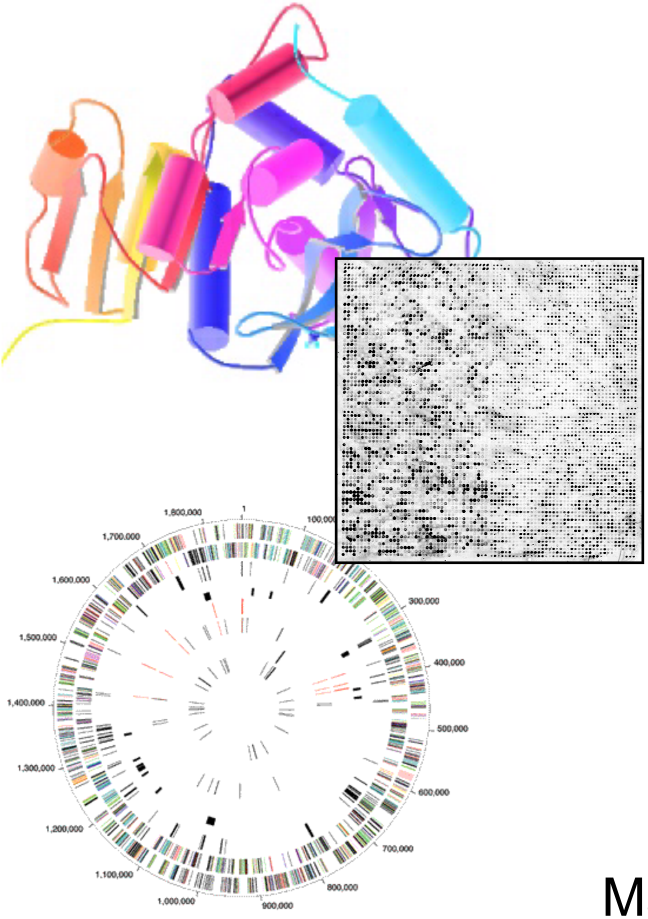
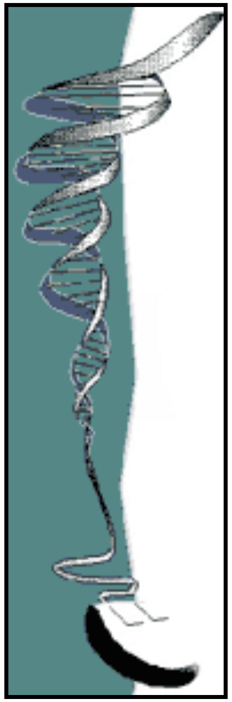
Bioinformatics: Predicting Networks





Mark Gerstein, Yale University
gersteinlab.org/courses/452
(last edit in Spring '18)

Origin of Biological Networks

Origin of Networks

- Protein-protein interactions
  - ◊ Phosphorylation networks
- Metabolic Networks
- Regulatory networks
  - ◊ from Chip-Seq (see next slide)

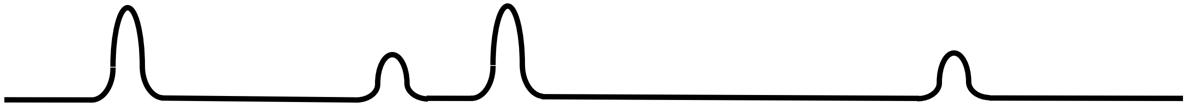
- “Squared” scale
  - ◊ 6K genes in yeast but ~18M potential interactions (6000 chose 2 pairs of interactions)

