بسم الله الرحمن الرحیم

Balance Theory of Signed Genetic Interactions Reveals Differences in Cancerous and Healthy Cells

Abbas K. Rizi

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School of Science

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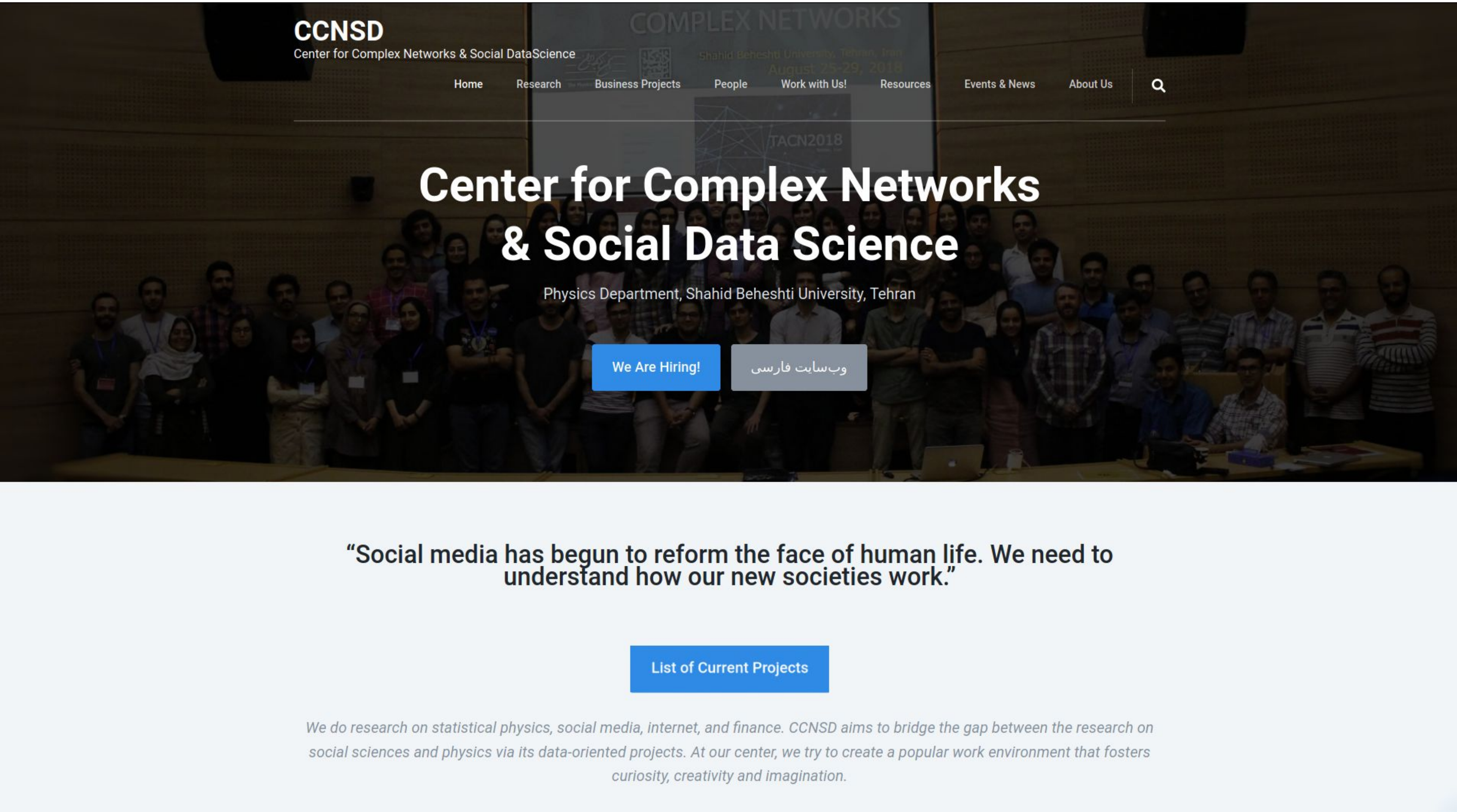

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We Are Hiring!
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“Social media has begun to reform the face of human life. We need to understand how our new societies work.”
List of Current Projects
We do research on statistical physics, social media, internet, and finance. CCNSD aims to bridge the gap between the research on social sciences and physics via its data-oriented projects. At our center, we try to create a popular work environment that fosters curiosity, creativity and imagination.

I am going to talk about:

- Balance Theory
- Molecular Biology
- Inference Problems (Inverse Stat. Phys.)
- Results!

Balance Theory

Heider, Fritz (1958). *The Psychology of Interpersonal Relations*. John Wiley & Sons.

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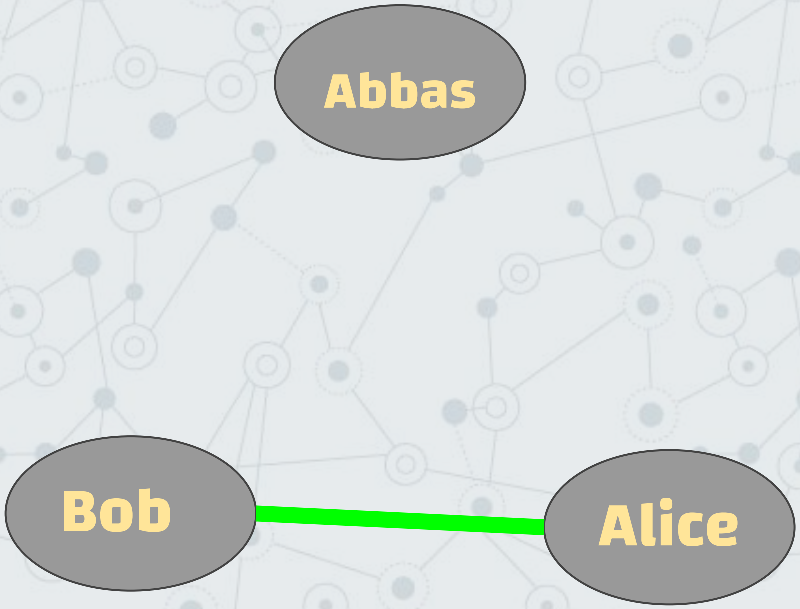

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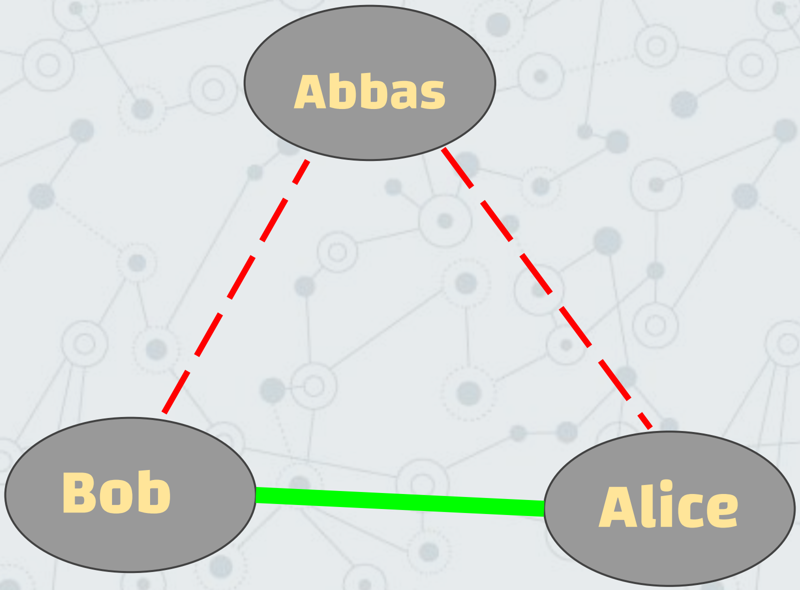

