

# Essays on Bioinformatics and Social Network Analysis

## Statistical and Computational Methods for Complex Systems

George G Vega Yon

University of Southern California, Department of Preventive Medicine

June 22, 2020



On the Prediction of Gene Functions Using Phylogenetic Trees (Ch. 2 & 4)

Exponential Random Graph Models for Small Networks (Ch. 5)

Goodness-of-fit for Small Networks (Ch. 3 & 6)

Connecting the Dots: Phylogenetic Modeling with ERGMs (Ch. 4)

Next Steps (Ch. 7)

You can download the slides from <https://github.com/gvegayon/faculty-talk>

# On the Prediction of Gene Functions Using Phylogenetic Trees

*Joint with:* Paul D Thomas, Paul Marjoram, Huaiyu Mi, Duncan Thomas, and John Morrison  
(Chapters 2 and 4)



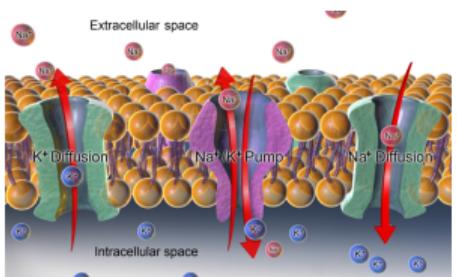
- ▶ The GO project has  $\sim 44,400$  validated terms [► more](#),  $\sim 7.9M$  annotations on  $\sim 4,600$  species.
- ▶ About  $\sim 550,000$  are on human genes.
- ▶ Yet, less than 10% of those annotations are based on experimental evidence.

**source:** Statistics from <http://pantherdb.org> and <http://geneontology.org>

Gene functions can be classified in three types:

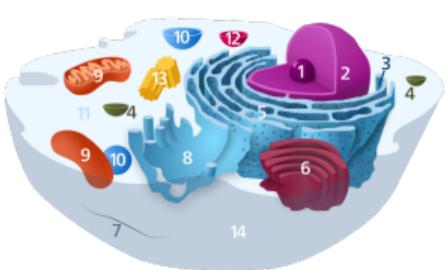
## Molecular function

Active transport GO:0005215



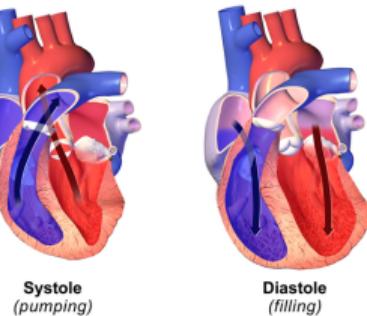
## Cellular component

Mitochondria GO:0004016



## Biological process

Heart contraction GO:0060047



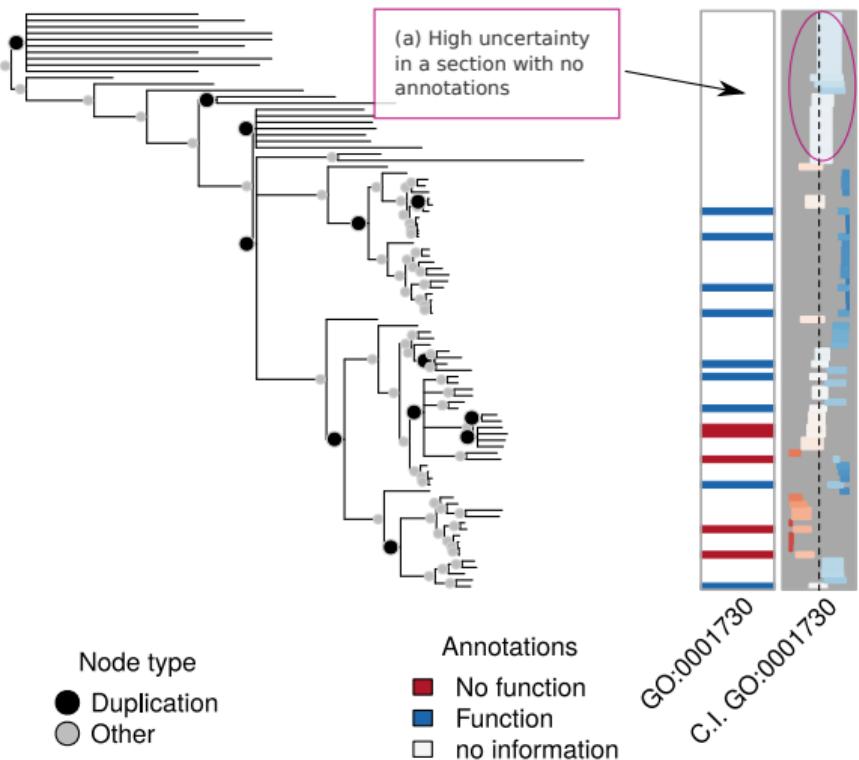
## GO Annotations and Phylogenetic Trees

**Family:** PTHR11258

**Type:** Molecular Function

**Name:** 2'-5'-oligoadenylate synthetase activity

**Desc:** GO:0001730 involved in the process of cellular antiviral activity (wiki on [interferon](#)).



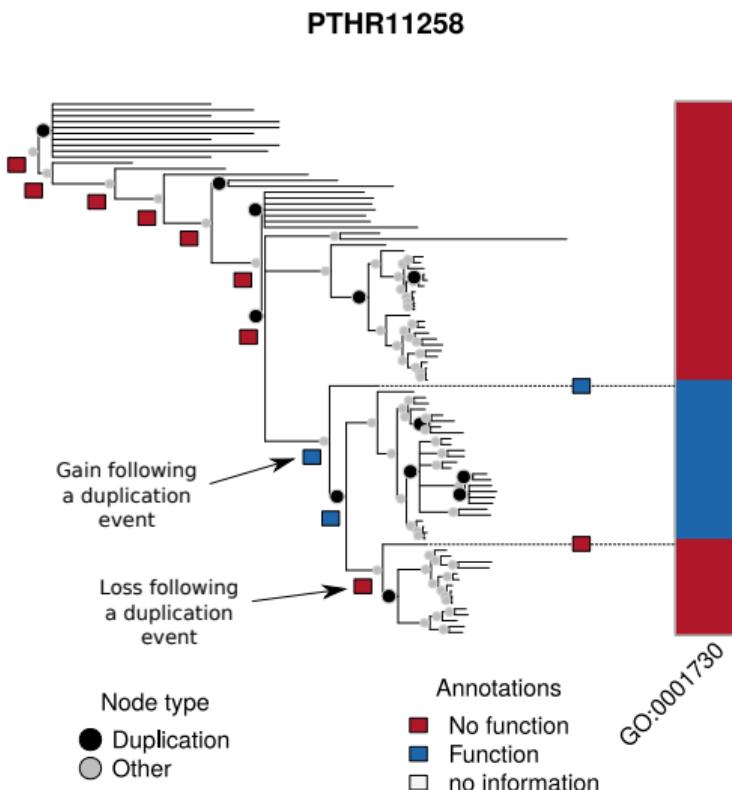
# An evolutionary model of gene functions

Imagine a relay race...



**Figure 1** ISTAF 2019 4 × 100 m relay race (Martin Rulsch, wikimedia)

# An evolutionary model of gene functions



- ▶ Starting with the root node (no function in this case).
- ▶ Passes the baton to its offspring.
- ▶ Possibly without change (on this particular function).
- ▶ Or, with some probability, gaining... or loosing the function.
- ▶ Until the *baton* reaches the end of the tree (modern genes).

▶ more on duplication

▶ alt view

# Example of Data + Predictions

**Family: PTHR11258**

**Type:** Molecular Function

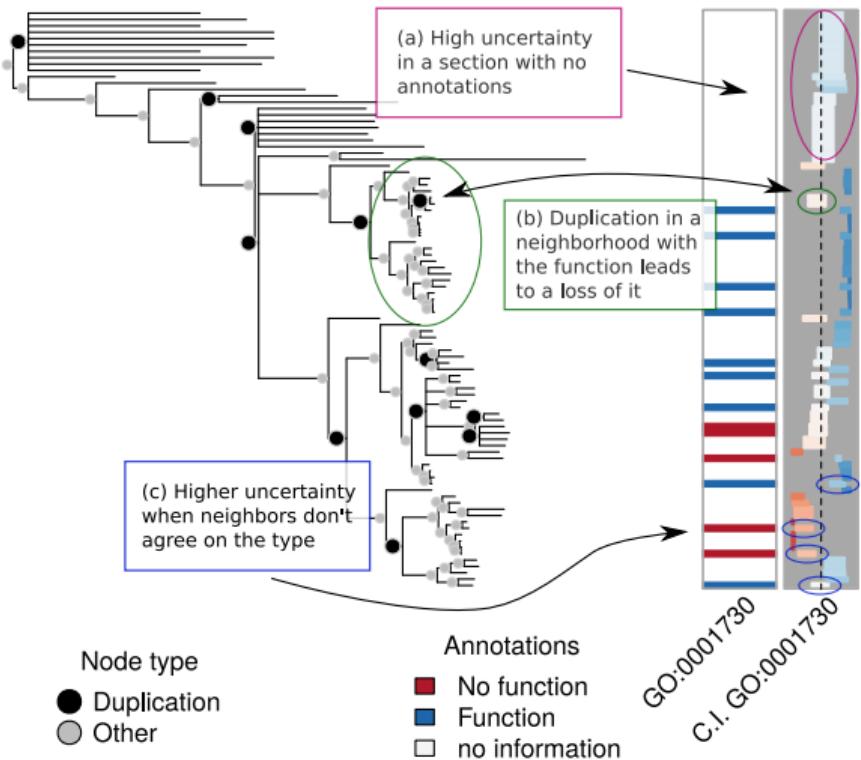
**Name:** 2'-5'-oligoadenylate synthetase activity

