Entropy and functional redundancy in biological networks

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1. How can we **understand robustness** in biological networks?

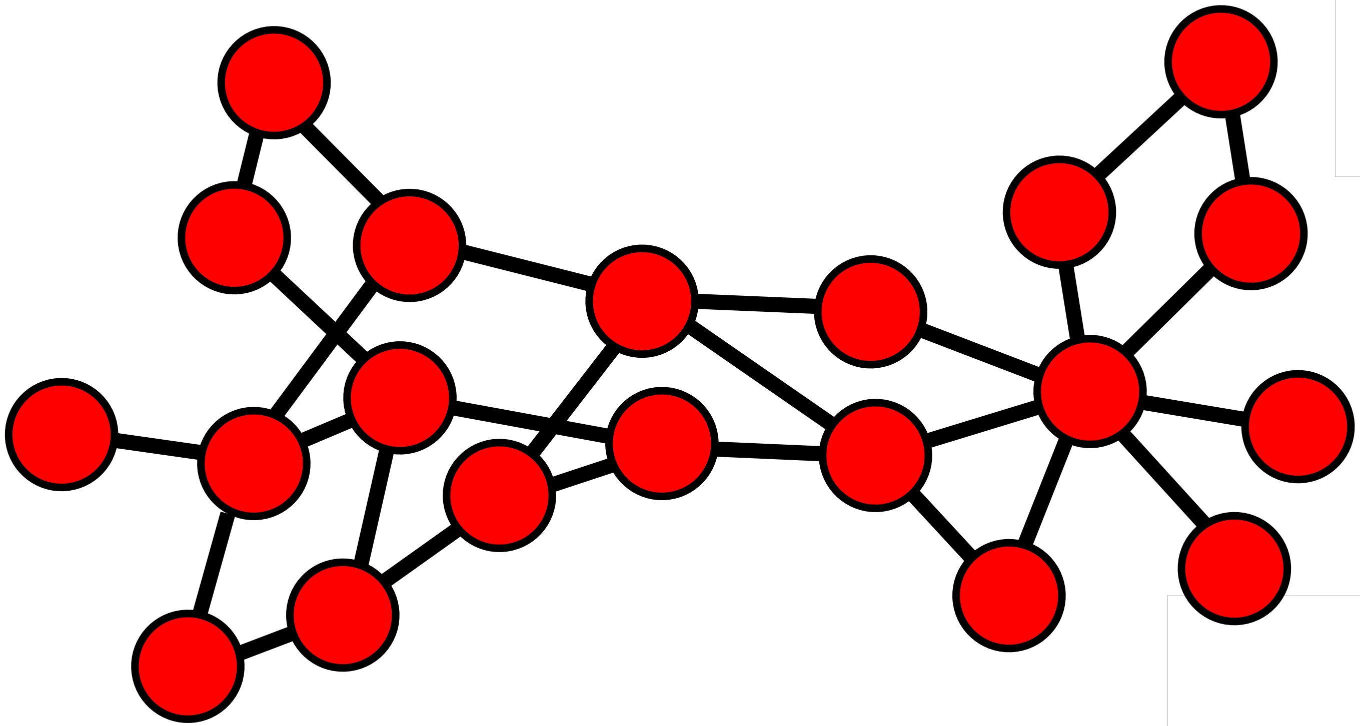
2. How can we **measure redundancy** in biological networks?

3. Which **network motifs** contribute to redundancy?

4. Why is this **cool**?

Robustness of biological networks

Robustness of biological networks



$$\mathcal{N} = (V, E)$$

$$A_{ij} = \begin{cases} 1 & \text{if } e_{ij} \in E \\ 0 & \text{else} \end{cases}$$