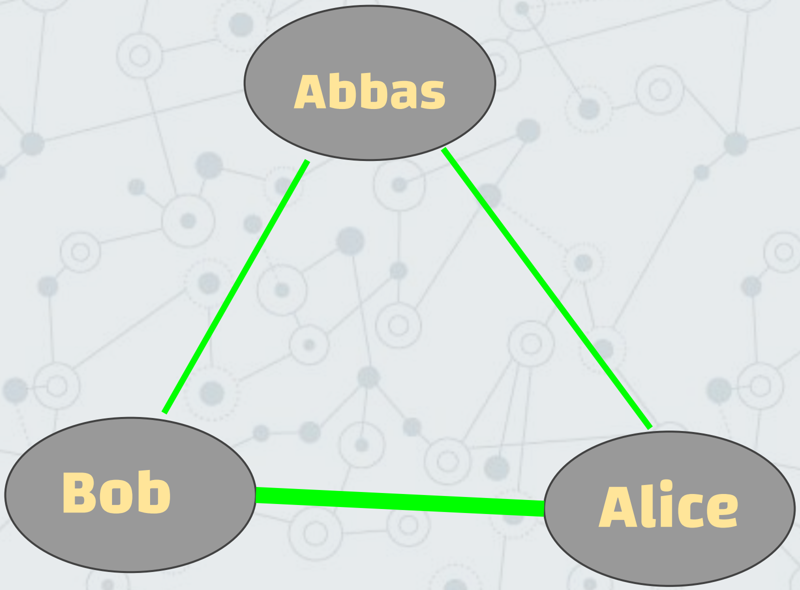

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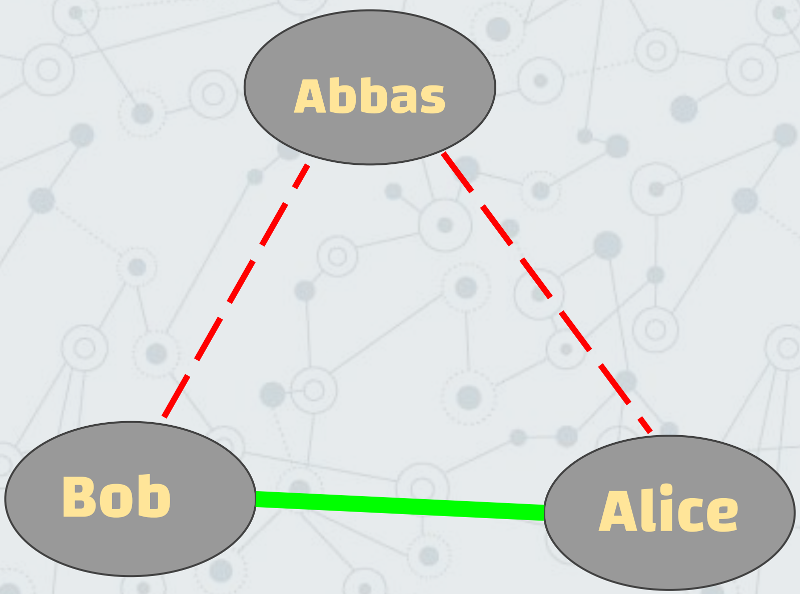
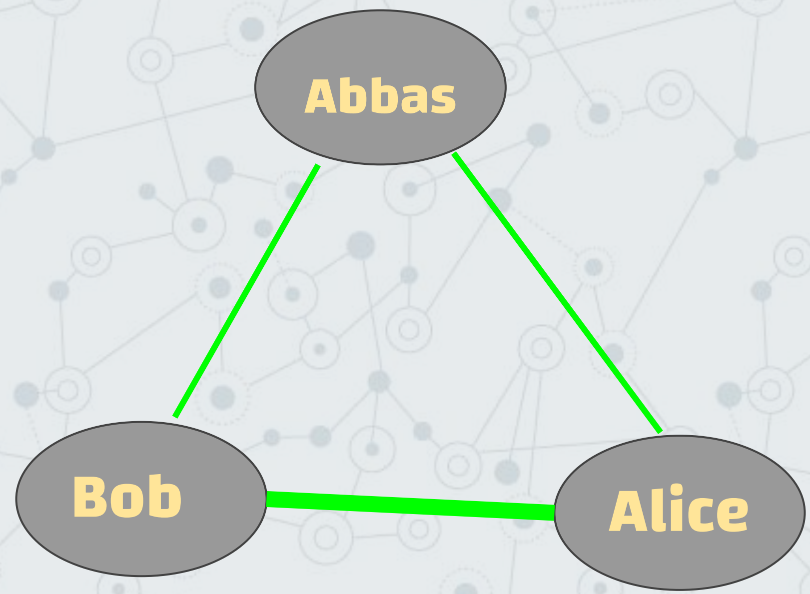


balanced



balanced

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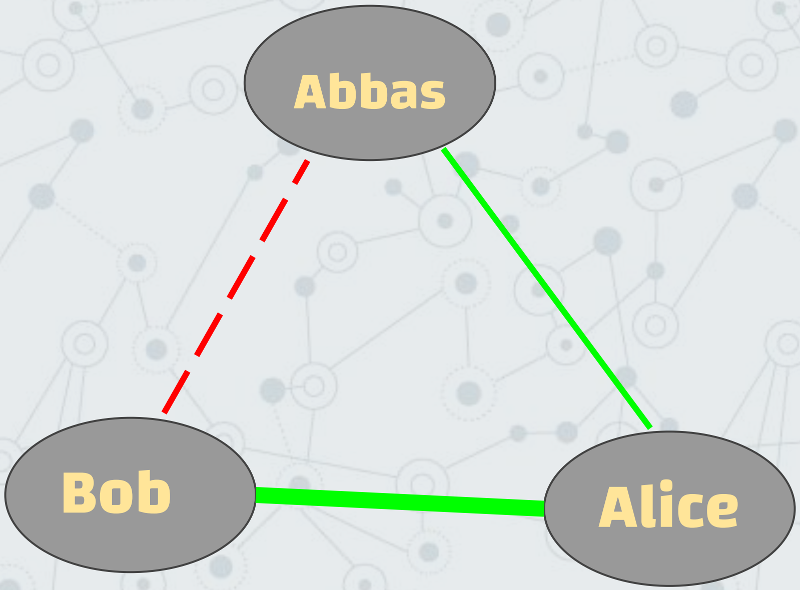

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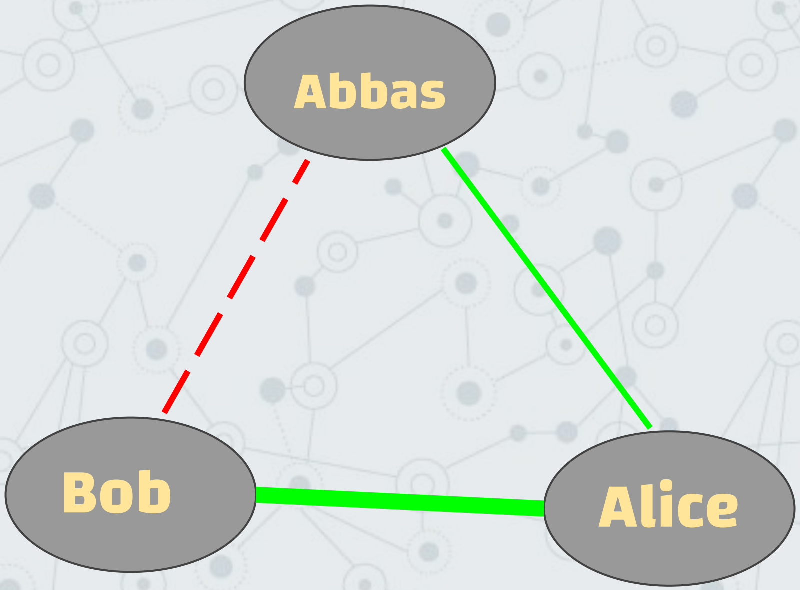

imbalanced

Balance Theory

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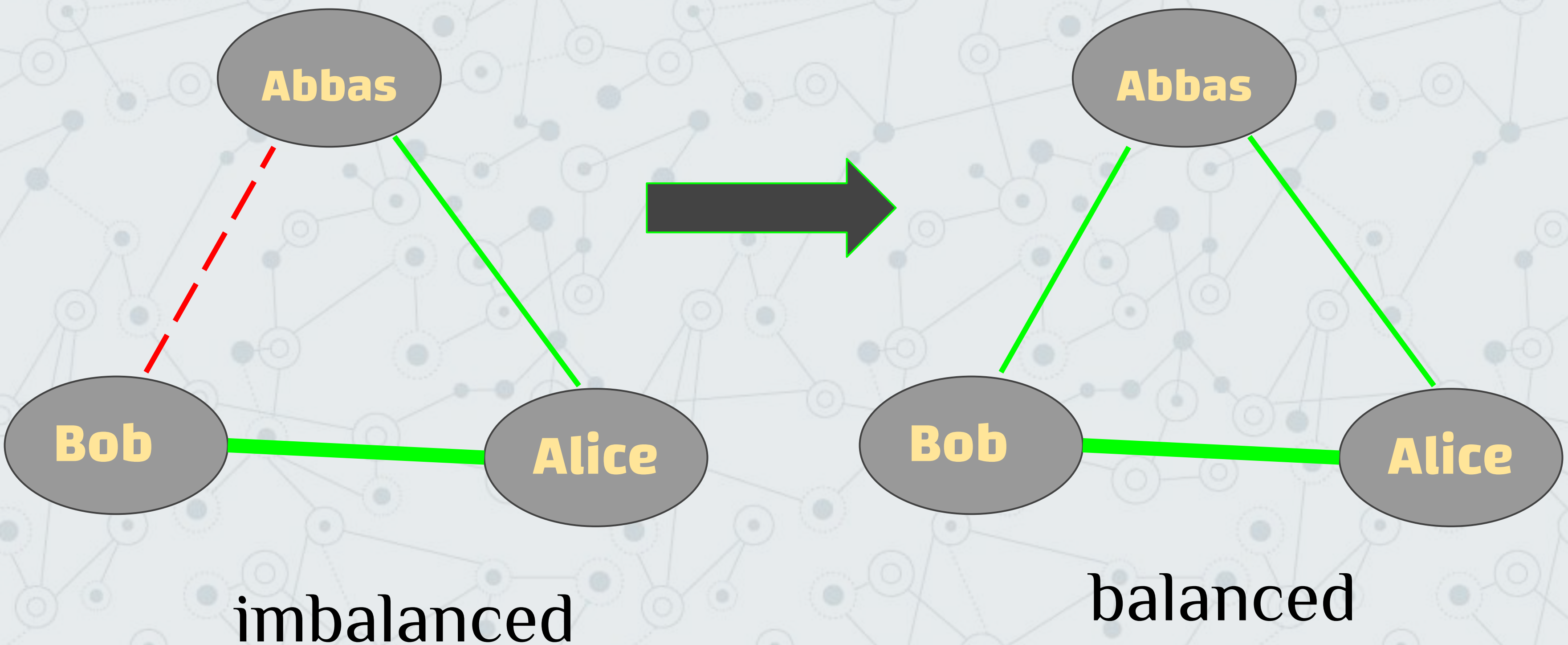

