Applications of Statistical Computing in Complex Social and Biological Systems Modeling

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The University of Utah

(virtual)

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Funding and support

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National Cancer Institute Grant #1P01CA196596.

U.S. Army Research Laboratory and the U.S. Army Research Office under grant number W911NF-15-1-0577.

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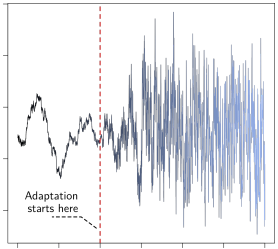

Bayesian, Non-parametric, Spatial

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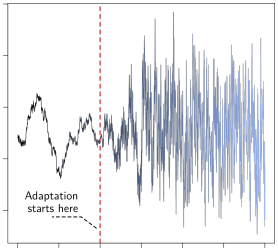

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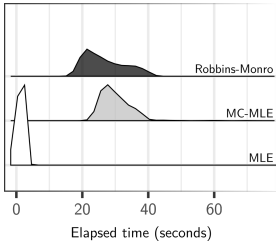

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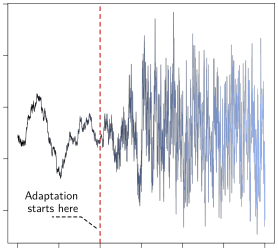

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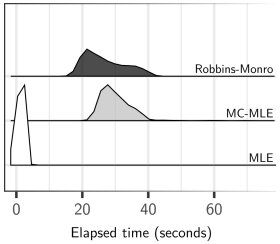

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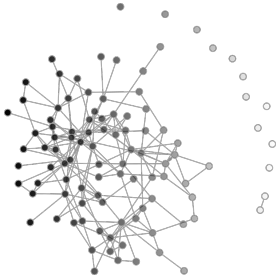
Complex Systems



social, biological, technical

Contents

Part I: Exponential Random Graph Models for Small Networks

Part II: A general framework for modeling functional evolution

Part II: Other Projects and Future Research

You can download the slides from ggv.cl/slides/utah-epi

Part I: Exponential Random Graph Models for Small Networks

Joint with: Andrew Slaughter and Kayla de la Haye

(published in the journal *Social Networks*)

Social Networks

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

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- If COVID-19 has taught us something it is that networks matter.

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- 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.

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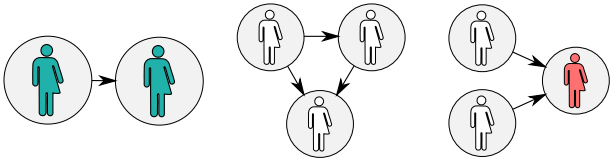

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A vector of model parameters

A vector of sufficient statistics

$$\mathbb{P}\left(\mathbf{G}=\mathbf{g} \mid X=x\right)=\frac{\exp\left\{\theta^{\mathrm{t}} s\left(\mathbf{g}, x\right)\right\}}{\sum_{\mathbf{g}^{\prime} \in \mathcal{G}} \exp\left\{\theta^{\mathrm{t}} s\left(\mathbf{g}^{\prime}, x\right)\right\}}, \quad \forall \mathbf{g} \in \mathcal{G}$$

Observed data

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... I implemented this in the **ergmito** R package

more theory more terms

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Premise

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- Full enumeration $\neq$ All networks with k ties

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Extra features

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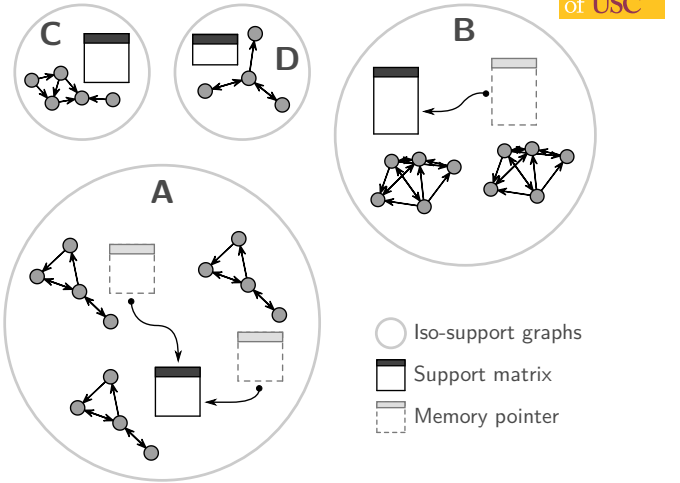

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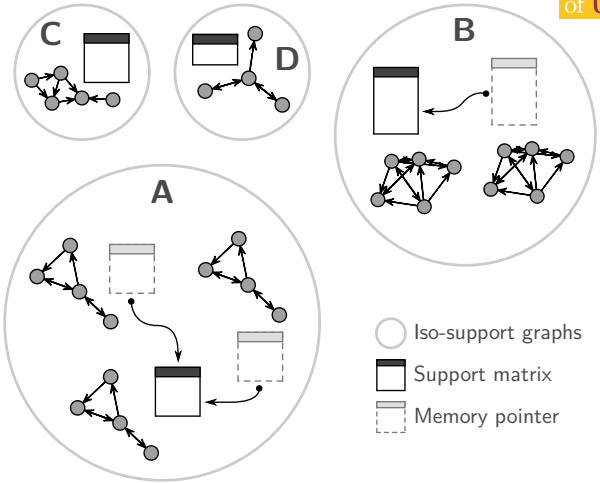

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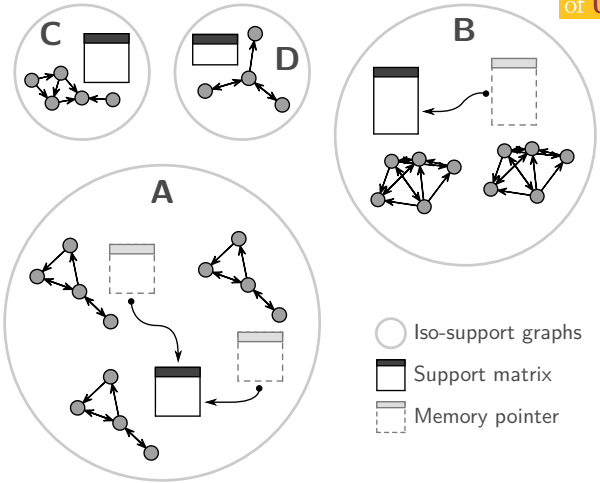
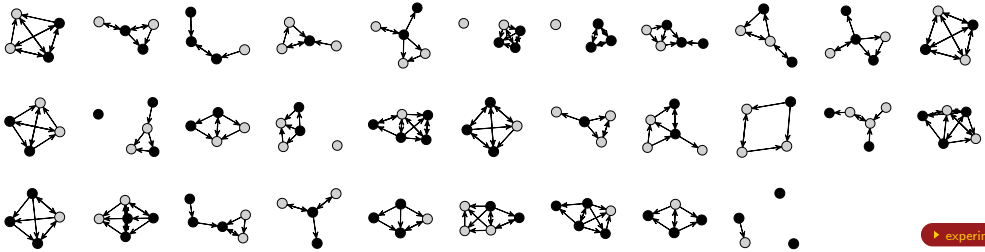
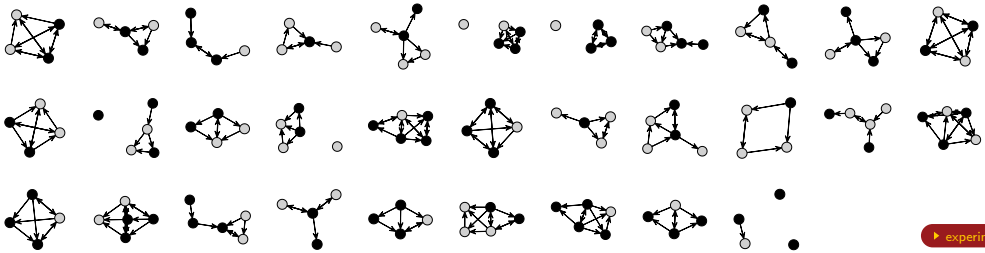


Fitting a pooled-data ERGMito with 80K nodes in 20K small nets $\sim$ 4s

ergmito featured example: Advice seeking networks in small teams (de la Haye et al, 2020)



▸ experiment



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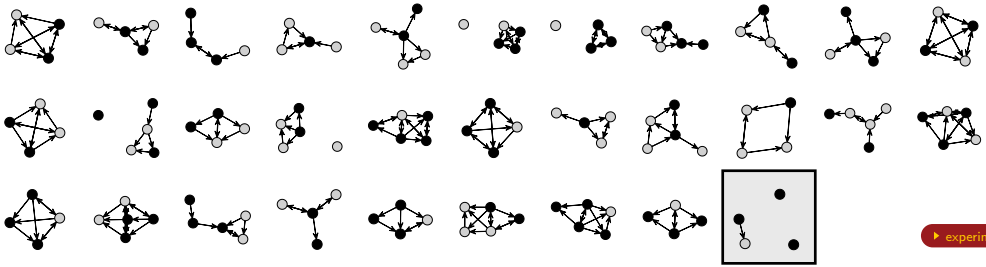

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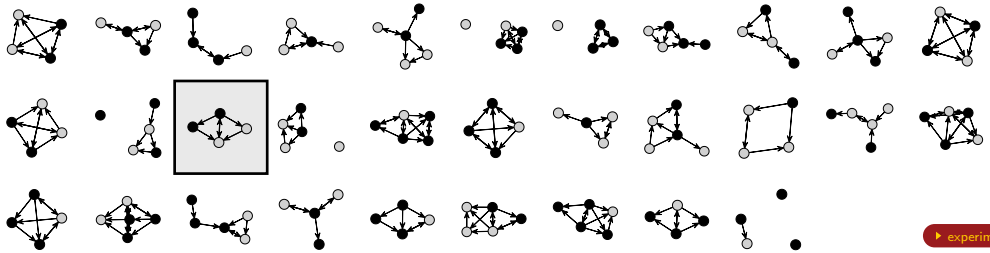