$$\mathbf{x} := (x_1, x_2, x_3, \dots, x_N)^T$$

$$d\mathbf{x} = f(\mathbf{x}, \mathbf{A}, \xi)$$

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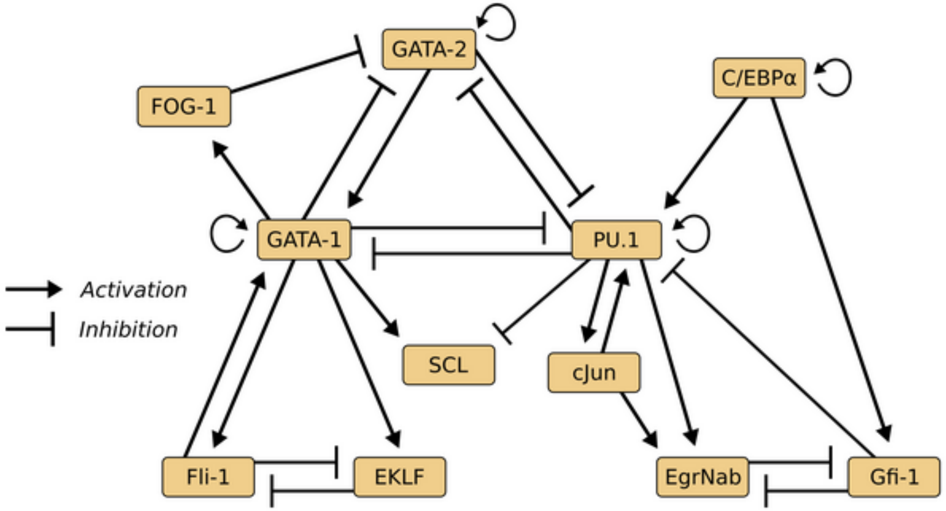
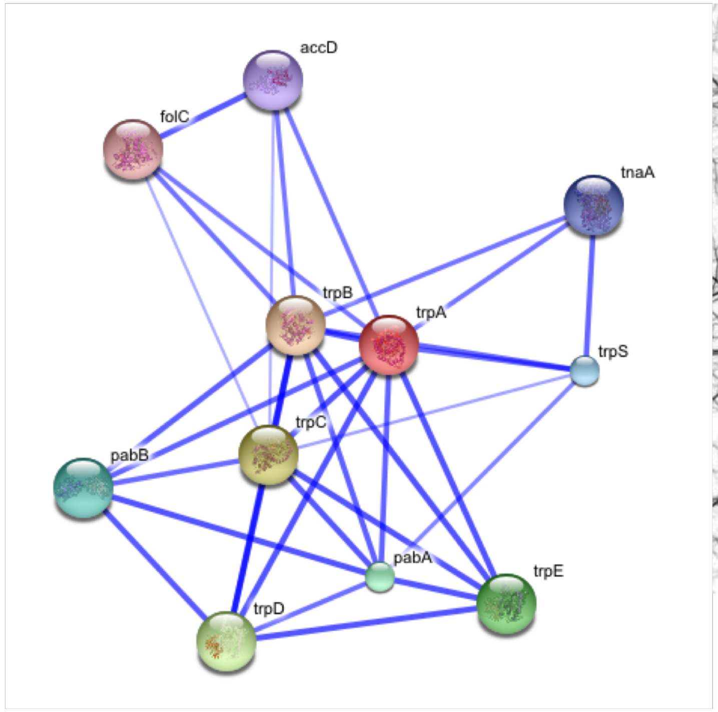
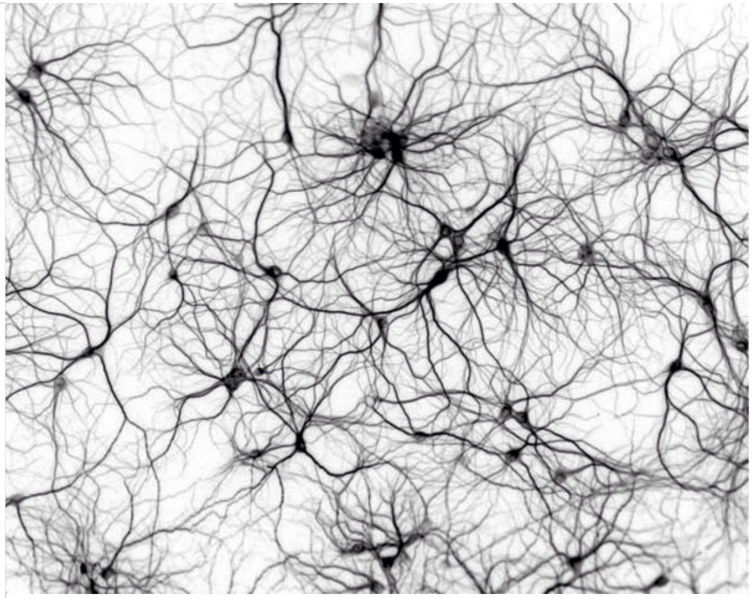


J. Krumsiek, et al. *PloS one* 6.8 (2011): e22649.



STRING Database (2009)



M. Humphries, The Spike (2016)

Robustness of biological networks

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- Robustness of a ***function*** of a ***system*** to a ***perturbation***

Robustness of biological networks

- Robustness of a ***function*** of a ***system*** to a ***perturbation***
- In biological networks:

function	=	viability
system	=	organism/cell
perturbation	=	environmental changes/ mutations

Structural and functional redundancy

- ***Structural redundancy*** indicates the existence of structurally similar subsystems that can perform the same function.
- ***Functional redundancy*** indicates the existence of structurally different subsystems that can perform the same function.

G. M. Edelman and J. A. Gally. *Proceedings of the National Academy of Sciences* 98.24 (2001): 13763-13768.

Structural and functional redundancy

Or: How to recruit for your pirate ship

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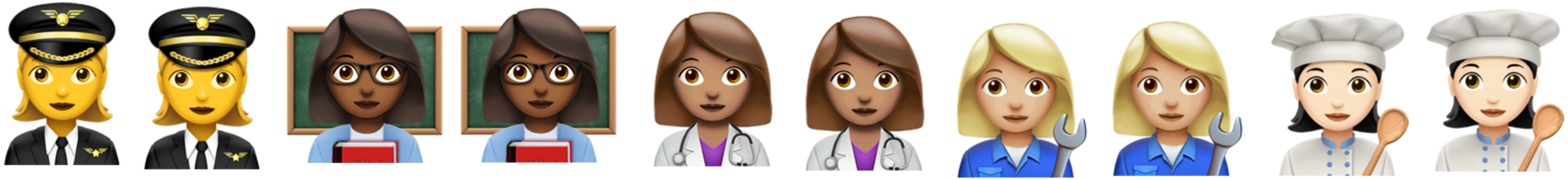
Minimal crew with *"structurally redundant"* members (10):



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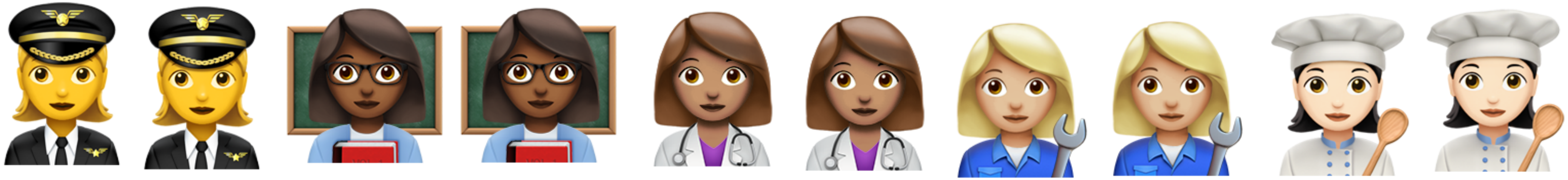

Minimal crew with *"functionally redundant"* members (6):

