The Whole-Cell Network of *Mycoplasma genitalium*

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Complex Networks

The "Social Graph" behind Facebook
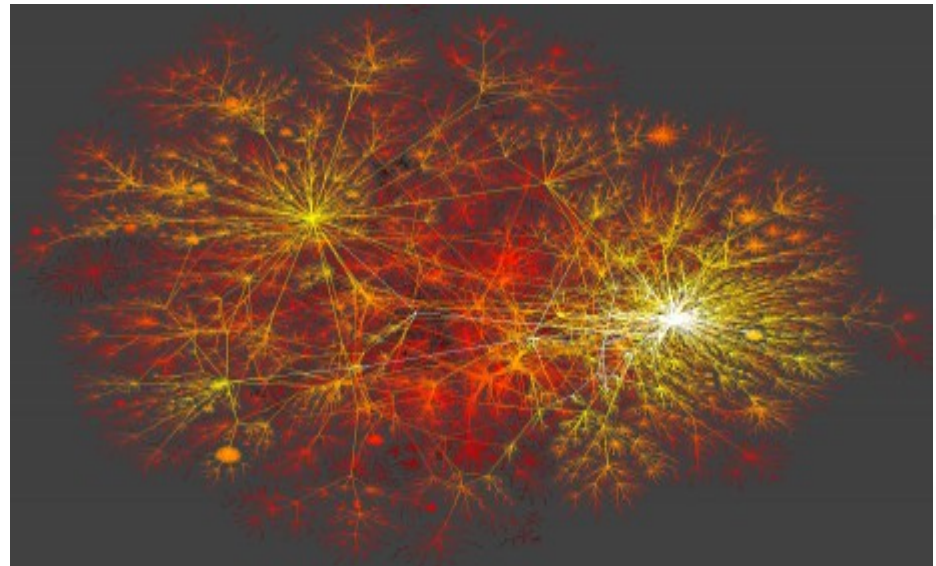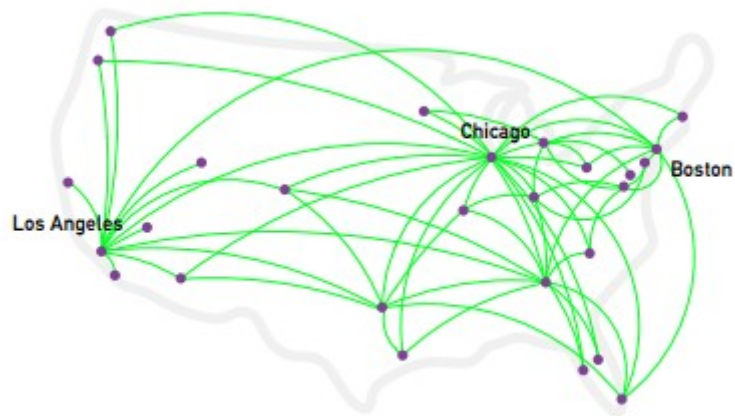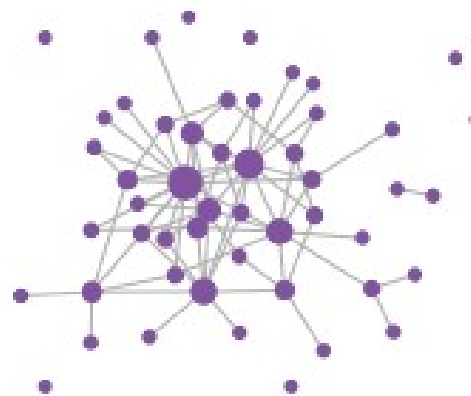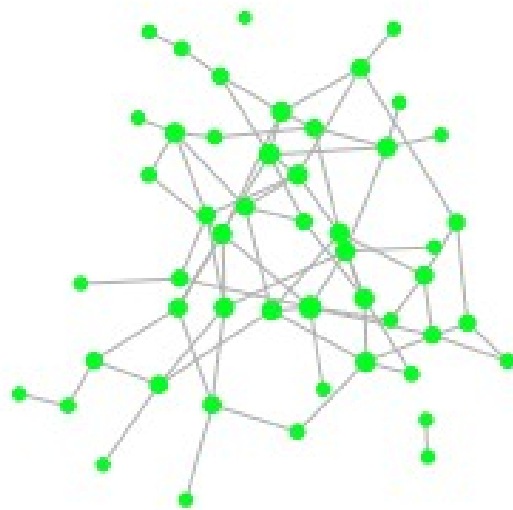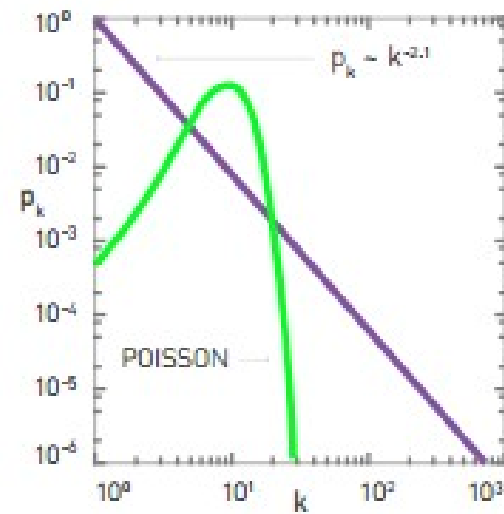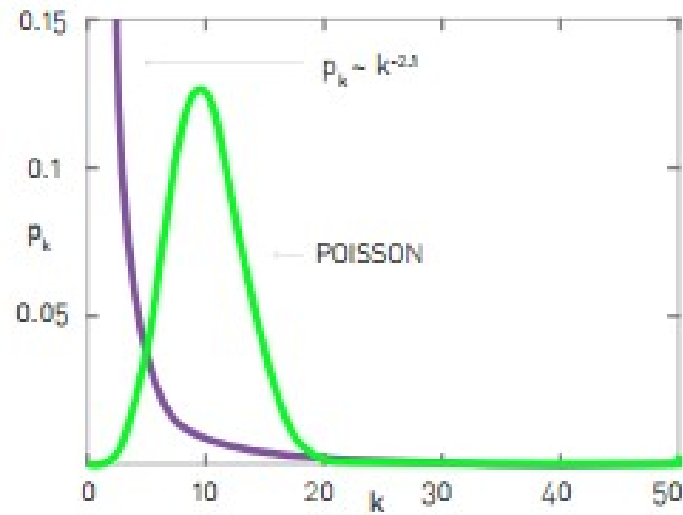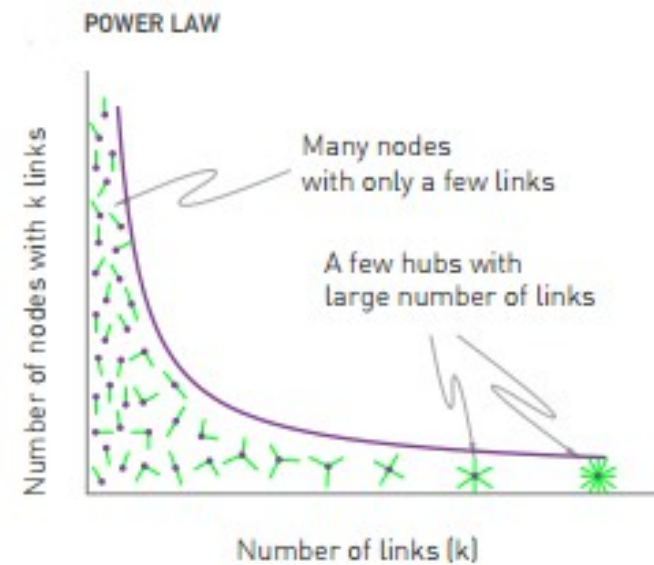