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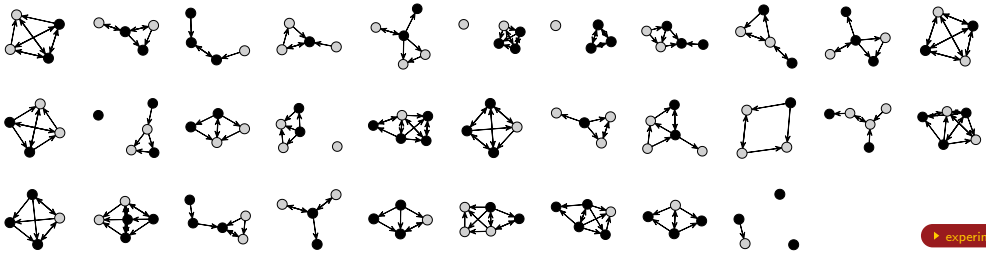

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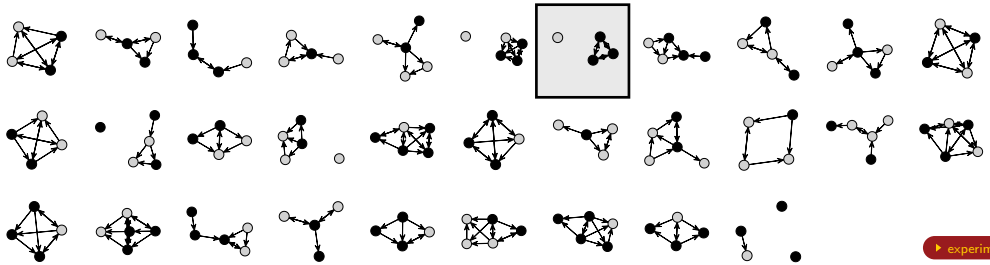

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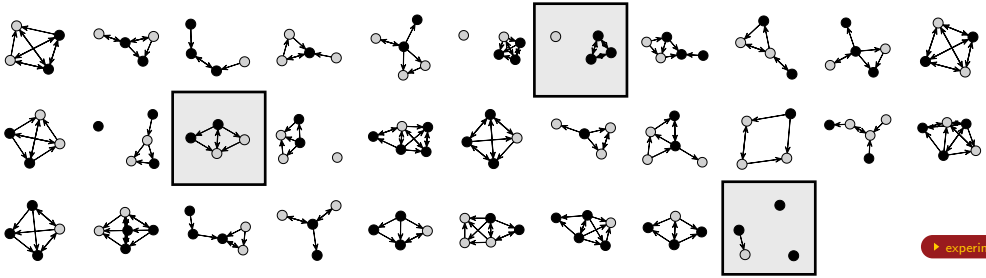

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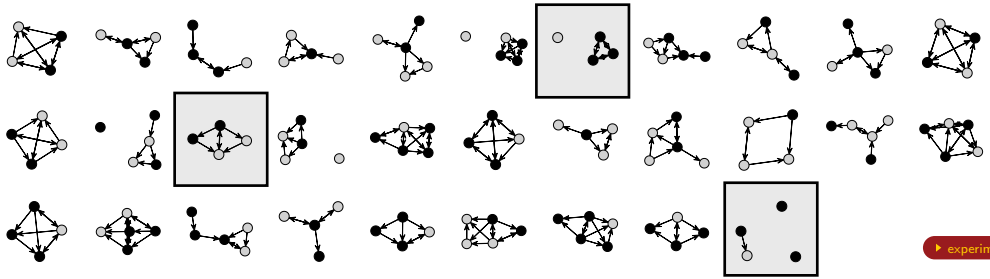

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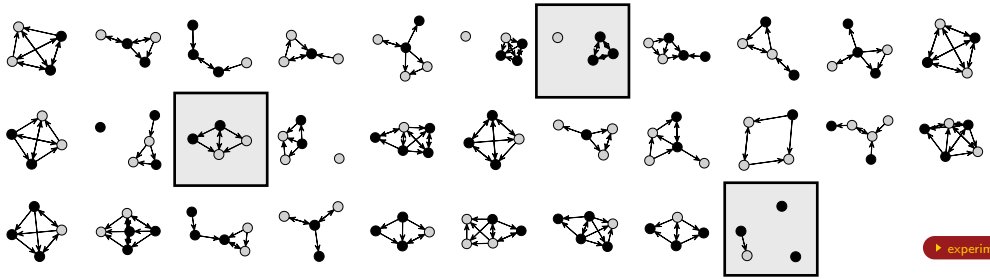

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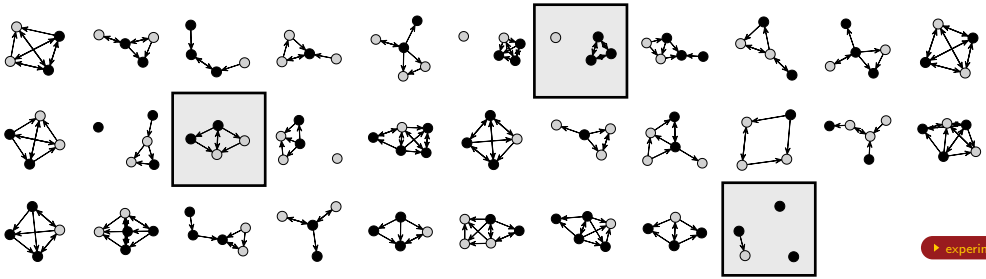

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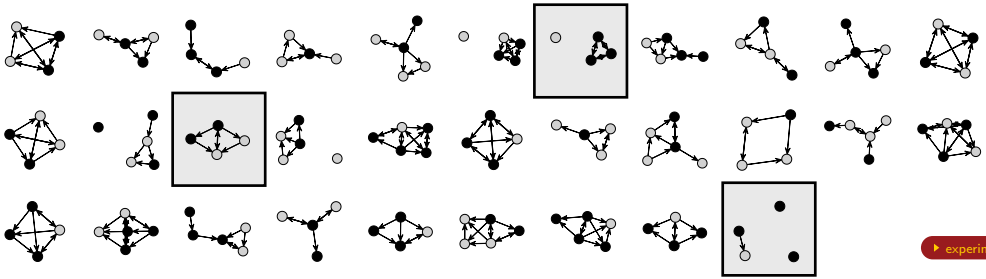

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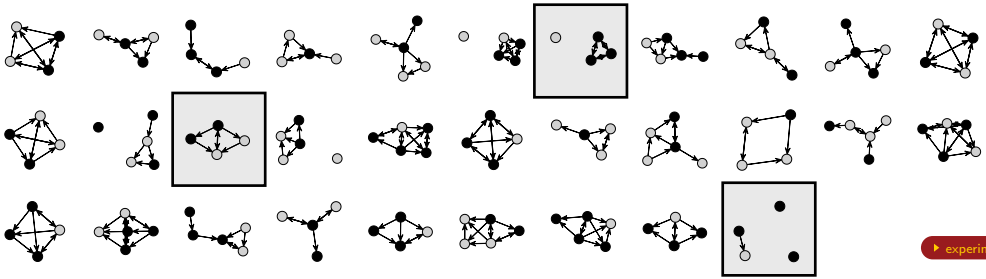

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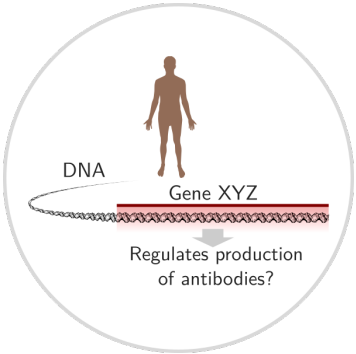
▸ details ▸ gof ▸ data

Part II: A general framework for modeling functional evolution

Is gene *XYZ* involved in process *ABC*?



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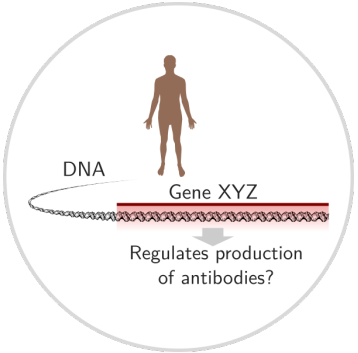

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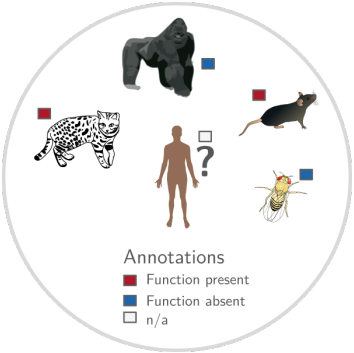

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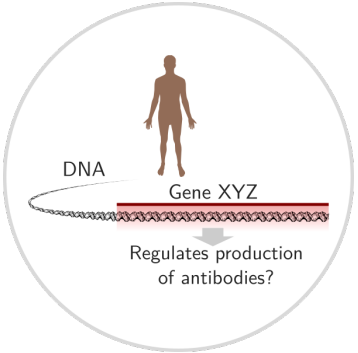

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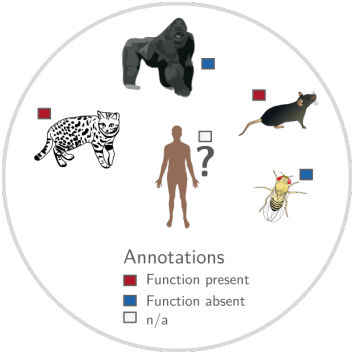

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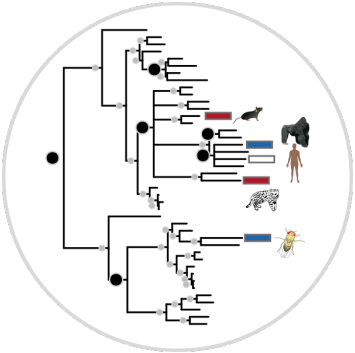

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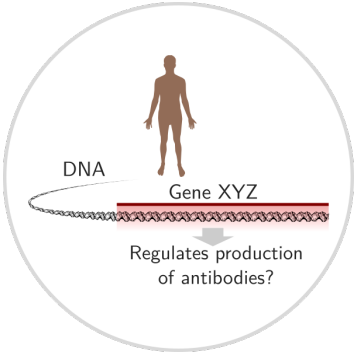

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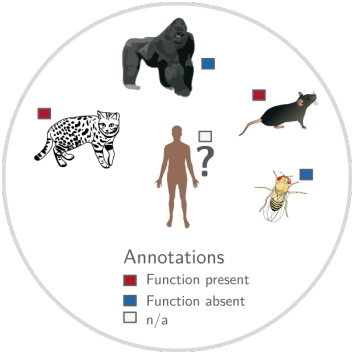

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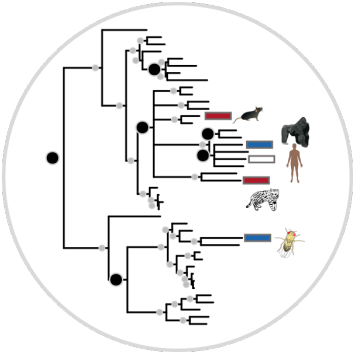

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... let's rephrase the question.

