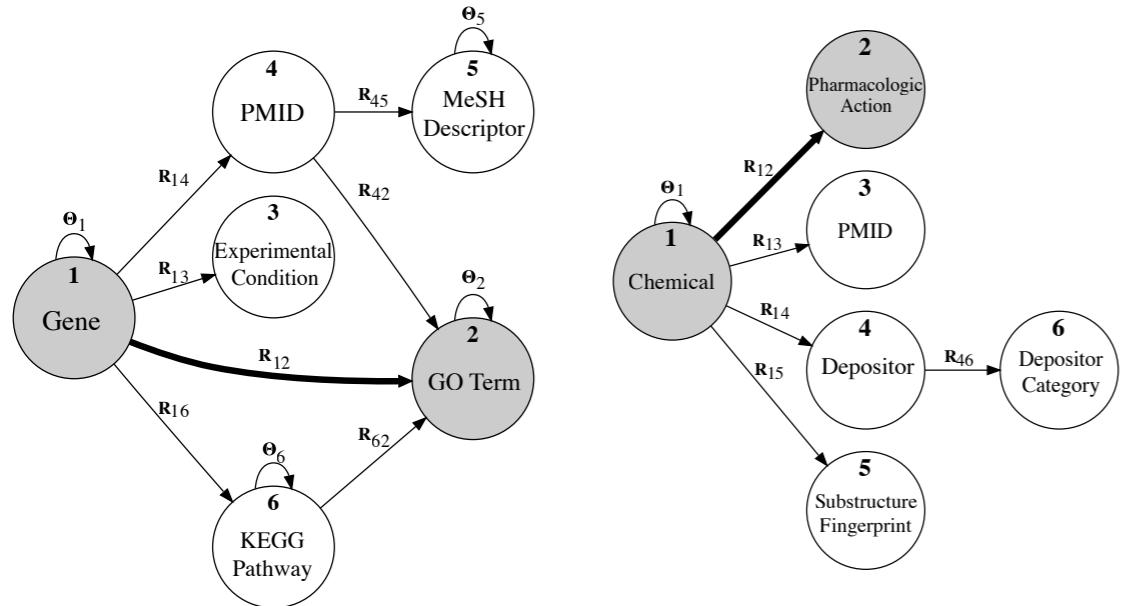
Prediction task	DFMF		MKL		RF		tri-SPMF	
	F_1	AUC	F_1	AUC	F_1	AUC	F_1	AUC
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#2: Functional Genomics



Prediction task	DFMF		MKL		RF		tri-SPMF	
	F_1	AUC	F_1	AUC	F_1	AUC	F_1	AUC
100 <i>D. discoideum</i> genes	0.799	0.801	0.781	0.788	0.761	0.785	0.731	0.724
1000 <i>D. discoideum</i> genes	0.826	0.823	0.787	0.798	0.767	0.788	0.756	0.741
Whole <i>D. discoideum</i> genome	0.831	0.849	0.800	0.821	0.782	0.801	0.778	0.787
Pharmacologic actions	0.663	0.834	0.639	0.811	0.643	0.819	0.641	0.810

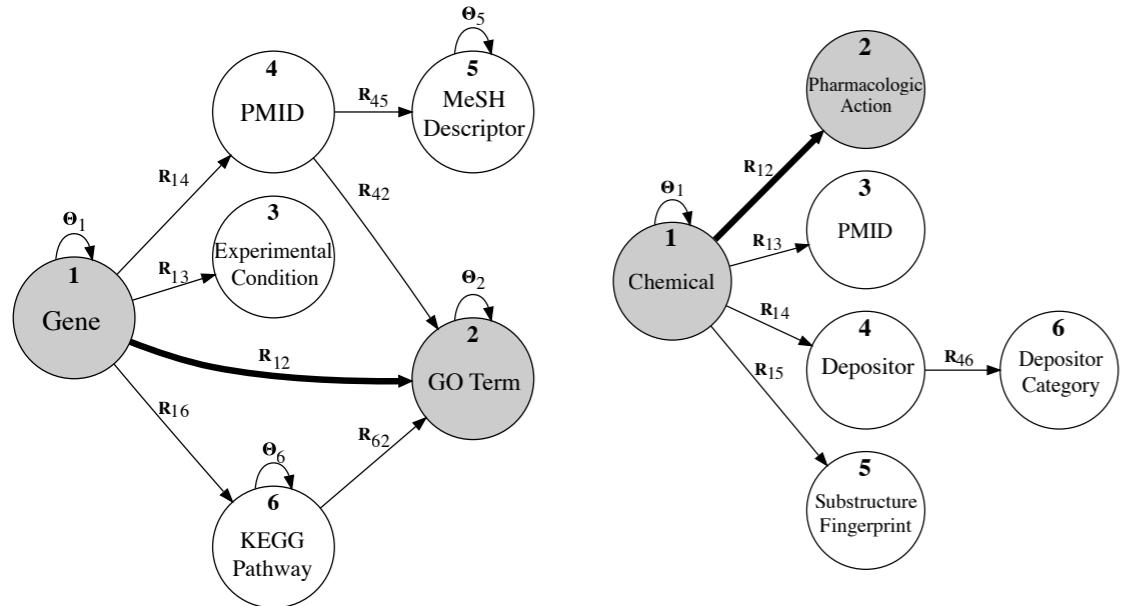
#2: Functional Genomics



Mining disease associations
Žitnik et al *Scientific Reports* 2013

Prediction task	DFMF		MKL		RF		tri-SPMF	
	F_1	AUC	F_1	AUC	F_1	AUC	F_1	AUC
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1000 <i>D. discoideum</i> genes	0.826	0.823	0.787	0.798	0.767	0.788	0.756	0.741
Whole <i>D. discoideum</i> genome	0.831	0.849	0.800	0.821	0.782	0.801	0.778	0.787
Pharmacologic actions	0.663	0.834	0.639	0.811	0.643	0.819	0.641	0.810

#2: Functional Genomics



Mining disease associations

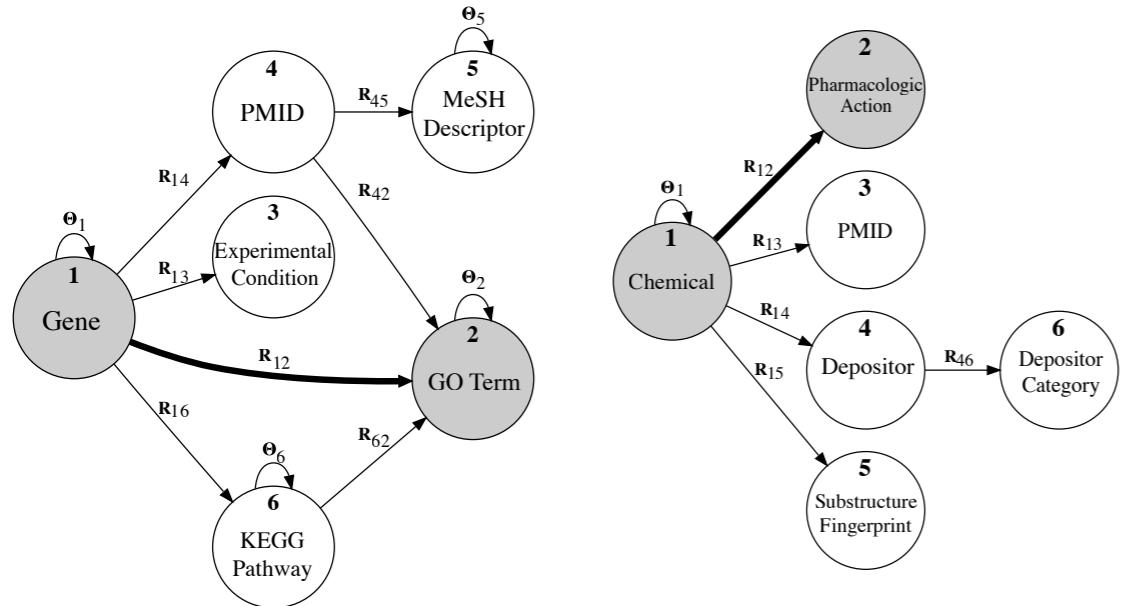
Žitnik et al *Scientific Reports* 2013

Predicting drug toxicity

Žitnik & Zupan *Systems Biomedicine* 2014 (CAMDA Award)

Prediction task	DFMF		MKL		RF		tri-SPMF	
	F_1	AUC	F_1	AUC	F_1	AUC	F_1	AUC
100 <i>D. discoideum</i> genes	0.799	0.801	0.781	0.788	0.761	0.785	0.731	0.724
1000 <i>D. discoideum</i> genes	0.826	0.823	0.787	0.798	0.767	0.788	0.756	0.741
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#2: Functional Genomics



Mining disease associations

Žitnik et al *Scientific Reports* 2013

Predicting drug toxicity

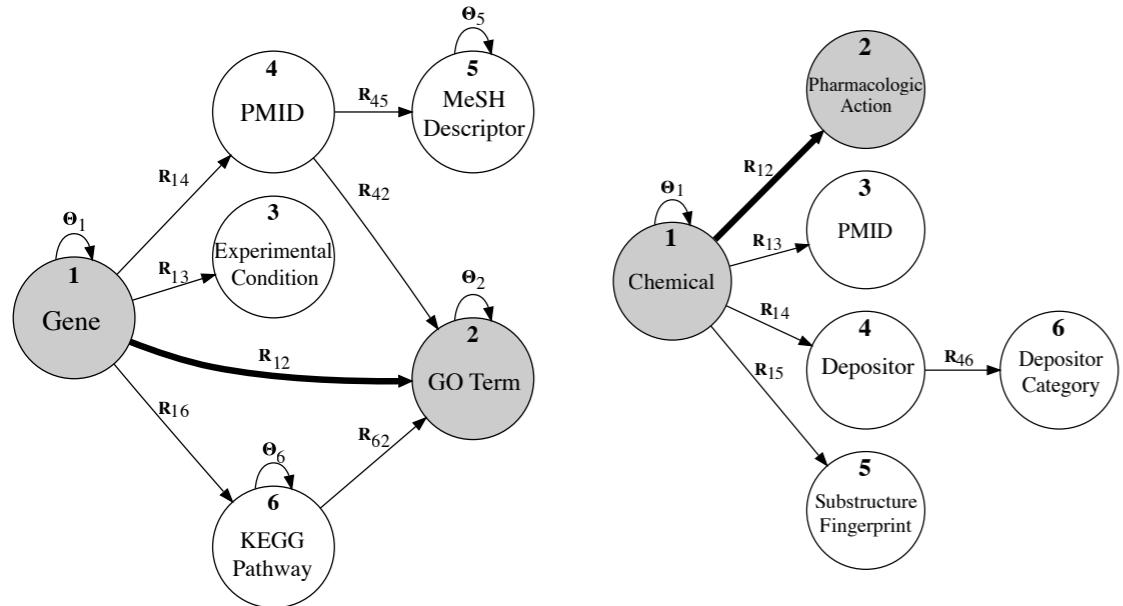
Žitnik & Zupan *Systems Biomedicine* 2014 (CAMDA Award)

Predicting gene functions

Žitnik & Zupan *In PSB* 2014

Prediction task	DFMF		MKL		RF		tri-SPMF	
	F_1	AUC	F_1	AUC	F_1	AUC	F_1	AUC
100 <i>D. discoideum</i> genes	0.799	0.801	0.781	0.788	0.761	0.785	0.731	0.724
1000 <i>D. discoideum</i> genes	0.826	0.823	0.787	0.798	0.767	0.788	0.756	0.741
Whole <i>D. discoideum</i> genome	0.831	0.849	0.800	0.821	0.782	0.801	0.778	0.787
Pharmacologic actions	0.663	0.834	0.639	0.811	0.643	0.819	0.641	0.810

#2: Functional Genomics



Mining disease associations

Žitnik et al *Scientific Reports* 2013

Predicting drug toxicity

Žitnik & Zupan *Systems Biomedicine* 2014 (CAMDA Award)

Predicting gene functions

Žitnik & Zupan *In PSB* 2014

Predicting cancer survival

Žitnik & Zupan *Systems Biomedicine* 2015 (CAMDA Award)

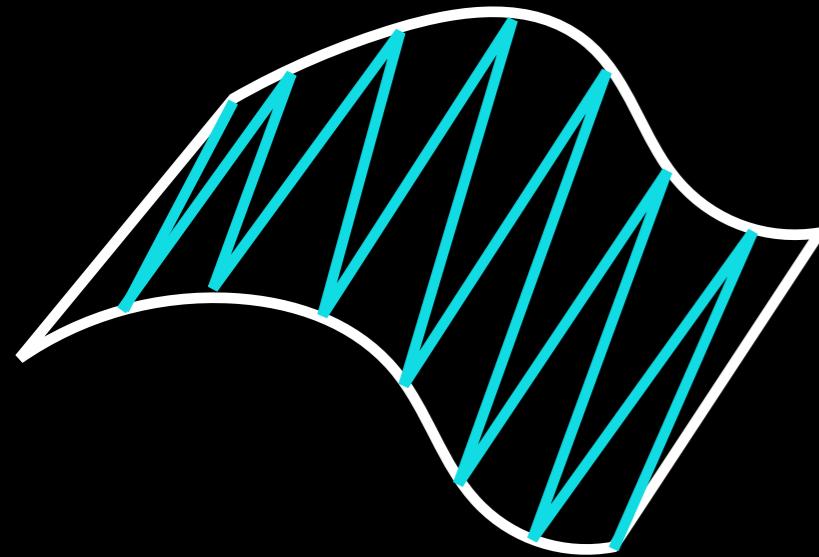
Prediction task	DFMF		MKL		RF		tri-SPMF	
	F_1	AUC	F_1	AUC	F_1	AUC	F_1	AUC
100 <i>D. discoideum</i> genes	0.799	0.801	0.781	0.788	0.761	0.785	0.731	0.724
1000 <i>D. discoideum</i> genes	0.826	0.823	0.787	0.798	0.767	0.788	0.756	0.741
Whole <i>D. discoideum</i> genome	0.831	0.849	0.800	0.821	0.782	0.801	0.778	0.787
Pharmacologic actions	0.663	0.834	0.639	0.811	0.643	0.819	0.641	0.810