Image: ALBERT-LÁSZLÓ BARABÁSI, NETWORK SCIENCE, chapters 1 and 4

Scale-Free Networks

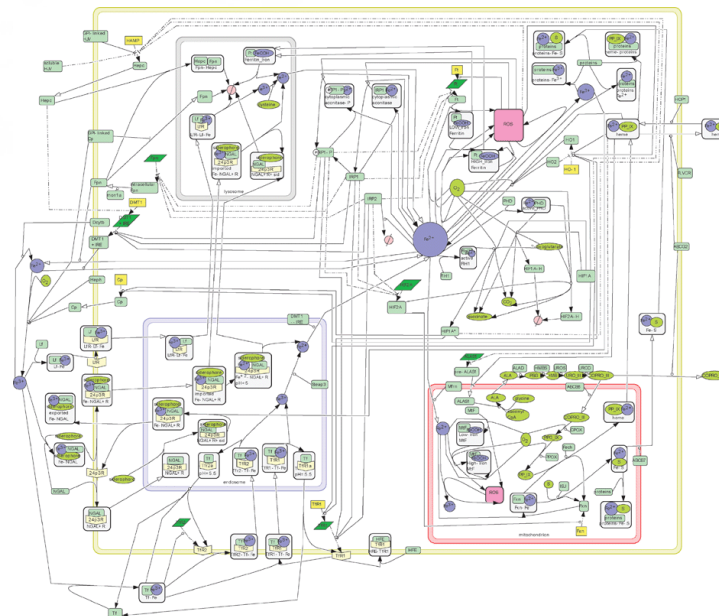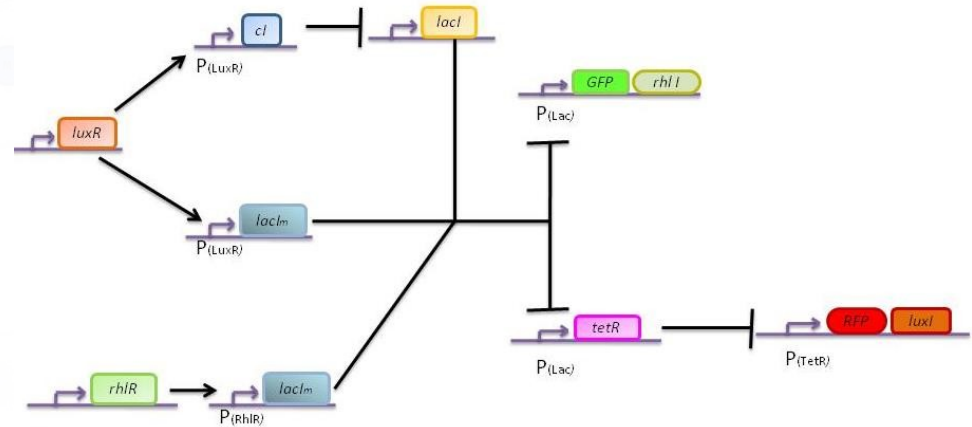