Data Flow: Chip-seq expts. to co-associating peaks

119 TFs from 458 ChIP-Seq experiments (2 Tb tot.)

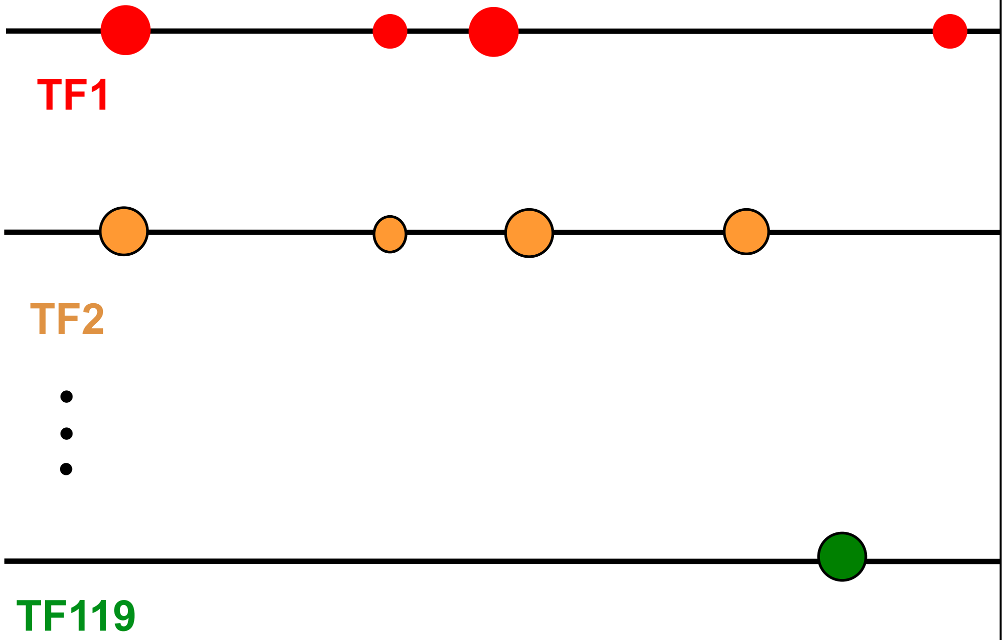
↓

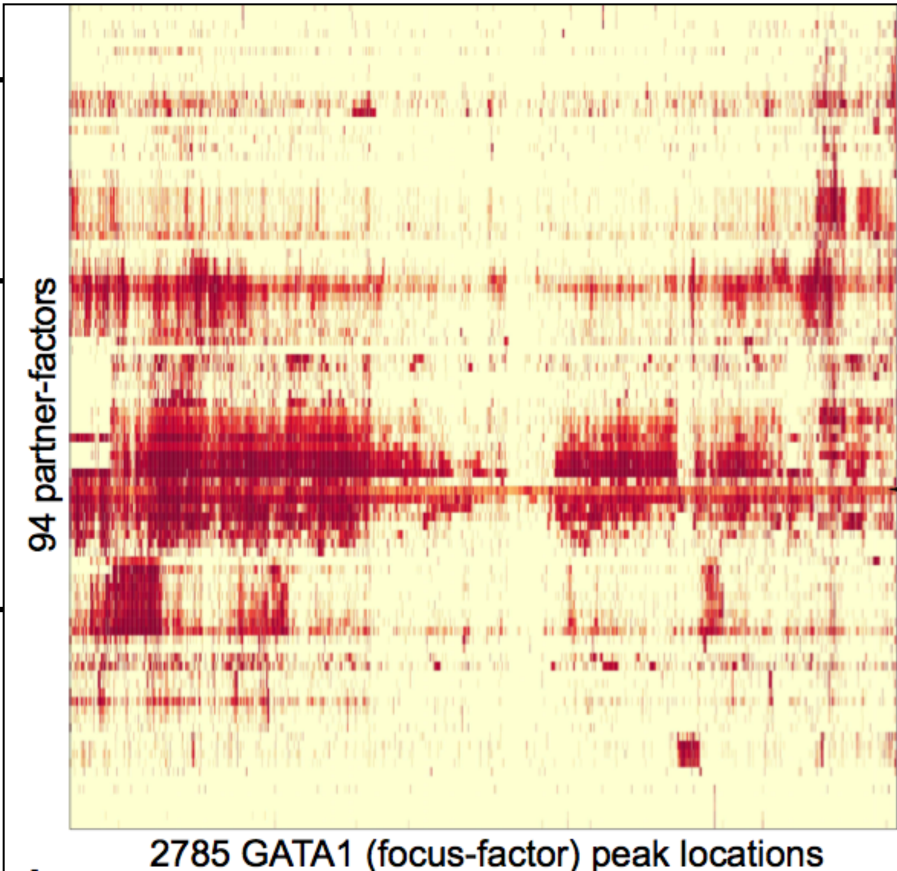
Signal Tracks



↓

7M Peaks from Uniform Peak Calling



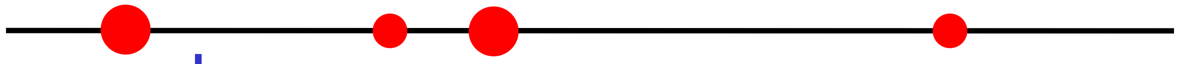


[Gerstein et al. Nature (in press, '12)]