Key Idea: Transfer of Knowledge

θ  θ  θ  θ 

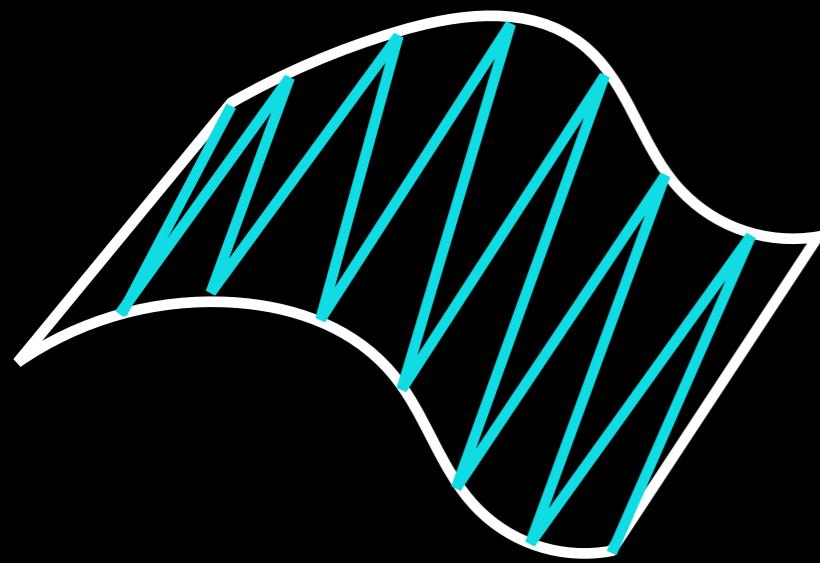
θ Model parameters

Key Idea: Transfer of Knowledge

 $\theta_{\text{[cyan]}}$ $\theta_{\text{[green]}}$ $\theta_{\text{[purple]}}$ $\theta_{\text{[red]}}$