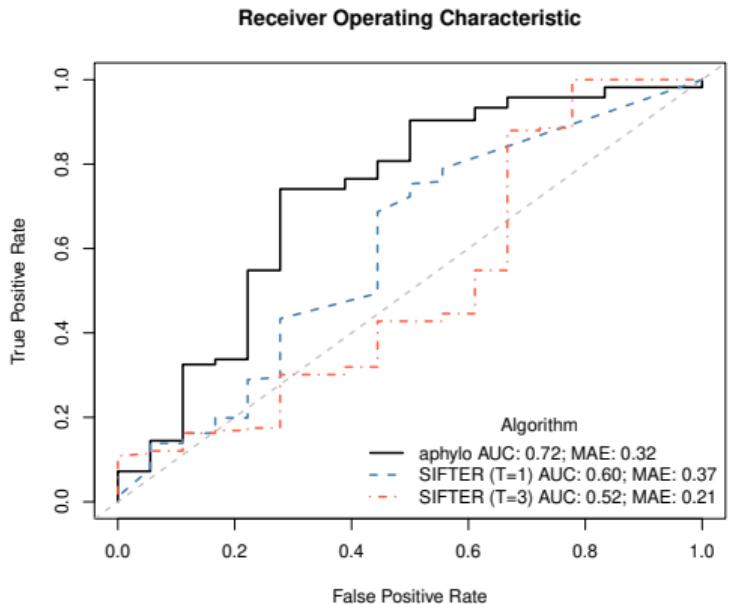
**Desc:** GO:0001730 involved in the process of cellular antiviral activity (wiki on [interferon](#)).

**MAE:** 0.34

**AUC:** 0.91

[see a bad one](#)





Comparing aphylo vs SIFTER (the current state-of-the-art phylo-based evolutionary model) on 147 proteins:

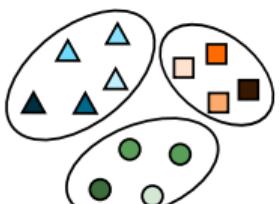
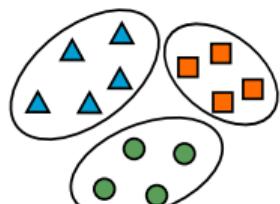
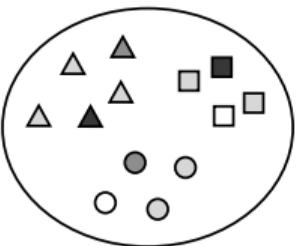
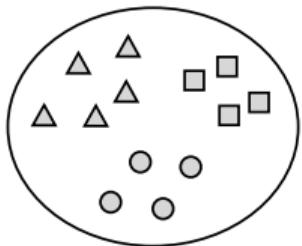
Fast

SIFTER took about 110 minutes to calculate the posterior probabilities, aphylo took 1 second.

Accurate

aphylo reported higher accuracy levels in LOO cross-validation (0.72 vs 0.60 AUC).

## Phylogenetics Modeling: Pooling data



- (a) Featured in the first version of the model.
- (b) “Full glory” Hierarchical Bayes (1,001 parameters for the 141 functions).
- (c) Distilled version (a), improves accuracy.
- (d) Model estimated for Molecular Function (using Empirical Bayes) without significant improvements.

All methods are now available in the `aphylo` package: `aphylo_mle`, `aphylo_mcmc`, and `aphylo_hier`.

# Overview of Prediction Results

	Pooled	Type of Annotation		
		Molecular Function	Biological Process	Cellular Comp.
<b>Mislabeling</b>				
$\psi_{01}$	0.23	0.18	0.09	
$\psi_{10}$	0.01	0.01	0.01	
<b>Duplication Events</b>				
$\mu_{d01}$	0.97	0.97	0.10	
$\mu_{d10}$	0.52	0.51	0.03	
<b>Speciation Events</b>				
$\mu_{s01}$	0.05	0.05	0.05	
$\mu_{s10}$	0.01	0.01	0.02	
<b>Root node</b>				
$\pi$	0.79	0.71	0.88	
Trees	141	74	45	22
<b>Accuracy under the by-aspect model</b>				
AUC	-	0.77	0.83	
MAE	-	0.34	0.26	
<b>Accuracy under the pooled-data model</b>				
AUC	-	0.77	0.75	
MAE	-	0.35	0.34	

Previously, joint estimates out-performed one-at-a-time

- ▶ **Molecular Function** No change.
- ▶ **Biological Process** Significantly better.
- ▶ **Cellular Component** Does not converge.

Molecular Function  $\neq$  Biological Process ? Cellular Component

▶ [data](#)

# Exponential Random Graph Models for Small Networks

*Joint with:* Andrew Slaughter and Kayla de la Haye  
(Chapter 2)

- ▶ If COVID-19 has taught us something it is that networks matter.
- ▶ And especially small networks: Families, teams, friends, etc. The cornerstone of larger social systems.
- ▶ We can study networks using ERGMs.

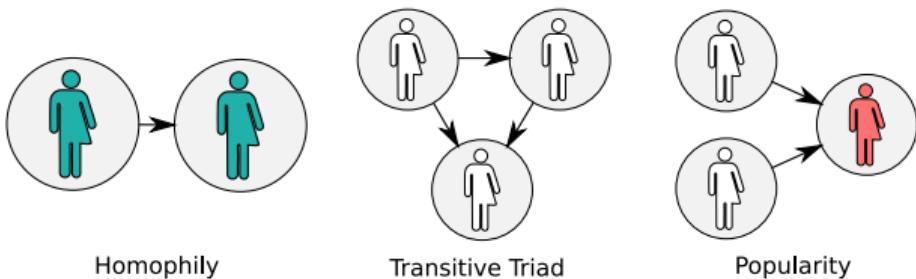
Data: Friendship network of a UK university faculty  
from `igraphdata`. Viz: R package `netplot` (yours truly,  
[github.com/usccana/netplot](https://github.com/usccana/netplot))



# What are Exponential Random Graph Models

Exponential Family Random Graph Models, aka **ERGMs** are:

- ▶ Statistical models of (social) networks.
- ▶ Not about individual ties, but about local structures.



A vector of model parameters	A vector of sufficient statistics
$\mathbb{P}(\mathbf{G} = \mathbf{g} \mid X = x) = \frac{\exp\{\theta^t s(\mathbf{g}, x)\}}{\sum_{\mathbf{g}' \in \mathcal{G}} \exp\{\theta^t s(\mathbf{g}', x)\}}, \quad \forall \mathbf{g} \in \mathcal{G}$	 The normalizing constant
Observed data	All possible networks

- ▶ For any 0/1 matrix of size  $(n \times m)$ , there are  $2^{(n \times m)}$  possible realizations.
  - ▶ A directed graph of size 5 has 1,048,576 possible configurations!
  - ▶ Most (all) applications use **approximations**... yet, for sufficiently small graphs we “can be exact”.

► more theory

► more terms

# ergmito: Estimation of Small ERGM using Exact Statistics

Using exact statistics means:

- Higher convergence rate.
- Lower type-I error rate.
- Smaller bias.
- More power.
- Faster.
- More flexible.

downloads 5649

CRAN - Package ergmito

ergmito: Exponential Random Graph Models for Small Networks

Simulation and estimation of Exponential Random Graph Models (ERGMs) for small networks using exact statistics. As a difference from the 'ergm' package, 'ergmito' circumvents using Markov-Chain Maximum Likelihood Estimator (MC-MLE) and instead uses Maximum Likelihood Estimator (MLE) to fit ERGMs for small networks. As exhaustive enumeration is computationally feasible for small networks, this R package takes advantage of this and provides tools for calculating likelihood functions, and other relevant functions, directly, meaning that in many cases both estimation and simulation of ERGMs for small networks can be faster and more accurate than simulation-based algorithms.

Version: 0.2-1  
Depends: R (≥ 3.3.0)  
Imports: ergm, network, MASS, Rcpp, texreg, stats, parallel, utils, methods, graphics  
LinkingTo: Rcpp, RcppArmadillo  
Suggests: covr, sna, lmtest, fmcmc, coda, knitr, rmarkdown, tinytest  
Published: 2020-02-12  
Author: George Vega Yon [cre, aut], Kayla de la Haye [ths], Army Research Laboratory and the U.S. Army Research Office [fnd] (Grant Number W911NF-15-1-0577)

Exponential Random Graph

ergmito 0.2-1-9999

ergmito: Exponential Random Graph Models for Small Networks

This R package, which has been developed on top of the amazing work that the Statnet team has done, implements estimation and simulation methods for Exponential Random Graph Models of small networks, in particular, less than 7 nodes. In the case of small networks, the calculation of the likelihood of ERGMs becomes computationally feasible, which allows us avoiding approximations and do exact calculation, ultimately obtaining MLEs directly.