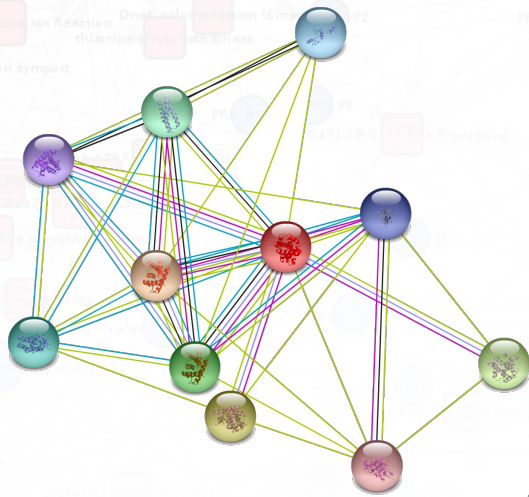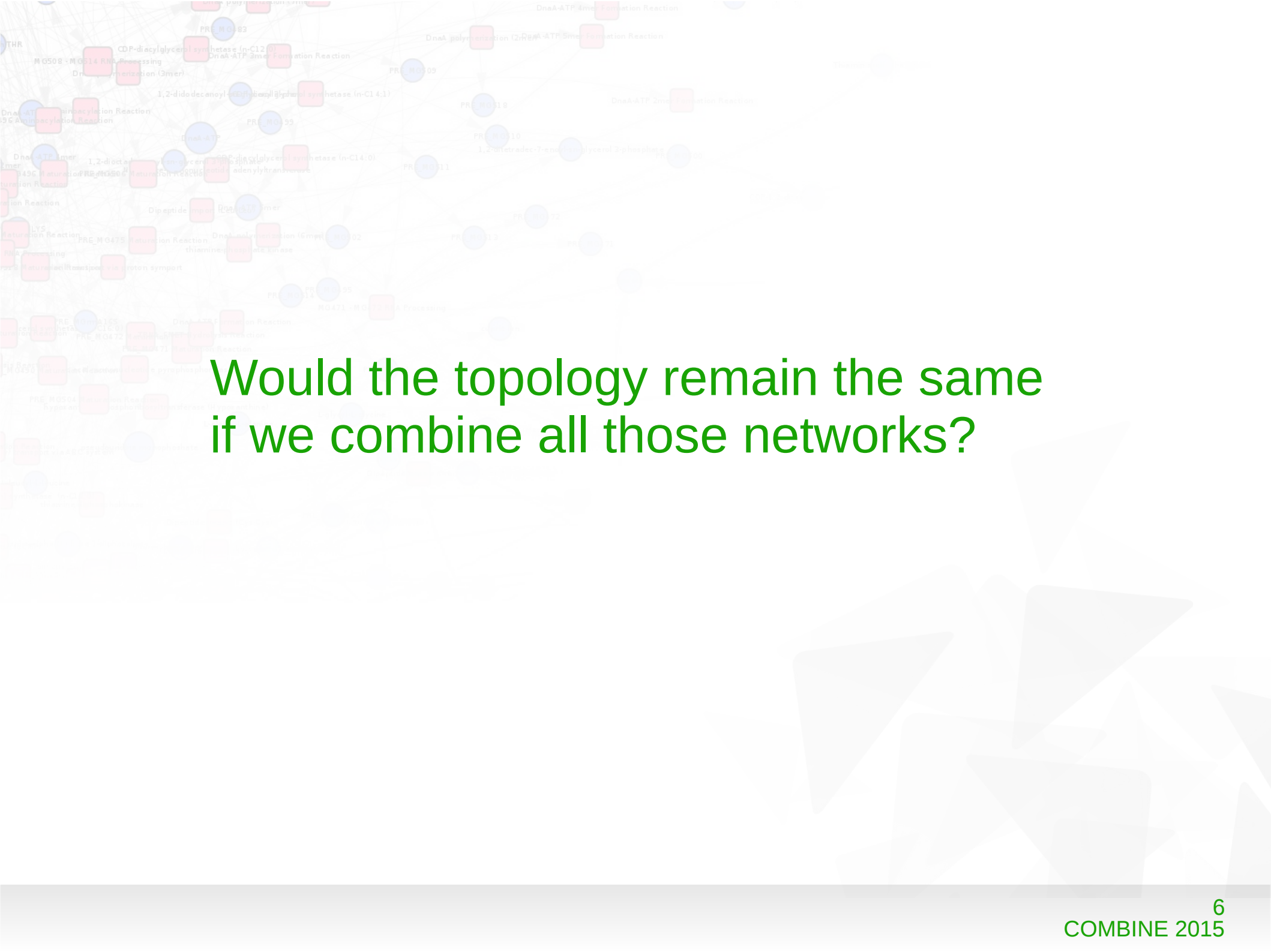Image: ALBERT-LÁSZLÓ BARABÁSI, NETWORK SCIENCE, chapter 4