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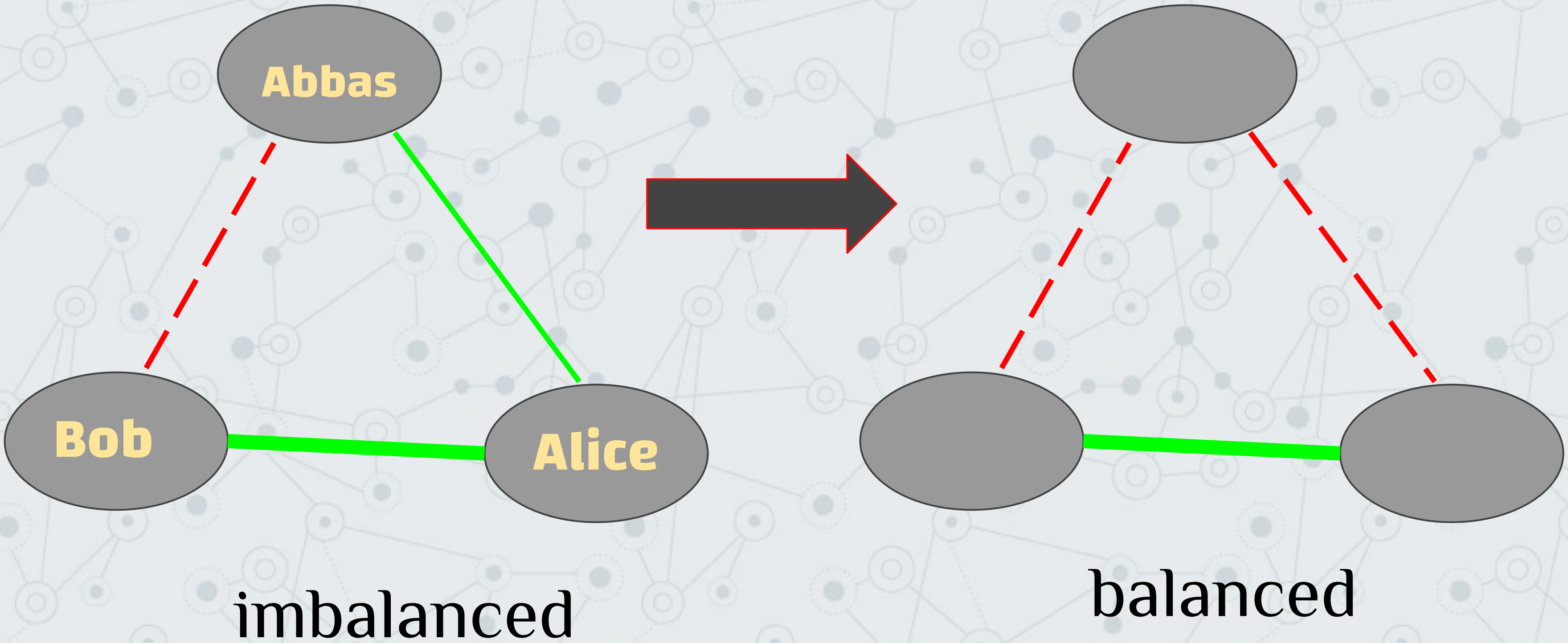

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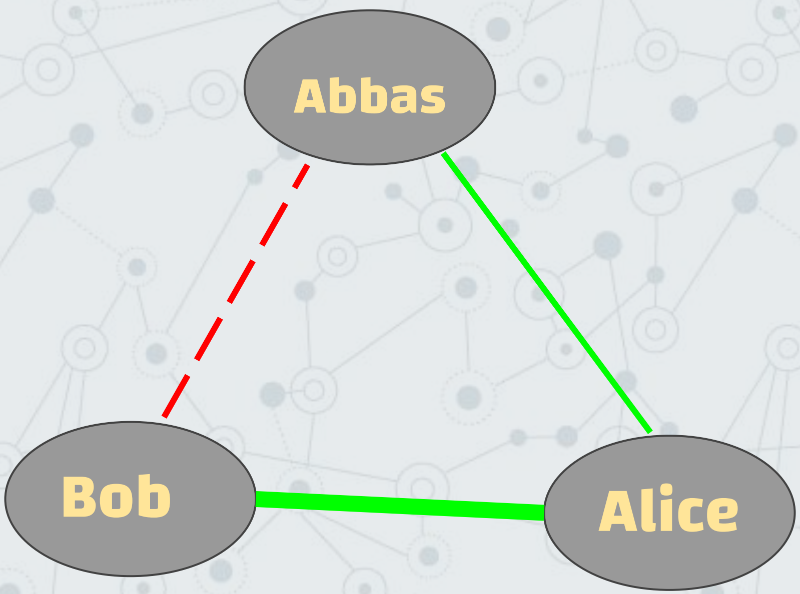

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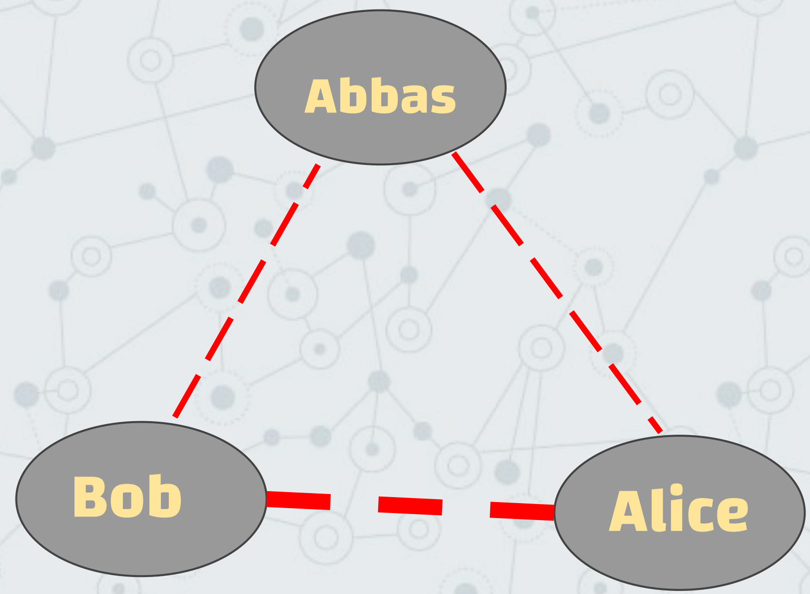

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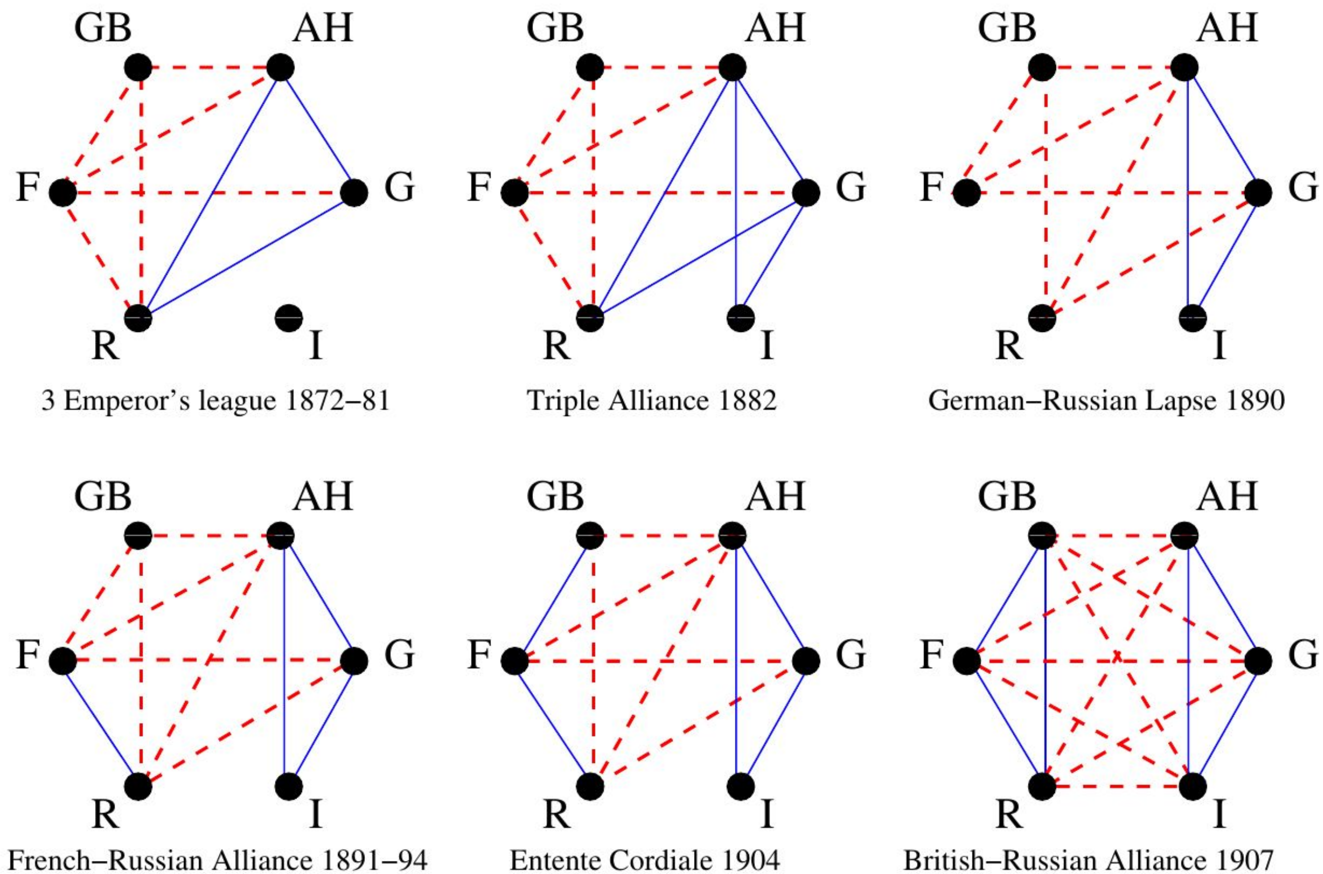
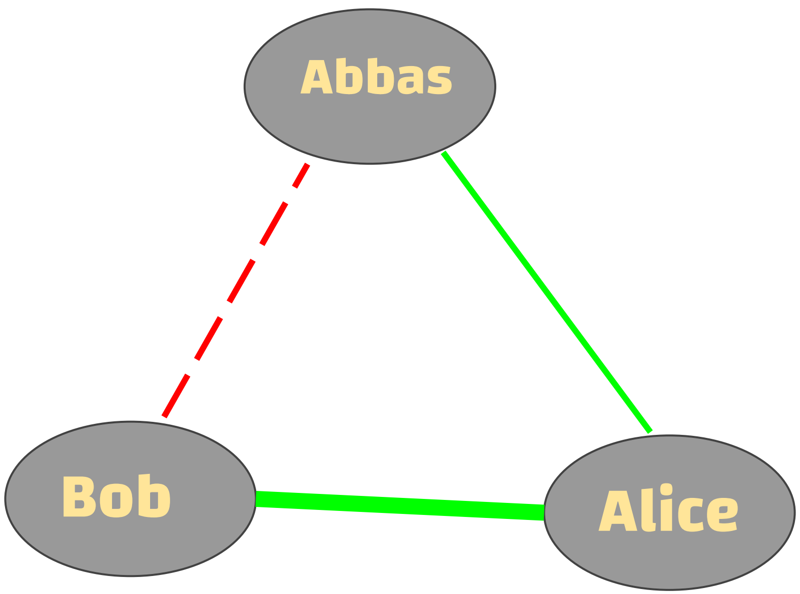


Evolution of the major relationship changes between the protagonists of World War I from 1872–1907.
GB = Great Britain, AH = Austria-Hungary, G = Germany, I = Italy, R = Russia, and F = France.