θ Model parameters

Key Idea: Transfer of Knowledge

 θ_{cyan} θ_{green} θ_{purple} θ_{red} 

Objects of one type



Data view

 θ Model parameters

Key Idea: Transfer of Knowledge

 θ_{cyan} θ_{green} θ_{purple} θ_{red} 

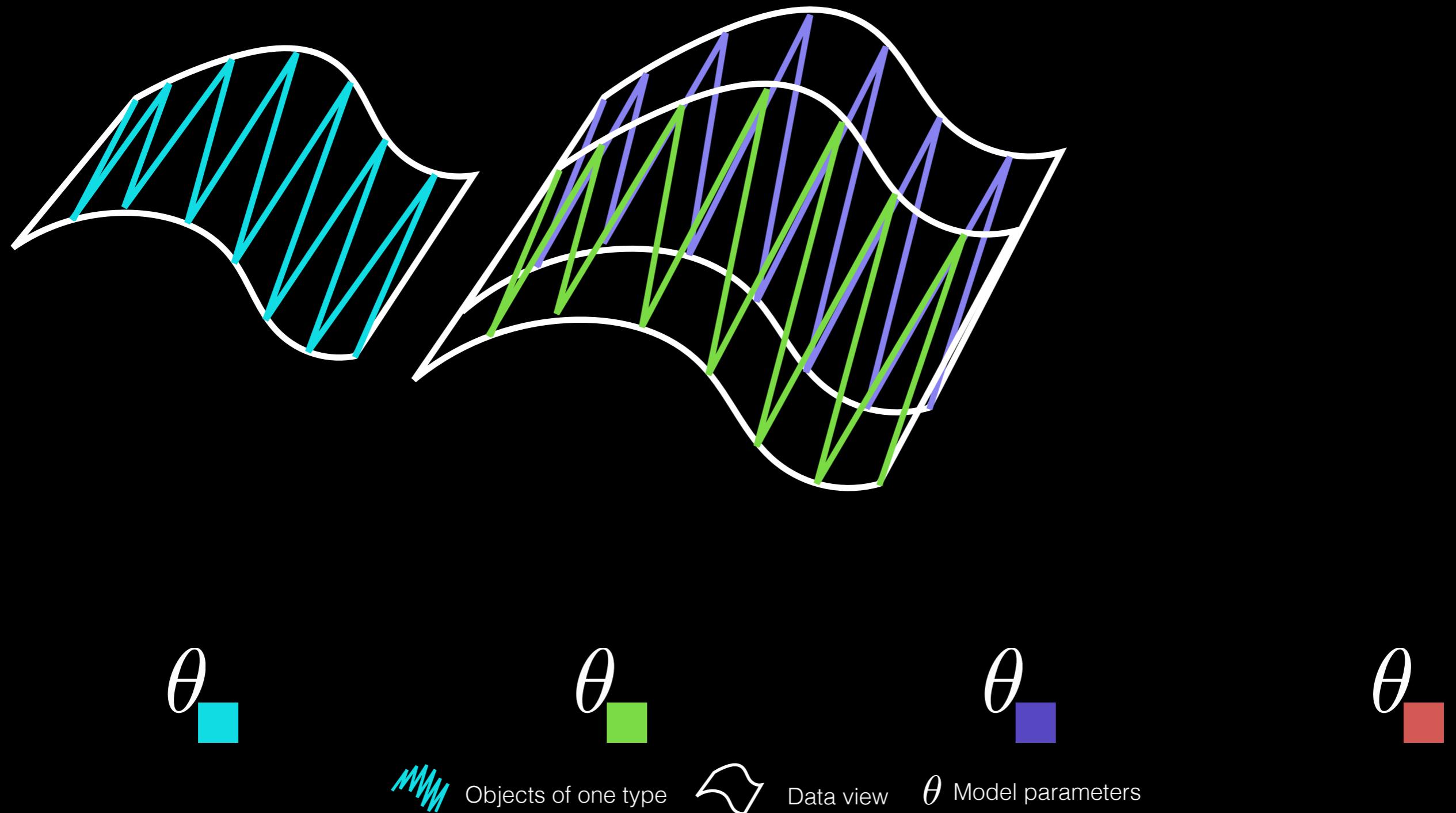
Objects of one type



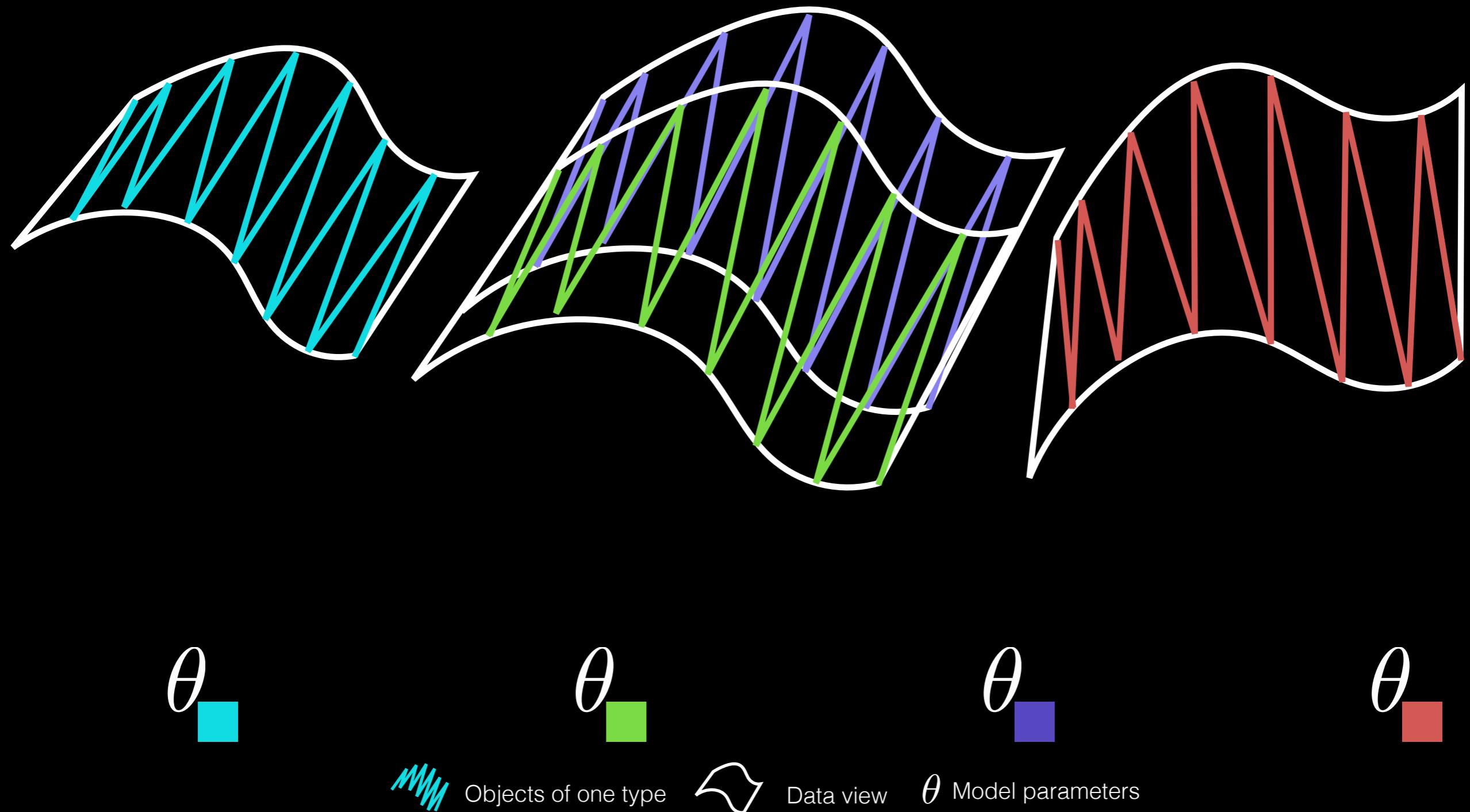
Data view

 θ Model parameters

Key Idea: Transfer of Knowledge

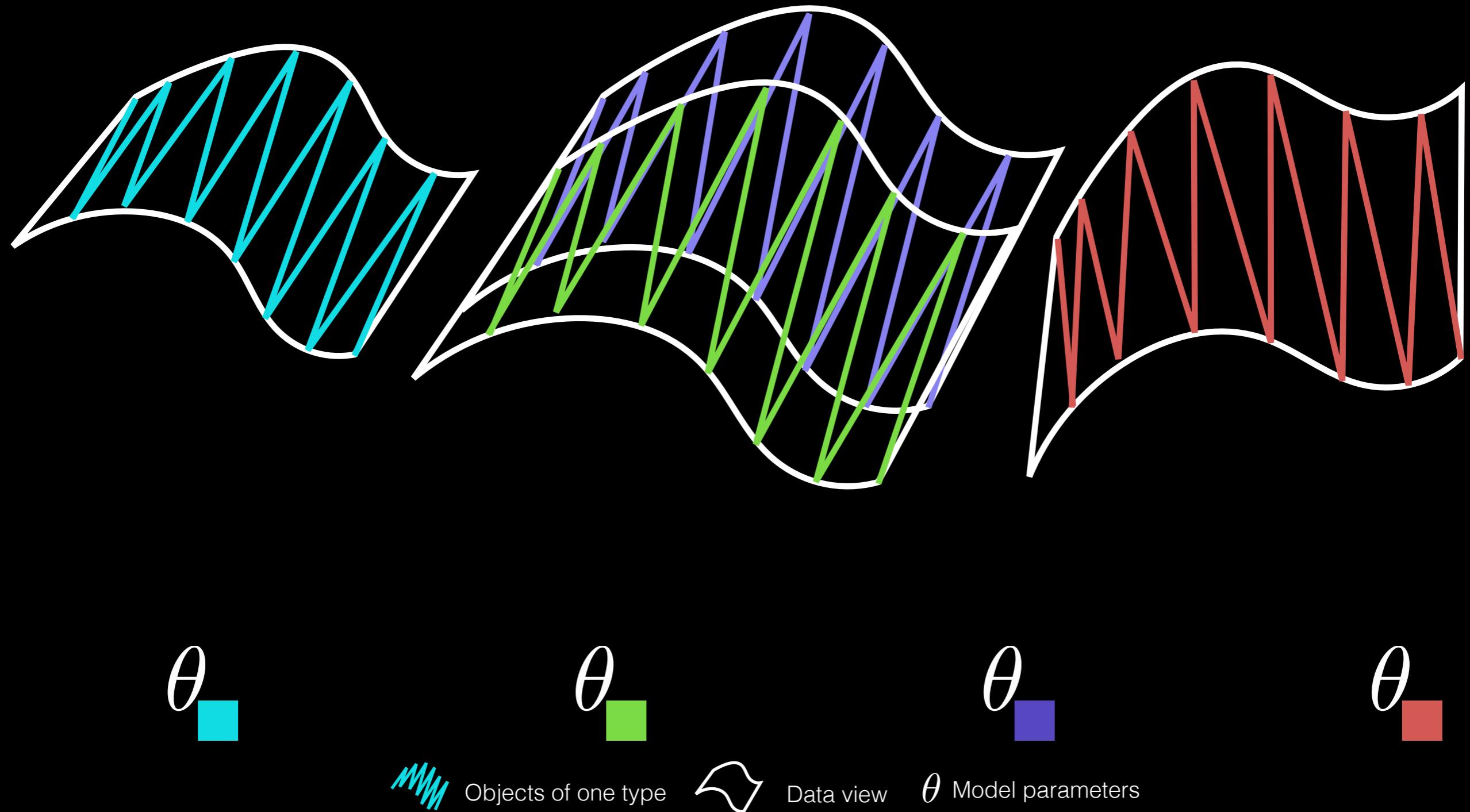


Key Idea: Transfer of Knowledge



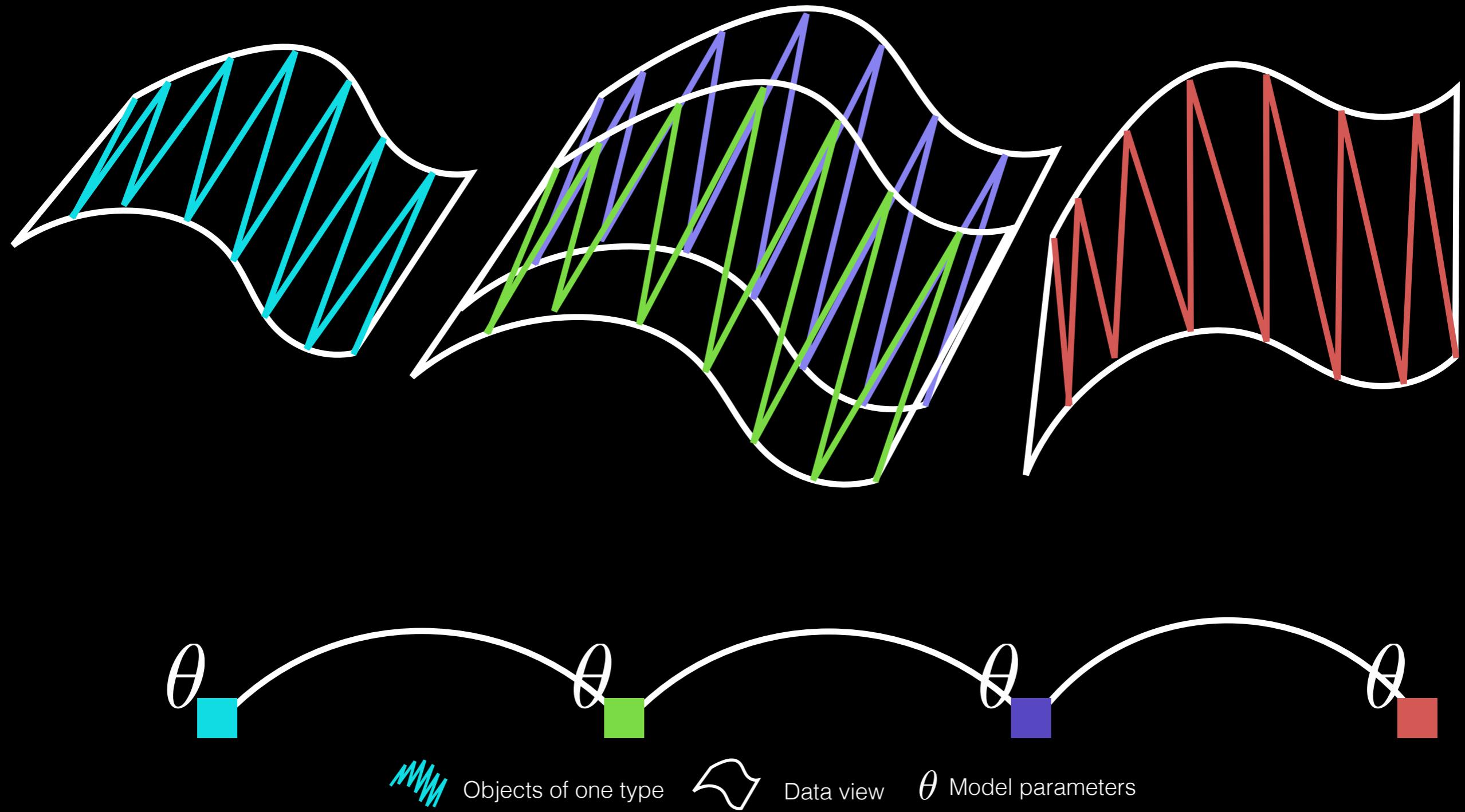
Key Idea: Transfer of Knowledge

Heterogeneous data domain space



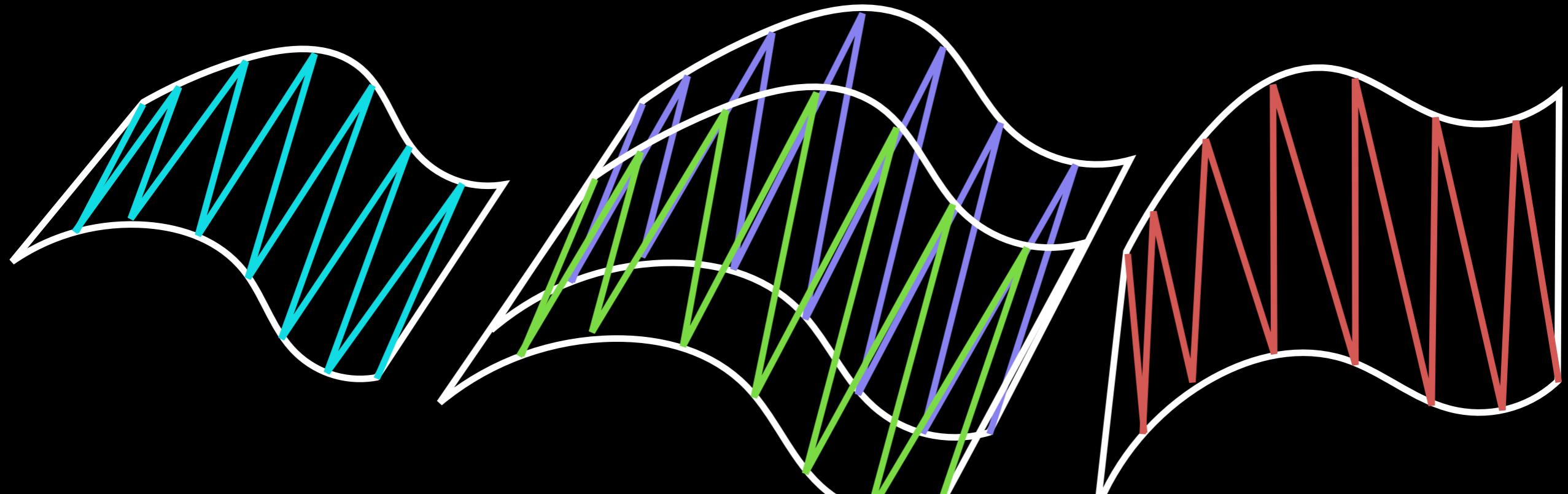
Key Idea: Transfer of Knowledge

Heterogeneous data domain space

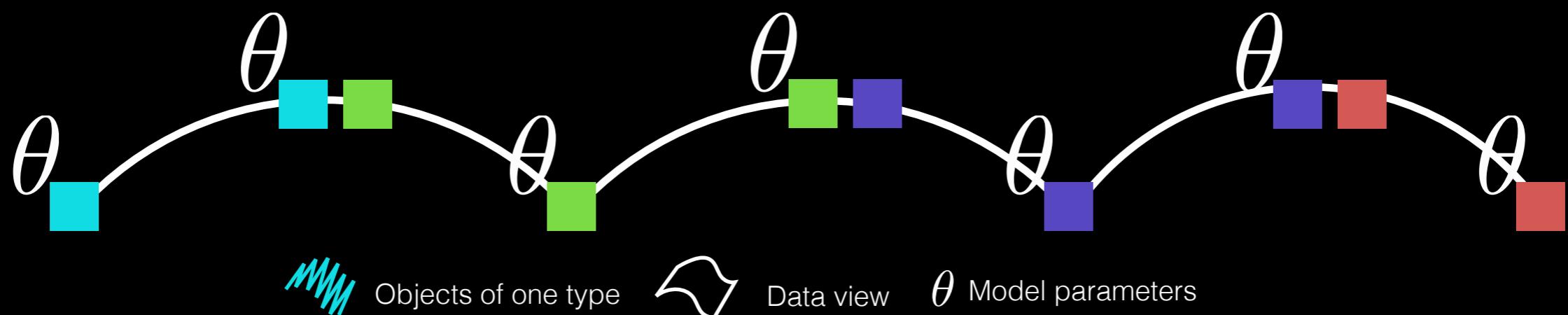


Key Idea: Transfer of Knowledge

Heterogeneous data domain space

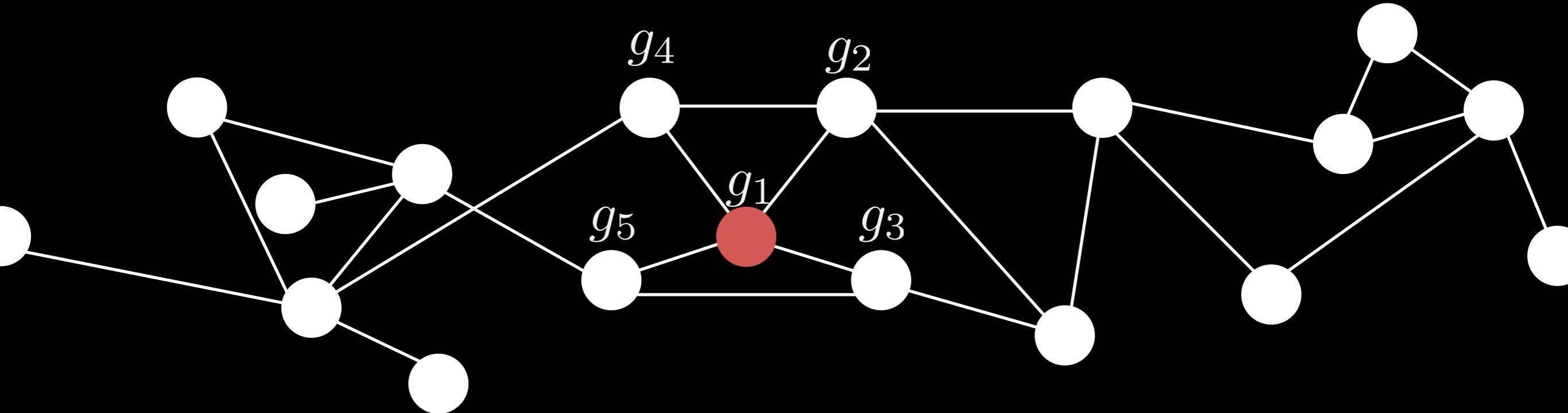


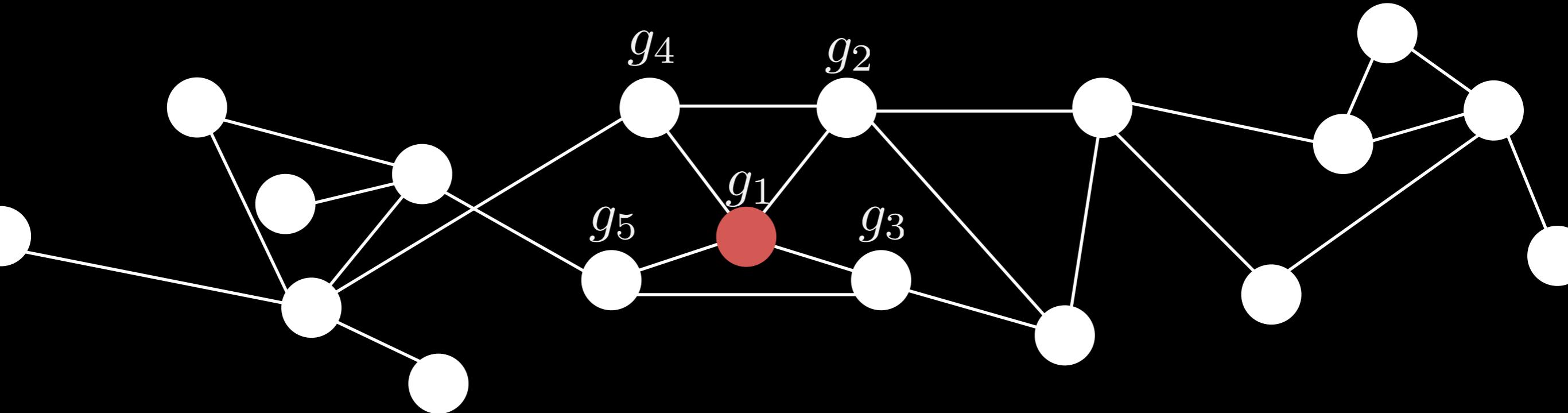
Context jumping in the latent space



Transfer of Knowledge: Another Example

Network Inference from Mixed Data

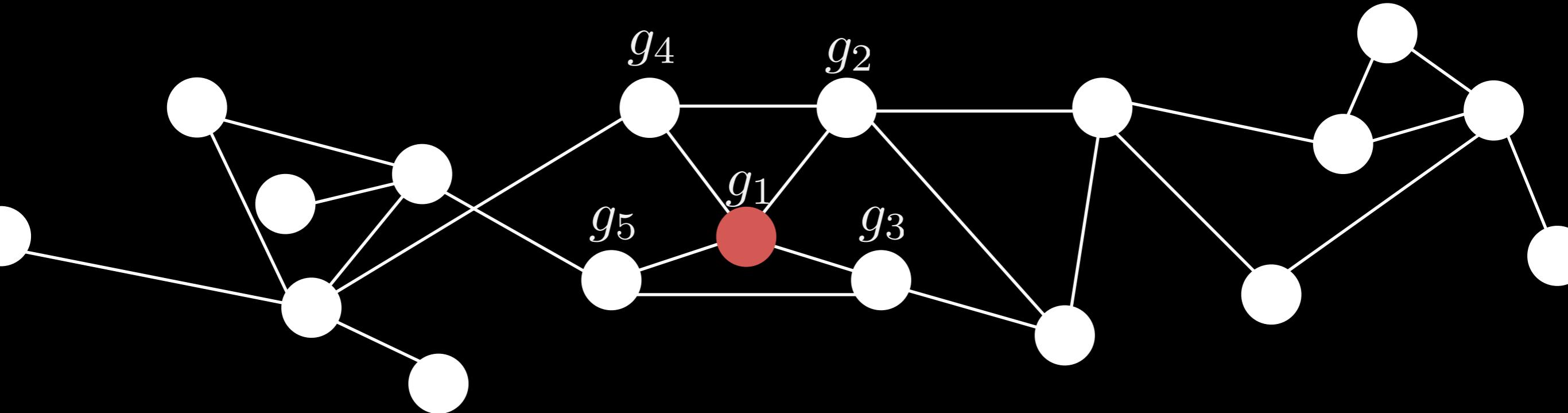




Direct inference

$$\mathcal{N}(g_1) = \{g_i \in V \setminus \{g_1\} : \text{sim}(g_1, g_i) \geq T\}$$

threshold value



Direct inference

$$\mathcal{N}(g_1) = \{g_i \in V \setminus \{g_1\} : \text{sim}(g_1, g_i) \geq T\}$$

threshold value

Model-based inference

$$g_1 = \theta_2 g_2 + \theta_3 g_3 + \theta_4 g_4 + \theta_5 g_5 + \dots + \theta_n g_n$$