## Support

This material is based upon work support by, or in part by, the U.S. Army Research Laboratory and the U.S. Army Research Office under grant number W911NF-15-1-0577

Computation for the work described in this paper was supported by the University of Southern California's Center for High-Performance Computing (www.usc.edu/cmp).

more

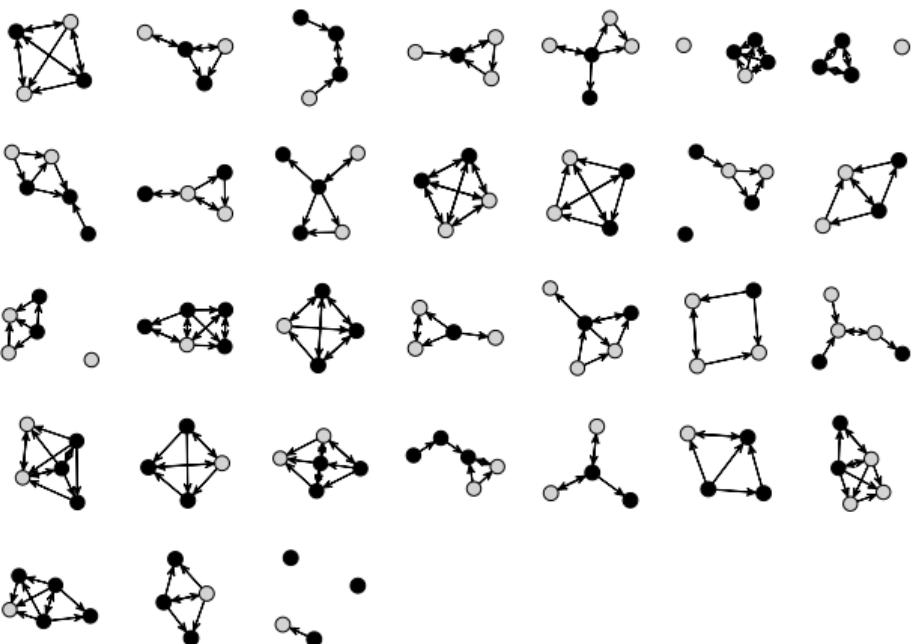
# Featured Application: Small Teams

## Sample

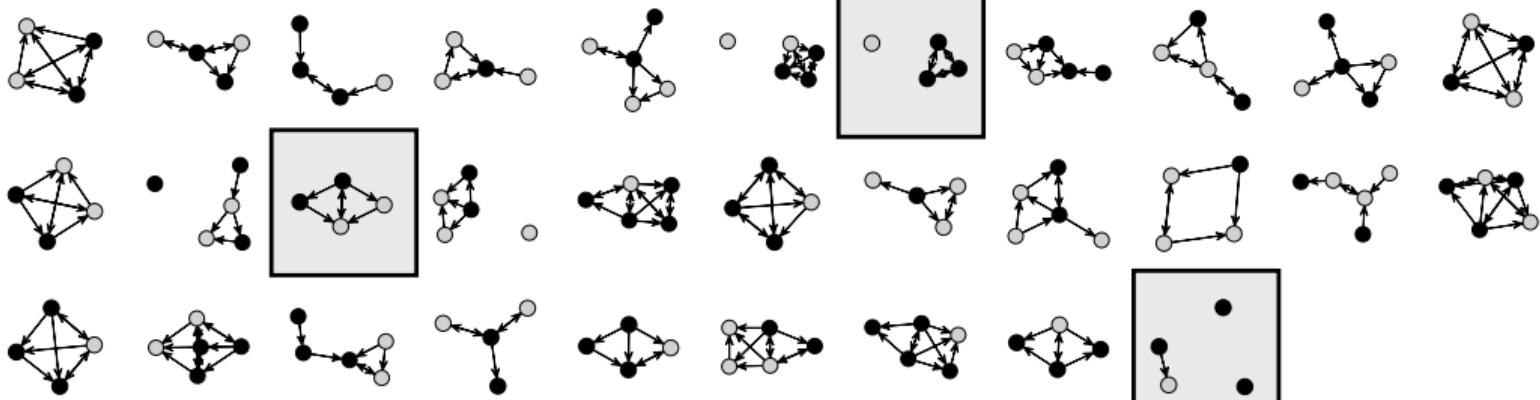
- ▶ 31 mixed-gender teams (4-5 members).
- ▶ University students.
- ▶ Don't know each other.
- ▶ At least one female/male per team.

## Experiment

- ▶ Complete 1 hour of group tasks.
- ▶ Captured network data using name generator survey: *Who did you go to for advice, information or help to complete the group task?*



Is Gender Homophily a feature of these graphs?



Key findings

- ▶ Low density.
- ▶ High balance (transitive triads).
- ▶ No evidence of gender homophily.
- ▶ Females are more likely to ask for advice.

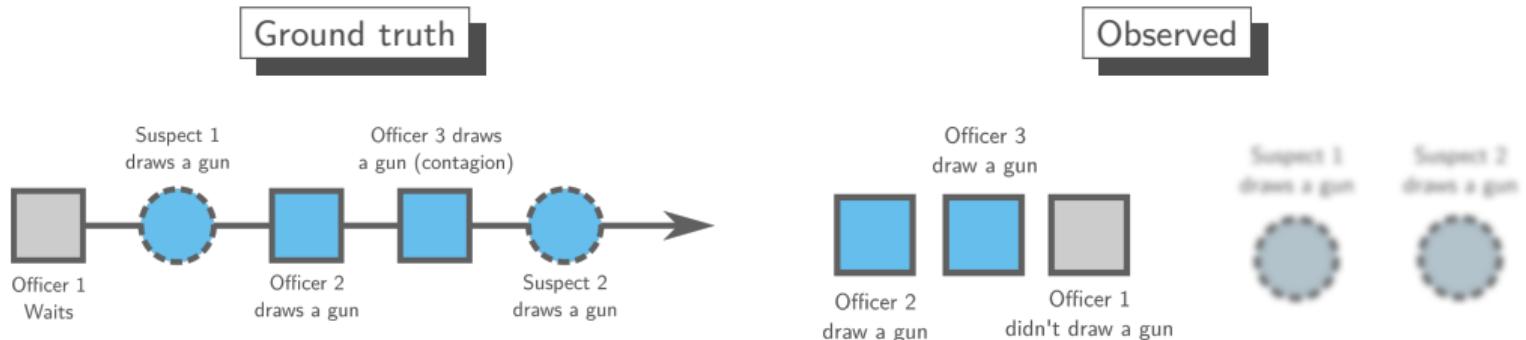
What's different (from regular ERGMs)?

- ▶ Interaction effects: edges  $\times 1$  ( $n = 5$ ).
- ▶ Constrained support: edge  $> 4$ .
- ▶ Transformed variables:  $(\text{Homophily})^{1/2}$ .
- ▶ Bootstrapping: 1,000 replicates in less than 1.5 minutes...  
... if you are lucky, using “regular” ERGMs would take you about 5 hours.

▶ details ▶ gof ▶ data

# Goodness-of-fit for Small Networks

(Chapters 3 and 6)



- ▶ Sequence of actions
- ▶ Subjects' Behavior
- ▶ Peer influence
- ▶ Other situational factors
  
- ▶ We only observe draw/no draw
- ▶ We are unaware of subjects' behavior
- ▶ Don't know if there's contagion/anti-contagion
- ▶ Other factors are unobserved as well

- ▶ Assuming no peer effect/influence/contagion

$$\mathbb{P}(Y_{it} = 1 \mid \mathbf{X}_{it}, \mathbf{z}_t) = \text{logit}^{-1}(\mathbf{x}_{it}\boldsymbol{\theta} + \mathbf{z}_t)$$

Yet,  $\mathbf{z}_t$  (subjects' behavior, etc.) is unobserved.

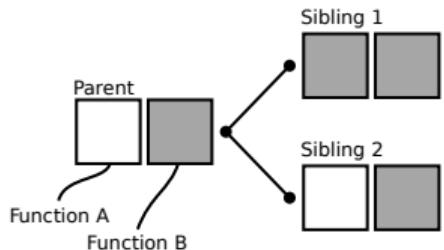
- ▶ Conditioning on  $\sum_i y_{it}$ , we can instead estimate the following

$$\mathbb{P}\left(\mathbf{Y}_t = \mathbf{y}_t \mid \sum_i Y_{it} = k, \mathbf{X}_{it}\right) = \frac{\exp\left\{\sum_i y_{it}\mathbf{x}_{it}\boldsymbol{\theta}\right\}}{\sum_{\mathbf{y}' \in \mathcal{P}(k)} \exp\left\{\sum_i y'_{it}\mathbf{x}_{it}\boldsymbol{\theta}\right\}}$$

A conditional Logit model.