Is the human gene **XYZ** involved in process **ABC**, given what we know about that for other *related* species?

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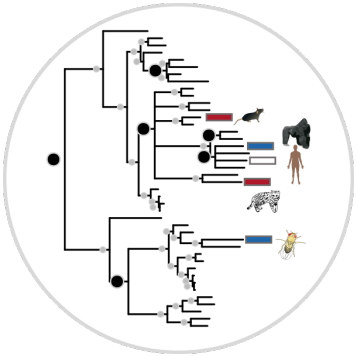

GENEONTOLOGY
Unifying Biology

more

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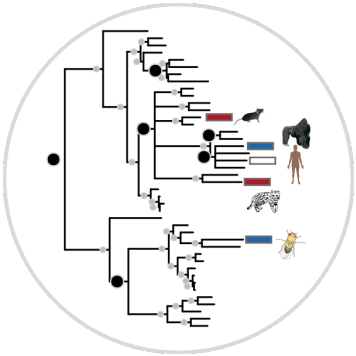

GENEONTOLOGY
Unifying Biology

- $\sim$ 15,000 phylogenetic trees

more

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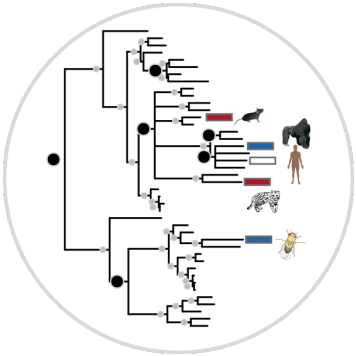

GENEONTOLOGY
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- $\sim$ 15,000 phylogenetic trees
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more

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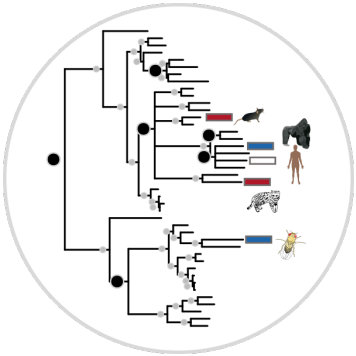

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more

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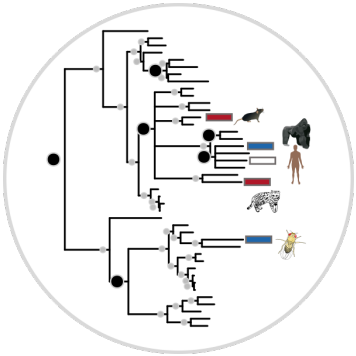

GENEONTOLOGY
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- $\sim <$ 10% are based on experimental evidence...

more

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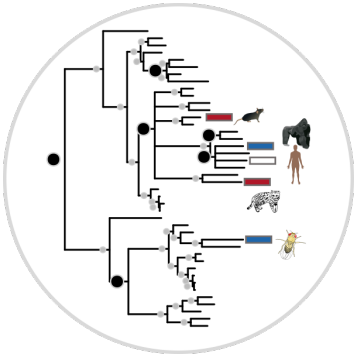

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more

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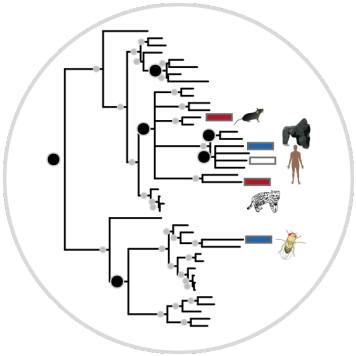

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Unifying Biology

- $\sim$ 15,000 phylogenetic trees
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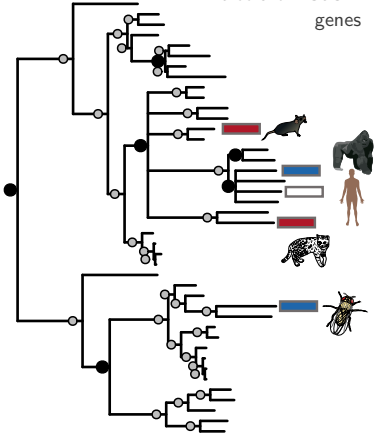
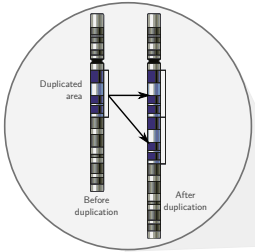
Only on 2020, 2,000+ COVID-19 papers using the GO (Google Scholar)

more

The tips of the tree are **modern** genes



● nodes are **Duplication** Events



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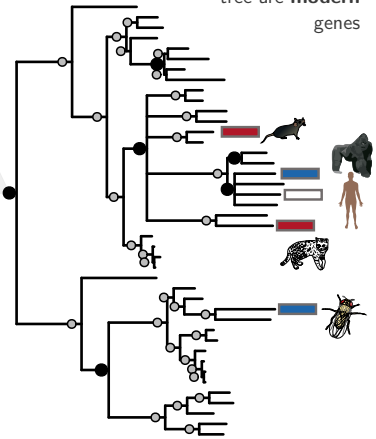
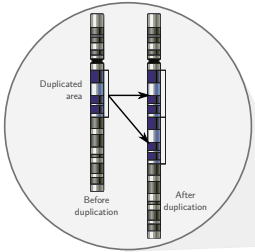


go back

● nodes are **Duplication** Events



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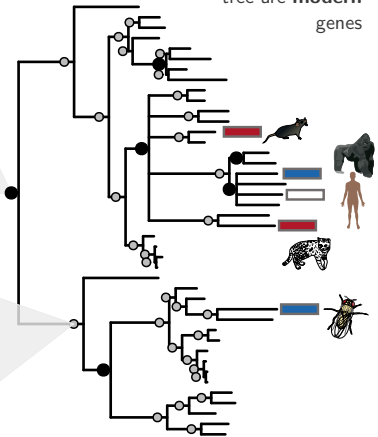
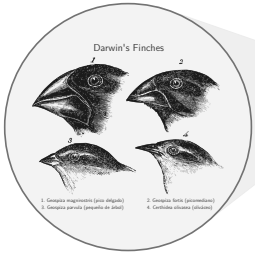


○ nodes are **Speciation** Events



go back

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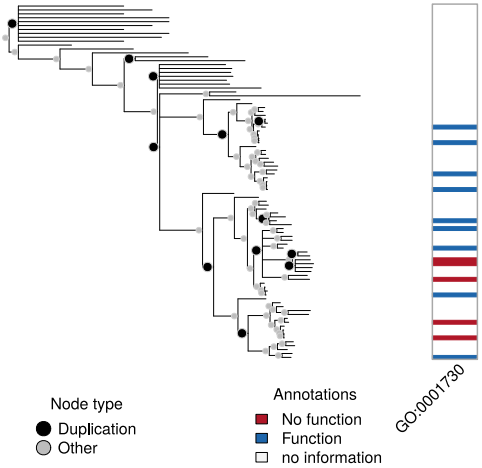
Name: 2'-5'-oligoadenylate synthetase activity

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



Example: Molecular function in family PTHR1128

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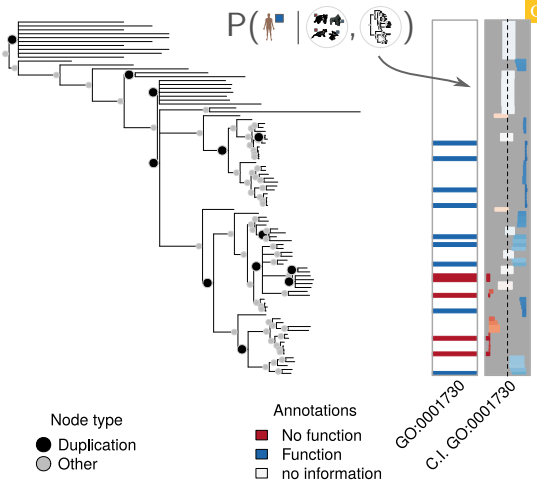
Name: 2'-5'-oligoadenylate synthetase activity

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

MAE: 0.34

AUC: 0.91



Example: Molecular function in family PTHR1128

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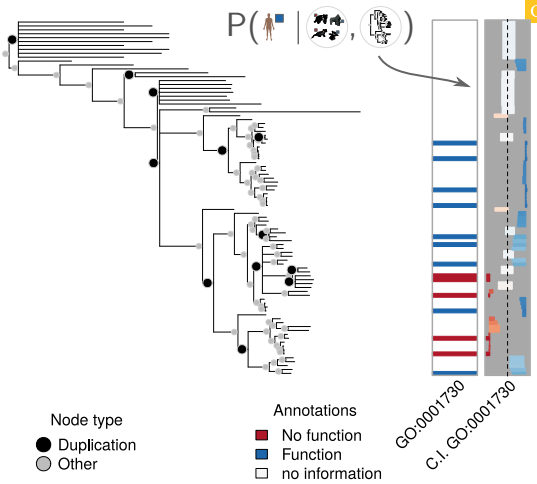
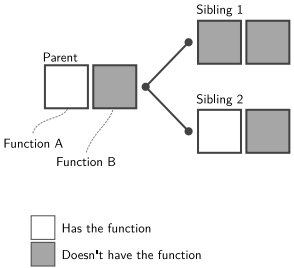
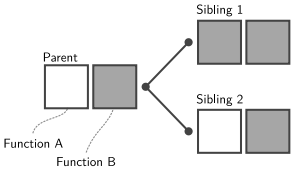
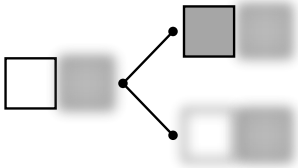


Note: Prediction made using **aphylo** (Vega Yon and *et al*, PLOS Comp. Bio 2021) see details


Sibling 1
Parent
Sibling 2
Function A
Function B
Has the function
Doesn't have the function





(a) Sibling and Function Conditional Independence

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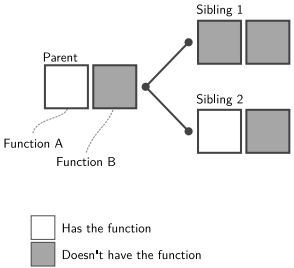