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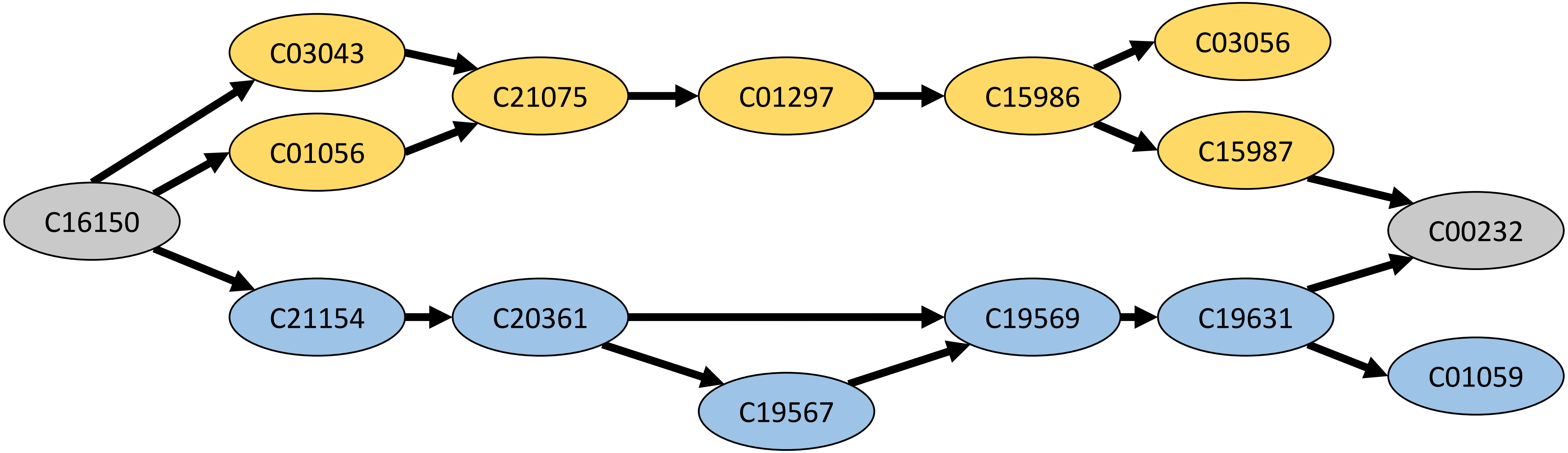

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   Hypothesis: Functional redundancy is important for robustness

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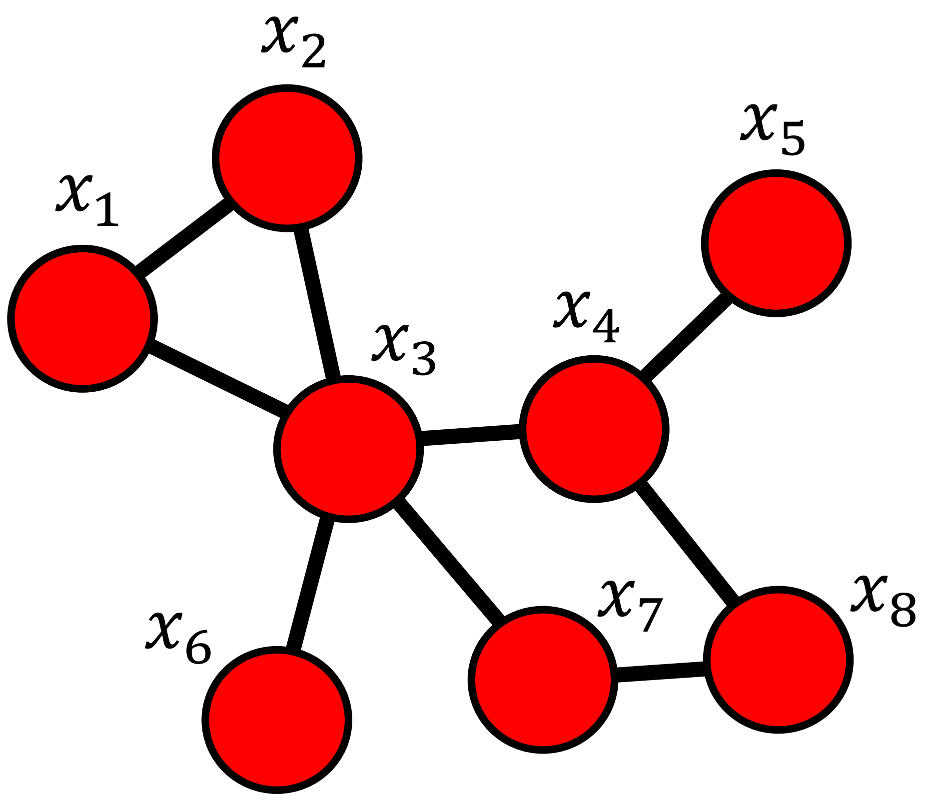
Information-based measures of redundancy

$$\mathbf{x} := (x_1, x_2, x_3, \ldots, x_N)^T$$
$$d\mathbf{x} = f(\mathbf{x}, \mathbf{A}, \xi)$$

$$H(\mathbf{x}) := \frac{1}{2}\ln\left[(2\pi e)^N \det(\mathbf{COV}(\mathbf{x}))\right]$$



O. Sporns, G. Tononi, and G. M. Edelman. *Cerebral cortex* 10.2 (2000): 127-141.

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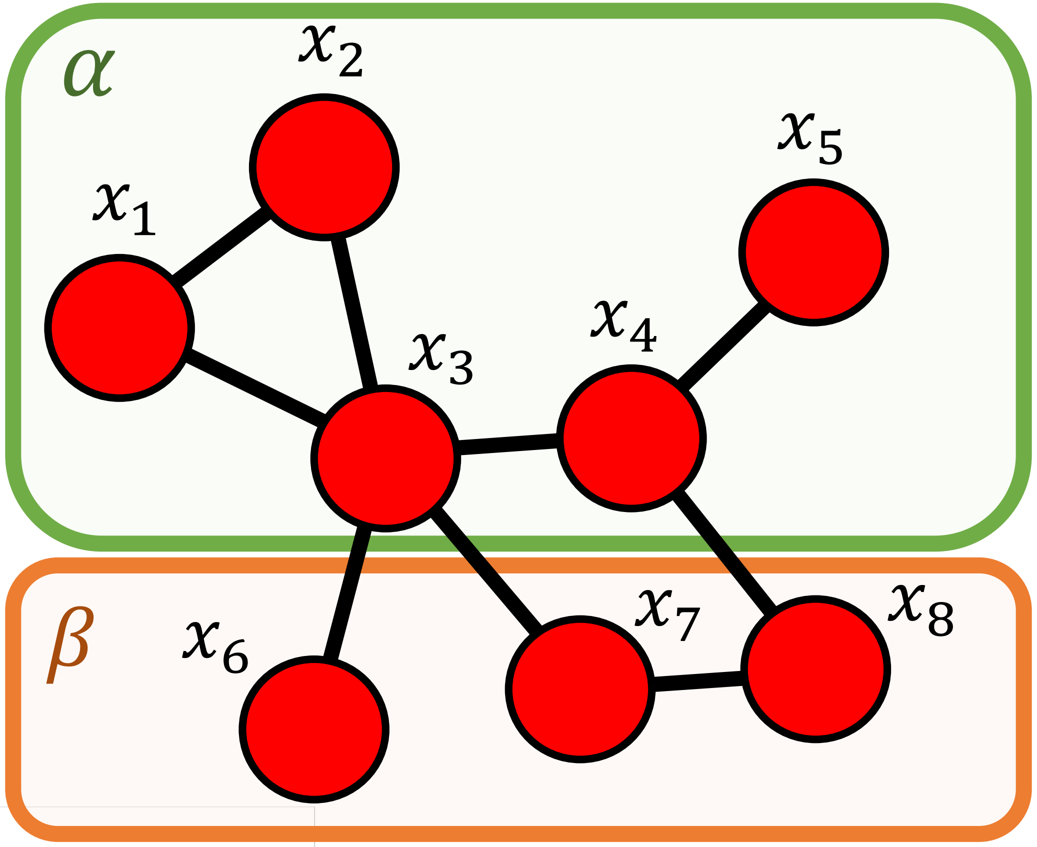
$$d\mathbf{x} = f(\mathbf{x}, \mathbf{A}, \xi)$$