T. Antal, P. L. Krapivsky, and S. Redner,
"Social Balance on Networks: The Dynamics of Friendship and Enmity,"

Balance Theory

Heider, Fritz (1958). *The Psychology of Interpersonal Relations*. John Wiley & Sons.



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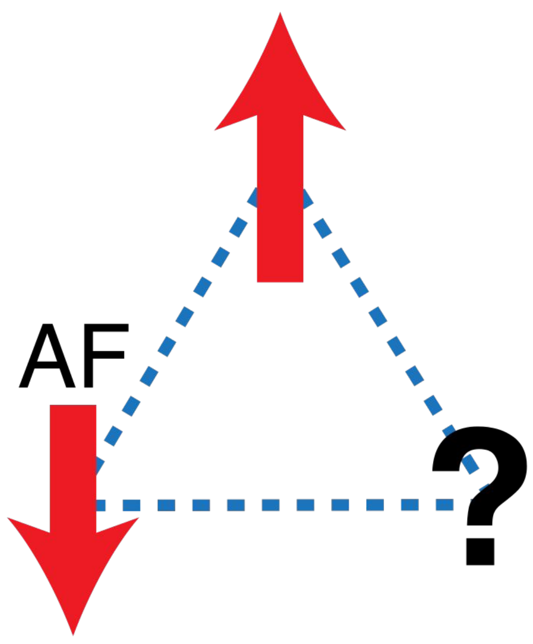
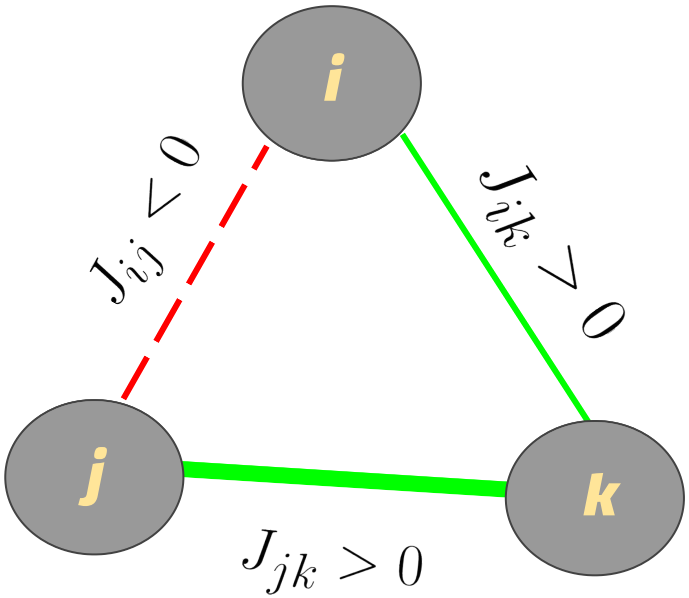


frustration

The Energy Landscape of Social Balance

Seth A. Marvel, Steven H. Strogatz, and Jon M. Kleinberg



$$E_{\triangle} = -J_{ij} J_{jk} J_{ki}$$

$J_{ij} \in R$

The Energy Landscape of Social Balance

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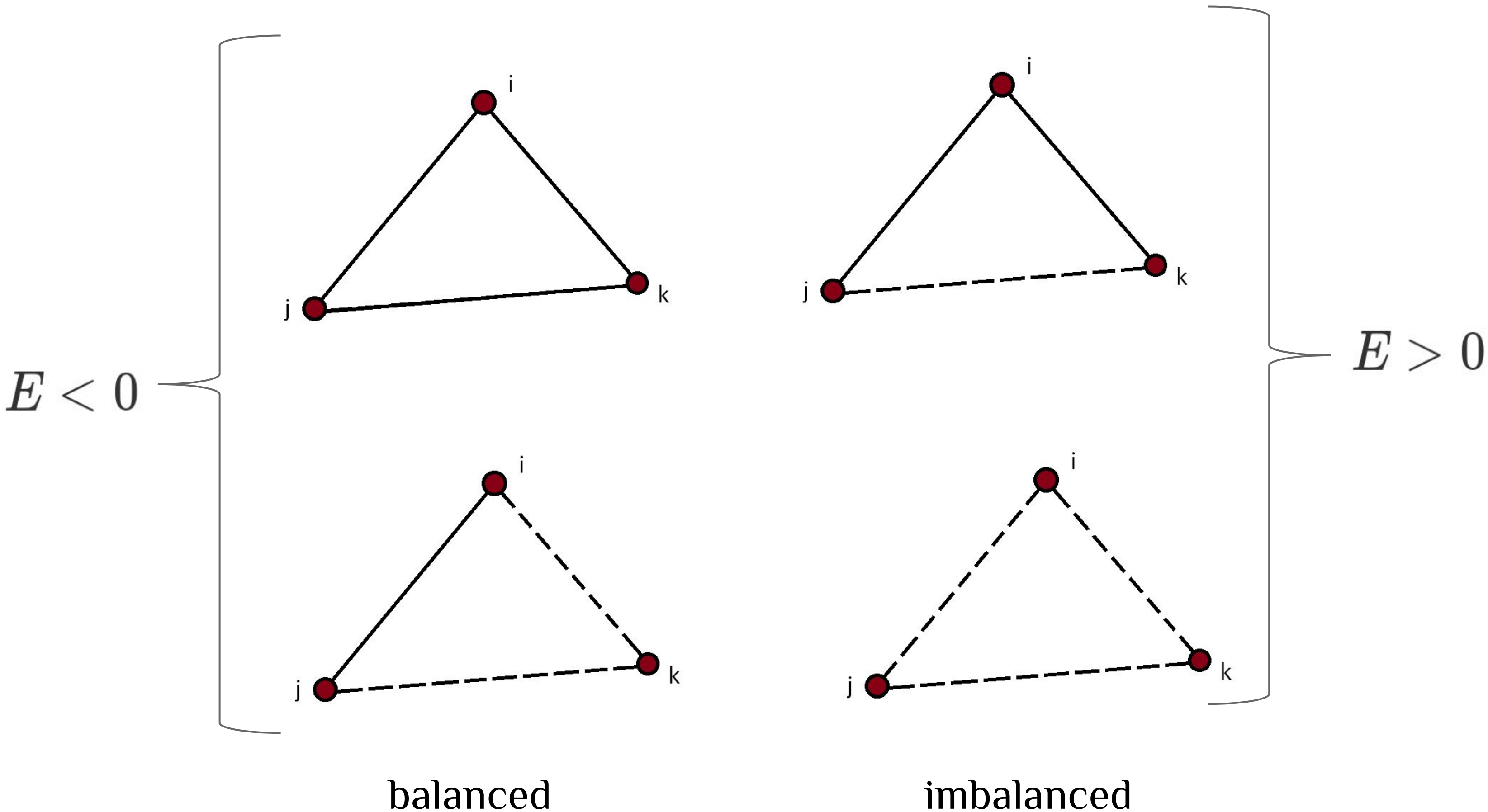

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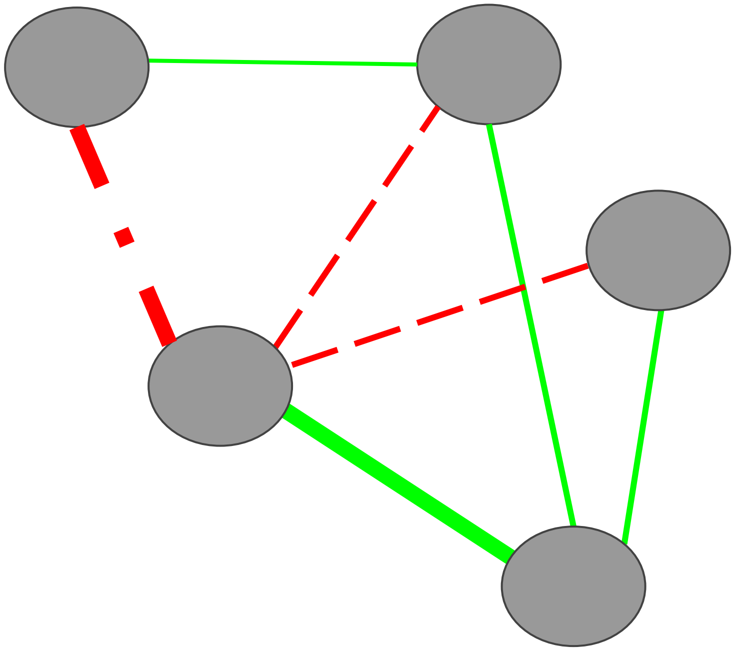

$$E_{Net} = \sum_{\triangle} E_{\triangle}$$

$$E_{\triangle} = -J_{ij} J_{jk} J_{ki}$$

$$J_{ij} \in R$$

International Networks

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- A. Bramson, K. Hoefman, M. van den Heuvel, B. Vandermarliere, and K. Schoors, Springer 108, (2017).

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Considered a role for nodes, disease-spreading process on the network

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Temperature as a parameter of randomness or tension in society

- F. Rabbani, Amir H. Shirazi, and G. R. Jafari Phys. Rev. E 99, 062302 (2019).