# Connecting the Dots: Phylogenetic Modeling with ERGMs

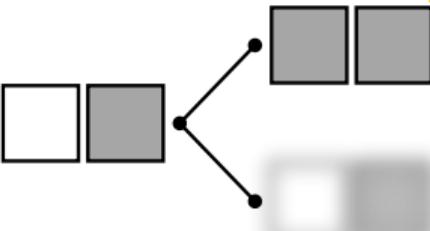
(Chapter 4)



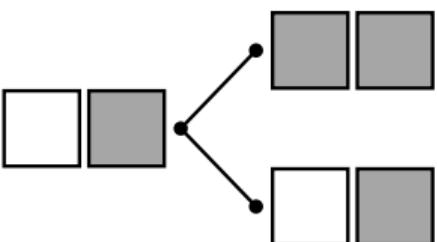
Has the function  
 Doesn't have the function



(a) Sibling and Function Conditional Independence



(b) Sibling Conditional Independence



(c) No conditional independence

Imagine that we have 3 functions (rows) and that each node has 2 siblings (columns)

		Transitions to	
		Case 1	Case 2
Parent	A	$\begin{bmatrix} 0 \\ 1 \end{bmatrix}$	$\begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix}$
	B	$\begin{bmatrix} 1 \\ 1 \end{bmatrix}$	$\begin{bmatrix} 1 & 0 \\ 1 & 1 \end{bmatrix}$
	C	$\begin{bmatrix} 1 \\ 1 \end{bmatrix}$	$\begin{bmatrix} 0 & 1 \\ 0 & 1 \end{bmatrix}$

### Sufficient statistics

# Gains	1	1
Only one offspring changes (yes/no)	1	0
# Changes (gain+loss)	2	3
Subfunctionalizations (yes/no)	0	1

# What Drives Evolution: a game changer

In the model with 3 functions and 2 offspring per node:

- ▶ Full Markov transition matrix:  $2^3 \times 2^6 = 512$
- ▶ Using sufficient statistics:

Pairwise co-evolution: 3 terms,

Pairwise Neofunctionalization: 3 terms,

Pairwise Subfunctionalization: 3 terms,

Function specific gain: 3 terms,

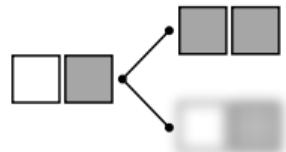
Function specific loss: 3 terms,

Total: 15 parameters.

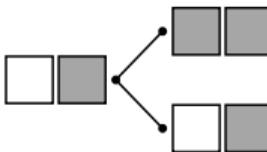
- ▶ Easier to fit and interpret.



(a) Sibling and Function  
Conditional Independence



(b) Sibling Conditional  
Independence



(c) No conditional  
independence

# Next Steps

(Chapter 7)

# Barry

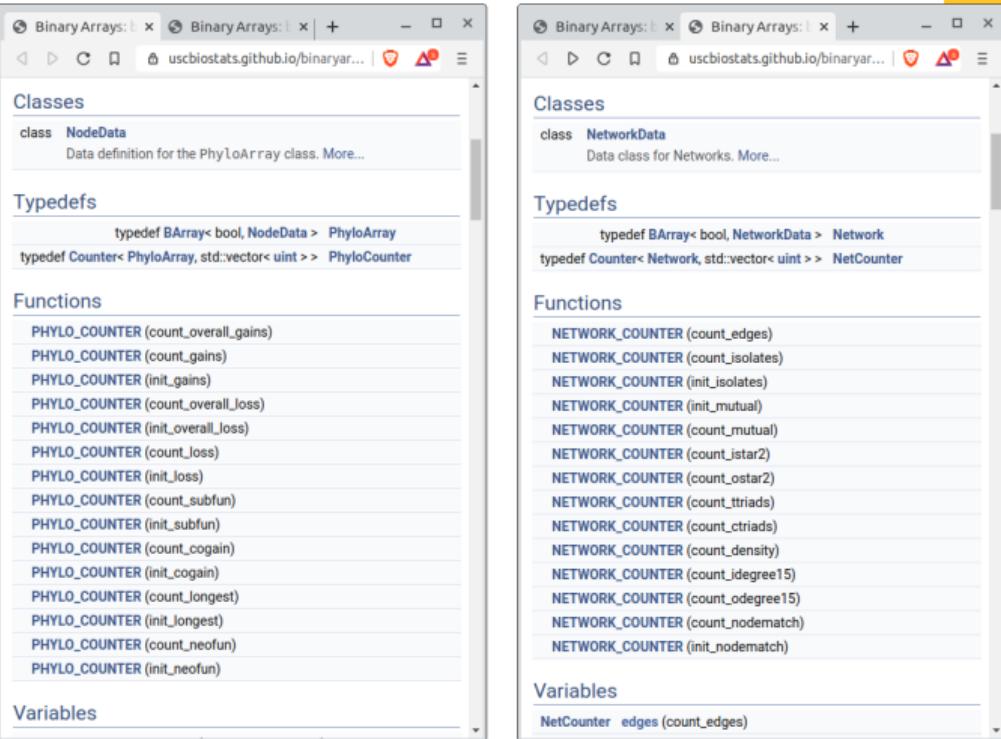
C++ header-only library for counting structures in binary arrays

"The Sniffing Accountant" (Seinfeld, Season 5, Episode 4)

## Barry: your go-to *motif* accountant

- ▶ Sparse matrix represented using double hashmaps (fast row/column access).
- ▶ Template implementation for flexible weights and metadata.
- ▶ Fast counting using change statistics (Ch. 4).
- ▶ Calculation of support for sufficient stats.

[https://USCbiostats.github.io/  
binaryarrays](https://USCbiostats.github.io/binaryarrays)



**Figure 2** Screenshots from the project's website on GitHub.

# Concluding Remarks

## Before my dissertation

### Predicting gene functions

- ▶ “Small scale”.
- ▶ Detached from theory.

### ERGMs

- ▶ Only approximations.
- ▶ Small networks overlooked.
- ▶ Limited alternatives for small nets.

## After my dissertation

### Predicting gene functions

- ▶ Scale-up the problem.
- ▶ More biology (via ERGMs).
- ▶ New ways to look at phylo data.

### ERGMs

- ▶ Revisited exact methods.
- ▶ New light on small networks.
- ▶ Many opportunities for methodological innovations.

## Products

### Publications

6 journal publications (*Journal of Open Source Software*, *Stata Journal*, *Journal of health and social behavior*, *Translational behavioral medicine*, *Social Science & Medicine*) +2 submitted  
(*PLOS Comp. Bio*, *Social Networks*)

### Published software

- ▶ `ergmito` downloads 5649
- ▶ `slurmR` downloads 4819
- ▶ `fmcmc` downloads 7301
- ▶ `netdiffuseR` downloads 20K

### Other tools

`similR`, `gnet`, `aphylo`, `polygons`, `pruner`, `netplot`, `rphyloxml`, `jsPhyloSVG`, and **Barry**

**Essays on Bioinformatics and Social Network Analysis**  
**Statistical and Computational Methods for Complex Systems**

**Thank you!**

## References |

-  Dodd, Diane M. B. (1989). "Reproductive Isolation as a Consequence of Adaptive Divergence in *Drosophila pseudoobscura*". In: *Evolution* 43.6, pp. 1308–1311. ISSN: 00143820, 15585646. URL: <http://www.jstor.org/stable/2409365>.
-  Handcock, Mark S. (2003). "Assessing Degeneracy in Statistical Models of Social Networks". In: *Working Paper No. 39* 76.39, pp. 33–50. ISSN: 1936900X. DOI: 10.1.1.81.5086. URL: <http://citeseerx.ist.psu.edu/viewdoc/summary?doi=10.1.1.81.5086>.

## Example of GO term

---

<b>Accession</b>	GO:0060047
<b>Name</b>	heart contraction
<b>Ontology</b>	biological_process
<b>Synonyms</b>	heart beating, cardiac contraction, hemolymph circulation
<b>Alternate IDs</b>	None
<b>Definition</b>	The multicellular organismal process in which the heart decreases in volume in a characteristic way to propel blood through the body. Source: GOC:dph

---

**Table 1** Heart Contraction Function. source: amigo.geneontology.org

You know what is interesting about this function?

◀ go back

These four species have a gene with that function... and two of these are part of the same evolutionary tree!