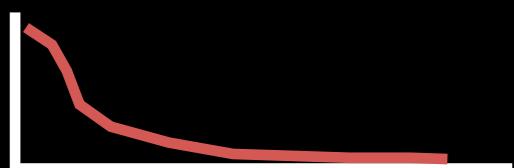
$$\mathcal{N}(g_1) = \{g_i \in V \setminus \{g_1\} : \theta_i \neq 0\}$$

model parameters

Mixed Data

Mixed Data

RNA-seq count data



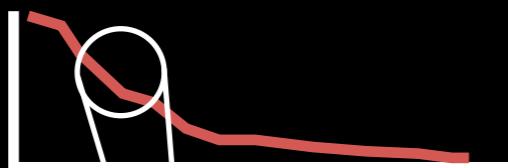
g_1



g_2



g_3



g_4

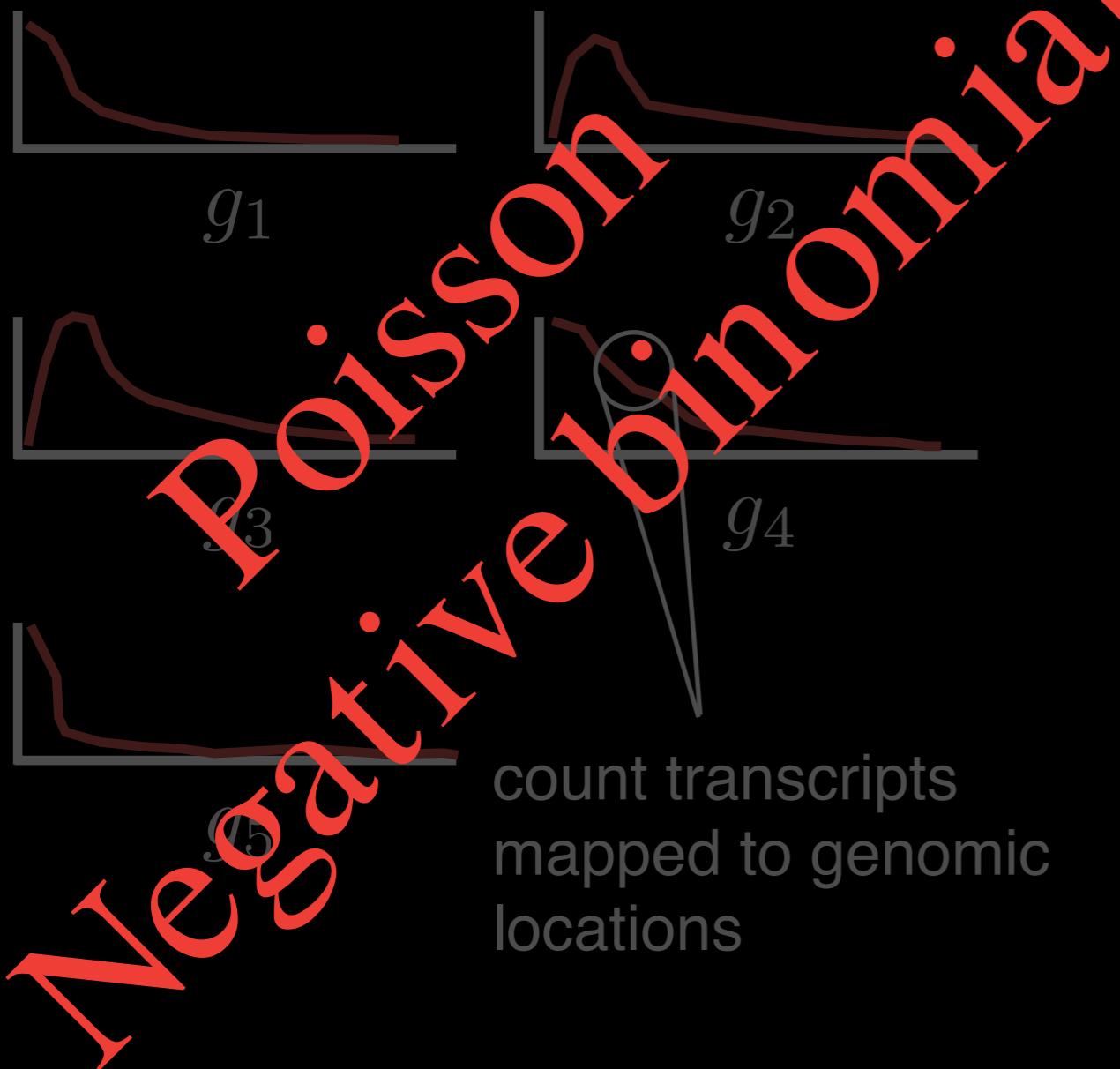


g_5

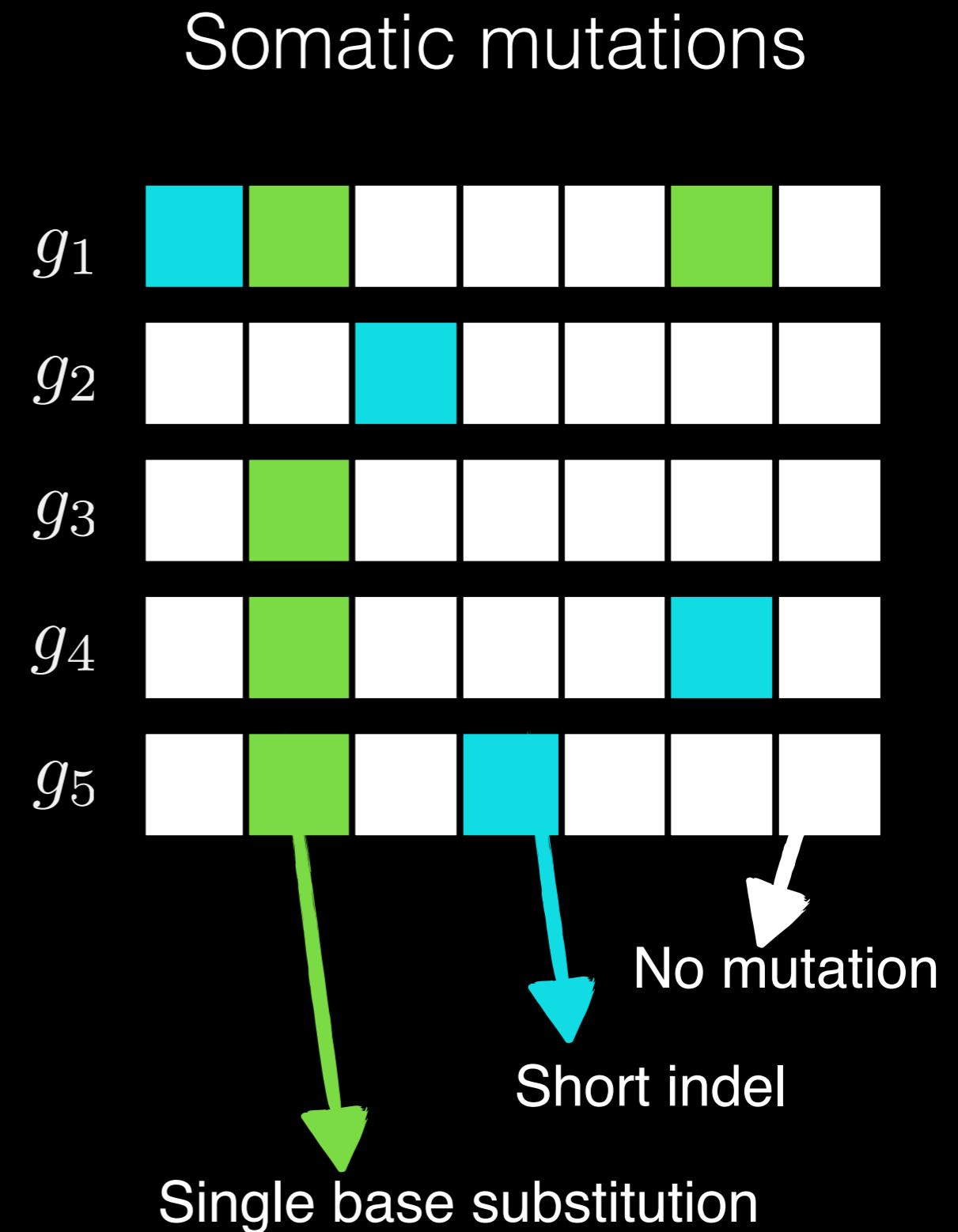
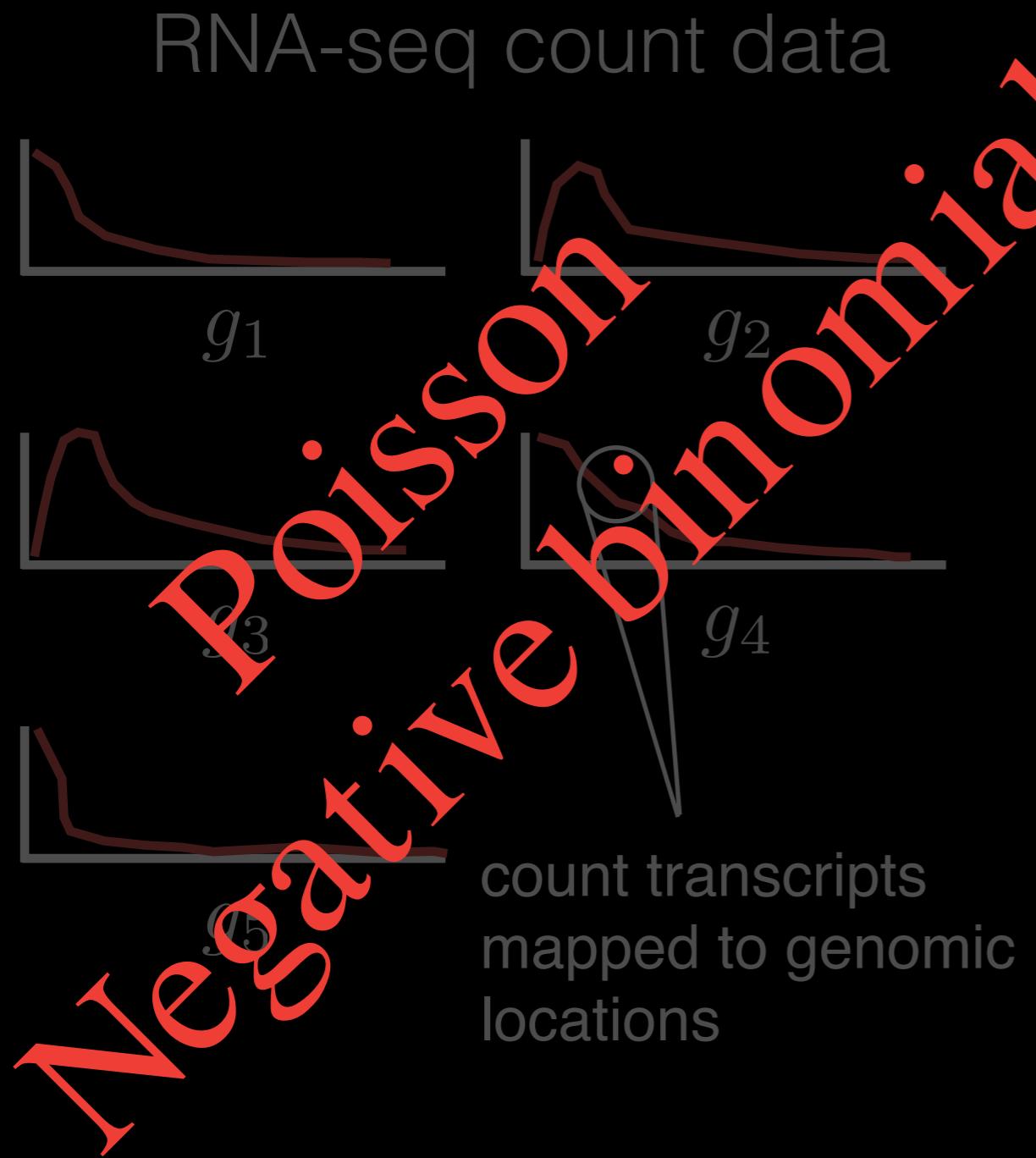
count transcripts
mapped to genomic
locations