USA Airport Network

Scale-Free Topology of Biological Networks

Would the topology remain the same if we combine all those networks?

Whole-Cell Network set of rules

◥ Each molecule or structure in the cell should be represented by a unique molecule node;

◥ Each different state of a molecule (e.g., active and inactive protein) should be represented by a different molecule node;

◥ Each molecular interaction should be represented by a single reaction node;

◥ Multi-step reactions (e.g., polymerization, degradation) should be condensed into single reaction nodes;

◥ Edges should only run between different types of nodes;

◥ The incoming edges of the reaction nodes can be of two types: reactant edges, which link molecule nodes that are consumed during the reactions, and modifier edges, which link molecule nodes representing catalysts or molecules that do not change during the reactions;

◥ The outgoing edges of the reaction nodes target the molecule nodes produced by interactions;

◥ The weight of each edge determines its stoichiometry in the interaction.

Biological Model

Mycoplasma genitalium

- Pathogenic bacteria

- Smallest known genome (580 kb)

- 525 genes

Modeling

I. Model molecular interactions with the whole-cell modeling rules.

(a) Enz, Met1, Met2 → Biochemical Reaction → Met3

(b) Ligand, Protein → Inhibition → Inactive Protein

(c) Enz, Block1, Block2, Block3 → Polymerization → Polymer

(d) Transporter, Compart1 Mol → Transport → Compart2 Mol

(e) Prot1, Prot2 → Complex Formation → Complex

Modeling

I. Model molecular interactions with the whole-cell modeling rules.

(a)
Met1 — 1 → Biochemical Reaction
Enz → Biochemical Reaction
Met2 — 1 → Biochemical Reaction
Biochemical Reaction — 1 → Met3

(b)
Ligand — 1 → Inhibition
Protein — 1 → Inhibition
Inhibition — 1 → Inactive Protein

(c)
Enz → Polymerization
Block1 — 20 → Polymerization
Block2 — 32 → Polymerization
Block3 — 16 → Polymerization
Polymerization — 1 → Polymer

(d)
Transporter → Transport
Compart1 Mol — 1 → Transport
Transport — 1 → Compart2 Mol

(e)
Prot1 — 1 → Complex Formation
Prot2 — 1 → Complex Formation
Complex Formation — 1 → Complex

II. Feed model with large-scale data regarding a desired organism.

- Id: MG_063_DIMER
- Name:1-phosphofructokinase
- Ann.: Protein Complex

- Id: F1P
- Name:D-Fructose 1-phosphate
- Ann.: Metabolite

- Id: FruK1
- Name:fructose-1-phosphate kinase
- Ann.: ALT_CARBON_METABOLISM
- Process: Metabolism