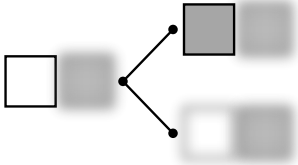

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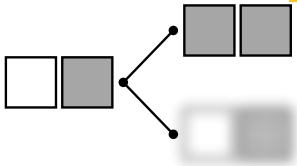
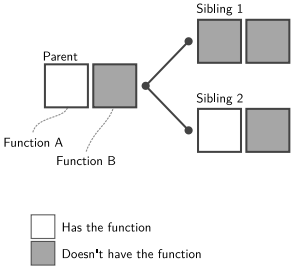
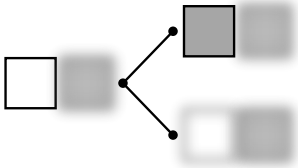


(b) Sibling Conditional Independence





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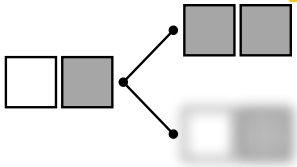

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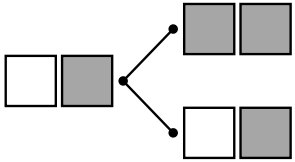
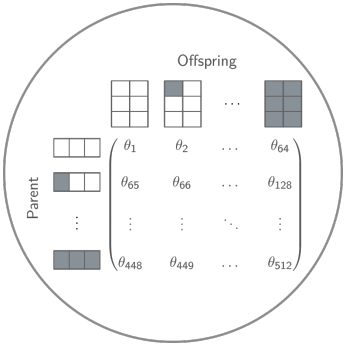


(c) No conditional independence

If we wanted to build a model with 3 functions, we would need to estimate...

Full Markov Transition Matrix



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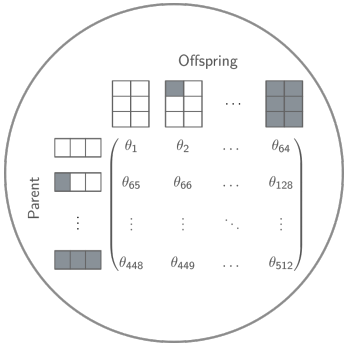

- 512 parameters

If we wanted to build a model with 3 functions, we would need to estimate...

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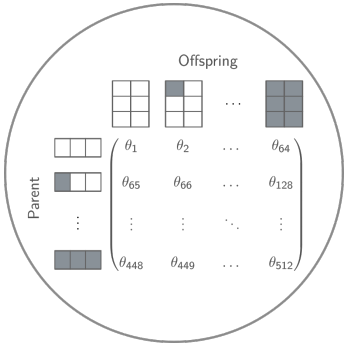

- 512 parameters
- Finding this many parameters not easy.

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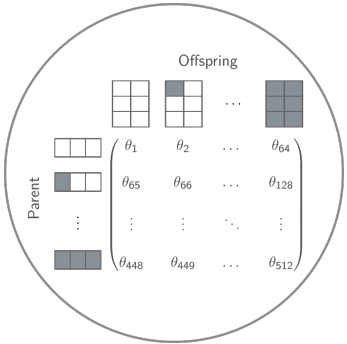

- 512 parameters
- Finding this many parameters not easy.
- Even if you can, interpretation is awkward.

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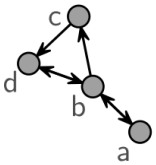
Social Network



	a	b	c	d
a		■		
b	■		■	■
c				■
d		■		

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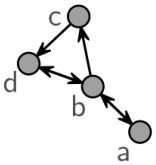
Social Network



	a	b	c	d
a		■		
b	■		■	■
c				■
d		■		

- Not about individual ties.

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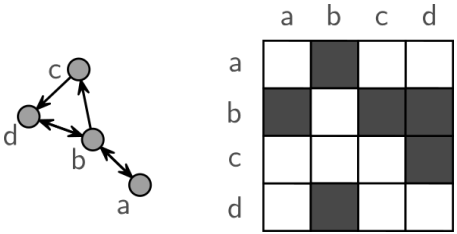
Social Network



- Not about individual ties.
- Statistical inference on *motifs* (triangles, dyads, homophily, etc.)

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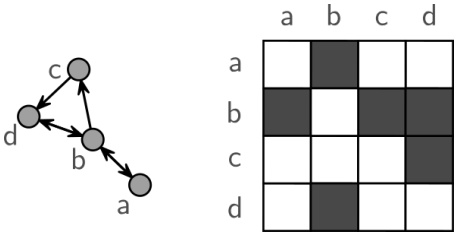
Social Network



- Not about individual ties.
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Ultimately...

ERGM $\equiv$ Modeling binary arrays

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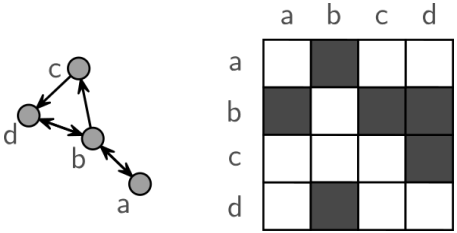
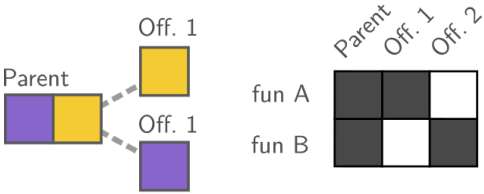
Social Network



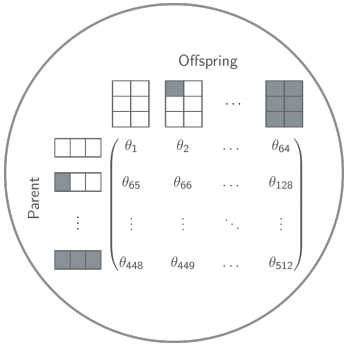
Evolutionary Event



Social Networks are usually represented as **adjacency matrices**, and so can evolutionary events!

If we wanted to build a model with 3 functions, we would need to estimate...

Full Markov Transition Matrix



512 parameters

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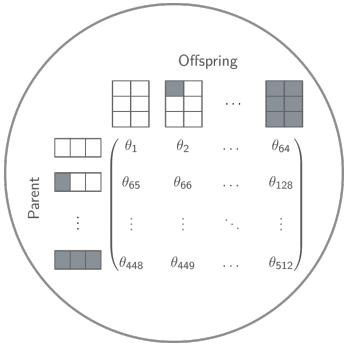
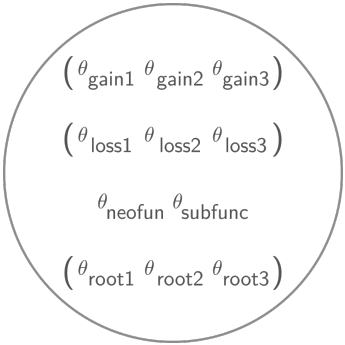


512 parameters

Sufficient statistics



11 parameters (for example)

If we wanted to build a model with 3 functions, we would need to estimate...

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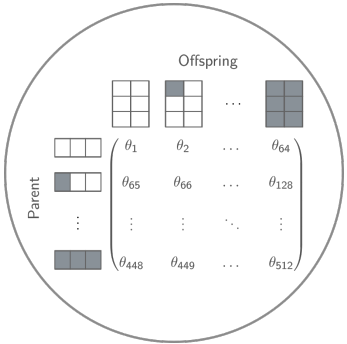

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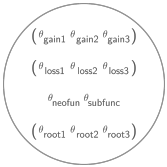
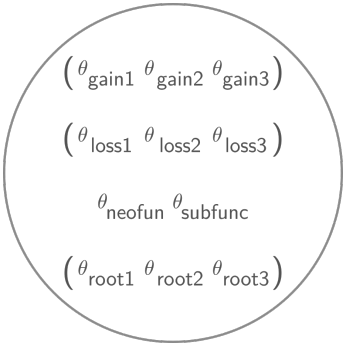


Easier to fit

Easier to interpret

Sufficient statistics



11 parameters (for example)

numeric example

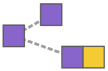
Representation	Description	Definition
	Gain of function	$(1 - x_p) \sum_{n:n \in Off} x_n$
	Loss of function	$x_p \sum_{n:n \in Off} (1 - x_n)$
	Subfunctionalization	$x_p^k x_p^j \sum_{n \neq m} x_n^k (1 - x_n^j)(1 - x_m^k) x_m^j$
	Neofunctionalization	$x_p^k (1 - x_p^j) \sum_{n \neq m} x_n^k (1 - x_n^j)(1 - x_m^k) x_m^j$
	Longest branch gains	$(1 - x_p^k)\mathbf{1}\left(x_m^k : m = \text{argmax}_n \text{blength}_n\right)$

Table 1 Example of sufficient statistics for evolutionary transitions.

Also known as *dynamic programming* or *postorder tree traversal*

All possible transitions from $\mathbf{x}_n$

Transition Probability (ERGM)

$$\mathbb{P}\left(\tilde{D}_n \,\middle|\, \mathbf{x}_n, \Theta\right) = \sum_{\mathbf{x}} \mathbb{P}\left(\mathbf{x} \mid \mathbf{x}_n\right) \prod_{m \in \mathbf{O}(n)} \mathbb{P}\left(\tilde{D}_m \,\middle|\, \mathbf{x}_m\right)$$

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Also known as *dynamic programming* or *postorder tree traversal*

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Model Parameters

Vector of Sufficient Statistics

$$\mathbb{P}\left(\mathbf{x} \mid \mathbf{x}_n\right) = \frac{\exp\left\{\Theta^{\mathsf{t}} s(\mathbf{x}, x_n)\right\}}{\sum_{\mathbf{x}'} \exp\left\{\Theta^{\mathsf{t}} s(\mathbf{x}', x_n)\right\}}$$

Normalizing Constant

the ***lingua franca*** of SNA

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Gene state given the data

It's parent state given the data

$$\mathbb{P}\left(\mathbf{x}^p = \mathbf{x} \,\middle|\, \tilde{D}\right) = \underbrace{\left\{\prod_{m \in \mathbf{O}(p)} \mathbb{P}\left(\tilde{D}_m \,\middle|\, x_m\right)\right\}}_{\text{Everything below } x^p} \underbrace{\sum_{x_p} \mathbb{P}\left(x_p \,\middle|\, \tilde{D}\right) \frac{\mathbb{P}\left(\mathbf{x}^p = \mathbf{x} \mid x_p\right)}{\mathbb{P}\left(\tilde{D}_p \,\middle|\, x_p\right)}}_{\text{Everything above } x^p}$$