Mixed Data

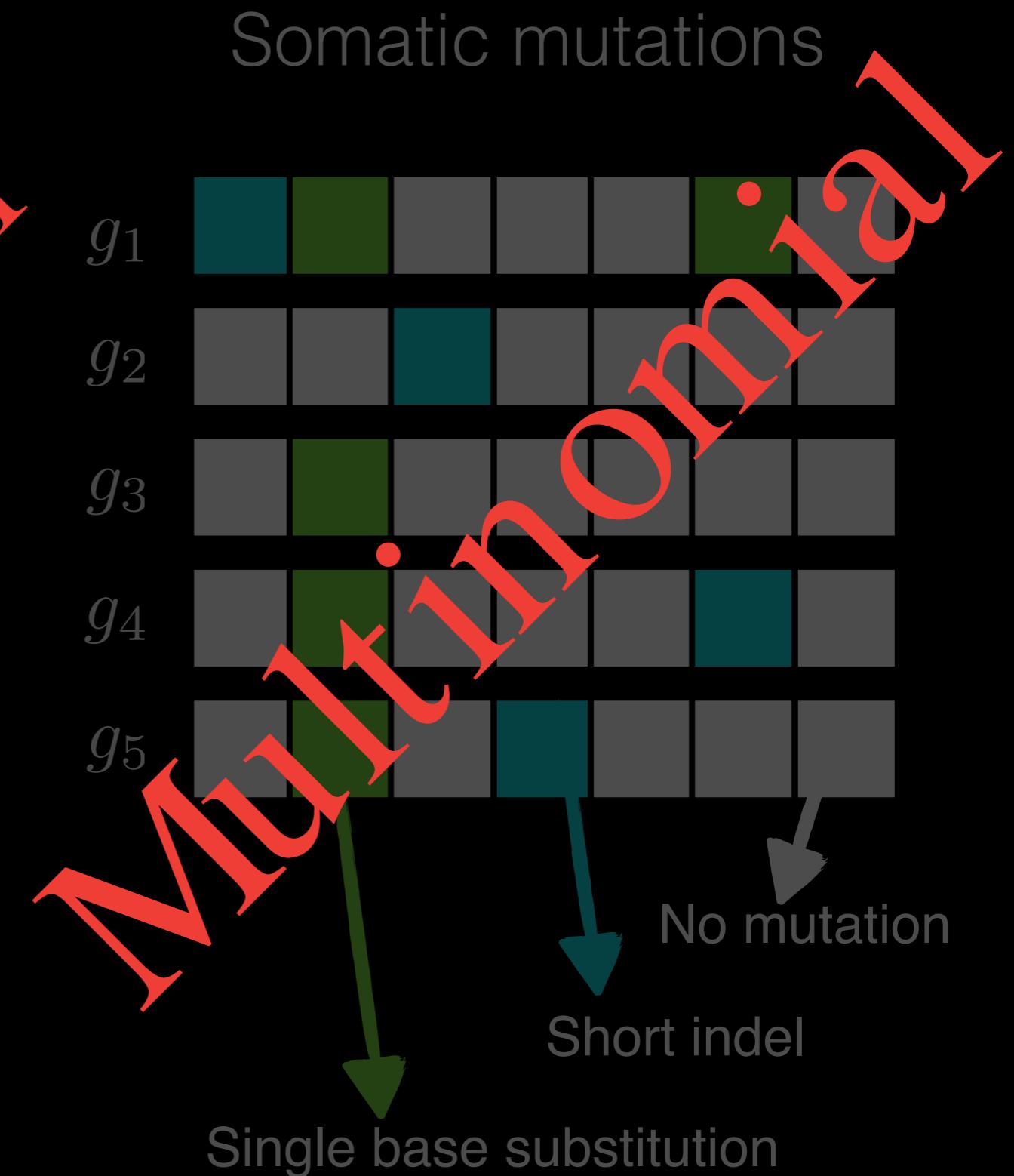
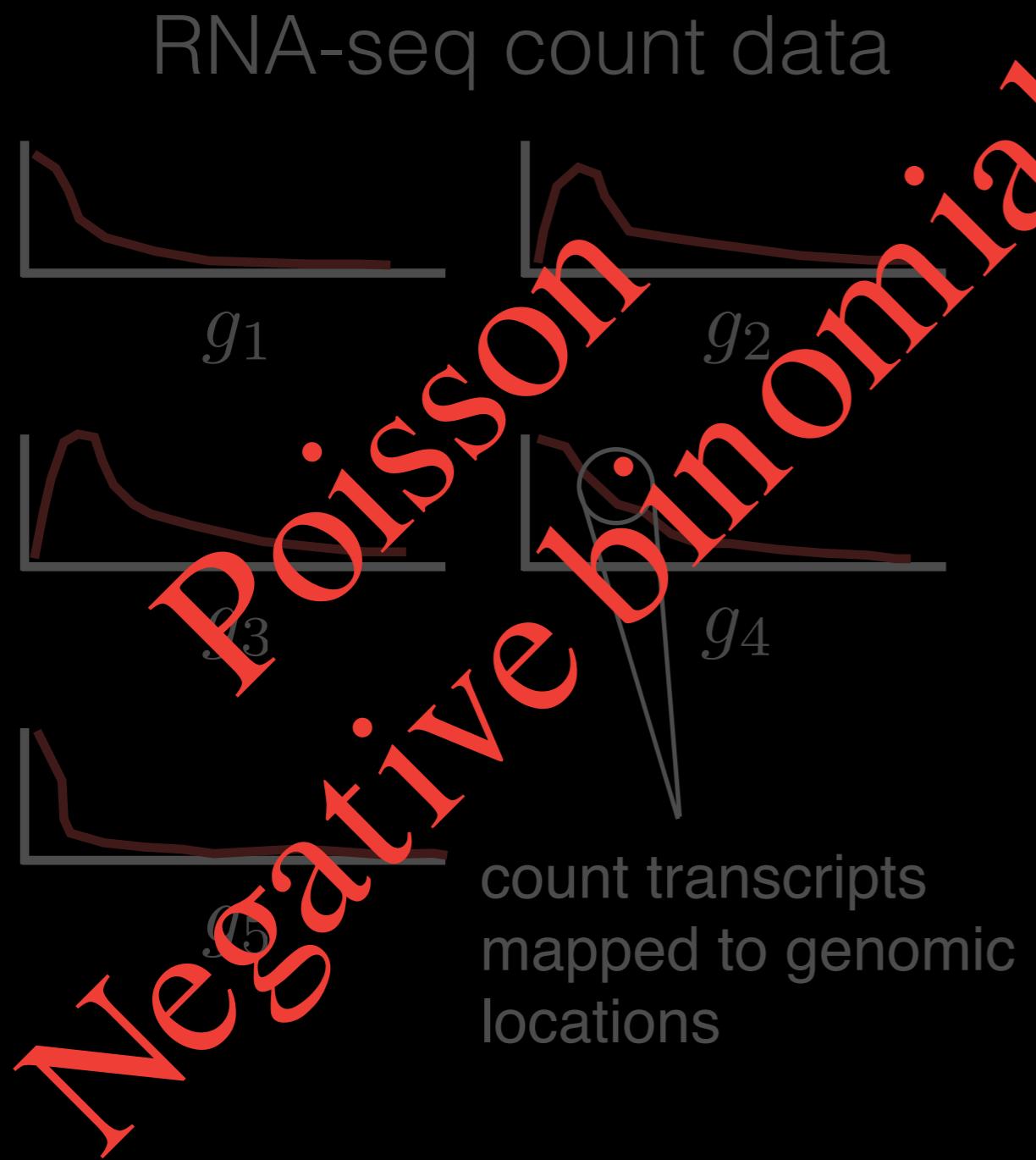
RNA-seq count data



Mixed Data



Mixed Data



Network Inference from Mixed Data

$$P_{\Theta}(X) \propto \exp\left(\sum_{g \in V} \theta_g \phi_g(X_g) + \sum_{(g,h) \in E} \theta_{gh} \phi_{gh}(X_g, X_h)\right)$$

Network Inference from Mixed Data

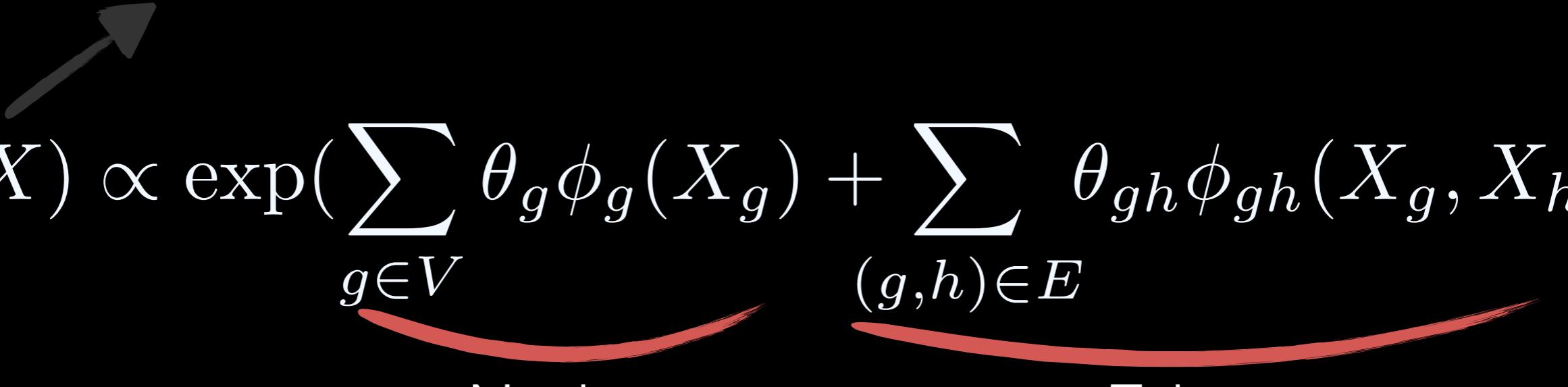
$X = (X_1, X_2, \dots, X_n)$, X_i is an object of interest



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Nodes

Edges

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Nodes

Edges

$\theta_g = \mathbf{U}_g$

Object weights

The diagram illustrates the components of the network inference formula. A grey arrow points to the vector X . A white arrow points to the term involving nodes, which is labeled "Nodes". A brown curved bracket underlines the term involving edges, which is labeled "Edges".

Network Inference from Mixed Data

$X = (X_1, X_2, \dots, X_n)$, X_i is an object of interest

$$P_{\Theta}(X) \propto \exp\left(\sum_{g \in V} \theta_g \phi_g(X_g) + \sum_{(g,h) \in E} \theta_{gh} \phi_{gh}(X_g, X_h)\right)$$

Nodes

Edges

$\theta_g = \mathbf{U}_g$
Object weights

$\theta_{gh} = \mathbf{U}_g^T \mathbf{W}^T \mathbf{W} \mathbf{U}_h$
Object-object interactions

Network Inference from Mixed Data

Objective function

Network Inference from Mixed Data

Objective function

$$\min_{\mathbf{U}, \mathbf{W}_x, \mathbf{W}_y} \sum_{g \in V} \ell_{g; P_x}(\mathbf{U}, \mathbf{W}_x; \mathbf{X})$$



Data \mathbf{X} following
distribution P_x

Network Inference from Mixed Data

Objective function

$$\min_{\mathbf{U}, \mathbf{W}_x, \mathbf{W}_y} \sum_{g \in V} \ell_{g; P_x}(\mathbf{U}, \mathbf{W}_x; \mathbf{X}) + \ell_{g; P_y}(\mathbf{U}, \mathbf{W}_y; \mathbf{Y}) + \text{reg. param.}$$



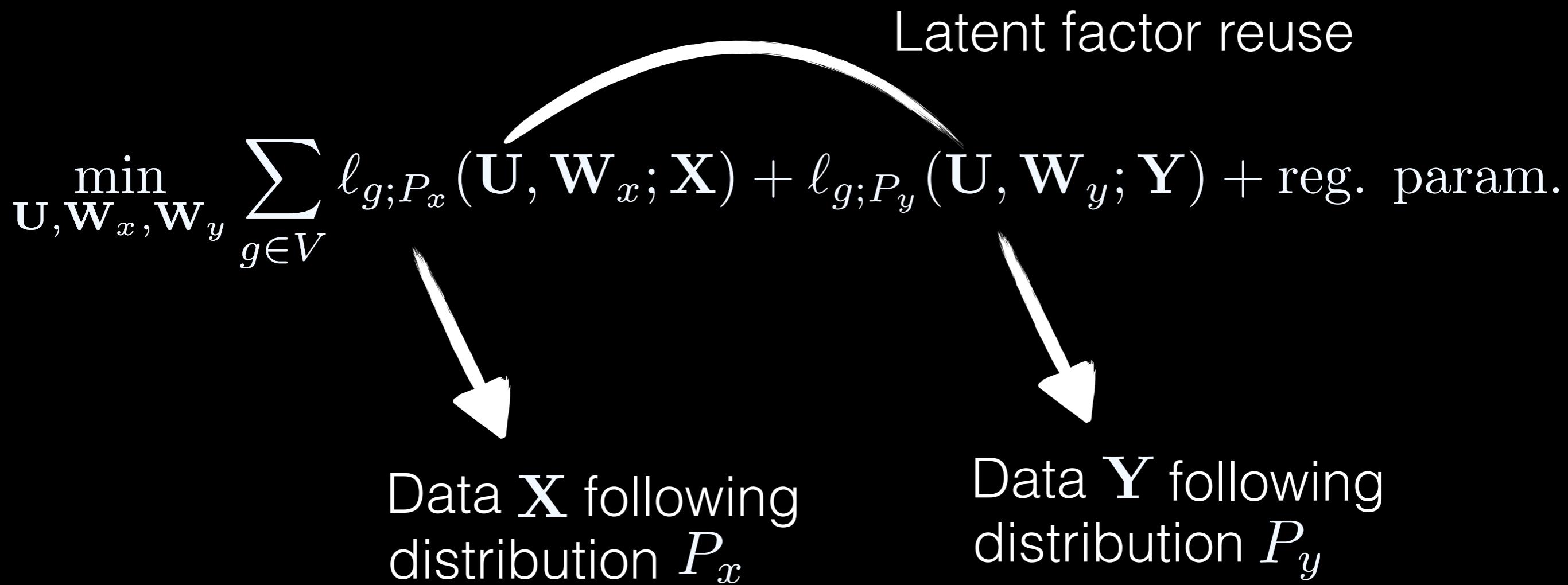
Data **X** following
distribution P_x



Data **Y** following
distribution P_y

Network Inference from Mixed Data

Objective function



Network Inference from Mixed Data

$$\min_{\mathbf{U}, \mathbf{W}_x, \mathbf{W}_y} \sum_{g \in V} \ell_{g; P_x}(\mathbf{U}, \mathbf{W}_x; \mathbf{X}) + \ell_{g; P_y}(\mathbf{U}, \mathbf{W}_y; \mathbf{Y}) + \text{reg. param.}$$