*Felis catus* pthr10037



*Oryzias latipes* pthr11521



*Anolis carolinensis* pthr11521



*Equus caballus* pthr24356

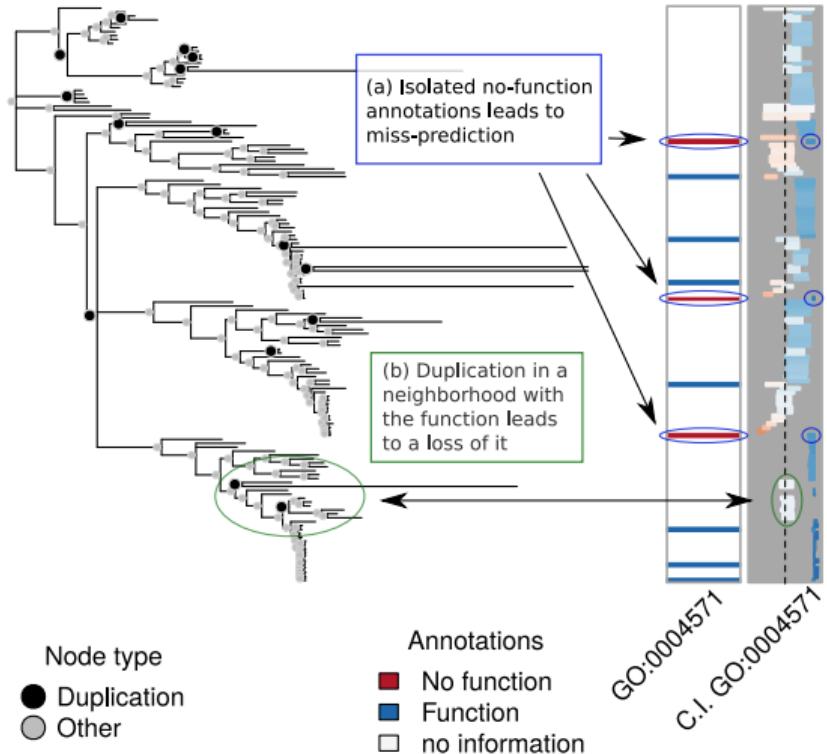
◀ go back

## Example 2: Bad quality prediction

MAE: 0.52

AUC: 0.33

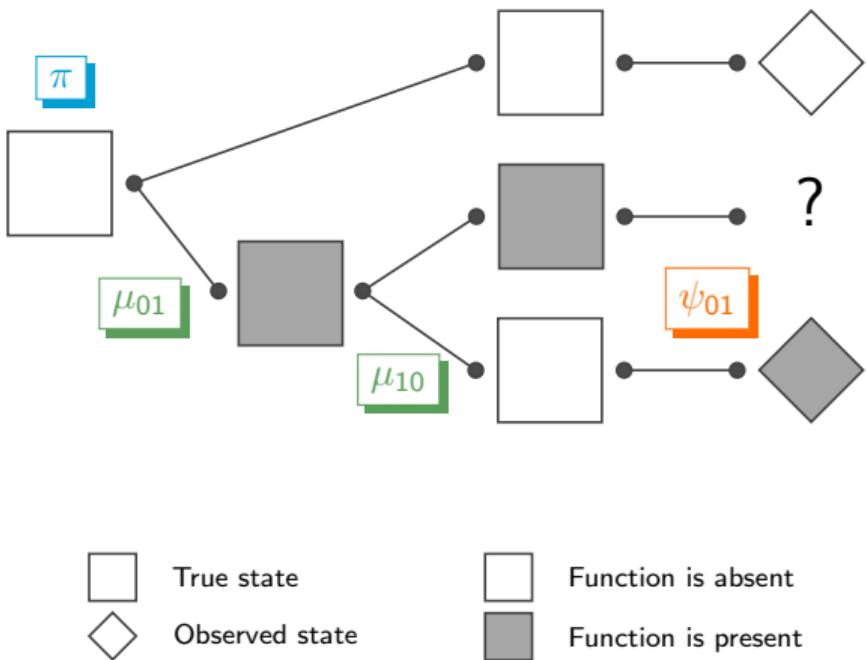
Type: Molecular Function

Name: mannosyl-oligosaccharide  
1,2-alpha-mannosidase activityDesc: GO:0004571 involved in  
synthesis of glycoproteins ([wiki](#)  
and [examples](#)).[◀ go back](#)

		Pooled-data	One-at-a-time	
		Beta prior	Unif. prior	Beta Prior
Pooled-data				
Unif. prior	Beta prior	[-0.02,-0.01]	[-0.14,-0.10]	[-0.06,-0.03]
	Beta prior	-	[-0.12,-0.09]	[-0.04,-0.01]
One-at-a-time				
Unif. prior		-	-	[ 0.06, 0.09]

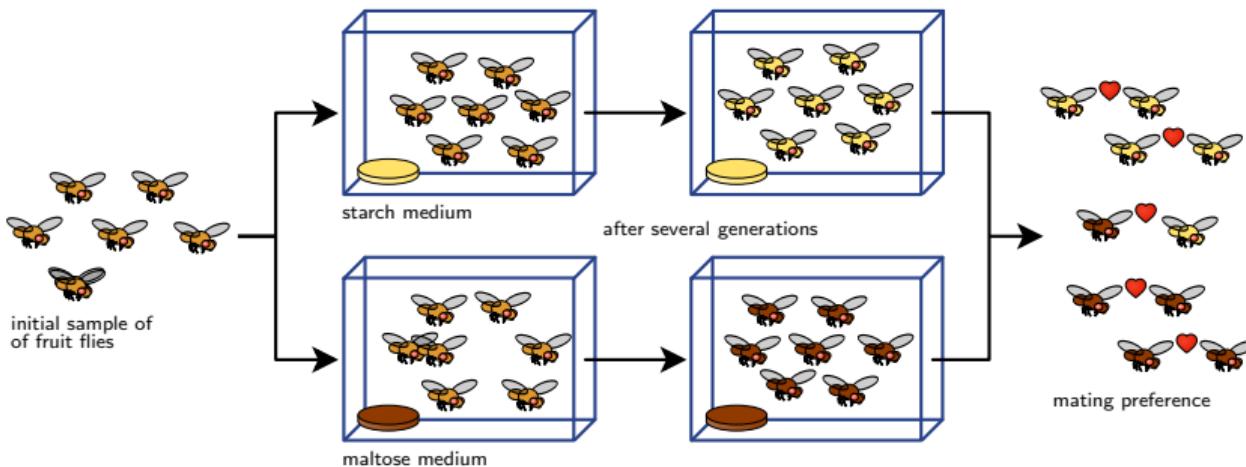
**Table 2** Differences in Mean Absolute Error [MAE]. Each cell shows the 95% confidence interval for the difference in MAE resulting from two methods (row method minus column method). Cells are color coded blue when the method on that row has a significantly smaller MAE than the method on that column; Conversely, cells are colored red when the method in that column outperforms the method in that row. Overall, predictions calculated using the parameter estimates from *pooled-data* predictions outperform *one-at-a-time*.

# An evolutionary model of gene functions



- ▶ Root has the function.
- ▶ Gain and loss (also depends on the type of event [► more](#)).
- ▶ Observed annotations may be incorrect.
- ▶ Only a fraction of the known genes have some form of annotation.

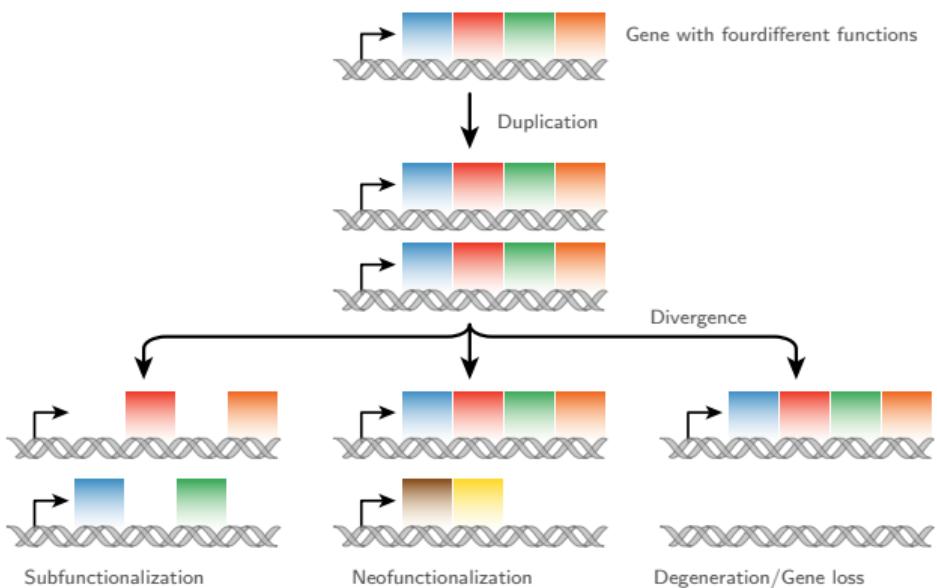
◀ go back



**Figure 3** Dodd 1989: After one year of isolation, flies showed a significant level of assortativity in mating (wikimedia)

◀ go back

# Duplication



**Figure 4** A key part of molecular innovation, gene duplication provides opportunity for new functions to emerge  
(wikimedia)