$$\mathbf{x}_\alpha = (x_1, \ldots, x_k)^T,$$
$$\mathbf{x}_\beta = (x_{k+1}, \ldots, x_N)^T$$

$$H(\mathbf{x}) := \frac{1}{2} \ln \left[(2\pi e)^N \det(\mathbf{COV}(\mathbf{x})) \right]$$

$$I(\mathbf{x}_\alpha, \mathbf{x}_\beta) := H(\mathbf{x}_\alpha) + H(\mathbf{x}_\beta) - H(\mathbf{x})$$



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Information-based measures of redundancy

- Kernel set

$$\mathbf{x}_\kappa = (x_1, \ldots, x_k)^T$$

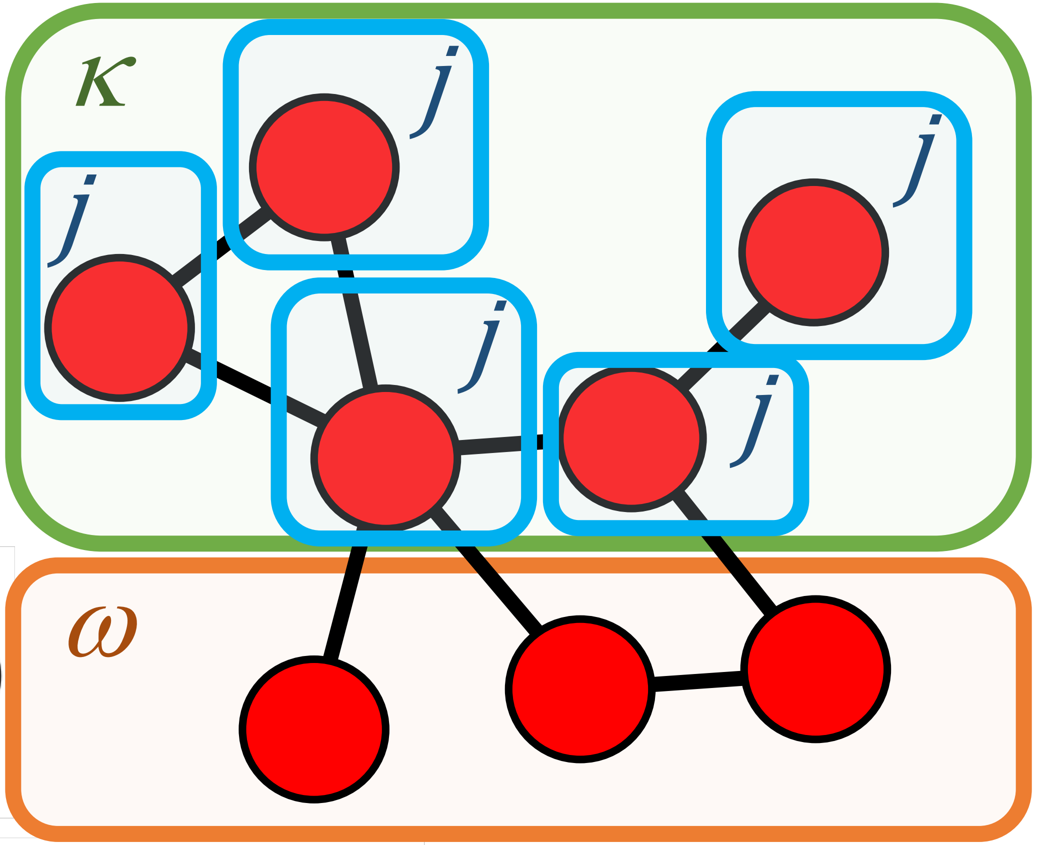
- Output set

$$\mathbf{x}_\omega = (x_{k+1}, \ldots, x_N)^T$$

- Redundancy

$$R(\mathbf{x}_\kappa, \mathbf{x}_\omega) := \sum_{j=1}^{k} I(x_j, \mathbf{x}_\omega) - I(\mathbf{x}_\kappa, \mathbf{x}_\omega)$$

$$R_F(\mathbf{x}_\kappa, \mathbf{x}_\omega) := \sum_{j=1}^{k} \left[\frac{j}{k} R(\mathbf{x}_\kappa, \mathbf{x}_\omega) - \langle R(\mathbf{x}_\iota, \mathbf{x}_\omega) \rangle_{\iota \subset_j \kappa} \right]$$