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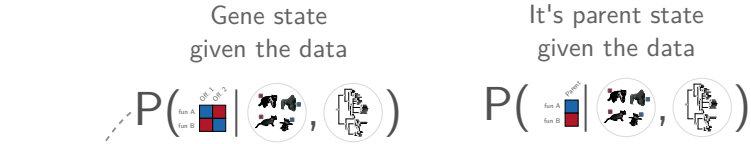
Gene state given the data

It's parent state given the data



... I implemented this (and more) on **geese**

GEne functional **E**volution using **S**ufficiency

... as part of **barry**, your to-go motif accountant

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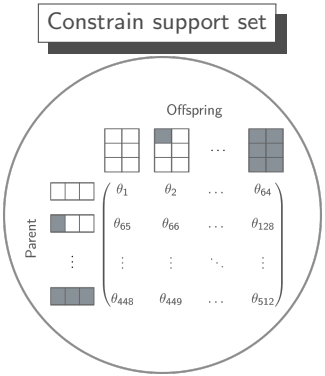

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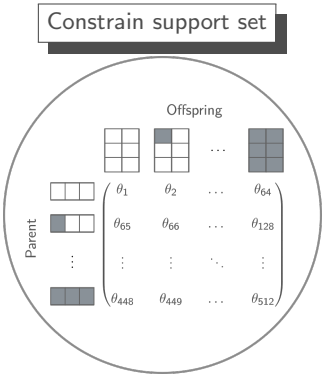

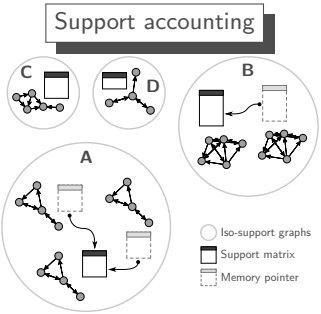

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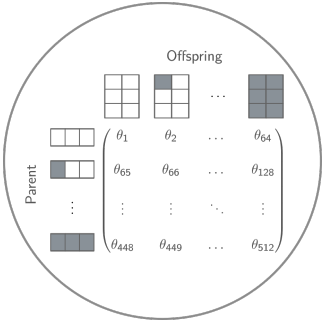
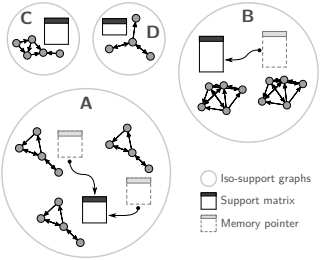
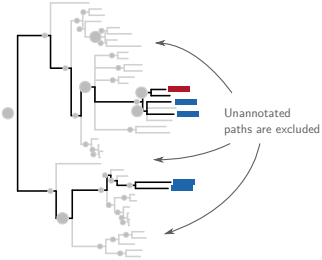
Constrain support set



Support accounting



Reduced peeling sequence



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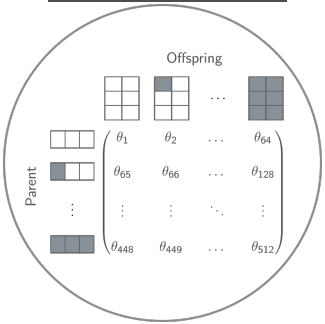
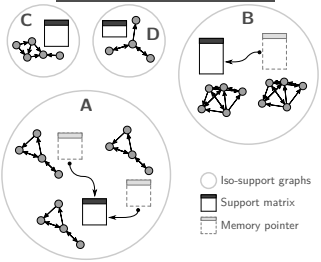
Constrain support set



Support accounting



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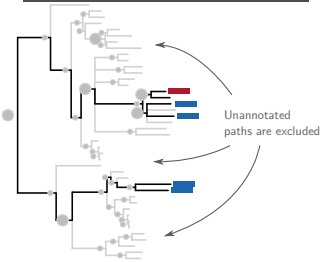

… how big can we go?

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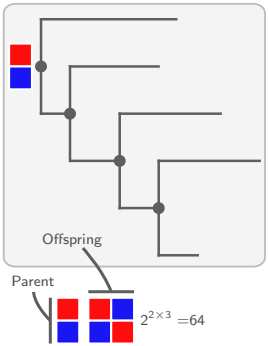
Whether the likelihood is tracktable or not depends on how large is the **"largest event"**

(a) Reconciled tree 2 functions



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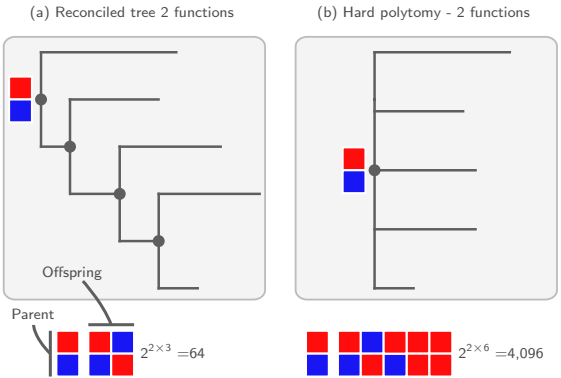

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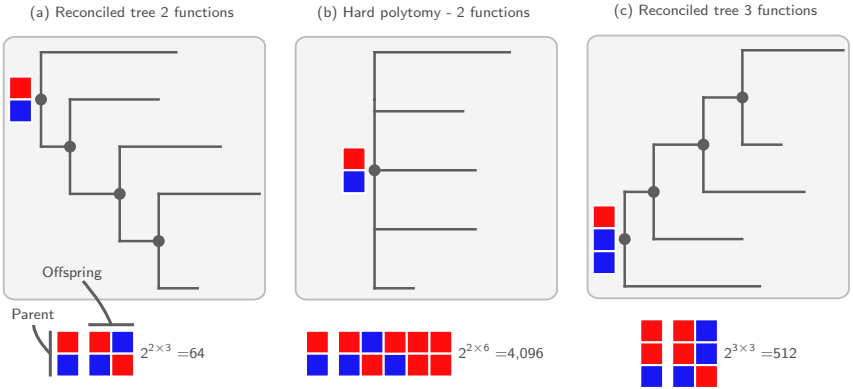

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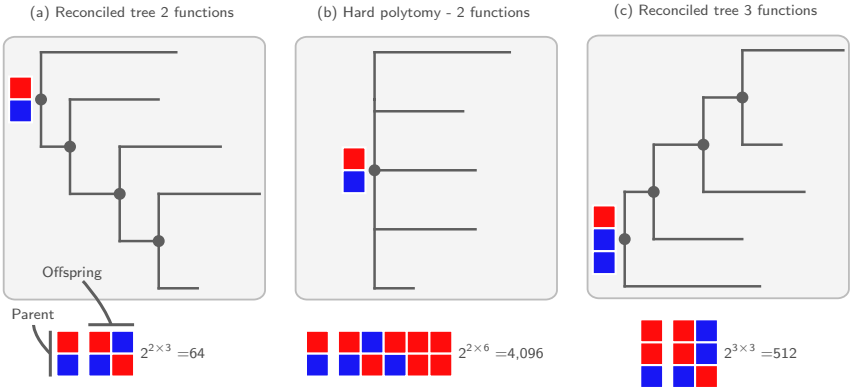

(in practice, arrays up to 32 cells, i.e., 4.3 billion comb., are feasible.)

With this modeling framework, we could tackle, e.g.,

What questions?

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- Potentially improve prediction accuracy.

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  "When was subfunctionalization more likely to happen?"

  "Where functions A and B gained at the same time?"
- and much more...

geese featured example: Analyzing 77 experimentally annotated trees (Vega Yon, *et al.*, WIP)

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Using data from Vega Yon et al. (2021), we re-estimated the models using **GEESE** and compared the results to those in the **aphylo** paper:

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- Both models used "informative" priors.
- Both were fitted using Adaptive Metropolis (**fmcmc** R package).

more

Example of code (R)

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After initializing a geese object named `model2fit`:

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After initializing a geese object named `model2fit`:

```r
# For later use (see last two lines)
term_overall_changes(model2fit, duplication = TRUE)
term_overall_changes(model2fit, duplication = FALSE)

# Couting how many genes change
term_genes_changing(model2fit, duplication = TRUE)

# Gain and loss at duplication
term_gains(model2fit, funs = 0:1, duplication = TRUE)
term_loss(model2fit, funs = 0:1, duplication = TRUE)

# Gain and loss at speciation
term_gains(model2fit, funs = 0:1, duplication = FALSE)
term_loss(model2fit, funs = 0:1, duplication = FALSE)

# Constraining the support set
rule_limit_changes(model2fit, id = 0, lb = 0, ub = 4, duplication = TRUE)
rule_limit_changes(model2fit, id = 1, lb = 0, ub = 4, duplication = FALSE)

```

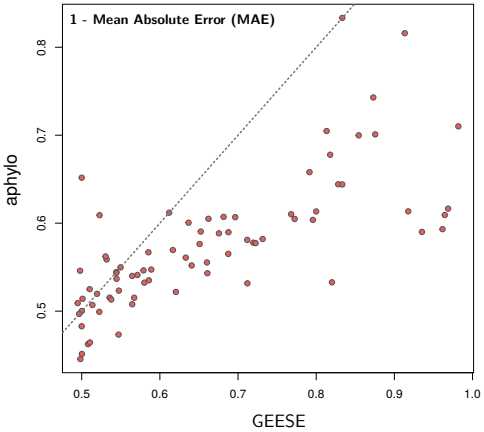

Figure 1 *Performance as Mean Absolute Error (MAE)*. Each set of coordinates shows the value of 1 minus the MAE of **GEESE**, x-axis, and **aphylo** (y-axis). The statistics were computed using leave-one-out based on individual parameter estimates. Overall, GEESE performs better than aphylo in most cases.