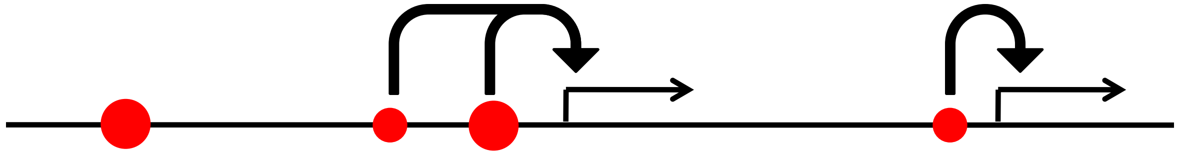
Data Flow: peaks to proximal & distal networks

[Cheng et al., *Bioinfo.* ('11);
Gerstein et al. *Nature* (in press, '12) ;
Yip et al., *GenomeBiology* (in press, '12)]

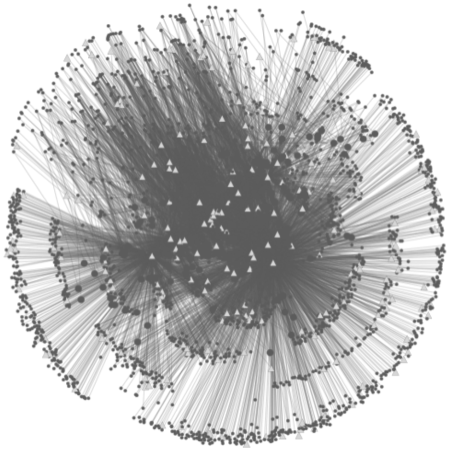
Peak Calling



Assigning TF binding sites to targets

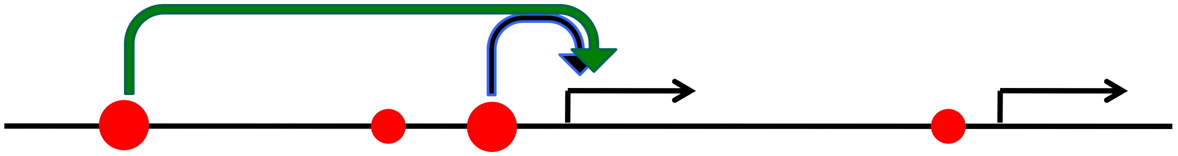


~500K Edges

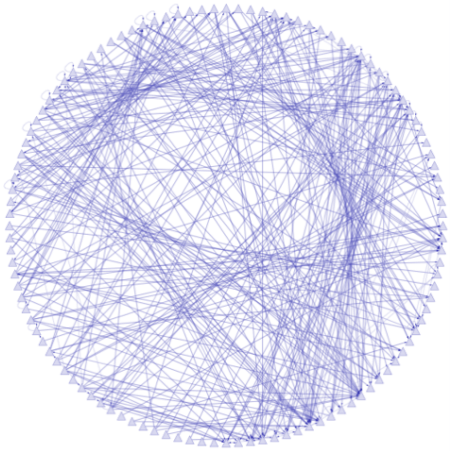


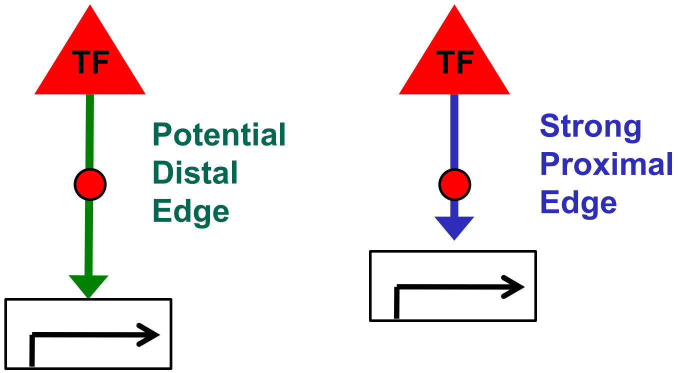
Filtering high confidence edges & distal regulation

Based on stat. model combining
signal strength & location relative to typical binding