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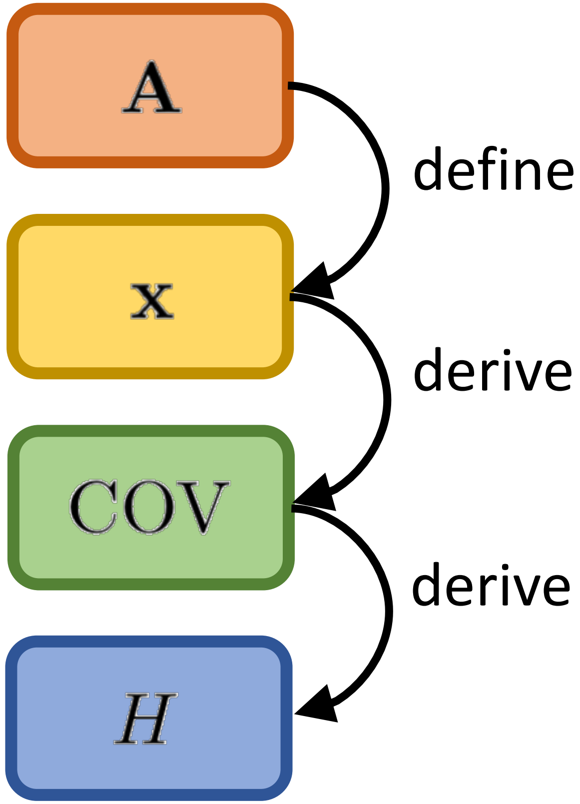
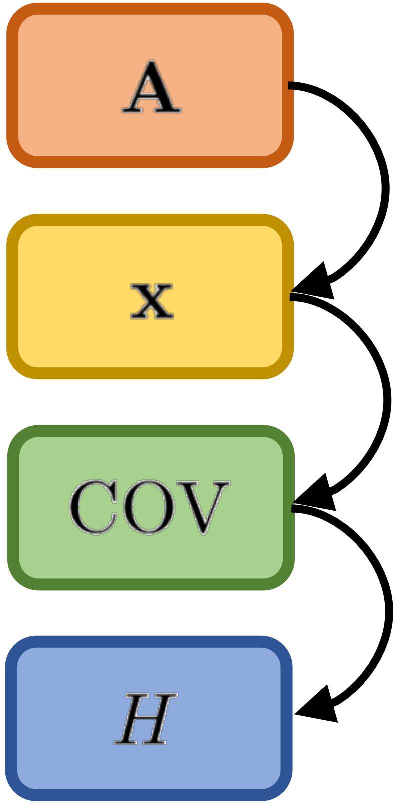
Information and network structure



L. Barnett, C. L. Buckley, and S. Bullock. *Physical Review E* 79.5 (2009): 051914.

Information and network structure



define $$d\mathbf{x}(t) = -\mathbf{x}(1 - \mathbf{A})dt + d\mathbf{W}(t)$$

derive $$\mathrm{COV} = (v_{ij}) = E(\mathbf{x}(t)^T\mathbf{x}(t))$$

derive $$H = \frac{1}{2}\ln\left[(2\pi e)^N \det(\mathrm{COV})\right]$$

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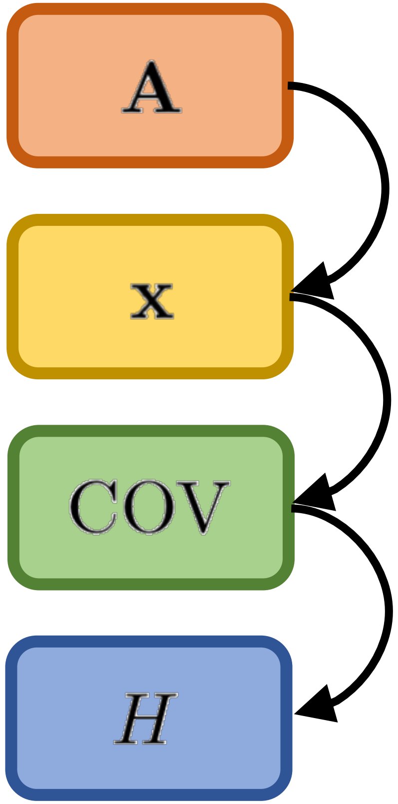

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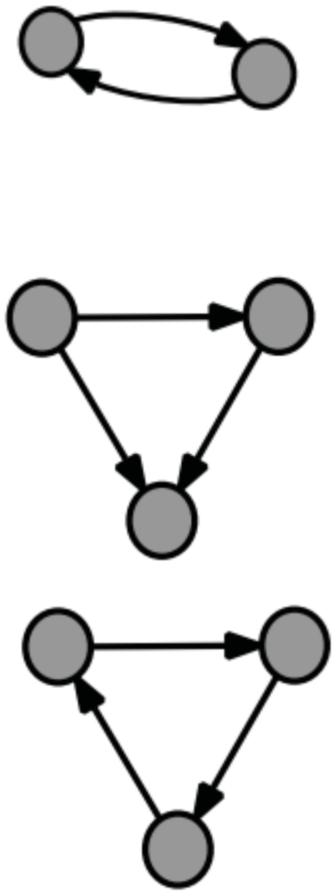

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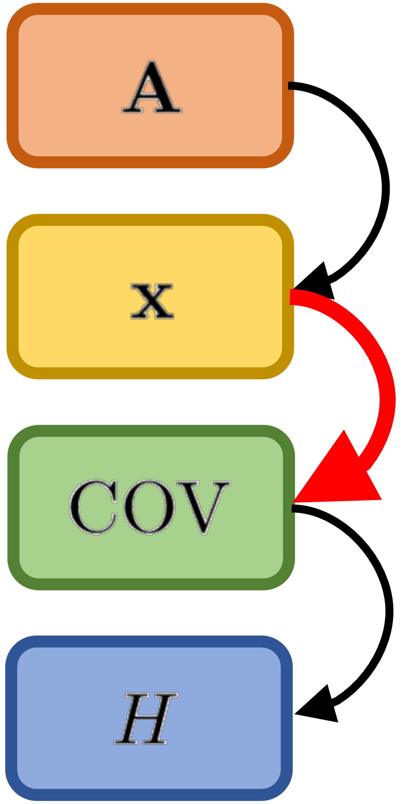