Network Inference from Mixed Data

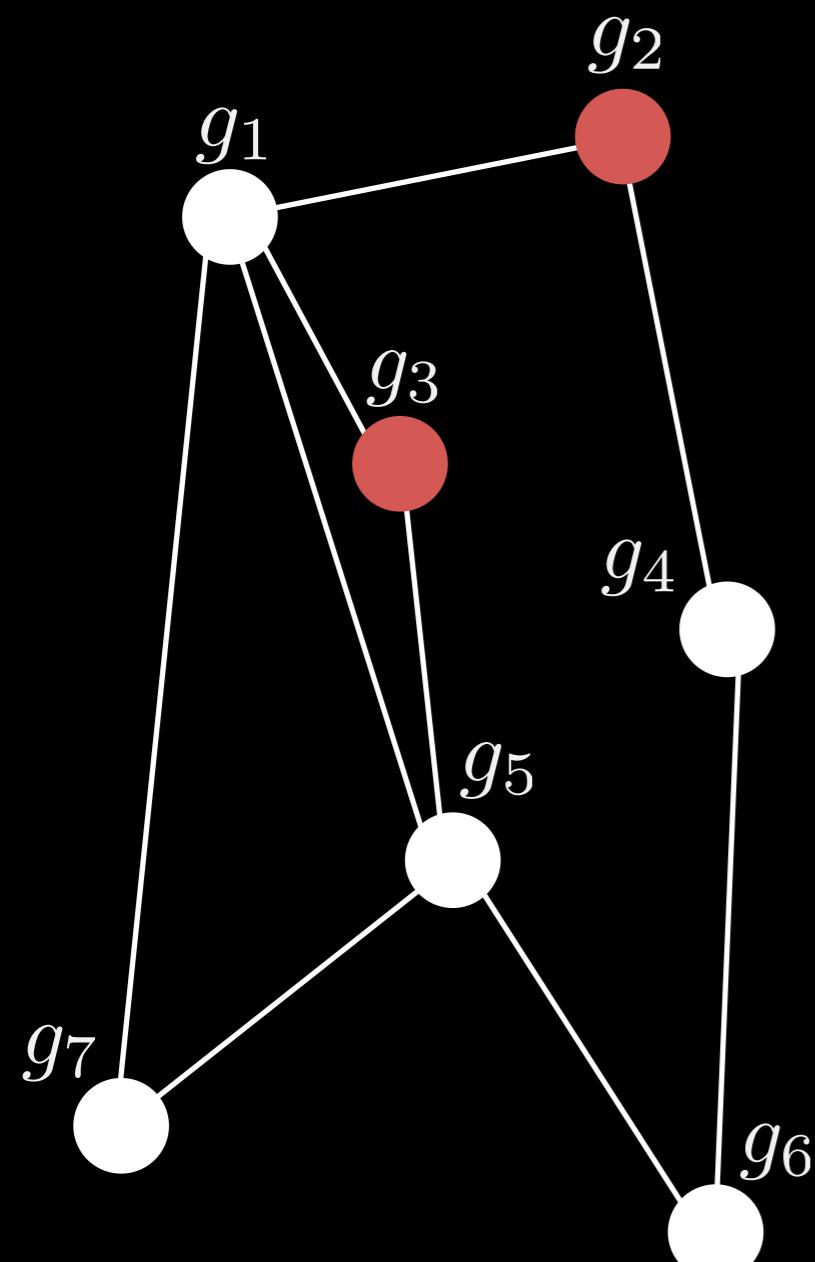
$$\min_{\mathbf{U}, \mathbf{W}_x, \mathbf{W}_y} \sum_{g \in V} \ell_{g; P_x}(\mathbf{U}, \mathbf{W}_x; \mathbf{X}) + \ell_{g; P_y}(\mathbf{U}, \mathbf{W}_y; \mathbf{Y}) + \text{reg. param.}$$

$$\hat{\mathcal{N}}(g) = \{h \in V \setminus \{g\} : \mathbf{U}_g^T \mathbf{W}_x^T \mathbf{W}_x \mathbf{U}_h \neq 0 \vee \mathbf{U}_g^T \mathbf{W}_y^T \mathbf{W}_y \mathbf{U}_h \neq 0\}$$

Data \mathbf{X}

Data \mathbf{Y}

Network Inference from Mixed Data



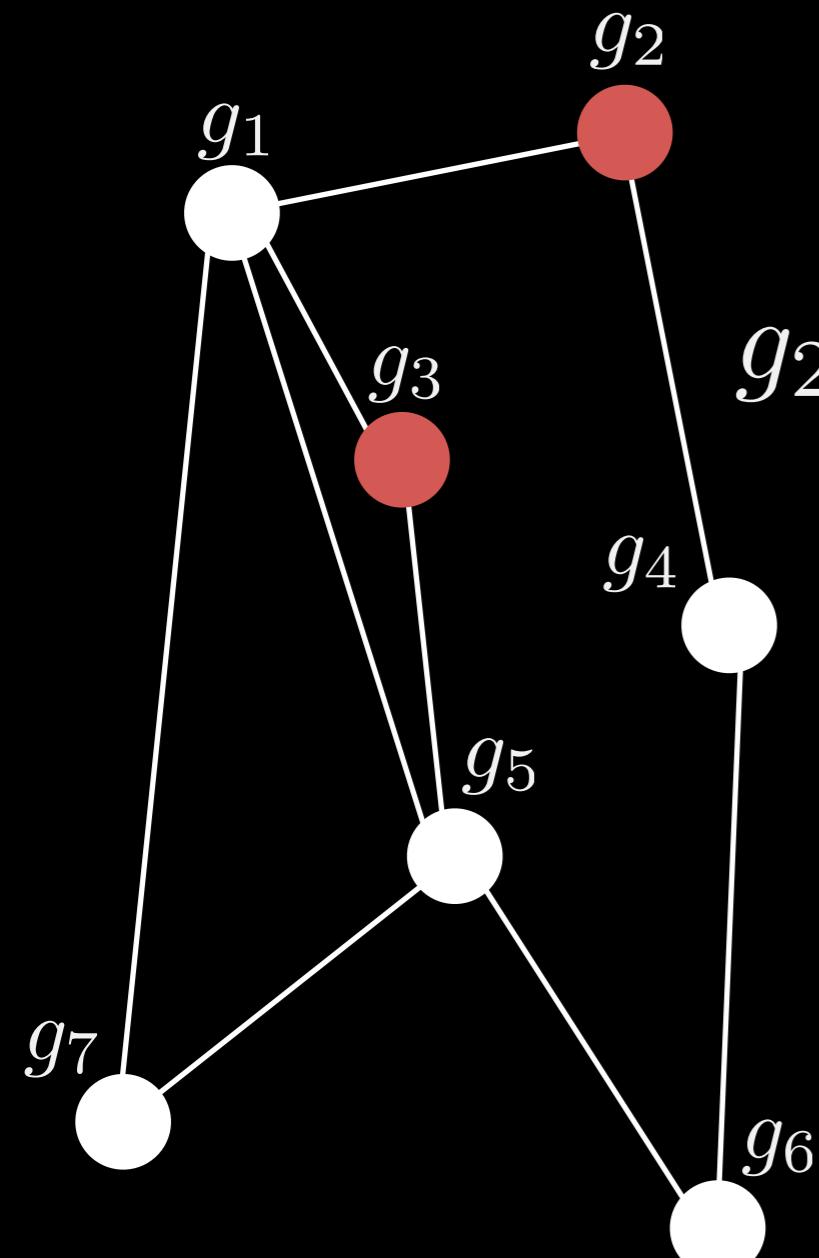
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Data X



Data Y

Network Inference from Mixed Data



$$g_2 \perp g_3 \mid \{g_1, g_4\}$$

$$\hat{\mathcal{N}}(g) = \{h \in V \setminus \{g\} : \mathbf{U}_g^T \mathbf{W}_x^T \mathbf{W}_x \mathbf{U}_h \neq 0 \vee \mathbf{U}_g^T \mathbf{W}_y^T \mathbf{W}_y \mathbf{U}_h \neq 0\}$$