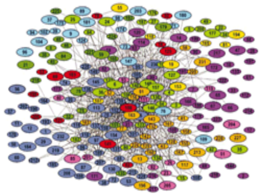


~26K Edges



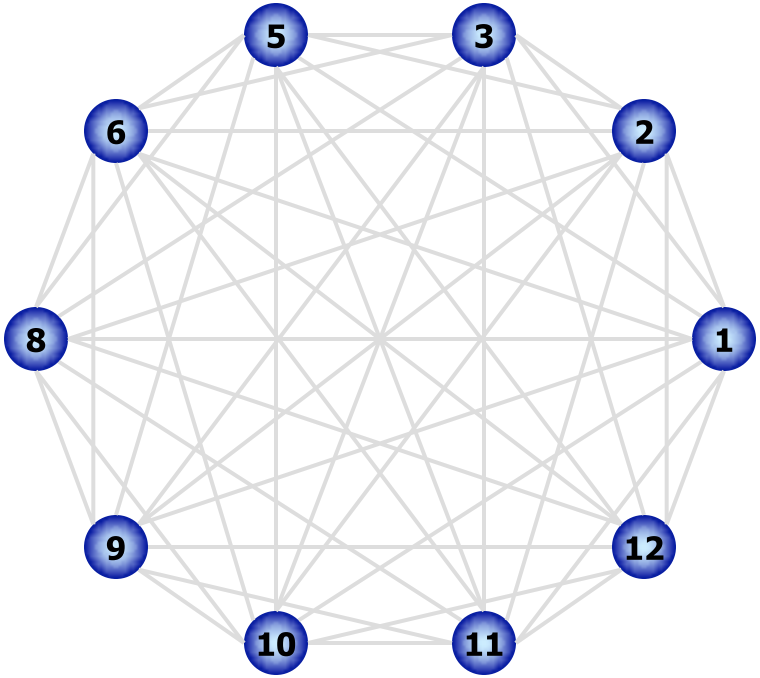


Predicting Networks via Bayesian Integration: Problem Motivation



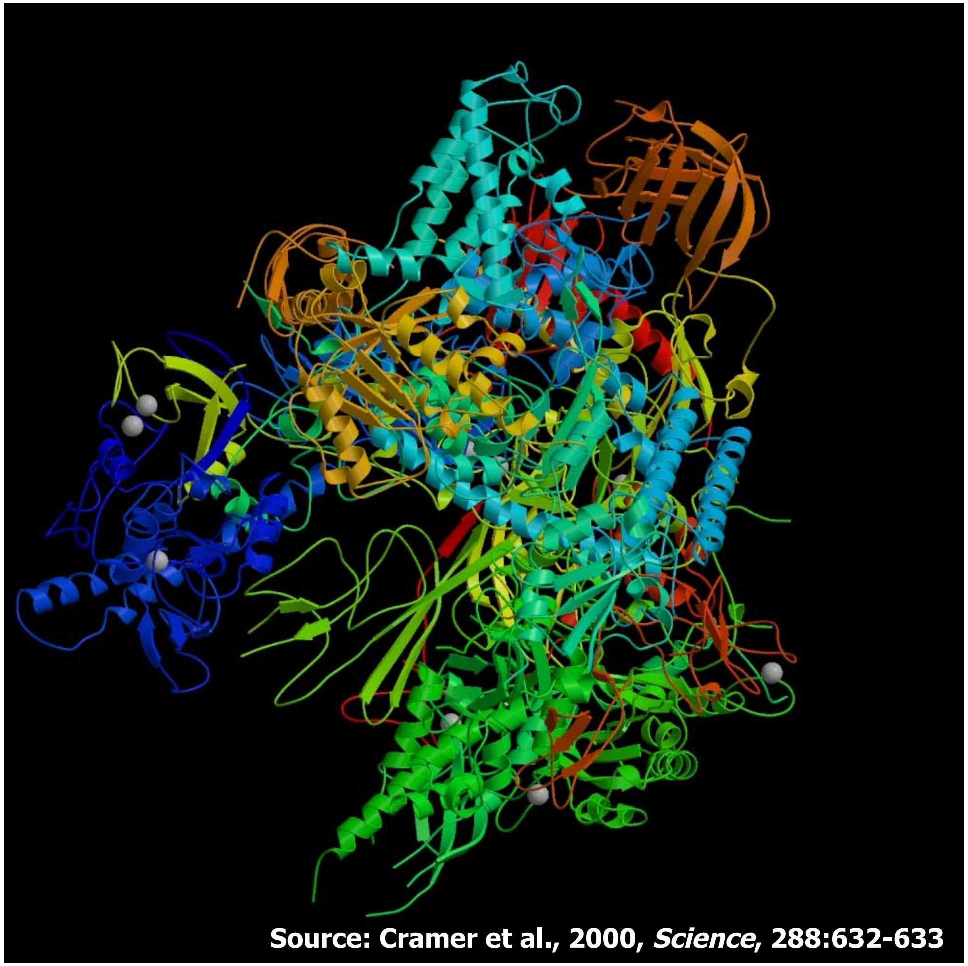
RNA polymerase II: Structure

Which subunits interact? Based on Binding experiments

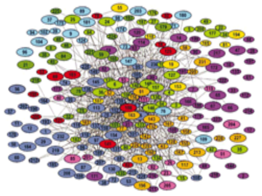


Source: Edwards et al., 2002, *Trends in Genetics*

Compare with Gold Std. Structure



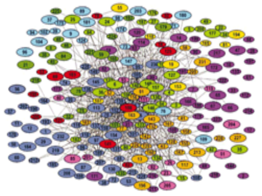
Source: Cramer et al., 2000, *Science*, 288:632-633



Binding Experiments on Subunit Pairs

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12