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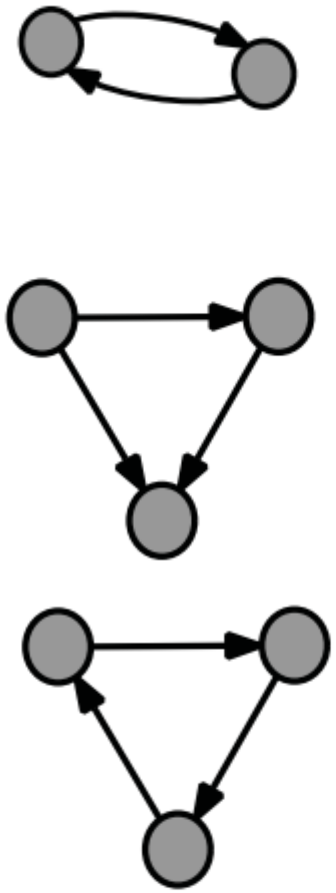

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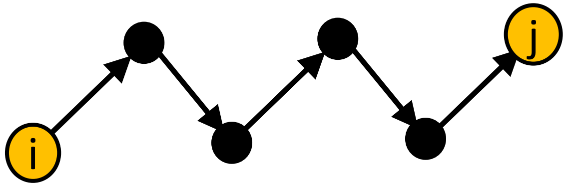
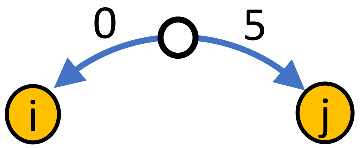
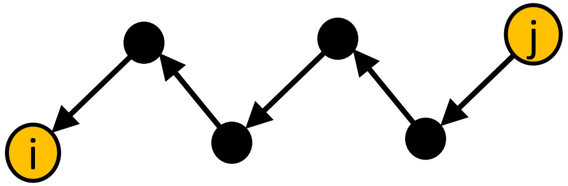
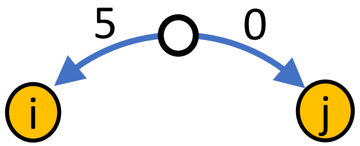
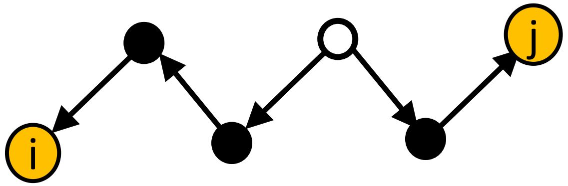
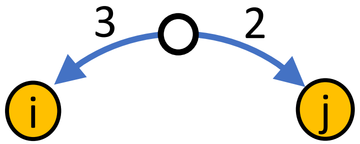
Information and network structure

COV

$$\mathrm{COV} = \frac{1}{2}\sum_{L=0}^{\infty} 2^{-L} \sum_{l=0}^{L} \binom{L}{l} (\mathbf{A}^{l})^{T}\mathbf{A}^{L-l}$$

Matrix	Graph diagramme	Chain diagramme
$\mathbf{A}^5$		
$(\mathbf{A}^{\mathrm{T}})^5$		
$(\mathbf{A}^{\mathrm{T}})^3\mathbf{A}^2$		

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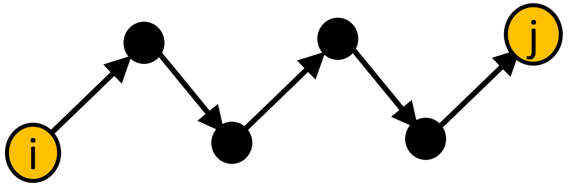
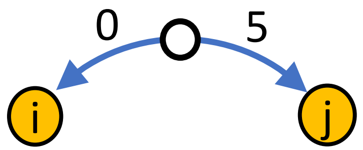
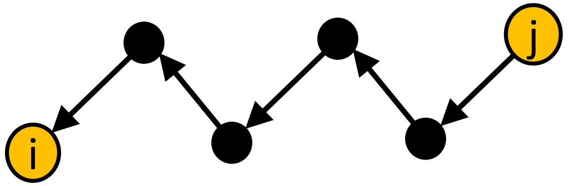
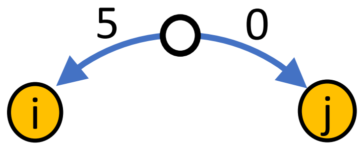
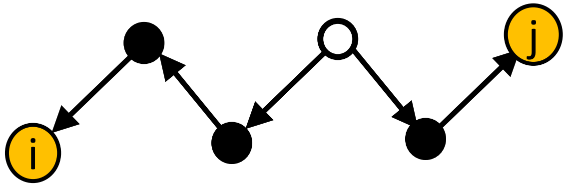
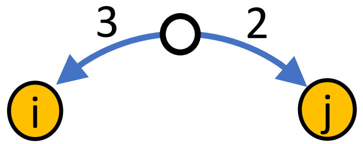
$\mathbf{A}^5$		
$(\mathbf{A}^T)^5$		
$(\mathbf{A}^T)^3\mathbf{A}^2$		