Modeling

I. Model molecular interactions with the whole-cell modeling rules.

(a) Met1, Met2, Enz → Biochemical Reaction → Met3
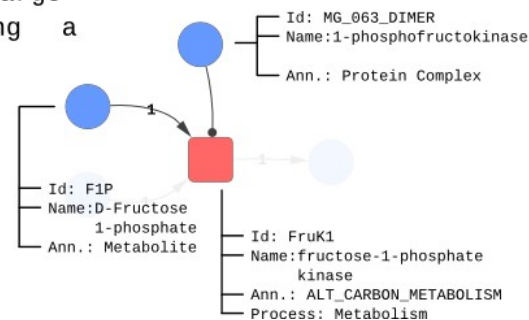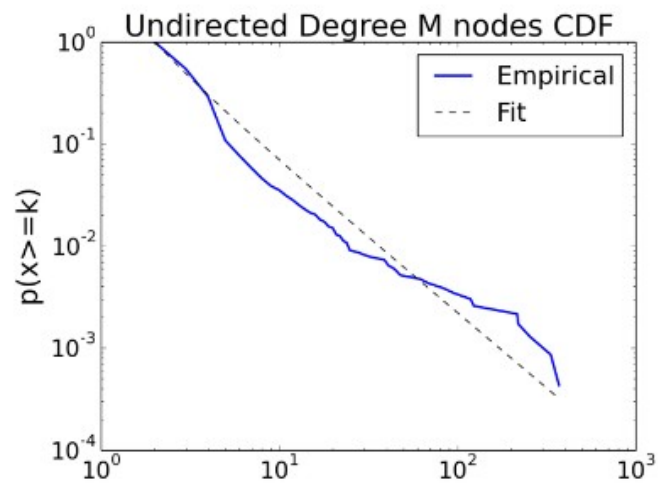
(b) Ligand, Protein → Inhibition → Inactive Protein

(c) Enz, Block1, Block2, Block3 → Polymerization → Polymer (20, 32, 15)