Pull-down 1		1	1	0	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1	1		1	1	0	1	0		0	0	0	0		0	1	0		0	0		0		
Pull-down 2		1	1	1	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1	1		0	1	0	1	0		0	0	0	0		0	0	0		0	0		0		
Pull-down 3		1								1								1	0	1	0	0	1	0																					
Cross-linking	1	1	1	1	1		0	1	1	1	1	1	0		1	1	1					1	1		1	0					1														
Far Western 1		1	1							1	1							1	0	0		0	0	0	0	1		0	0	0															
Far Western 2				1	1		1	1	1			1	1		1	1	1		0	0		0	1	0	0	0		0	0	0	0		0	0	0		0	0	0				0	0	0
Far Western 3																		1	0	0		0	1	0																					

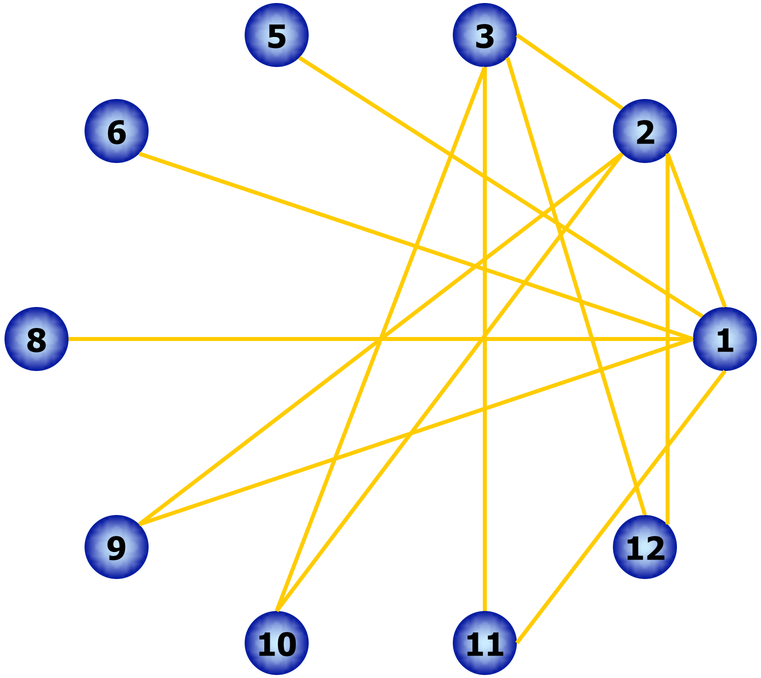
Interaction experiments
before structure was known