◀ go back

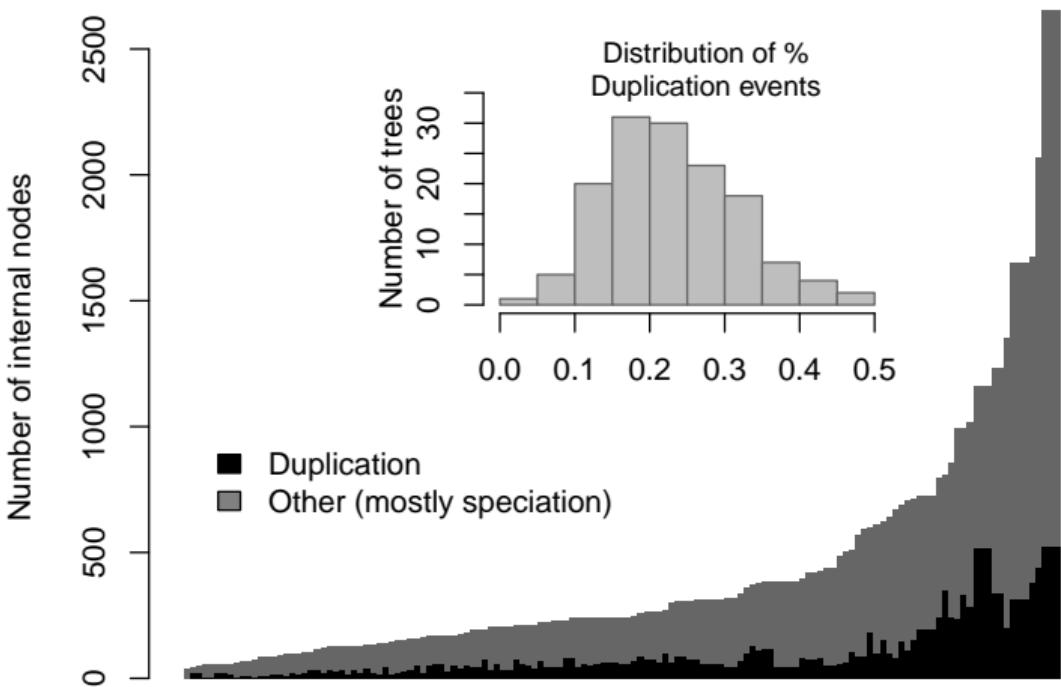
## Data: Phylogenetic trees

Sample of annotations (first 10 in a single tree, Phosphoserine Phosphatase [PTHR10000])

Internal id	Branch Length	type	ancestor
AN0		S	LUCA
AN1	0.06	S	Archaea-Eukaryota
AN2	0.24	S	Eukaryota
AN3	0.44	S	Unikonts
AN4	0.42	S	Opisthokonts
AN6	0.68	D	
AN9	0.79	S	Amoebozoa
AN10	0.18	D	
AN15	0.57	S	Dictyostelium
AN18	0.52	S	Alveolata-Stramenopiles

◀ go back

## Data: Node type (events)



◀ go back

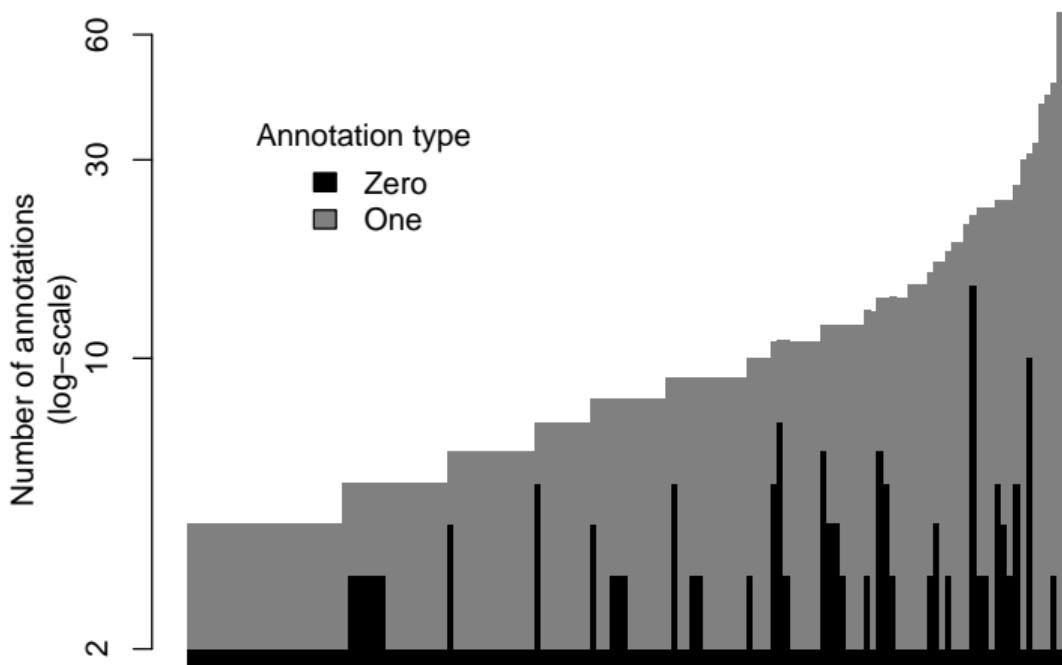
## Data: Annotations (example)

This is the first 10 of ~ 400,000 experimental annotations used:

	Family	Id	GO term	Qualifier
1	PTHR12345	HUMAN HGNC=15756 UniProtKB=Q9H190	GO:0005546	
2	PTHR11361	HUMAN HGNC=7325 UniProtKB=P43246	GO:0016887	CONTRIBUTES_TO
3	PTHR10782	MOUSE MGI=MGI=3040693 UniProtKB=Q6P1E1	GO:0045582	
4	PTHR23086	ARATH TAIR=AT3G09920 UniProtKB=Q8L850	GO:0006520	
5	PTHR32061	RAT RGD=619819 UniProtKB=Q9EPI6	GO:0043197	
6	PTHR46870	ARATH TAIR=AT3G46870 UniProtKB=Q9STF9	GO:1990825	
7	PTHR15204	MOUSE MGI=MGI=1919439 UniProtKB=Q9Z1R2	GO:0045861	
8	PTHR22928	DROME FlyBase=FBgn0050085 UniProtKB=Q9XZ34	GO:0030174	
9	PTHR35972	HUMAN HGNC=34401 UniProtKB=A2RU48	GO:0005515	
10	PTHR10133	DROME FlyBase=FBgn0002905 UniProtKB=O18475	GO:0097681	

◀ go back

## Data: Experimental Annotations



◀ go back

## Asymptotic Behavior of ERGMs

- ▶ In the case that  $s_l = s(\mathbf{g}, x)$  is on the boundary:  $s_l \rightarrow \pm\infty$
- ▶ Since the support space of  $s(\mathbf{g}, x) \in \mathcal{S}$  is bounded, e.g. # edges  $\in [0, n \times (n - 1)]$ , we have:

$$\lim_{\theta_l \rightarrow \infty} l(\theta), \quad \lim_{\theta_l \rightarrow \infty} \nabla l(\theta), \quad \lim_{\theta_l \rightarrow \infty} \mathbf{H}(\theta)$$

log-likelihood, its gradient, and hessian are finite.

- ▶ The direct implication is that, while  $s(\mathbf{g}, x)$  is on the boundary, the MLE for the other statistics exists.<sup>1</sup>
- ▶ All equations ultimately involve realizations of  $s(\mathbf{g}', x)$  that equal  $s_l$ , relevant in: Simulations, Bootstrapping, etc.

◀ go back

<sup>1</sup>Handcock 2003 briefly mentions this

- ▶ Long history in (soc.) network science.
- ▶ Common usage: Hypothesis test prevalence of a feature.

*Is the observed count of XYZ within the expected in a Bernoulli graph?*

*Are statistics A, B, and C different from graphs with 5 triangles?*

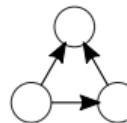
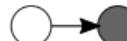
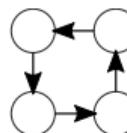
- ▶ Different names, same thing, e.g. CUG tests and rewiring algorithms.
- ▶  $\{\text{CUG, Rewiring}\} \subset \text{ERGM}$
- ▶ We can talk about *Conditional* ERGMs.

$$\mathbb{P}(s(\mathbf{G})_k = s_k \mid s(\mathbf{G})_l = s_l, \theta) = \frac{\exp\{\theta_{-l}^T s(\mathbf{g})_{-l}\}}{\sum_{\mathbf{g}' : s(\mathbf{g}')_l = s(\mathbf{g})_l} \exp\{\theta_{-l}^T s(\mathbf{g}')_{-l}\}} \quad (\text{Eq in 3.5 thesis})$$

In this equation, the marginal distribution of  $s(\mathbf{g})_k$  is orthogonal (independent) from  $\theta_l$ .