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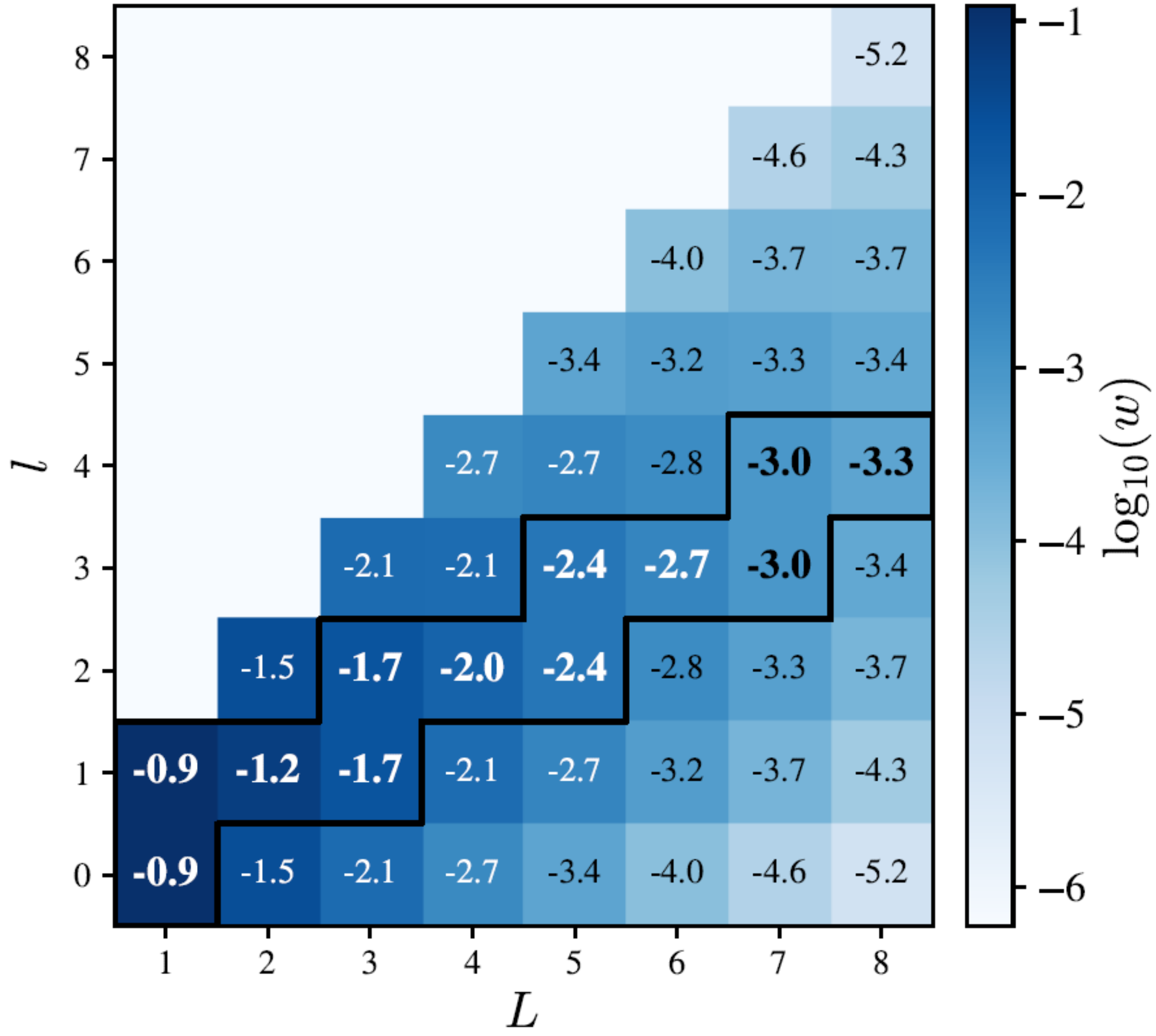

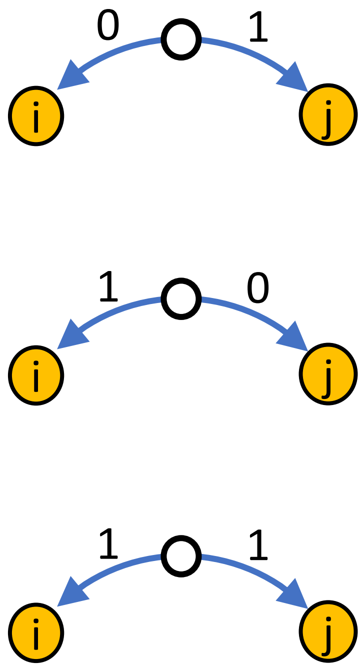

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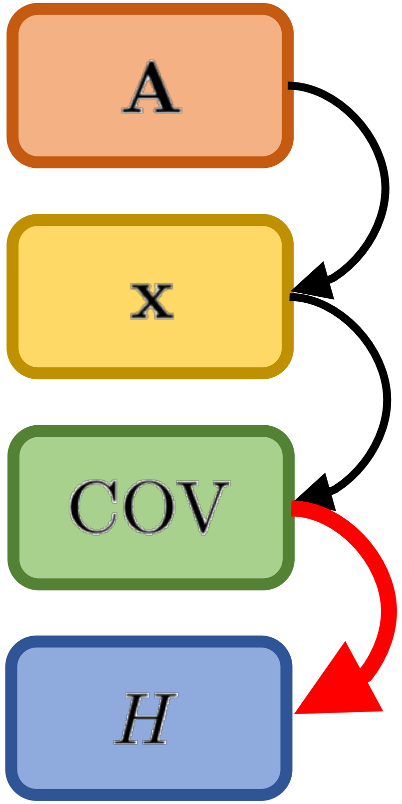

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H

$$H \propto \sum_{m \in \text{motifs}} w_m \, \#m$$

$$= \sum_{k=1}^{\infty} \sum_{\mathbf{x},\mathbf{y} \in \mathbb{N}^k} \frac{(-1)^{k+1}}{k} \prod_{i=1}^{k} 2^{-(x_i+y_i)} \binom{x_i + y_i}{x_i} \#m_{\mathbf{x},\mathbf{y}}$$

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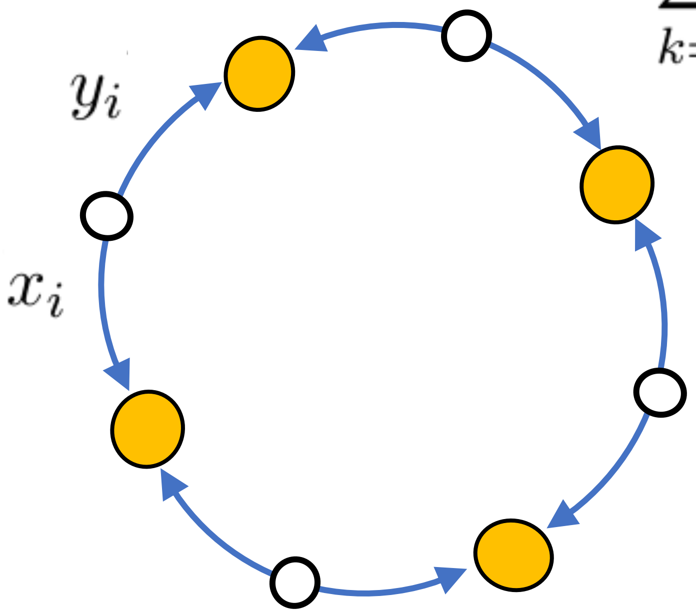