Tapping into computational scalability

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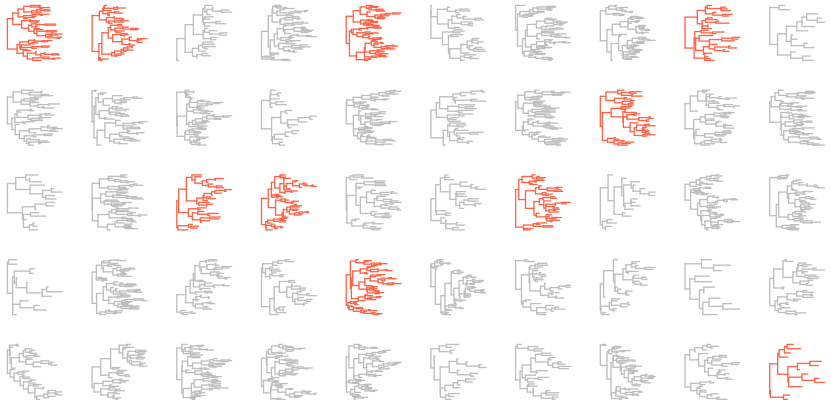
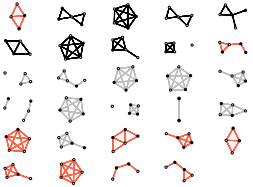


Figure 2 A dramatization of how a group of GEESE, i.e., a flock, looks like.

Part II: Other Projects and Future Research

Sociology

Using ERGMitos to model political discussion networks in Romania



Sociology

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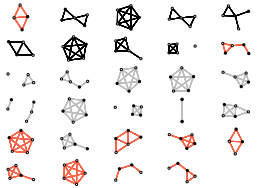

Criminology

The role of social networks on police use of force

Sociology

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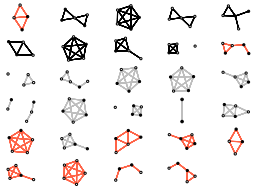
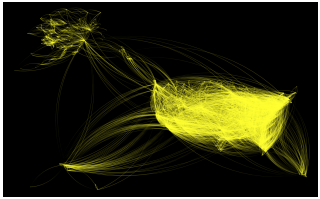


Criminology

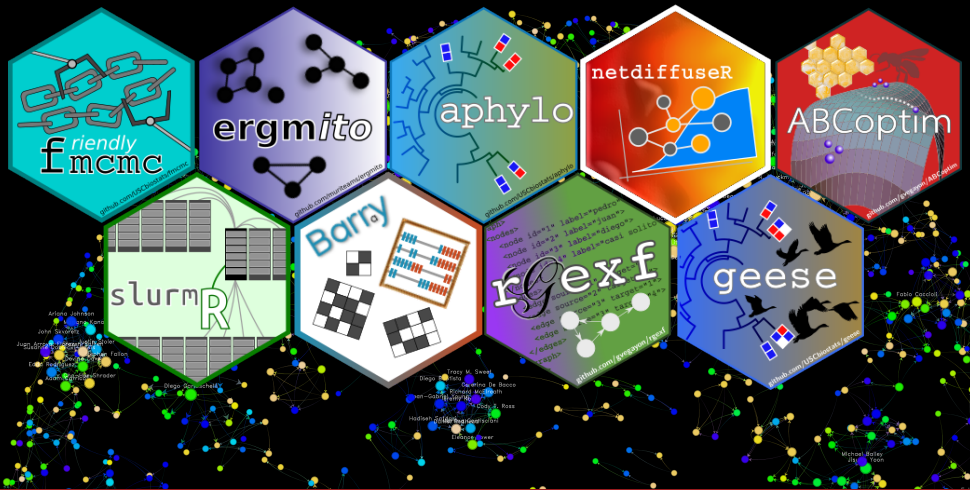
The role of social networks on police use of force

Statistical Computing

Leverage computing power to advance theory and application for studying complex systems...



Continue developing scientific software...



The future: Keep building bridges

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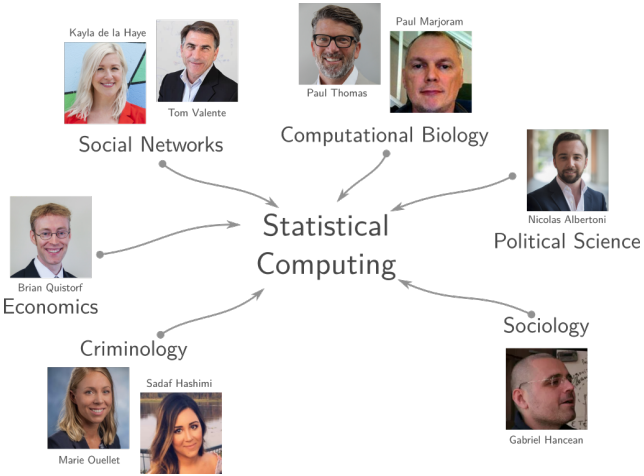

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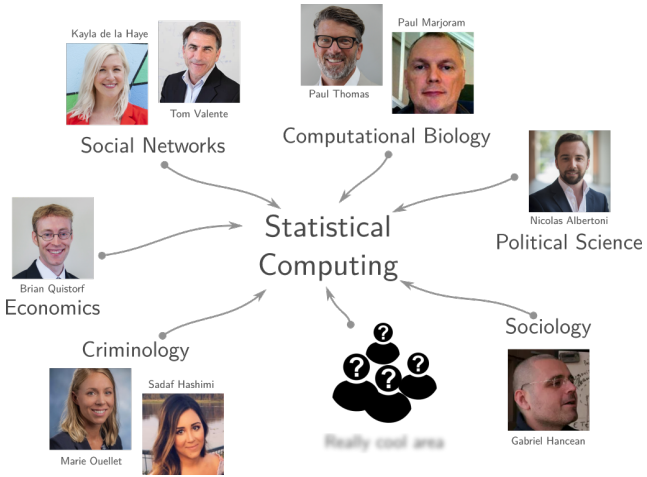

...you could be next!

Applications of Statistical Computing in Complex Social and Biological Systems Modeling

George G Vega Yon

https://ggvy.cl

vegayon@usc.edu

Thank you!

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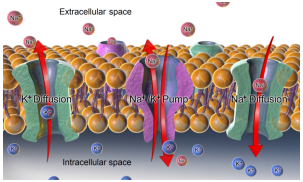
Gene functions can be classified in three types:

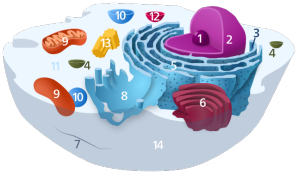
Molecular function

Active transport GO:0005215



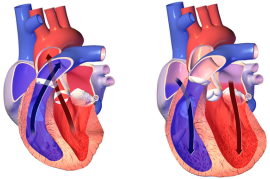
Cellular component

Mitochondria GO:0004016



Biological process

Heart contraction GO:0060047



go back

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Example of GO term

Accession	GO:0060047
Name	heart contraction
Ontology	biological_process
Synonyms	heart beating, cardiac contraction, hemolymph circulation
Alternate	IDs None
Definition	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 2 Heart Contraction Function. source: amigo.geneontology.org

You know what is interesting about this function?

go back

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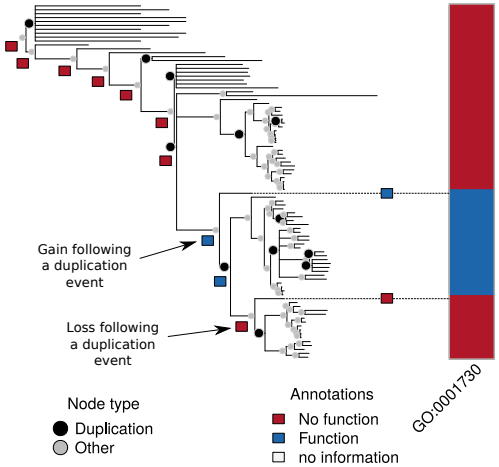

- Starting with the root node (no function in this case).
- Passes the baton to its offspring.
- Possibly without change (on this particular function).
- Or, with some probability, gaining... or loosing the function.
- Until it reaches the end of the tree (modern genes).

more on diplication | duplication vs speciation

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

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Family: PTHR11258

Type: Molecular Function

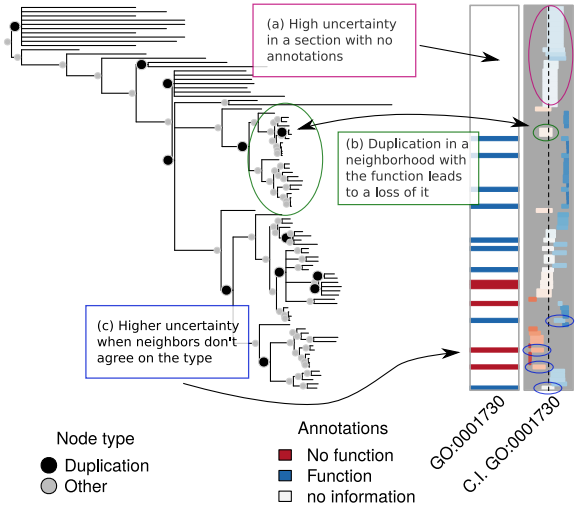
Name: 2'-5'-oligoadenylate synthetase activity

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

MAE: 0.34

AUC: 0.91

see a bad one | go back



Example 2: Bad quality prediction

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MAE: 0.52

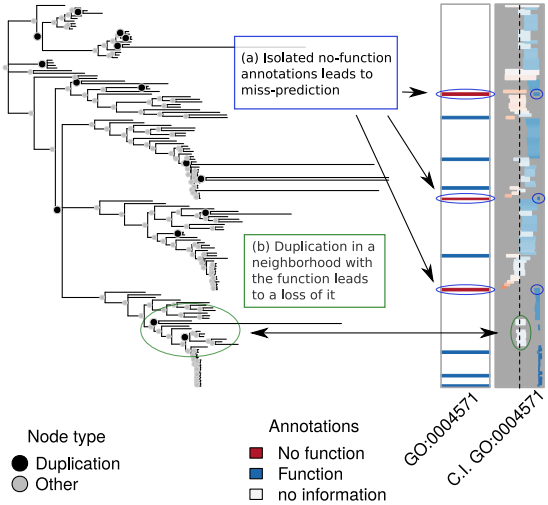
AUC: 0.33

Type: Molecular Function

Name: mannosyl-oligosaccharide 1,2-alpha-mannosidase activity

Desc: 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	[-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 3 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*.