(d) Transporter, Compart1 Mol → Transport → Compart2 Mol

(e) Prot1, Prot2 → Complex Formation → Complex

II. Feed model with large-scale data regarding a desired organism.

- Id: F1P
- Name:D-Fructose 1-phosphate
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- Name:1-phosphofructokinase
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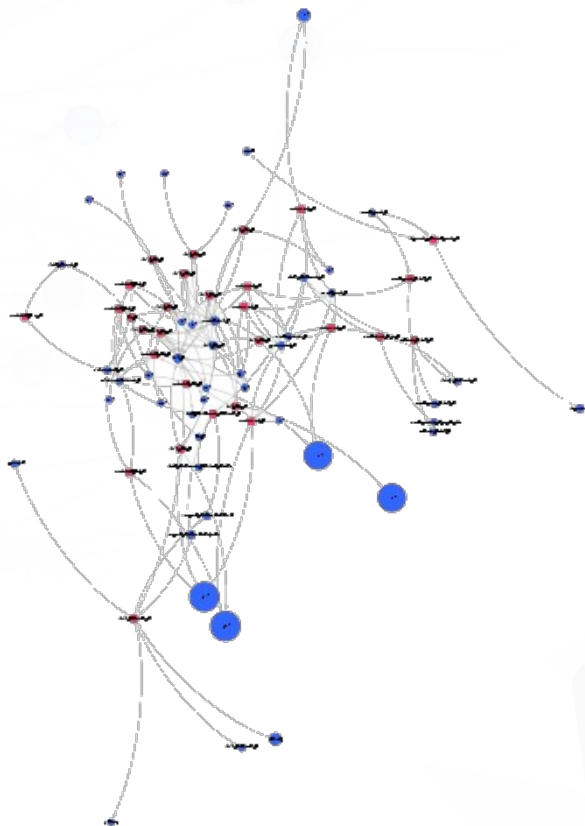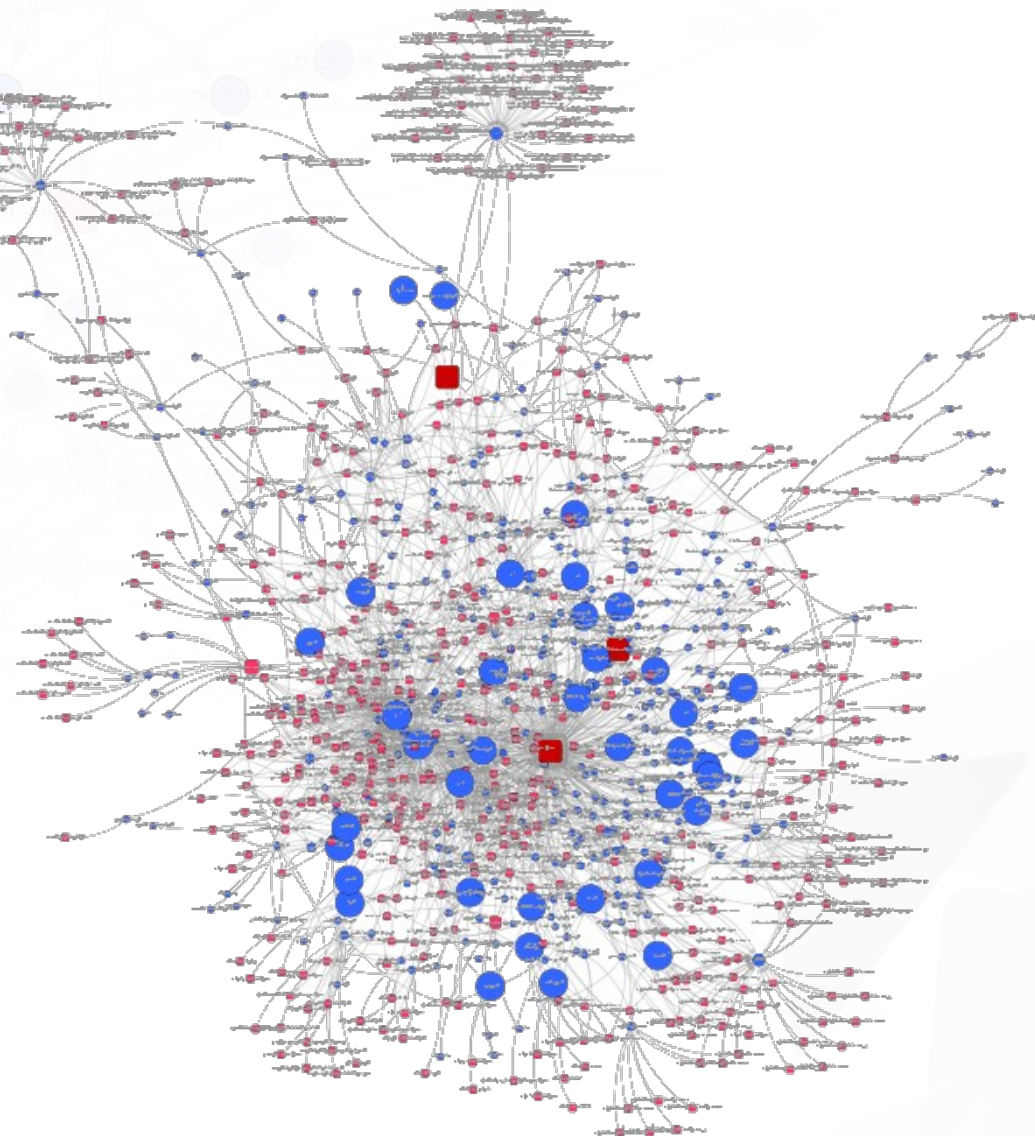**III.** Resultant whole-cell network which represents a whole organism.
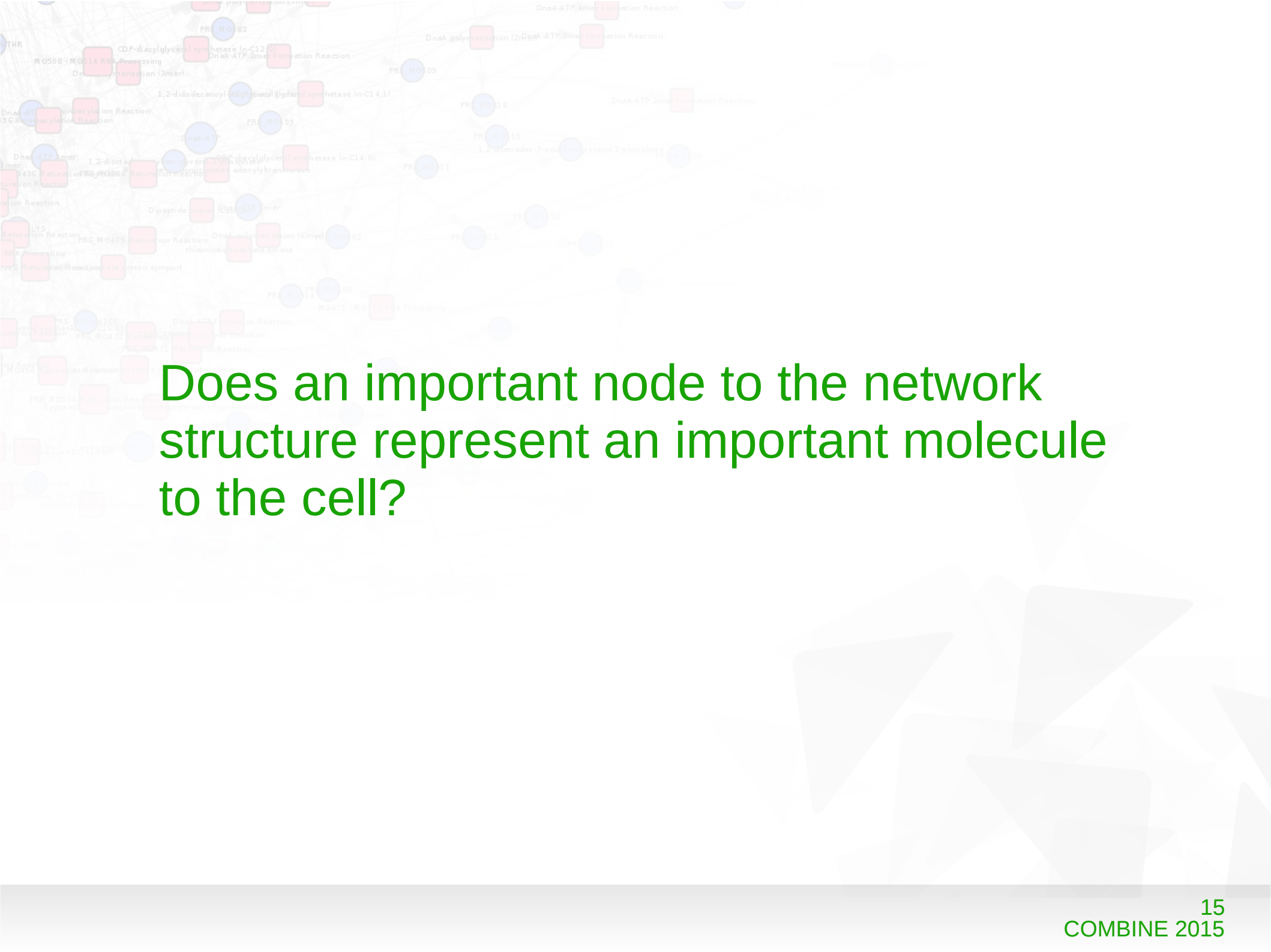
Topology
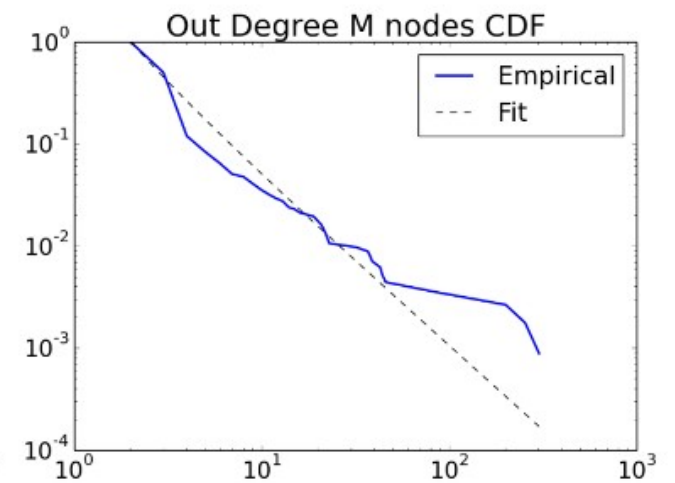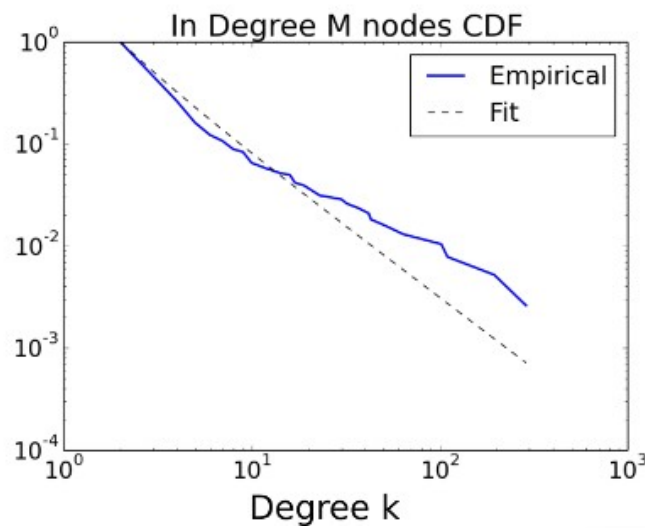
Pathway Interactions