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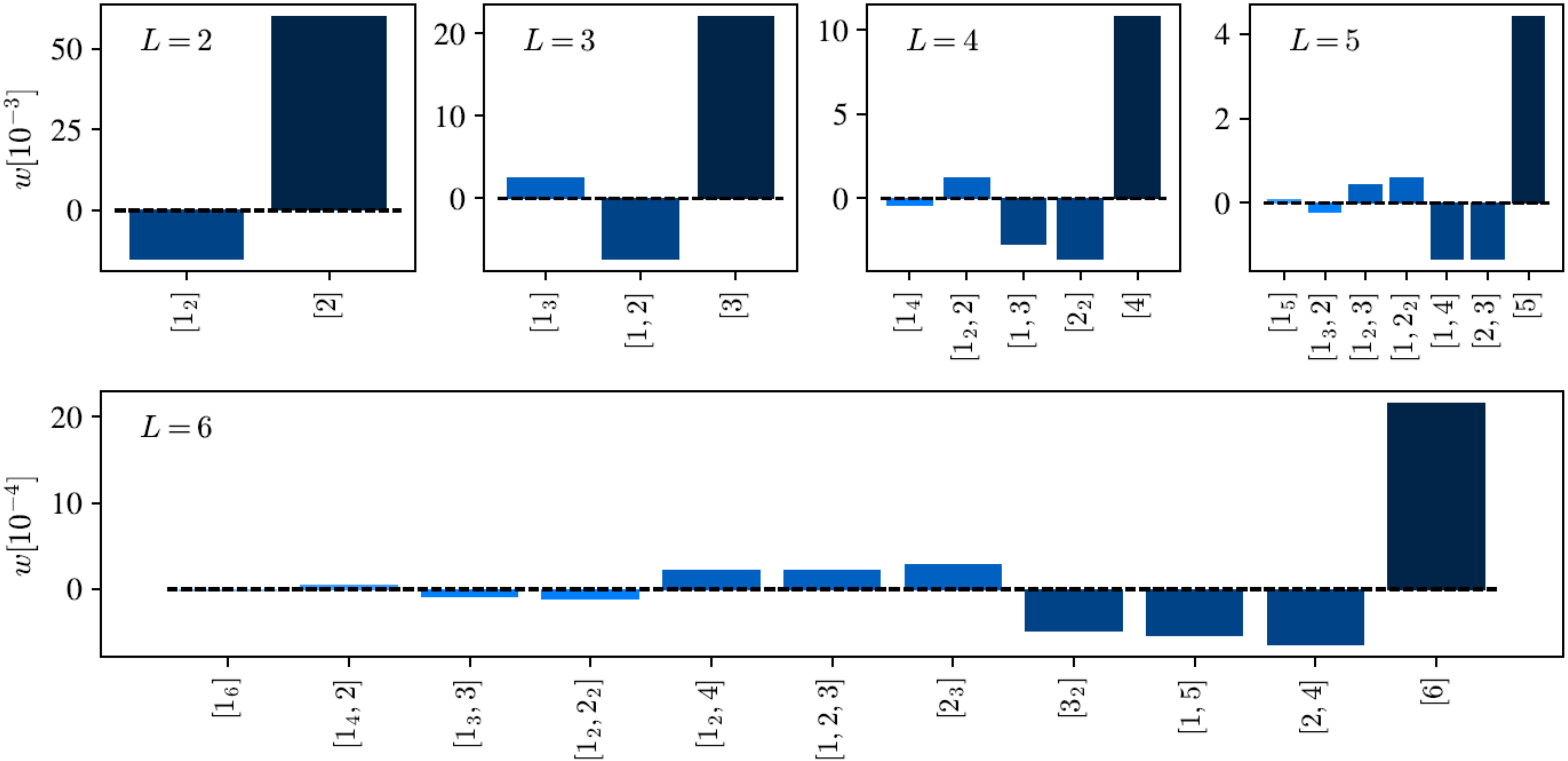

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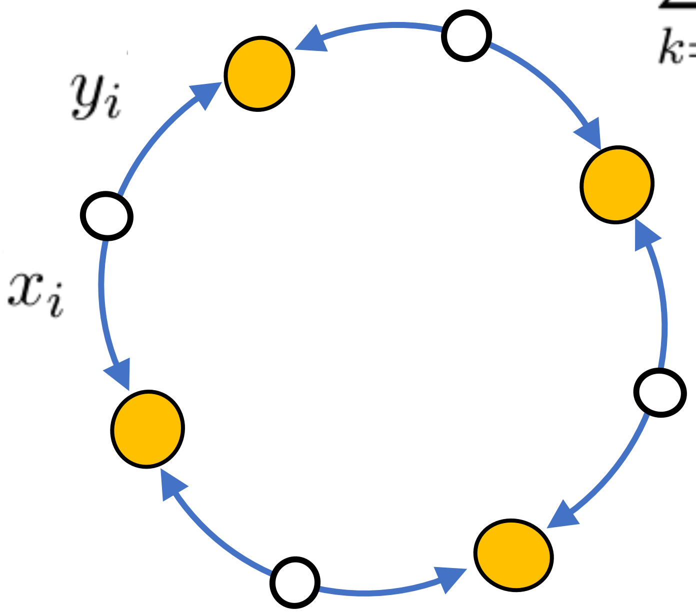

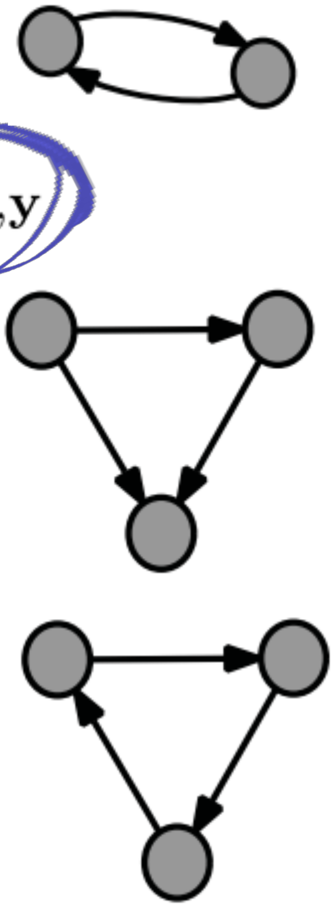

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   Ubiquity of functional redundancy
   Quantitative approach to redundancy
   Understanding the influence of dynamics