Quartic Balance Theory

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What About
Biological Networks?
e.g. The GRN

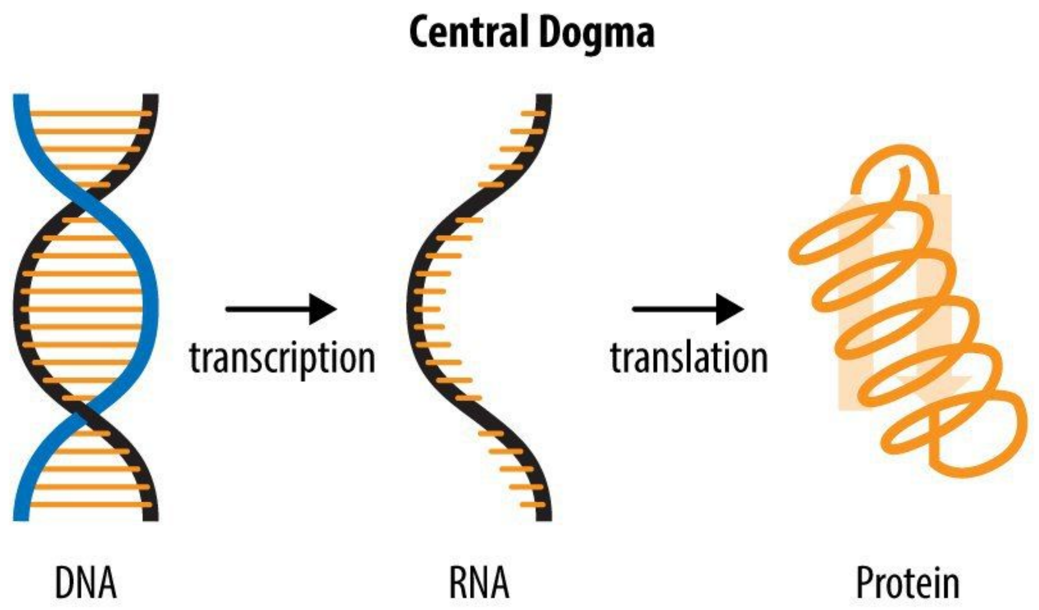
Central Dogma of Molecular Biology

All the information needed to run a cell is stored in a molecule called **DNA**.

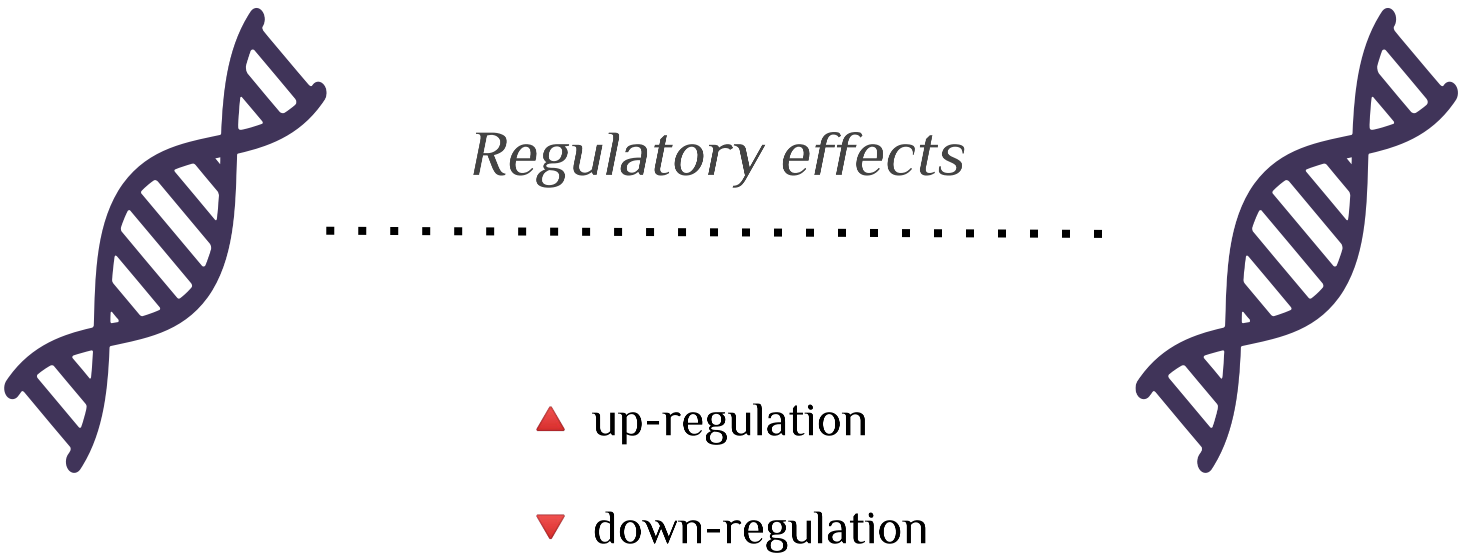
A section of DNA that encodes the information to make a protein (via mRNA) is called a **gene**.

The amount of mRNA produced from a given gene is called the **expression** of that gene.

Central Dogma of Molecular Biology



Gene Regulatory Network (GRN)



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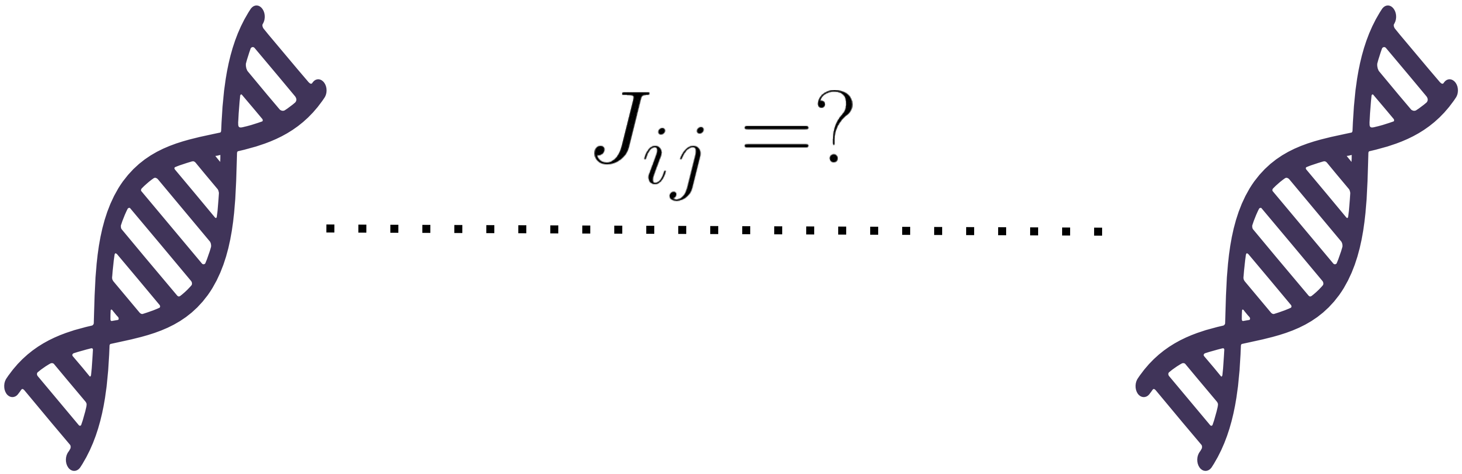
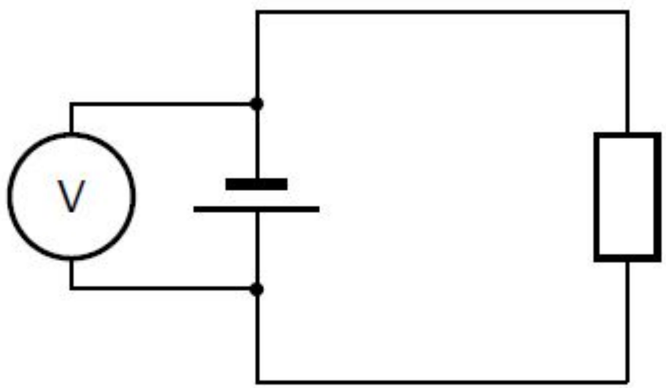


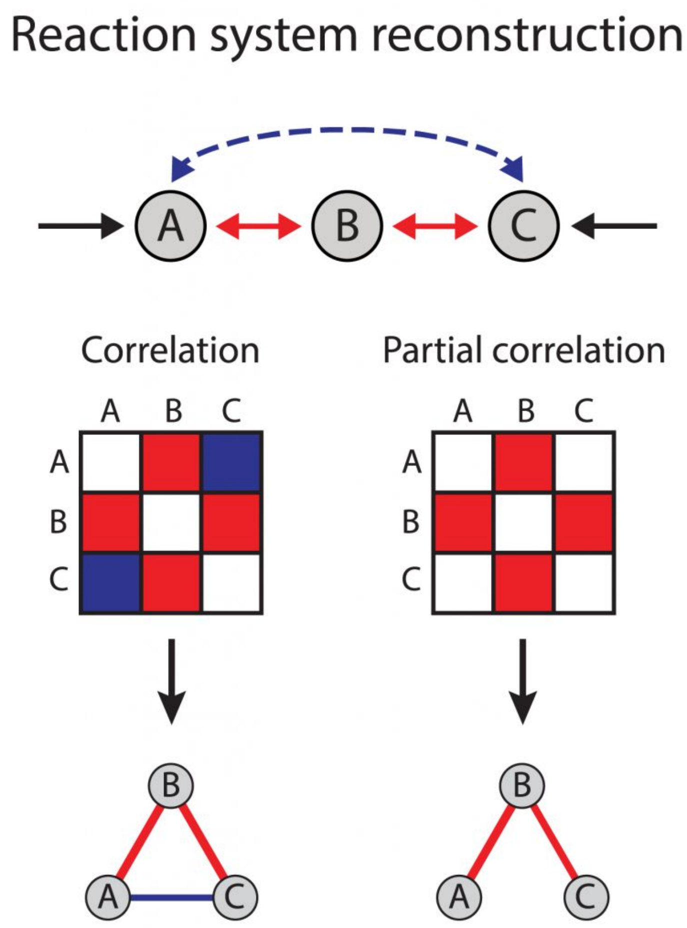
$$J_{ij} =?$$



Data Set

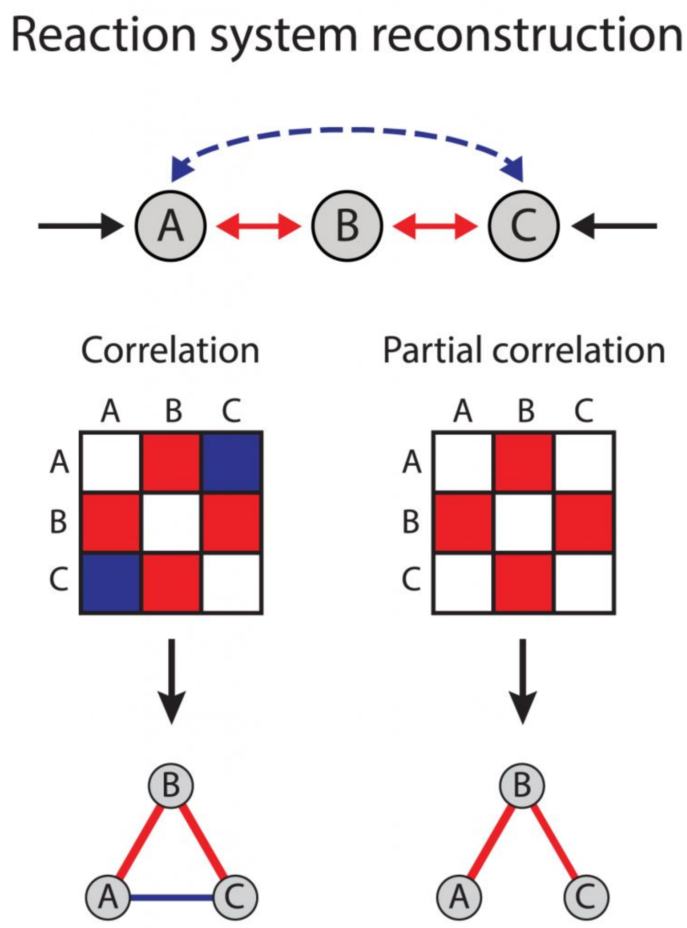
- BRCA: Breast Invasive Carcinoma
- The Cancer Genome Atlas (TCGA)
- RNA Sequencing
  (The state-of-the-art technology to measure mRNA)
- Expression Levels for 20532 Genes
- 114 Normal and 763 Cancerous Samples