Data X

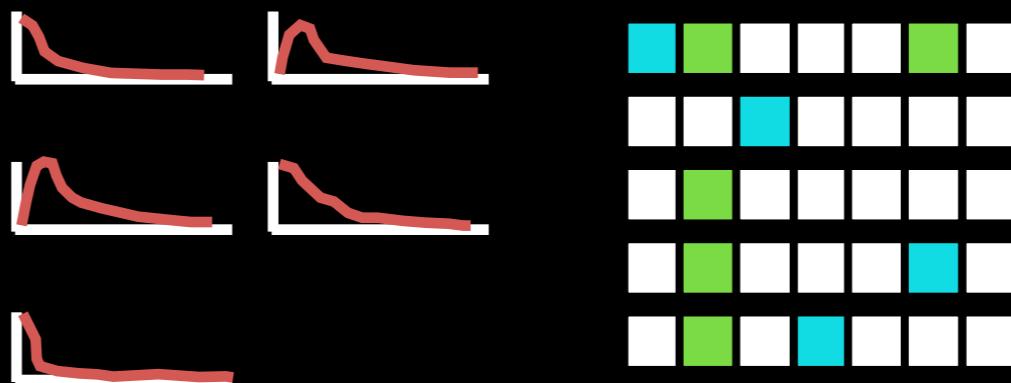


Data Y



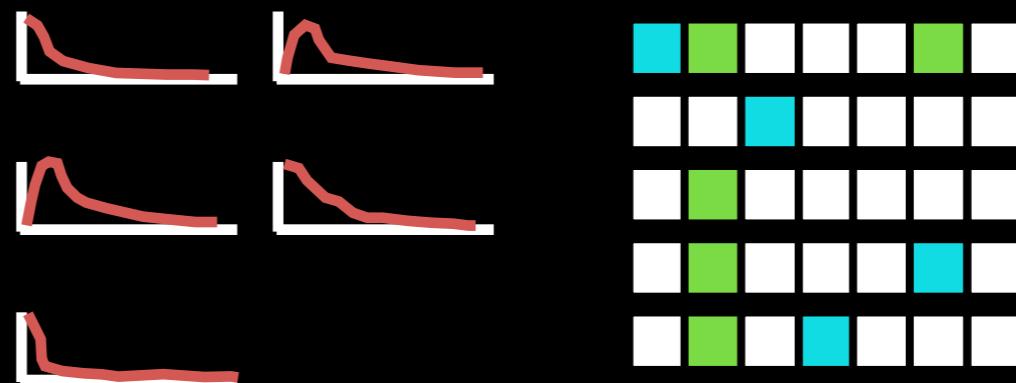
FuseNet

Data



FuseNet

Data



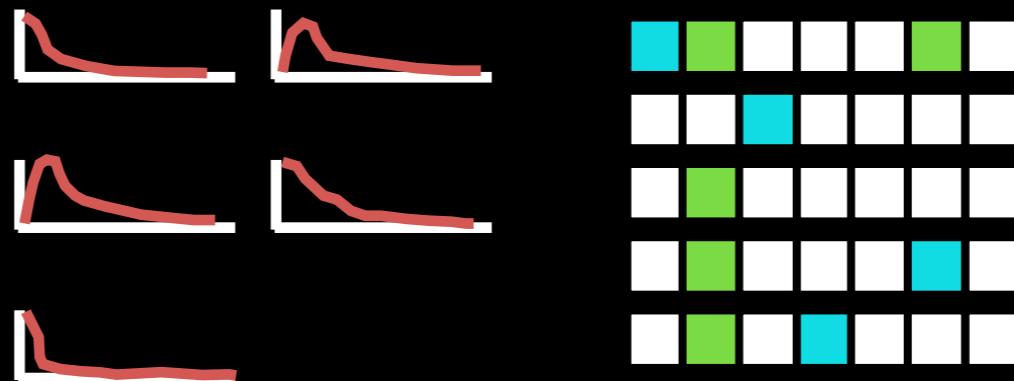
Model

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FuseNet

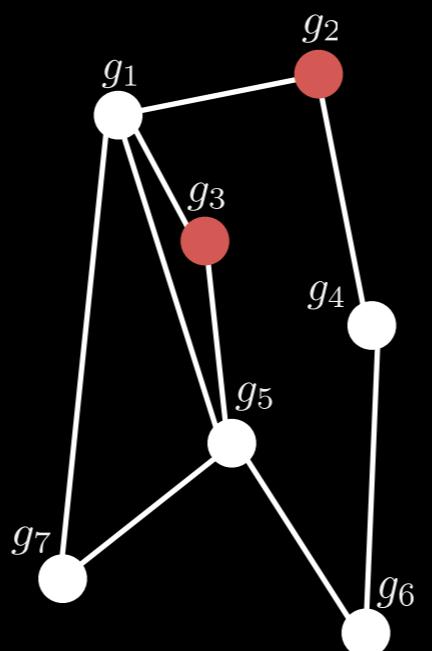
Data



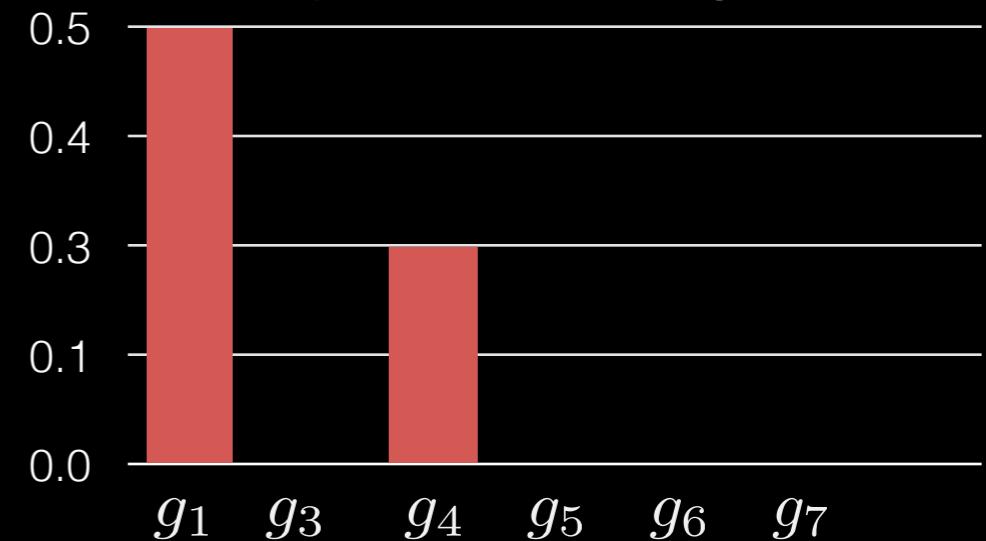
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Network



Neighborhood of g_2

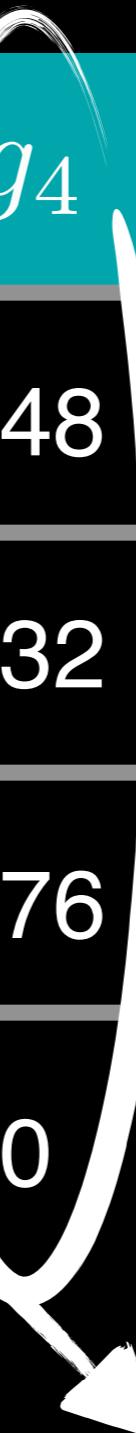


Poisson Data

	g_1	g_2	g_3	g_4	g_5	g_6	g_7	g_8
Sample 1	452	872	495	348	2	297	348	982
Sample 2	482	124	726	132	872	29	77	144
Sample 3	719	2	198	376	193	287	173	346
Sample 4	56	24	99	0	239	928	376	660

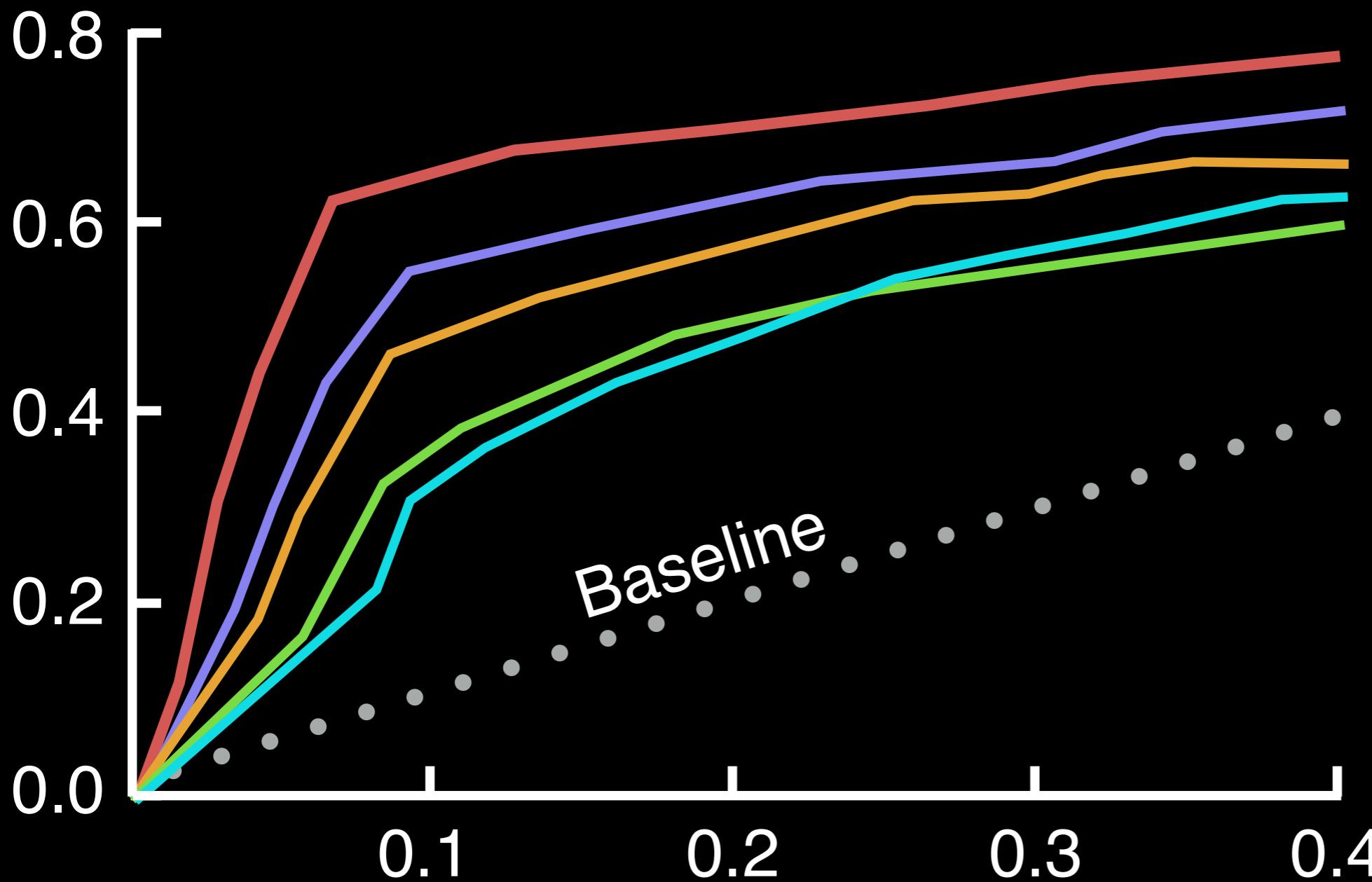
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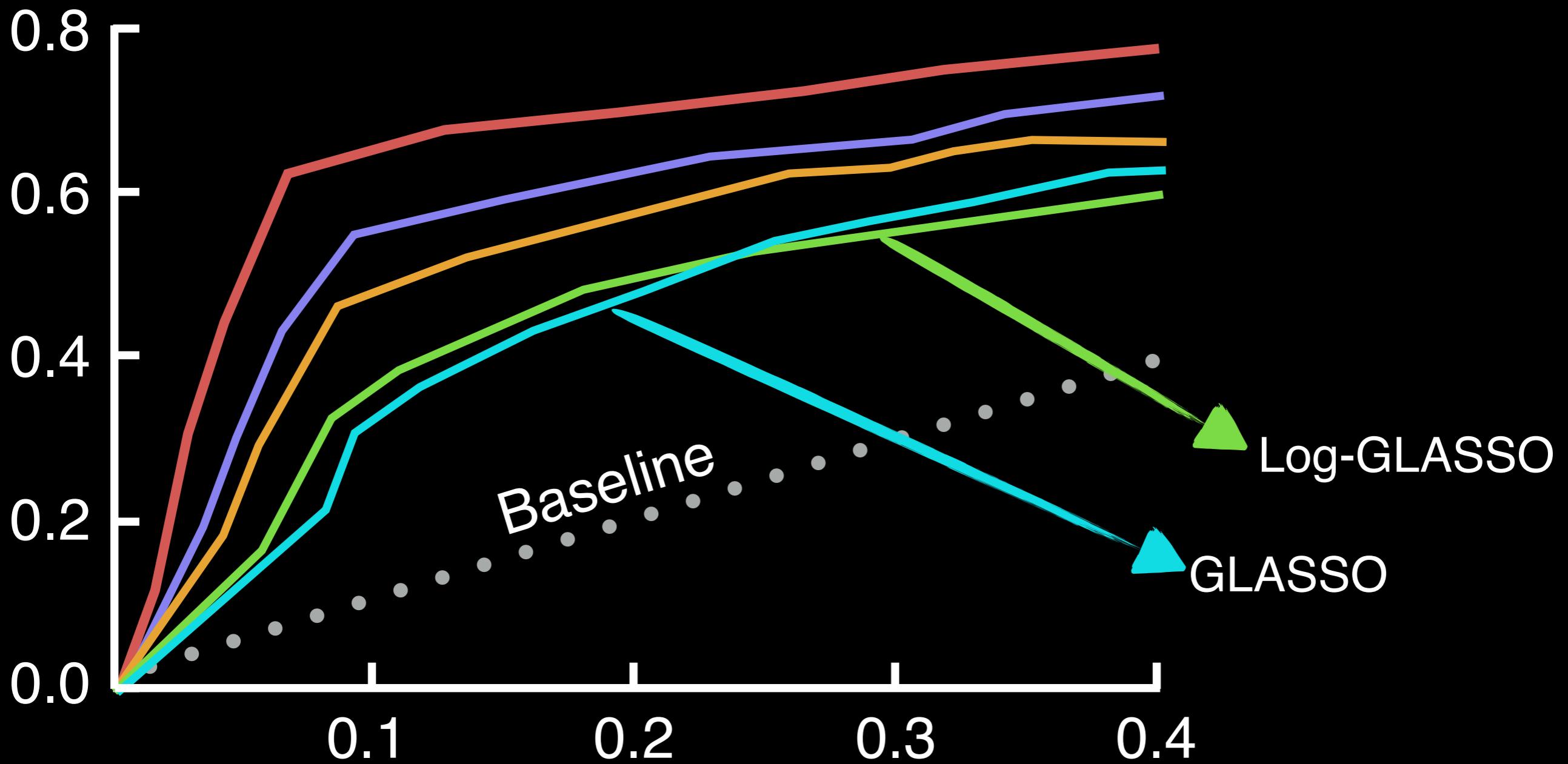
Poisson distribution

Recovery of Poisson Networks



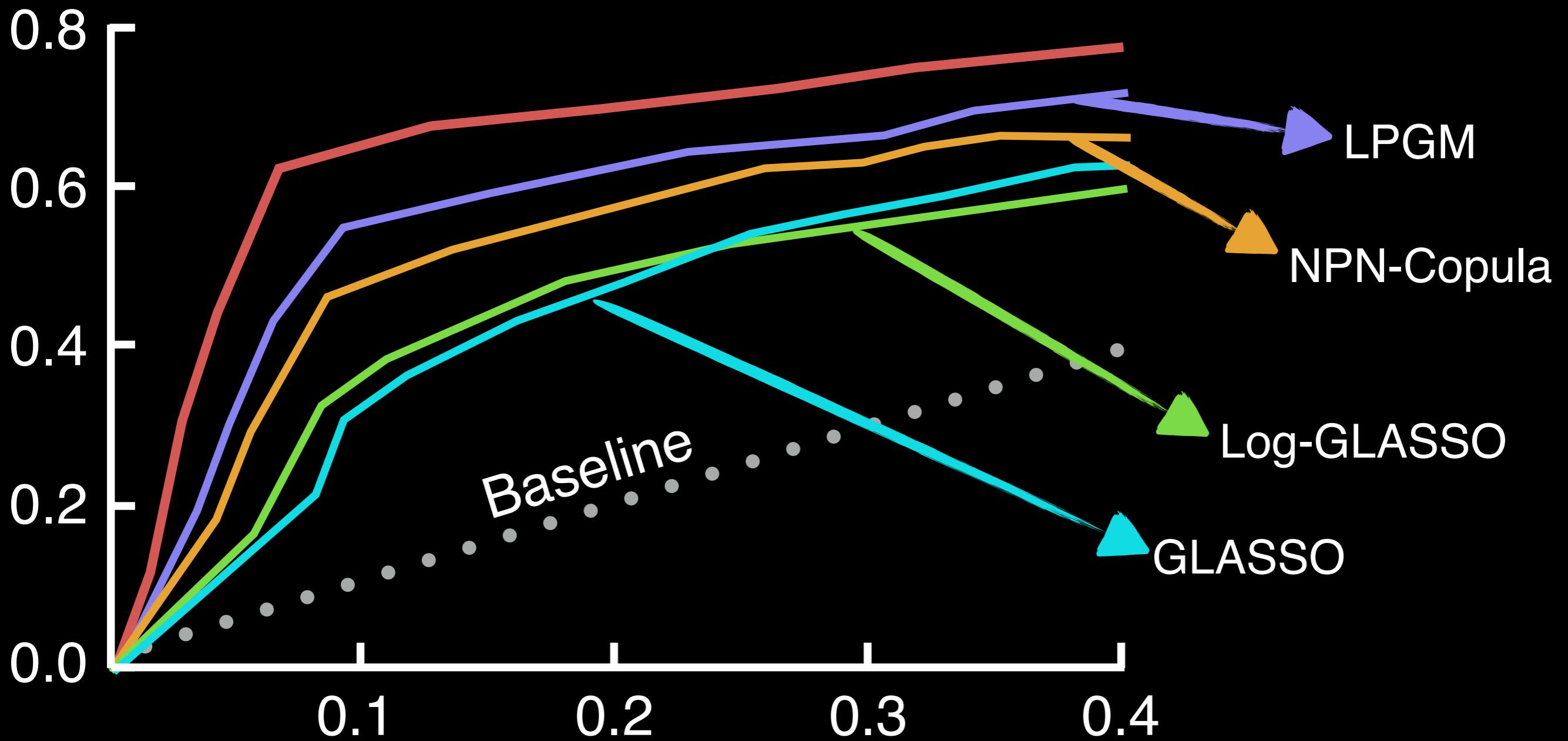
FuseNet - Our method; LPGM - Allen & Liu 2014; NPN-Copula - Liu et al. 2009;
log-GLASSO - Gallopin et al 2013; GLASSO - Friedman et al 2007