◀ go back

## Sufficient statistics have various forms

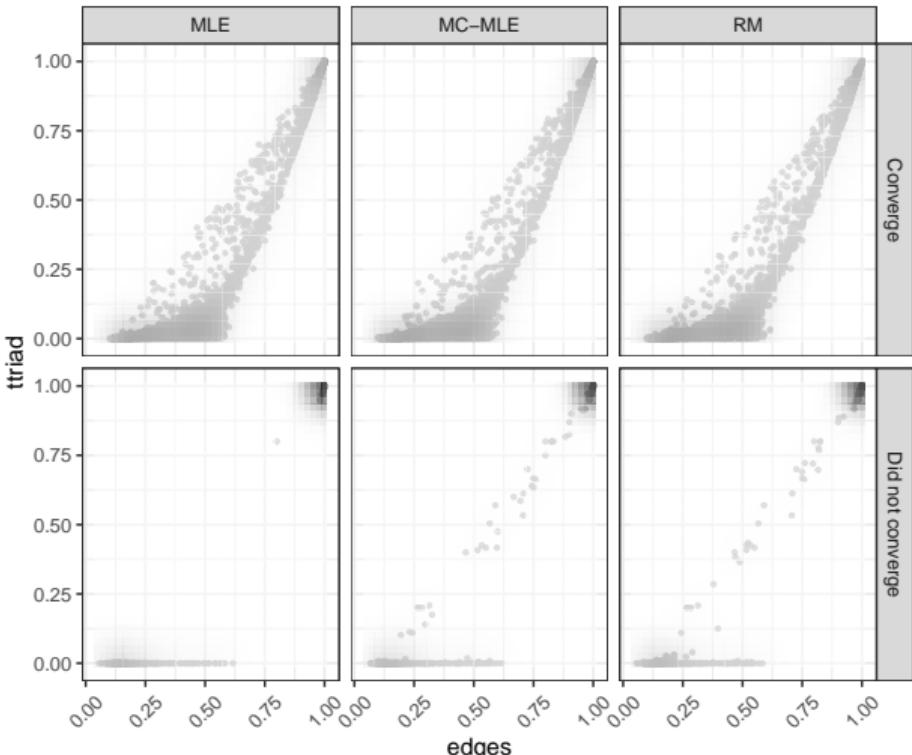
Representation	Description
	Mutual Ties (Reciprocity) $\sum_{i \neq j} y_{ij} y_{ji}$
	Transitive Triad (Balance) $\sum_{i \neq j \neq k} y_{ij} y_{jk} y_{ik}$
	Homophily $\sum_{i \neq j} y_{ij} \mathbf{1}(x_i = x_j)$
	Attribute-receiver effect $\sum_{i \neq j} y_{ij} x_j$
	Four Cycle $\sum_{i \neq j \neq k \neq l} y_{ij} y_{jk} y_{kl} y_{li}$

**Figure 5** Besides the common edge count statistic (number of ties in a graph), ERGMs allow measuring other more complex structures that can be captured as sufficient statistics.

◀ go back

## 1. Higher convergence rate

◀ return



1. Higher convergence rate
2. **Smaller bias**

◀ return

	MLE	MC-MLE	RM
edges	[0.27, 0.36]	[1.23, 1.65]	[0.55, 1.54]
ttriads	[-0.05, -0.03]	[-0.22, -0.16]	[-0.15, 0.48]

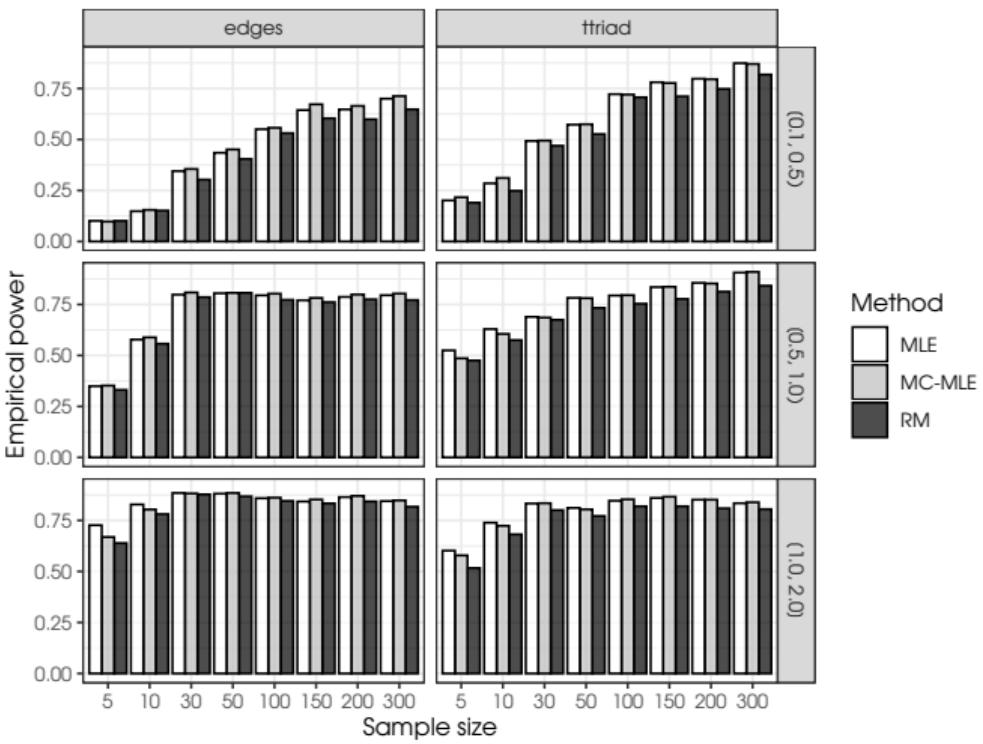
**Table 3** Empirical bias. Each cell shows the 95% confidence interval of each methods' empirical bias.

▶ alt take

# Simulation Study

1. Higher convergence rate
2. Smaller bias
3. **Higher power**

◀ return



1. Higher convergence rate

2. Smaller bias

3. Higher power

4. **Smaller type I error**

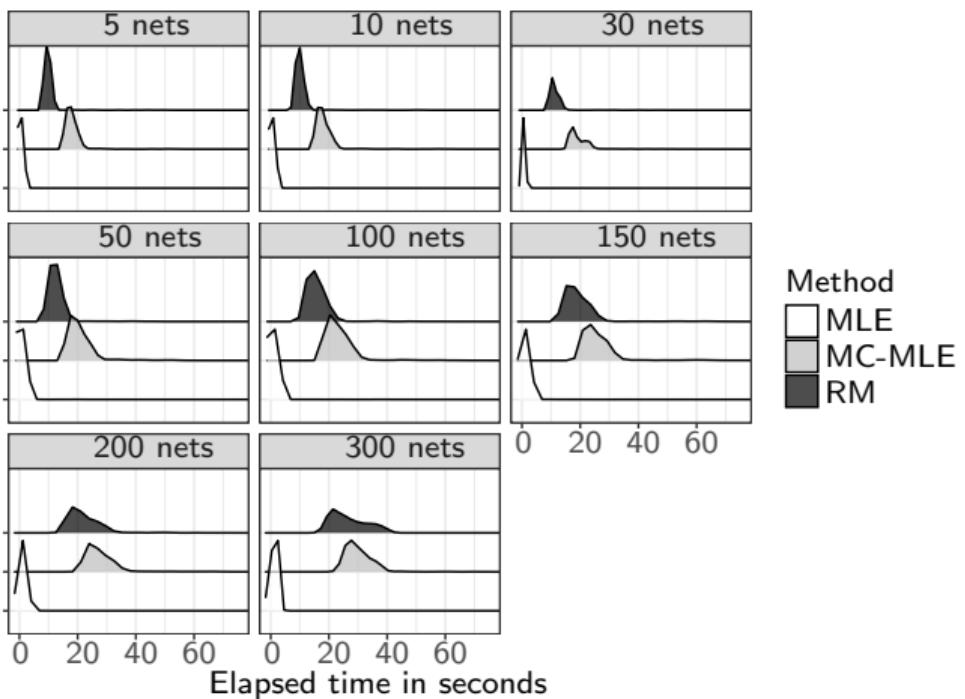
◀ return

	Sample size	N. Sims.	P(Type I error)		$\chi^2$ (vs MLE)		
			MLE	MC-MLE	RM	MC-MLE	RM
	5	4,325	0.066	0.086	0.086	11.36 ***	11.36 ***
	10	4,677	0.063	0.078	0.073	8.44 ***	3.73 *
	15	4,818	0.060	0.072	0.063	5.50 **	0.41
	20	4,889	0.054	0.065	0.061	5.30 **	2.05
	30	4,946	0.053	0.059	0.055	1.60	0.07
	50	4,987	0.053	0.055	0.047	0.16	1.67
	100	4,999	0.054	0.054	0.050	0.00	0.81

# Simulation Study

1. Higher convergence rate
2. Smaller bias
3. Higher power
4. Smaller type I error
5. **Elapsed time**

◀ return



	(1)	(2)	(3)	(4)	(5)	(4b)
edges	-0.52** (0.17)	-0.91*** (0.23)	-0.54** (0.18)	-0.72*** (0.19)	-0.48* (0.19)	-0.72*** (0.17)
ttriads	0.36*** (0.06)	0.46*** (0.06)	0.37*** (0.06)	0.36*** (0.06)	0.36*** (0.06)	0.36*** (0.05)
Homophily (gender)	-0.03 (0.20)	-0.01 (0.21)	-0.20 (0.46)	-0.12 (0.20)	-0.01 (0.20)	-0.12 (0.20)
edges × 1 ( $n = 5$ )	-0.53*** (0.12)	-0.47** (0.16)	-0.52*** (0.13)	-0.53*** (0.13)	-0.53*** (0.12)	-0.53*** (0.13)
(Homophily) $^{1/2}$			0.54 (1.32)			
Sender (female)				0.46* (0.18)		0.46* (0.18)
Receiver (female)					-0.08 (0.18)	
<i>Constraint (offset)</i>						
edge > 4		Yes				
AIC	639.26	569.93	641.08	634.68	641.07	634.68
BIC	655.99	586.66	661.99	655.59	661.98	655.59
Num. networks	31	28	31	31	31	31
Time (seconds)	2.26	2.32	2.28	5.10	5.19	83.97
N replicates					1000	