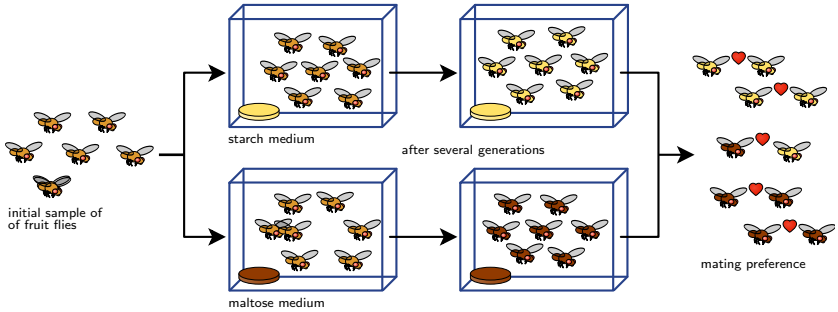


Figure 3 Dodd 1989: After one year of isolation, flies showed a significant level of assortativity in mating (wikimedia)

go back

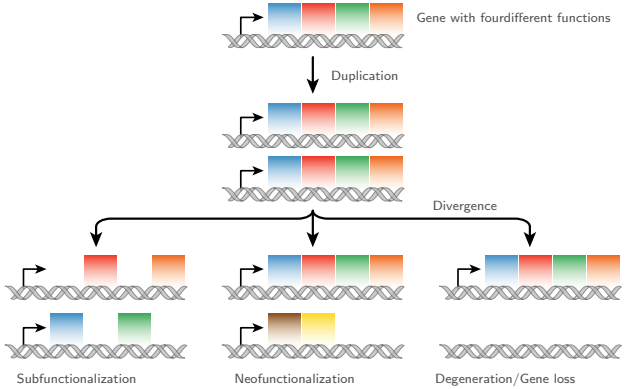


Figure 4 A key part of molecular innovation, gene duplication provides opportunity for new functions to emerge (wikimedia)

go back

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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

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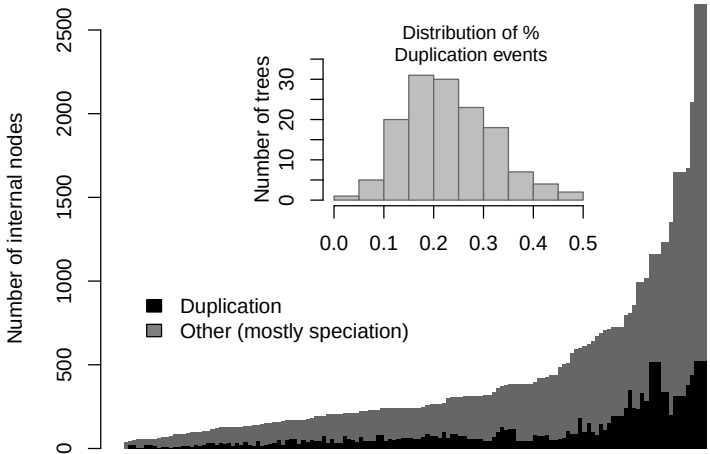

go back

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This is the first 10 of $\sim$ 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	

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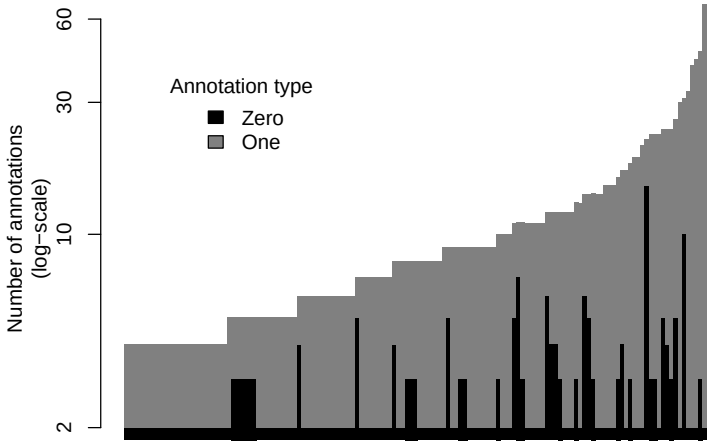

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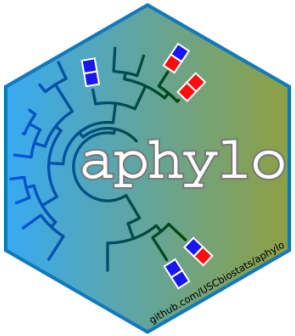
- Simulation, estimation, and prediction: **aphylo** R package.
- Large simulation study (all known trees, about 15,000) on USC's HPC cluster.
- Prediction quality assessment on $\sim$ 1,300 genes involving $\sim$ 130 families... estimation of parameters using a pooled-data model ($<$ 5 min). ◂ modeling ◂ estimates
- In a subset of $\sim$ 200 predictions we found 46 novel annotations ▸ more



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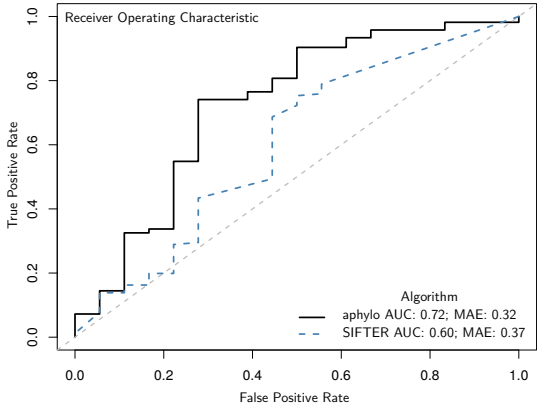
aphylo vs SIFTER (state-of-the-art phylo-based model) on 147 genes.



Fast 110 minutes (SIFTER) 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).

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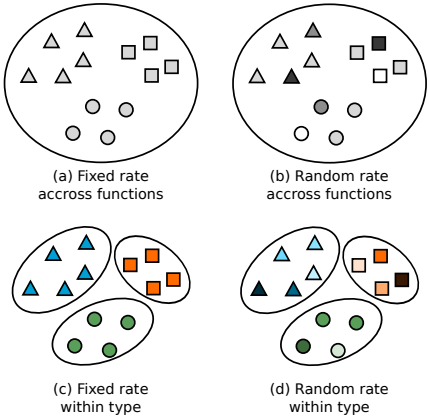

(a) Featured in the first version of the model.

(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`.

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Overview of Prediction Results

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	Pooled	Type of Annotation: Molecular Function	Type of Annotation: Biological Process	Type of Annotation: Cellular Comp.
Mislabeling				
ψ_{01}	0.23	0.18	0.09	
ψ_{10}	0.01	0.01	0.01	
Duplication Events				
μ_{d01}	0.97	0.97	0.10	
μ_{d10}	0.52	0.51	0.03	
Speciation Events				?
μ_{s01}	0.05	0.05	0.05	
μ_{s10}	0.01	0.01	0.02	
Root node				
π	0.79	0.71	0.88	
Trees	141	74	45	22
Accuracy under the by-aspect model				
AUC	-	0.77	0.83	
MAE	-	0.34	0.26	
Accuracy under the pooled-data model				
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

▸ go back

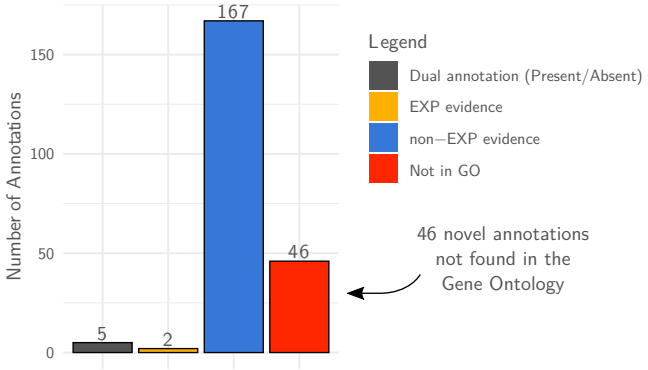

Figure 5 Distribution of predictions

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- In the case that $s_l = s(\mathbf{g}, x)$ is on the boundary: $s_l \to \pm\infty$
- 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:

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

  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.[1]
- All equations ultimately involve realizations of $s(\mathbf{g}', x)$ that equal s_l, relevant in: Simulations, Bootstrapping, etc.

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[1] Handcock 2003 briefly mentions this

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- 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.
- $\{\text{CUG}, \text{Rewiring}\} \subset \text{ERGM}$
- We can talk about *Conditional* ERGMs.

$$\mathbb{P}\left(s\left(\mathbf{G}\right)_k = s_k \;\middle|\; s\left(\mathbf{G}\right)_l = s_l, \theta\right) = \frac{\exp\left\{\theta^{\mathbf{t}}_{-l} s\left(\mathbf{g}\right)_{-l}\right\}}{\sum_{\mathbf{g}' : s(\mathbf{g}')_l = s(\mathbf{g})_l} \exp\left\{\theta^{\mathbf{t}}_{-l} s\left(\mathbf{g}'\right)_{-l}\right\}}$$

In this equation θ_l becomes a nuisance parameter.

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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 $\sum_{i \neq j} y_{ij} \mathbf{1}\left(x_i = x_j\right)$
	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 6 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.

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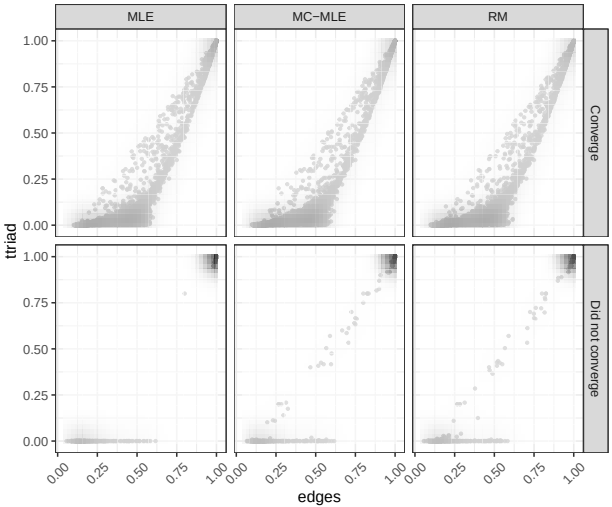
1. **Higher convergence rate**

return



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

alt take

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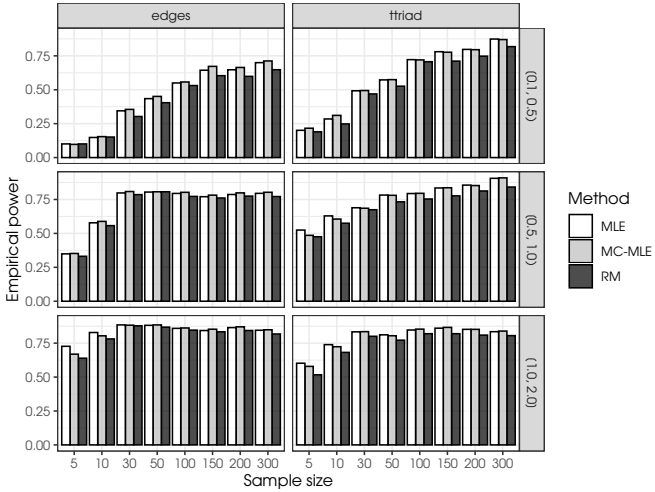
1. Higher convergence rate
2. Smaller bias
3. **Higher power**

return



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

return

Sample size	N. Sims.	P(Type I error)			χ^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