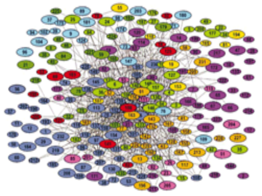


Gold-Standard Positives

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12

Gold-Standard Positive (GSTD+): 13

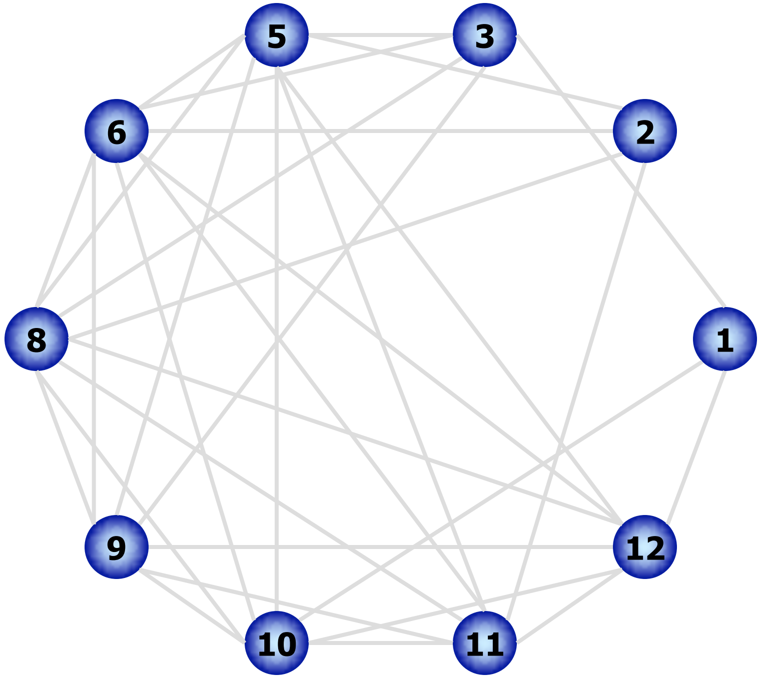


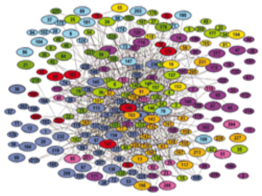


Gold-Standard Negatives

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12

Gold-Standard Negative (GSTD-): 32



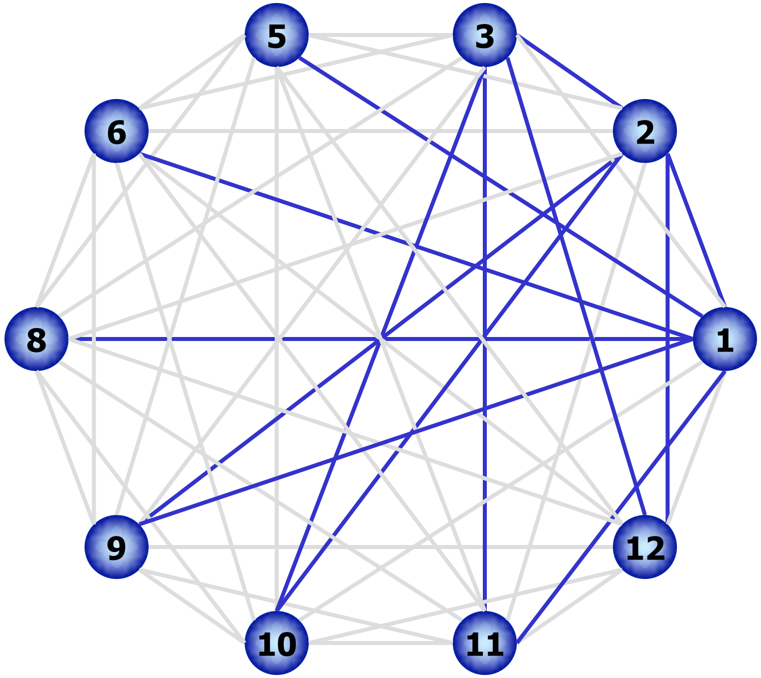


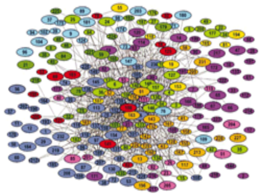
RNA Polymerase II: Gold-Standards

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12

Gold-Standard Positive (GSTD+): 13

Gold-Standard Negative (GSTD-): 32





Assess Quality and Coverage of PPints

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11
Pull-down 1		🟥 1	🟩 1	🟥 0	🟩 1	🟥 0	🟥 1	🟥 0		🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1	🟩 0		🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1
Pull-down 2		🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟥 1	🟥 0		🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1	🟩 0		🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1
Pull-down 3		🟥 1								🟩 1								🟥 1	🟩 0	🟥 1	🟩 0	🟥 0	🟩 1
Cross-linking	🟩 1	🟥 1	🟩 1	🟩 1	🟩 1		🟩 0	🟩 1	🟥 1	🟩 1	🟥 1	🟥 1	🟩 0		🟩 1	🟥 1	🟩 1					🟩 1	🟩 1
Far Western 1		🟥 1	🟩 1							🟩 1	🟥 1							🟥 1	🟩 0	🟩 0		🟥 0	🟥 0
Far Western 2				🟩 1	🟩 1		🟥 1	🟩 1	🟥 1			🟥 1	🟥 1		🟩 1	🟥 1	🟩 1		🟩 0	🟩 0		🟥 0	🟩 1
Far Western 3																		🟥 1	🟩 0	🟩 0		🟥 0	🟩 1

Subunits	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12
Pull-down 1		🟥 1	🟥 1	🟩 0	🟥 1	🟩 0		🟩 0	🟩 0	🟩 0	🟩 0		🟩 0	🟥 1	🟩 0		🟩 0	🟩 0		🟩 0		
Pull-down 2		🟩 0	🟥 1	🟩 0	🟥 1	🟩 0		🟩 0	🟩 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0		🟩 0	🟩 0		🟩 0		
Pull-down 3	🟥 0																					