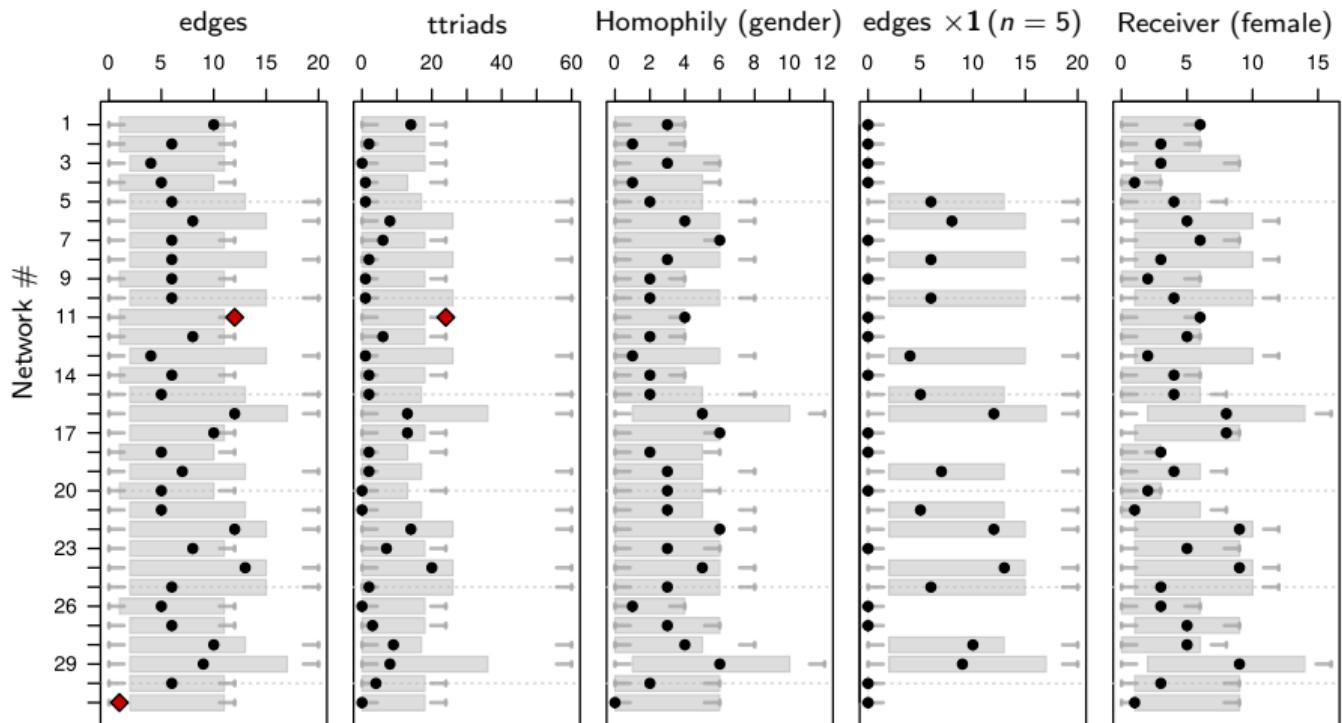
\*\*\*  $p < 0.001$ , \*\*  $p < 0.01$ , \*  $p < 0.05$

1. Interaction effects: seemingly included.
2. Transformed variables: also easy to add.
3. Using offset terms, we can constrain the support.
4. Each 1,000 bootstrap replicates took roughly 0.08 secs.
5. No support for gender homophily, but evidence of females sending more ties.

What about goodness-of-fit?

◀ go back

## What About Goodness-of-fit?



◀ go back

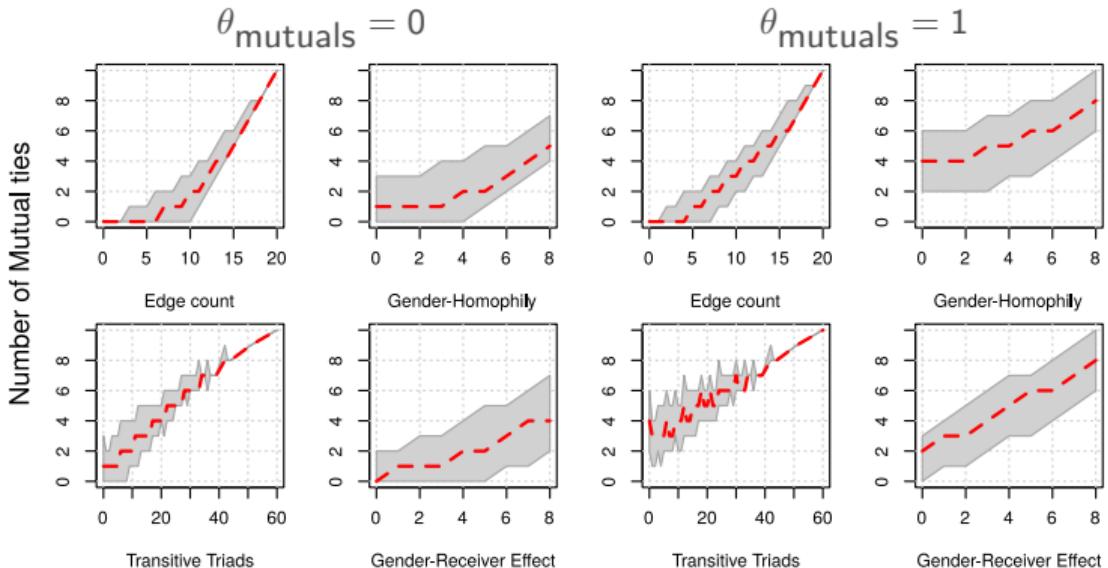
(1)	(2)	(3)	(4)	(5)	(6)
Size ( $n$ )	edges	ttriads	edges $\times$ $\mathbf{1} (n = 5)$	ttriads $\times$ $\mathbf{1} (n = 5)$	edges $\times$ $\log \{1/n\}$
4	10	14	0	0	-13.86
4	6	2	0	0	-8.32
4	4	0	0	0	-5.55
5	6	1	6	1	-9.66
5	8	8	8	8	-12.88
5	6	2	6	2	-9.66
... 25 more rows...					

**Table 4** Example of observed sufficient statistics for the team advice networks. Pooled-data ERGMs have multiple observed sufficient statistics (also known as target statistics). Furthermore, as shown here, we can manipulate common statistics as *edges* (2) and *ttriads* (3) to include, e.g. interaction effects (4) and (5), or more complex transformations, e.g. (6).

## Conditional Distribution: Mutual Ties

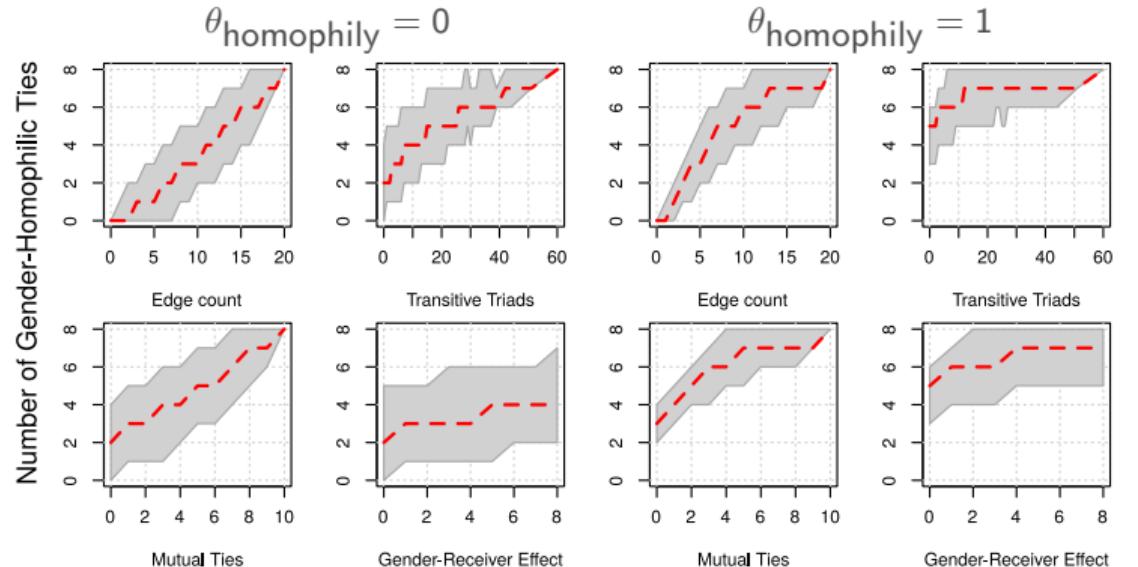


- ▶ Better predicted by other Markov structures.
- ▶ Non-Markov structures = poor prediction.
- ▶ No big impact of prevalence ( $\theta_{\text{mutual}}$ ).



◀ go back

## Conditional Distribution: Homophily



- ▶ No structure has high predictive power.
- ▶ Almost zero association with Receiver Effect.
- ▶ Prevalence ( $\theta_{\text{homophily}}$ ) has no effect.