GRN Reconstruction



Inferring the Interactions

1. Fixing a Good Model!
2. Inferring the Parameters



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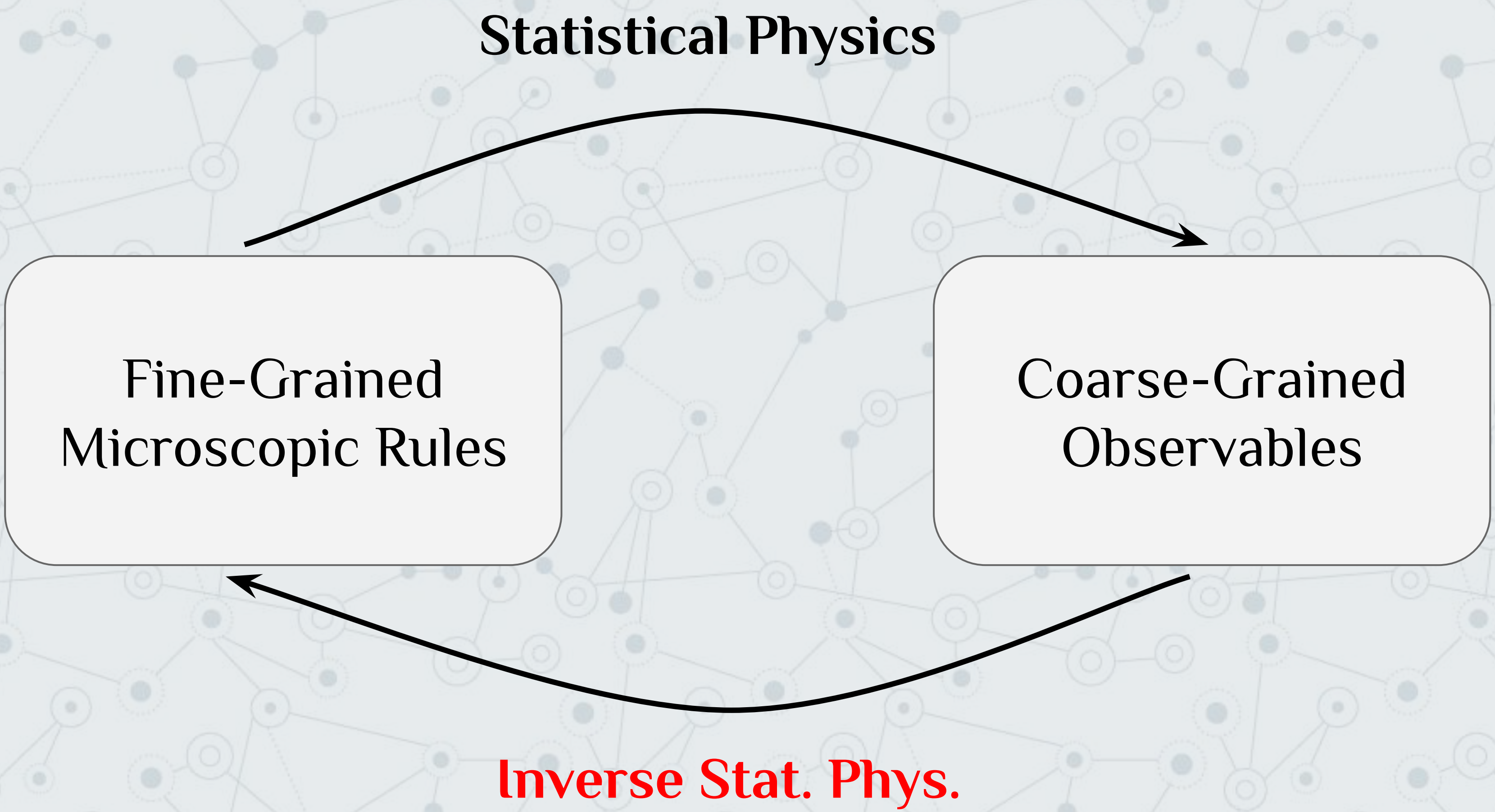
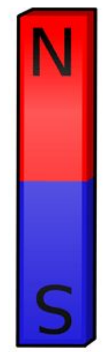
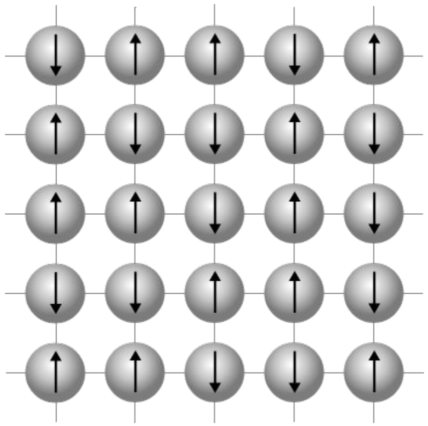


Ising Model in Statistical Physics





Fine-Grained
Microscopic Rules

$$P(\{X_i\}) = \frac{1}{Z} exp[\sum_{i<j} J_{ij} X_i X_j]$$

Ising Model in Statistical Physics

Coarse-Grained Observables

$$\begin{cases} M \equiv \langle X_i \rangle \\ \xi \equiv \langle X_i X_j \rangle \end{cases}$$

Fine-Grained Microscopic Rules

$$P(\{X_i\}) = \frac{1}{Z} exp[\sum_{i<j} J_{ij} X_i X_j]$$

Inverse Ising Problem

Coarse-Grained Observables

$$\begin{cases} M \equiv \langle X_i \rangle \\ \xi \equiv \langle X_i X_j \rangle \end{cases}$$

Fine-Grained Microscopic Rules

to be inferred

$$P(\{X_i\}) = \frac{1}{Z} exp[\sum_{i<j} J_{ij} X_i X_j]$$

GRN Reconstruction

1. Fixing a Good Model!

   Undirected Pairwise Maximum-Entropy Probability Model

$$P(\{X_i\}) = \frac{1}{Z} exp[\sum_{i<j} J_{ij} X_i X_j]$$

2. Inferring the Parameters,

   J =?

GRN Reconstruction

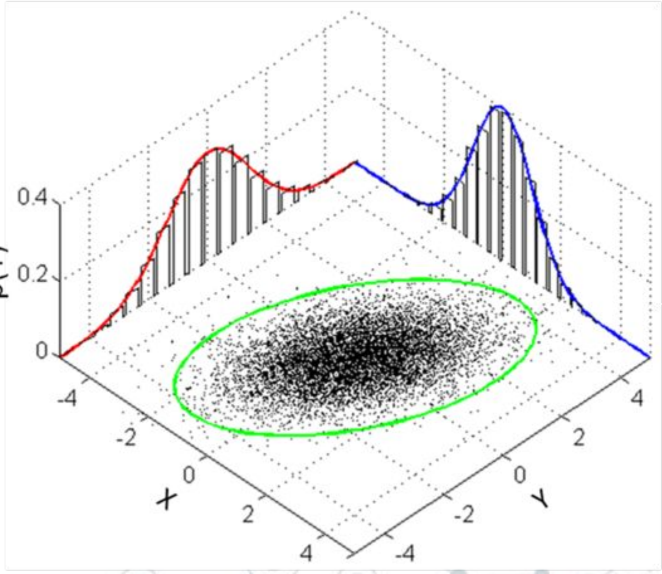
$$\text{maximize } S = -\int_{\mathbf{x}} P(\mathbf{x}) \ln P(\mathbf{x}) \, \mathrm{d}\mathbf{x}$$

$$\begin{cases} \int_{\mathbf{x}} P(\mathbf{x}) \, \mathrm{d}\mathbf{x} = 1, \\ \langle x_i \rangle = \int_{\mathbf{x}} P(\mathbf{x}) x_i \, \mathrm{d}\mathbf{x} = \frac{1}{M} \sum_{m=1}^{M} x_i^m = \overline{x_i}, \\ \langle x_i x_j \rangle = \int_{\mathbf{x}} P(\mathbf{x}) x_i x_j \, \mathrm{d}\mathbf{x} = \frac{1}{M} \sum_{m=1}^{M} x_i^m x_j^m = \overline{x_i x_j} \end{cases}$$

L = 20,532 and M = 764 + 114

GRN Reconstruction

$$P(\mathbf{x}; \langle \mathbf{x} \rangle, C) = (2\pi)^{-L/2} \det(C)^{-1/2} \exp\left(-\frac{1}{2}(\mathbf{x} - \langle \mathbf{x} \rangle)^{\mathrm{T}} C^{-1} (\mathbf{x} - \langle \mathbf{x} \rangle)\right)$$



Inferring Pairwise Interactions from Biological Data
Using Maximum-Entropy Probability Models