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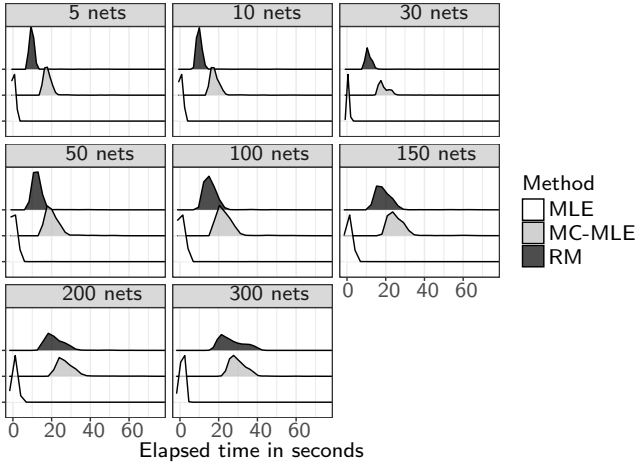
1. Higher convergence rate
2. Smaller bias
3. Higher power
4. Smaller type I error
5. **Elapsed time**

return



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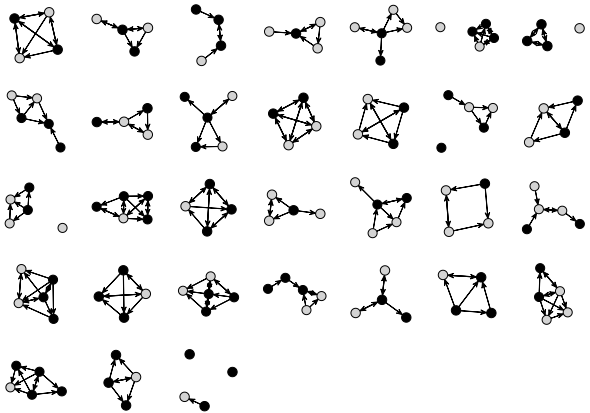
Sample

- 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?

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	(1)	(2)	(3)	(4)	(5)	(4b)
edges	-0.52^{**}	-0.91^{***}	-0.54^{**}	-0.72^{***}	-0.48^{*}	-0.72^{***}
	(0.17)	(0.23)	(0.18)	(0.19)	(0.19)	(0.17)
ttriads	0.36^{***}	0.46^{***}	0.37^{***}	0.36^{***}	0.36^{***}	0.36^{***}
	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.05)
Homophily (gender)	-0.03	-0.01	-0.20	-0.12	-0.01	-0.12
	(0.20)	(0.21)	(0.46)	(0.20)	(0.20)	(0.20)
edges $\times \mathbf{1}(n = 5)$	-0.53^{***}	-0.47^{**}	-0.52^{***}	-0.53^{***}	-0.53^{***}	-0.53^{***}
	(0.12)	(0.16)	(0.13)	(0.13)	(0.12)	(0.13)
$(\text{Homophily})^{1/2}$			0.54			
			(1.32)			
Sender (female)				0.46^{*}		0.46^{*}
				(0.18)		(0.18)
Receiver (female)					-0.08	
					(0.18)	
Constraint (offset)						
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?

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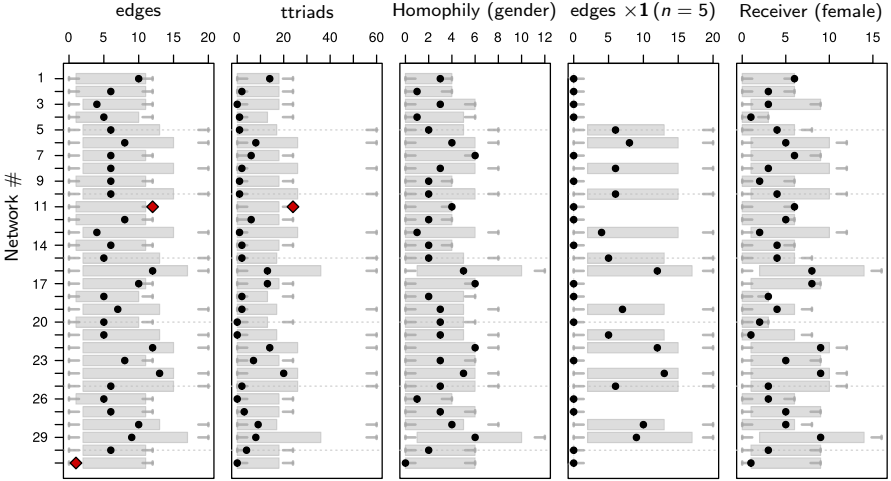
What About Goodness-of-fit?



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(1) Size (n)	(2) edges	(3) ttriads	(4) edges $\times$ $\mathbf{1}(n = 5)$	(5) ttriads $\times$ $\mathbf{1}(n = 5)$	(6) 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 5 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).

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- 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`

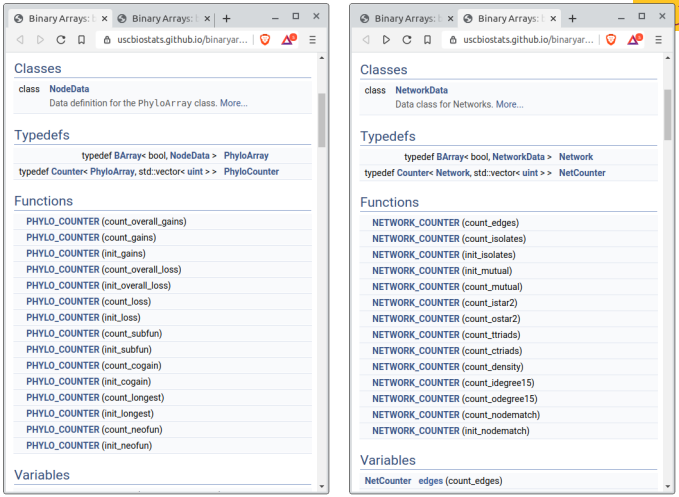

Figure 7 Screenshots from the project's website on GitHub.

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

			Transitions to	
			Case 1	Case 2
	A	$\begin{bmatrix} 0 \end{bmatrix}$	$\begin{bmatrix} 0 & 1 \end{bmatrix}$	$\begin{bmatrix} 0 & 1 \end{bmatrix}$
Parent	B	$\begin{bmatrix} 1 \end{bmatrix}$	$\begin{bmatrix} 1 & 0 \end{bmatrix}$	$\begin{bmatrix} 1 & 0 \end{bmatrix}$
	C	$\begin{bmatrix} 1 \end{bmatrix}$	$\begin{bmatrix} 1 & 1 \end{bmatrix}$	$\begin{bmatrix} 0 & 1 \end{bmatrix}$
Sufficient statistics				
# Gains			1	1
Only one offspring changes (yes/no)			1	0
# Changes (gain+loss)			2	3
Subfunctionalizations (yes/no)			0	1

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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

return

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: Simple model with two functions

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To illustrate, we will **simulate** and then **estimate** the parameters for the following process:

1. 100 genes on a simulated phylogenetic tree.
2. Two functions, **0** and **1**,
3. **Function 0** is likely to be gain **gained at a dupl. event**,
4. **Function 1** is gained as **neofunctionalization** (**from 0**) **at a dupl. event**,
5. There is a higher chance of **changes at duplication** (explicit).
6. Root node starts off without either function (i.e. prob $\to$ 0).

We will fit the model using Robust Adaptive Metropolis with a logistic prior centered at 0 with scale 2.

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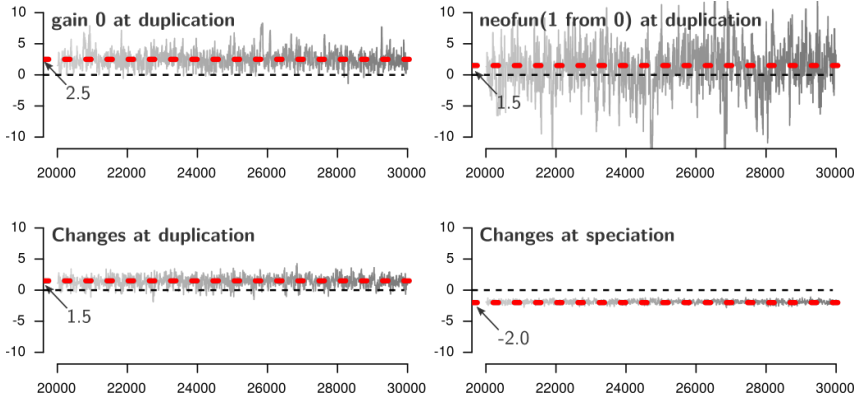

Figure 8 MCMC Trace of the functional gain of 0, neofunctionalization (1 from 0), and change rate (by event type).

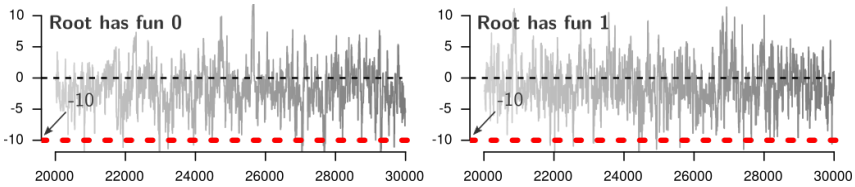

Figure 9 MCMC Trace of root parameters. The true population parameters are $(\theta_{root0}, \theta_{root1}) = (-10.0, -10.0)$. Root node probabilities are always hard to get.

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Repeated this experiment 5,000 times:

- MCMC for fitting.
- RAM kernel.
- Logistic prior at zero with scale two.
- Each tree took $<$ 1min estimation.

Figure 10 Distribution of parameter estimates from 5,000 phylo trees w/ 100 leafs.