Glycolysis pathway:
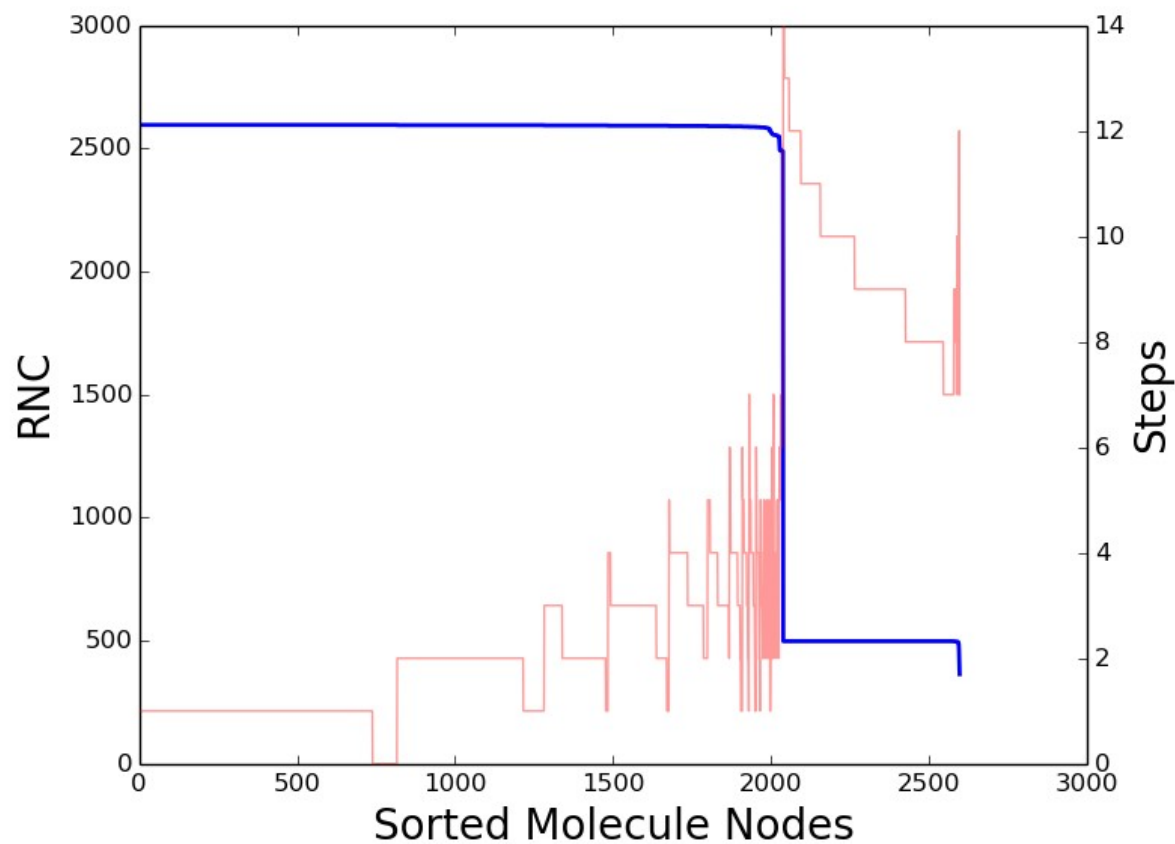
Pathway Interactions

Secondary
reactions that
involves
glycolysis
reactants and
products:

Does an important node to the network structure represent an important molecule to the cell?

Remaining Nodes Count

Essential Genes Prediction

	Karr's Model	Glass Set	*B. subtilis* orthologs	Mushegian& Koonin Set	Gil Core Set
Matches	379	261	389	300	375
False Positives	29	20	85	41	71
False Negatives	113	240	51	184	79
Accuracy	85.28%	89.85%	56.85%	79.19%	63.96%

Conclusions

- We found a good way to integrate different cellular processes;

- The whole-cell network of *Mycoplasma genitalium* have the scale-free topology;

- We could predict, with only structural information, good accuracy and low computational cost, 197 essential genes to the cell growth and reproduction.

Acknowledgements

Advisors:

Dr. Marcos G. Quiles

Dr. Claudia B. L. Camps

Thank you …

- … for the attention!