Richard R. Stein, Debora S. Marks, Chris Sander

PLOS

GRN Reconstruction

$$P(\mathbf{x}; \langle \mathbf{x} \rangle, C) = (2\pi)^{-L/2} \det(C)^{-1/2} \exp\left(-\frac{1}{2} (\mathbf{x} - \langle \mathbf{x} \rangle)^{\mathrm{T}} C^{-1} (\mathbf{x} - \langle \mathbf{x} \rangle) \right)$$

$$P(\{X_i\}) = \frac{1}{Z} exp[\sum_{i<j} J_{ij} X_i X_j]$$

$$\boxed{J = -C^{-1}}$$

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GRN Reconstruction

$$\boxed{J = -C^{-1}}$$

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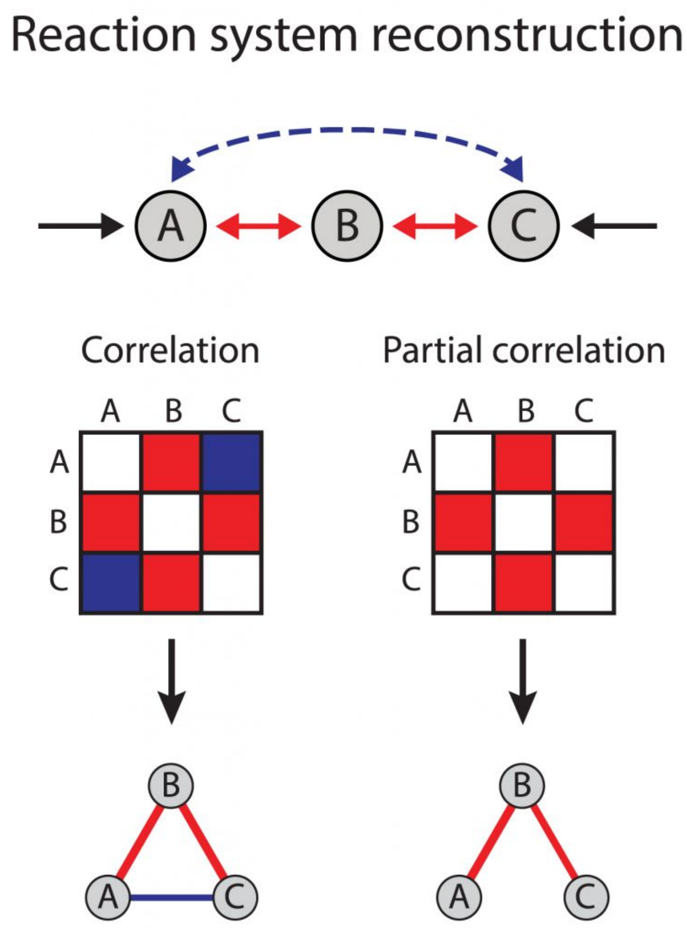
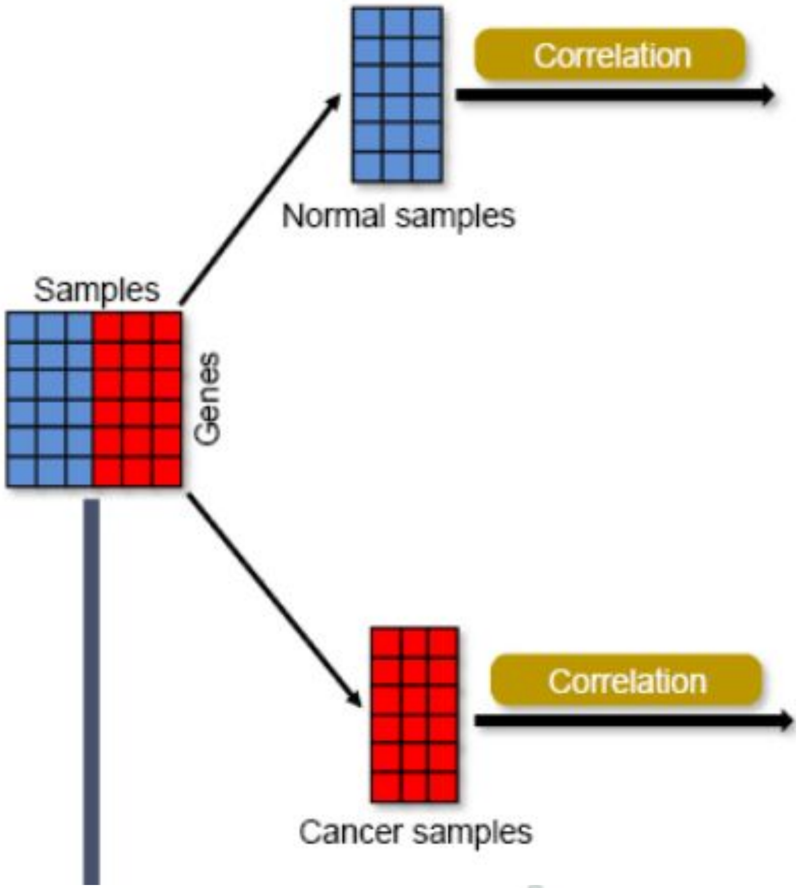


GRN Reconstruction



$$-C^{-1}$$

$$J = -C^{-1}$$

$$-C^{-1}$$

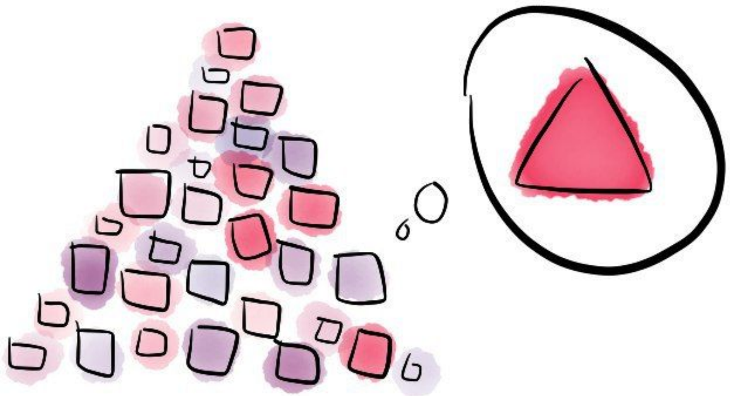
GLasso (Graphical Least Absolute Shrinkage and Selection Operator)

$$\begin{cases} X \sim N(0, \Sigma) \\ X_1, X_2, \ldots, X_n \end{cases}$$

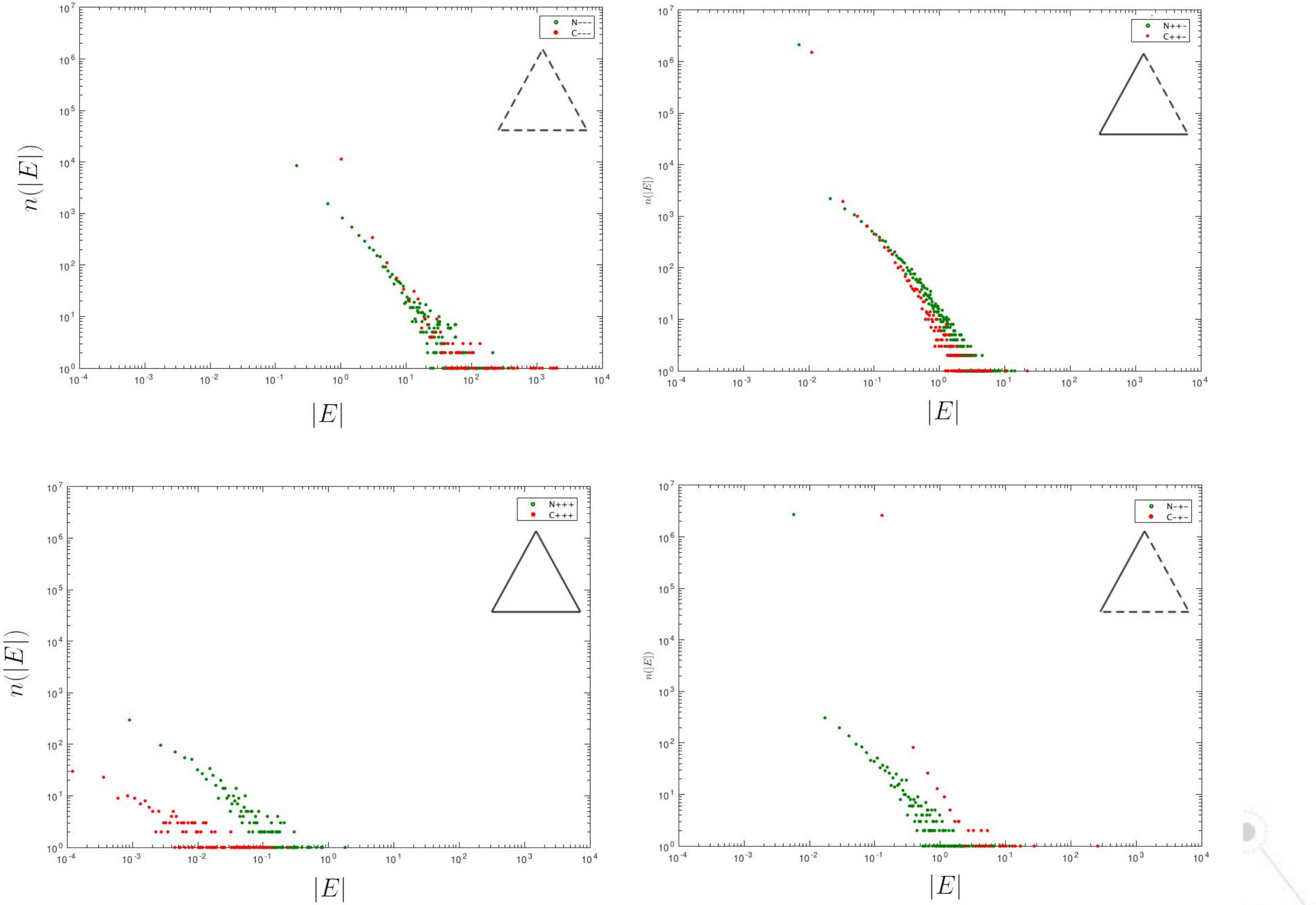
$$\Theta = \Sigma^{-1}$$

$$\hat{\Theta} = {}^{*}argmin_{\Theta \geq 0} \left(\operatorname{tr}(S\Theta) - \log\det(\Theta) + \lambda \sum_{j \neq k} |\Theta_{jk}| \right)$$