Cross-linking		🟥 1	🟩 0					🟥 1														
Far Western 1	🟥 0	🟩 0	🟥 1		🟩 0	🟩 0	🟩 0															
Far Western 2	🟥 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0				🟩 0	🟩 0	🟩 0
Far Western 3	🟥 0																					

🟦 GSTD+

⬜ GSTD-

🟩 True

🟥 False

(c) M Gerstein, gerstein.info/talks

Data integration: RNA polymerase II

Subunit A	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2
Subunit B	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10
structural contact	1	0	1	1	1	1	0	1	0	1	0	0	0	1	1
Far western		🟥1	🟩1							🟩1	🟥1				
Cross-linking	🟩1	🟥1	🟩1	🟩1	🟩1		🟩0	🟩1	🟥1	🟩1	🟥1	🟥1	🟩0		🟩1
Far western				🟩1	🟩1		🟥1	🟩1	🟥1			🟥1	🟥1		🟩1
Pull-down		🟥1	🟩1	🟥0	🟩1	🟥0	🟥1	🟥0		🟩1	🟥1	🟩0	🟥1	🟥0	🟩1
Pull-down		🟥1	🟩1	🟩1	🟩1	🟥0	🟥1	🟥0		🟩1	🟥1	🟩0	🟥1	🟥0	🟩1
Pull-down		🟥1								🟩1					
Far western															

Subunit A	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5
Subunit B	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12
structural contact	0	1	0	0	0	0	1	1	1	0	0	0	0	0	0
Far western			🟥1	🟩0	🟩0		🟥0	🟥0	🟥0	🟩0	🟥1		🟩0	🟩0	🟩0
Cross-linking	🟥1	🟩1					🟩1	🟩1		🟥1	🟩0				
Far western	🟥1	🟩1		🟩0	🟩0		🟥0	🟩1	🟥0	🟩0	🟩0		🟩0	🟩0	🟩0
Pull-down	🟩0		🟥1	🟥1	🟥1	🟩0	🟩1	🟩1		🟥1	🟥1	🟩0	🟥1	🟩0	
Pull-down	🟩0		🟥1	🟥1	🟥1	🟩0	🟩1	🟩1		🟩0	🟥1	🟩0	🟥1	🟩0	
Pull-down			🟥1	🟩0	🟥1	🟩0	🟥0	🟩1	🟥0						
Far western			🟥1	🟩0	🟩0		🟥0	🟩1	🟥0						

Subunit A	6	6	6	6	6	8	8	8	8	9	9	9	10	10	11
Subunit B	8	9	10	11	12	9	10	11	12	10	11	12	11	12	12
structural contact	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Far western															
Cross-linking	🟥1														
Far western	🟩0		🟩0	🟩0	🟩0		🟩0	🟩0	🟩0				🟩0	🟩0	🟩0
Pull-down	🟩0	🟩0	🟩0	🟩0		🟩0	🟥1	🟩0		🟩0	🟩0		🟩0		
Pull-down	🟩0	🟩0	🟩0	🟩0		🟩0	🟩0	🟩0		🟩0	🟩0		🟩0		
Pull-down															
Far western															