Recovery of Poisson Networks



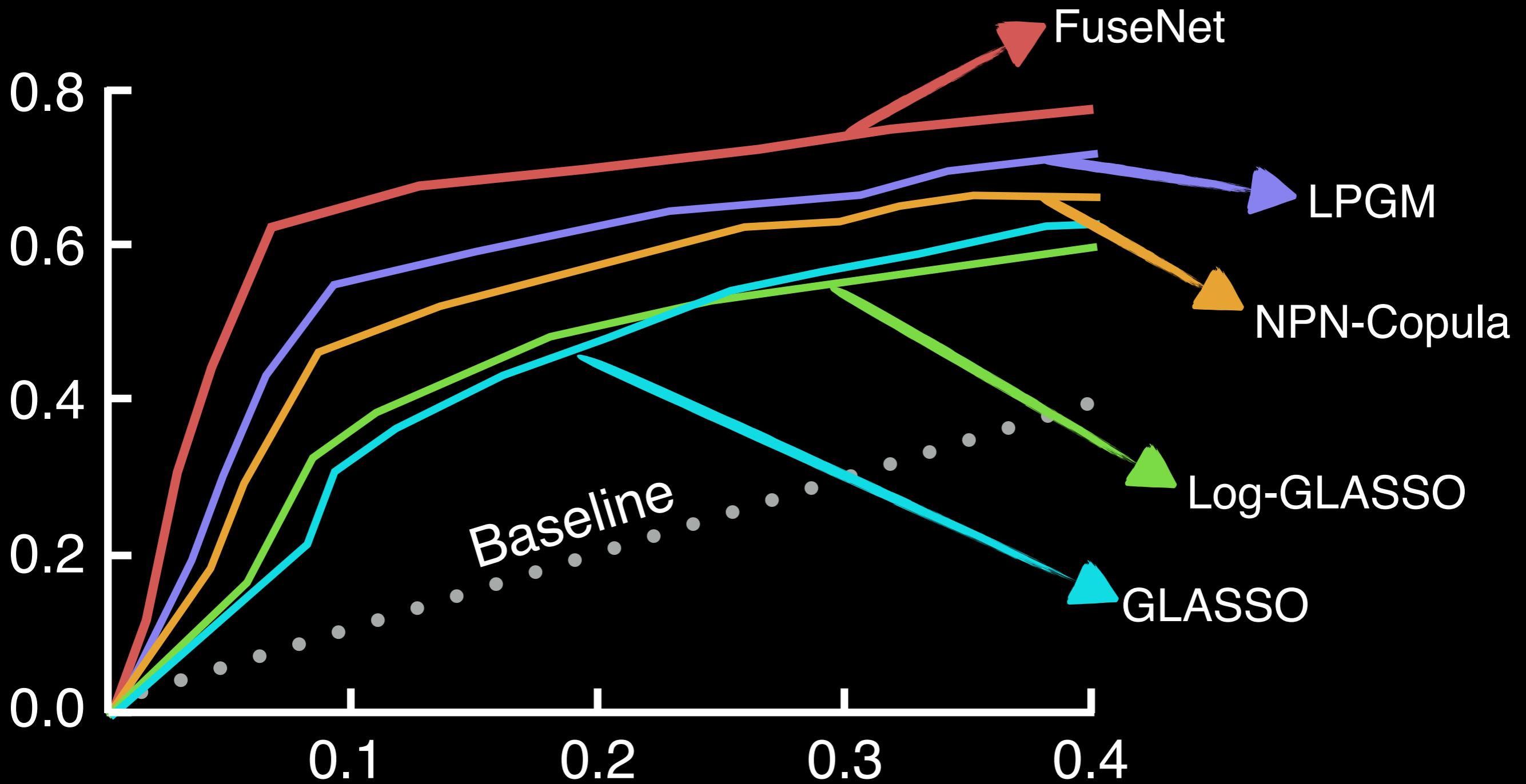
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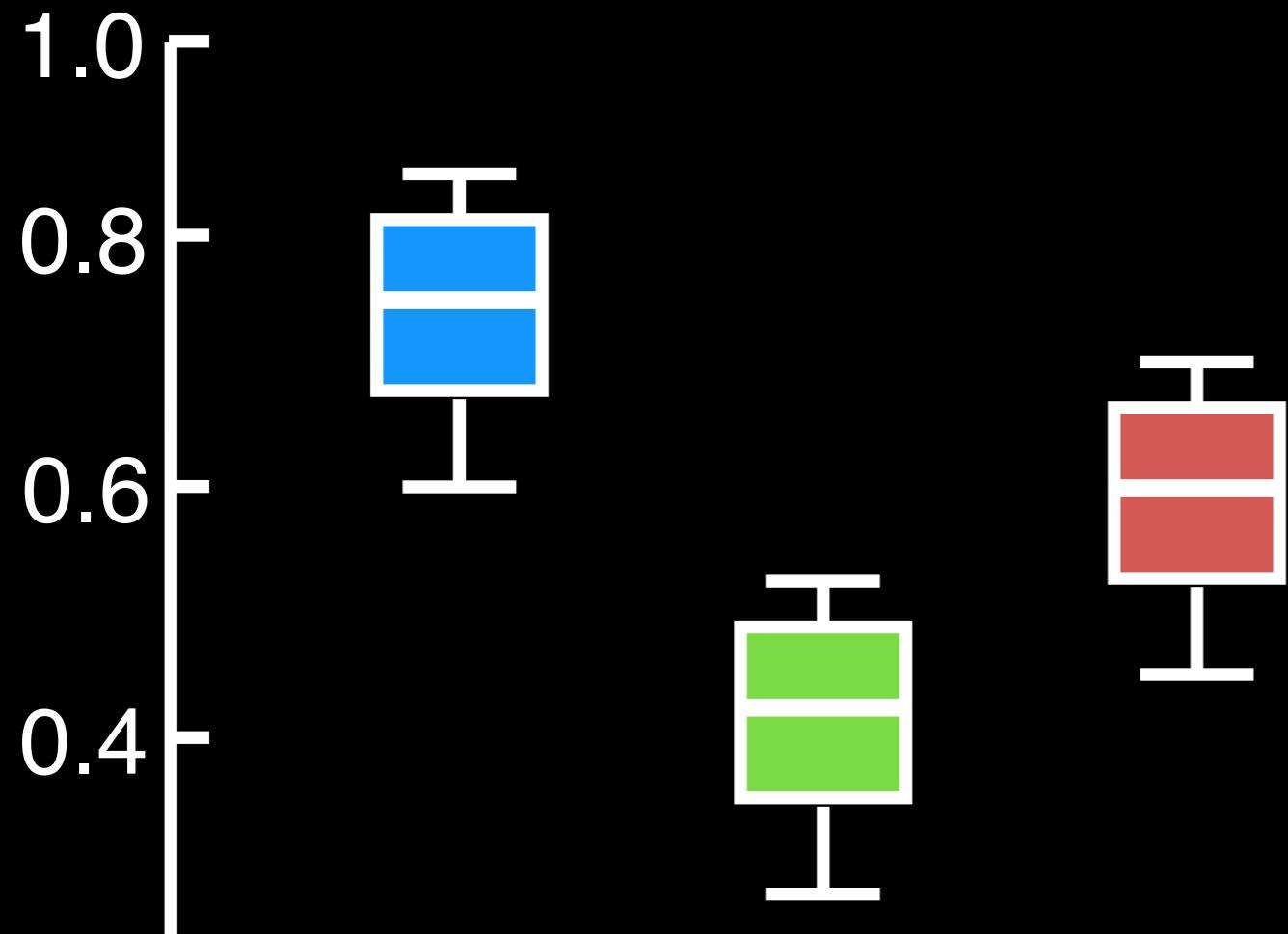
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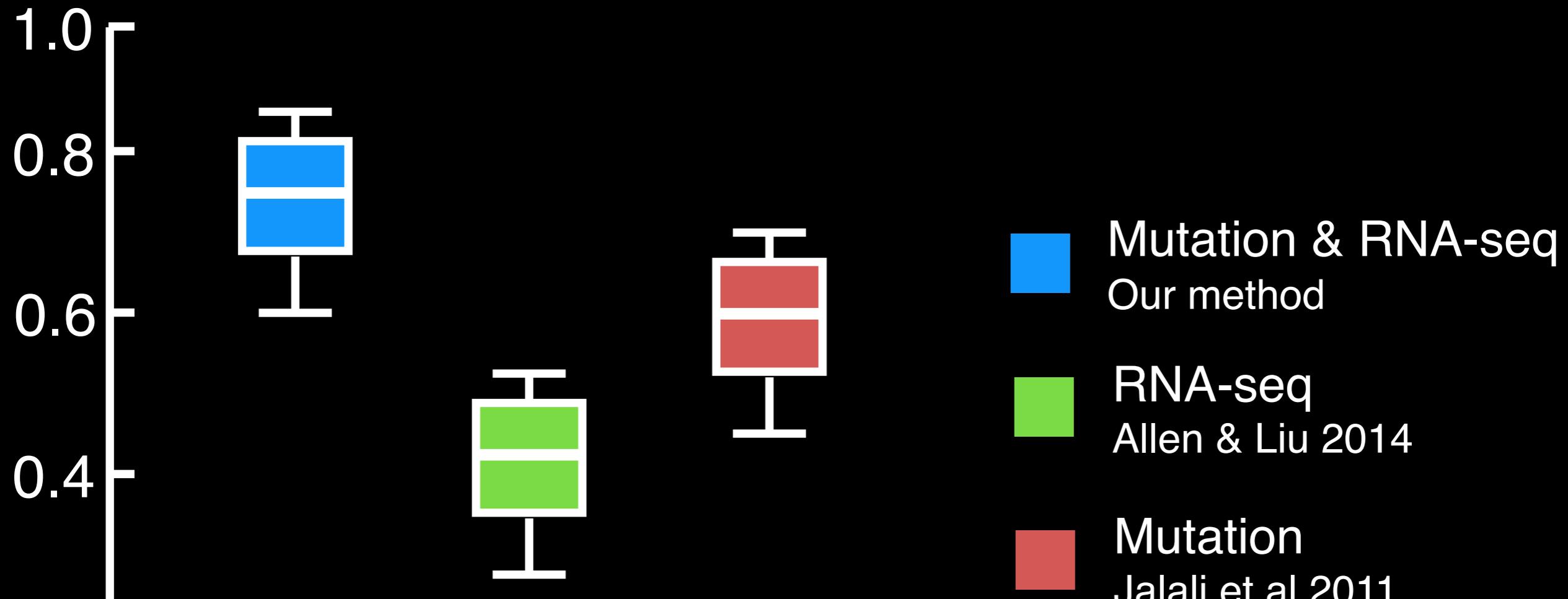
Functional Content of Inferred Cancer Networks



Higher score indicates a more informative network

Data from International Cancer Genome Consortium, BRCA

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Summary of Contributions

Relation Heterogeneity

Markov network inference for mixed data

Epistasis network inference

Collective pairwise classification for multi-way data

Z & Z. *JMLR* 2012;

Z & Z. *Bioinformatics* 2014 (in ISMB 2014);

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Z & Z. In PSB 2016

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Latent profile chaining

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Network guided matrix completion

Survival regression by data fusion

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Triple Heterogeneity

collective matrix factorization

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Exploring Heterogeneity

Sensitivity estimation using Frechet derivatives

ALL THIS EXCITEMENT
ABOUT DATA FUSION!

GENE FUNCTION PREDICTION,
DISEASE ASSOCIATIONS, PREDICTION
OF DRUG TOXICITY, GENE
PRIORITIZATION, CANCER NETWORKS,
DISEASE PROGRESSION, DRUG
INTERACTIONS, PHARMACOGENOMICS.

I WONDER WHAT'S NEXT?





biolab

Blaz Zupan



Uroš Petrovic
Petrá Kaferle

Charles Boone
Mojca M. Usaj



Karolinska
Institutet



SciLifeLab

Thomas Helleday
Jordi C. Puigvert

Natasa Przulj
Vuk Janjic

Imperial College
London

Stanford
University

Jure Leskovec



Adam Kuspa
Edward Nam
Chris Dinh

Baylor
College of
Medicine®



Gad Shaulsky
Rafael Rosengarten
Mariko Kurasawa
Balaji Santhanam