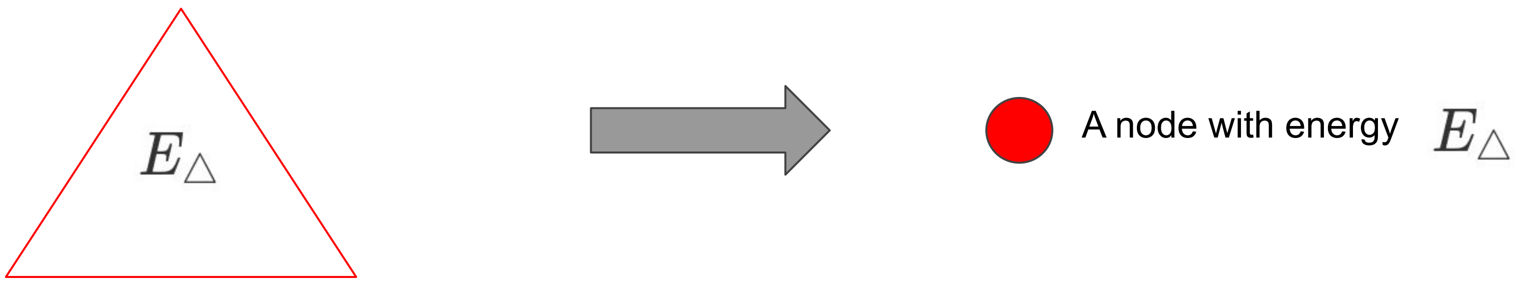
S: sample covariance
λ: penalizing parameter



Results



Coarse-graining the Network



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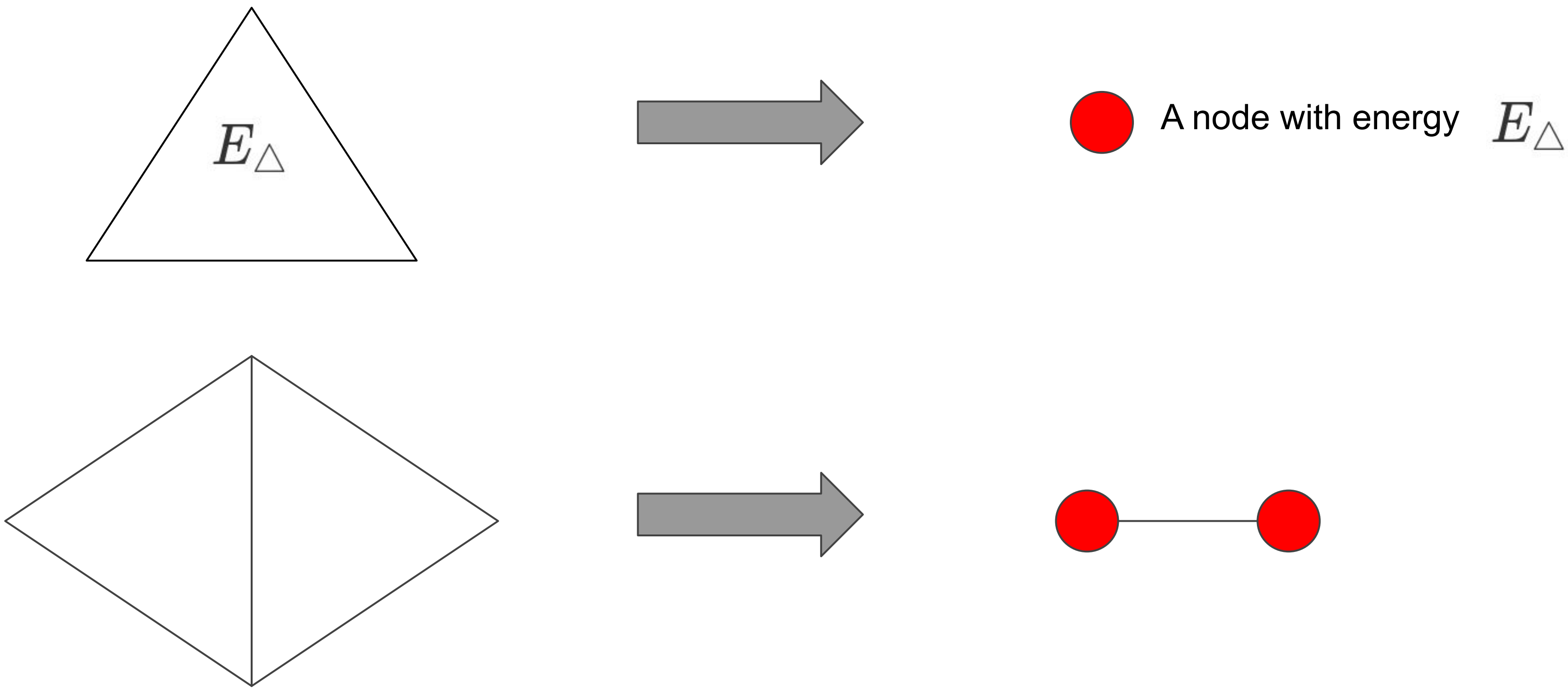
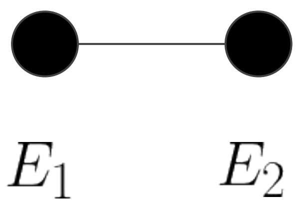
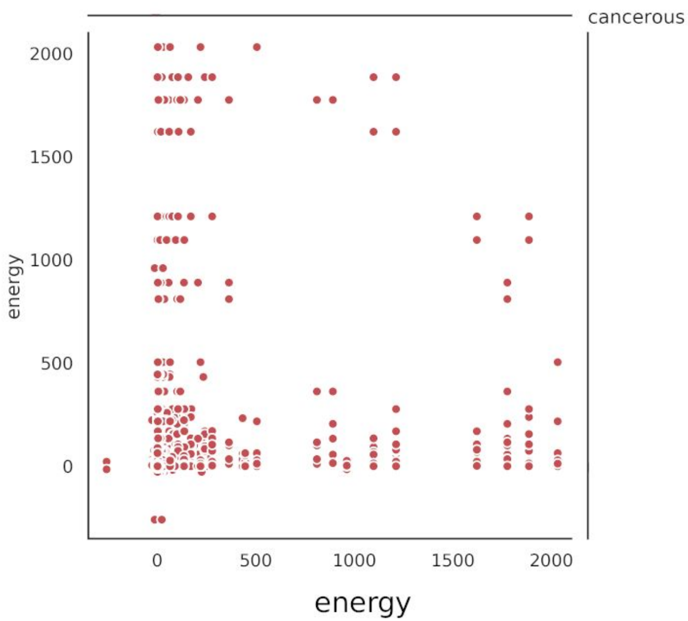


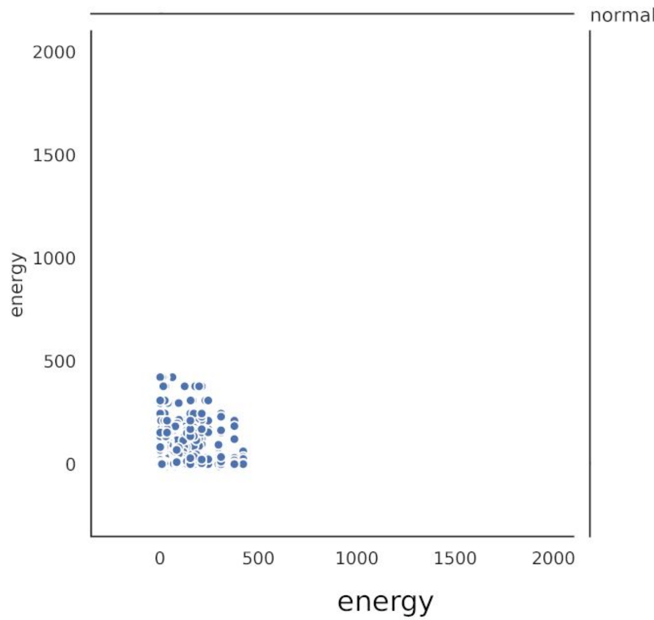
Results



E_1
E_2



cancerous
2000
1500
1000
500
0
energy
0
500
1000
1500
2000
energy

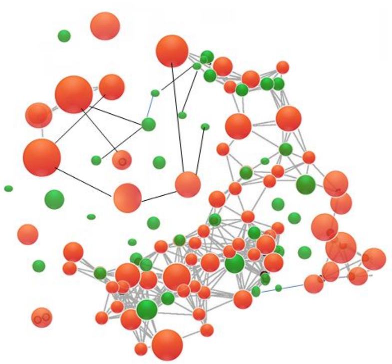


normal
2000
1500
1000
500
0
energy
0
500
1000
1500
2000
energy

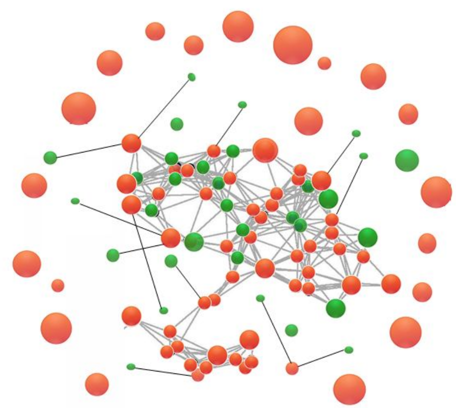
Results

35,984 units
27,239 units

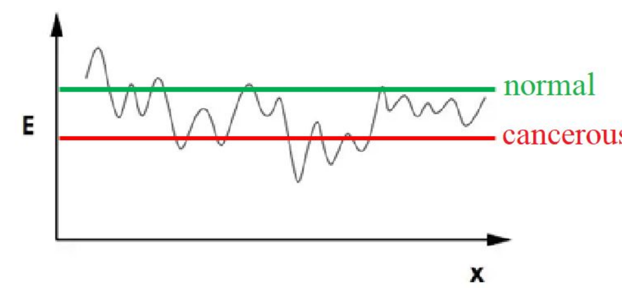
E Gap ~ 10,000 units



(a) *cancerous coarse-grained network*



(b) *normal coarse-grained network*



(c) *energy levels and local minima*

Thank You

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