🟥 = false

🟩 = true

Data integration: RNA polymerase II

Subunit A	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2
Subunit B	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10
structural contact	1	0	1	1	1	1	0	1	0	1	0	0	0	1	1
Far western		🟥 1	🟩 1							🟩 1	🟥 1				
Cross-linking	🟩 1	🟥 1	🟩 1	🟩 1	🟩 1		🟩 0	🟩 1	🟥 1	🟩 1	🟥 1	🟥 1	🟩 0		🟩 1
Far western				🟩 1	🟩 1		🟥 1	🟩 1	🟥 1			🟥 1	🟥 1		🟩 1
Pull-down		🟥 1	🟩 1	🟥 0	🟩 1	🟥 0	🟥 1	🟥 0		🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1
Pull-down		🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟥 1	🟥 0		🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1
Pull-down		🟥 1								🟩 1					
Far western															
Union	🟩 1	🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟥 1	🟩 1	🟥 1	🟩 1	🟥 1	🟥 1	🟥 1	🟥 0	🟩 1

Subunit A	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5
Subunit B	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12
structural contact	0	1	0	0	0	0	1	1	1	0	0	0	0	0	0
Far western			🟥 1	🟩 0	🟩 0		🟥 0	🟥 0	🟥 0	🟩 0	🟥 1		🟩 0	🟩 0	🟩 0
Cross-linking	🟥 1	🟩 1					🟩 1	🟩 1		🟥 1	🟩 0				
Far western	🟥 1	🟩 1		🟩 0	🟩 0		🟥 0	🟩 1	🟥 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0
Pull-down	🟩 0		🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1		🟥 1	🟥 1	🟩 0	🟥 1	🟩 0	
Pull-down	🟩 0		🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1		🟩 0	🟥 1	🟩 0	🟥 1	🟩 0	
Pull-down			🟥 1	🟩 0	🟥 1	🟩 0	🟥 0	🟩 1	🟥 0						
Far western			🟥 1	🟩 0	🟩 0		🟥 0	🟩 1	🟥 0						
Union	🟥 1	🟩 1	🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1	🟥 0	🟥 1	🟥 1	🟩 0	🟥 1	🟩 0	🟩 0

Subunit A	6	6	6	6	6	8	8	8	8	9	9	9	10	10	11
Subunit B	8	9	10	11	12	9	10	11	12	10	11	12	11	12	12
structural contact	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Far western															
Cross-linking	🟥 1														
Far western	🟩 0		🟩 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0				🟩 0	🟩 0	🟩 0
Pull-down	🟩 0	🟩 0	🟩 0	🟩 0		🟩 0	🟥 1	🟩 0		🟩 0	🟩 0		🟩 0		
Pull-down	🟩 0	🟩 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0		🟩 0	🟩 0		🟩 0		
Pull-down															
Far western															
Union	🟥 1	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟥 1	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0

🟥 = false

🟩 = true

Data integration: RNA polymerase II

Subunit A	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	11
Subunit B	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	12	12
structural contact	1	0	1	1	1	1	0	1	0	1	0	0	0	1	1	0	1	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Far western		1	1							1	1							1	0	0		0	0	0	0	1		0	0	0															
Cross-linking	1	1	1	1	1		0	1	1	1	1	1	0		1	1	1					1	1		1	0					1														
Far western				1	1		1	1	1			1	1		1	1	1		0	0		0	1	0	0	0		0	0	0	0		0	0	0		0	0	0				0	0	0
Pull-down		1	1	0	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1	1		1	1	0	1	0		0	0	0	0		0	1	0		0	0		0		
Pull-down		1	1	1	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1	1		0	1	0	1	0		0	0	0	0		0	0	0		0	0		0		
Pull-down		1								1								1	0	1	0	0	1	0																					
Far western																		1	0	0		0	1	0																					

Majority	1	1	1	1	1	0	1	0	1	1	1	0	1	0	1	0	1	1	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Intersection	1	1	1	0	1	0	0	0	1	1	1	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Union	1	1	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	0	1	1	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0

Data integration: RNA polymerase II

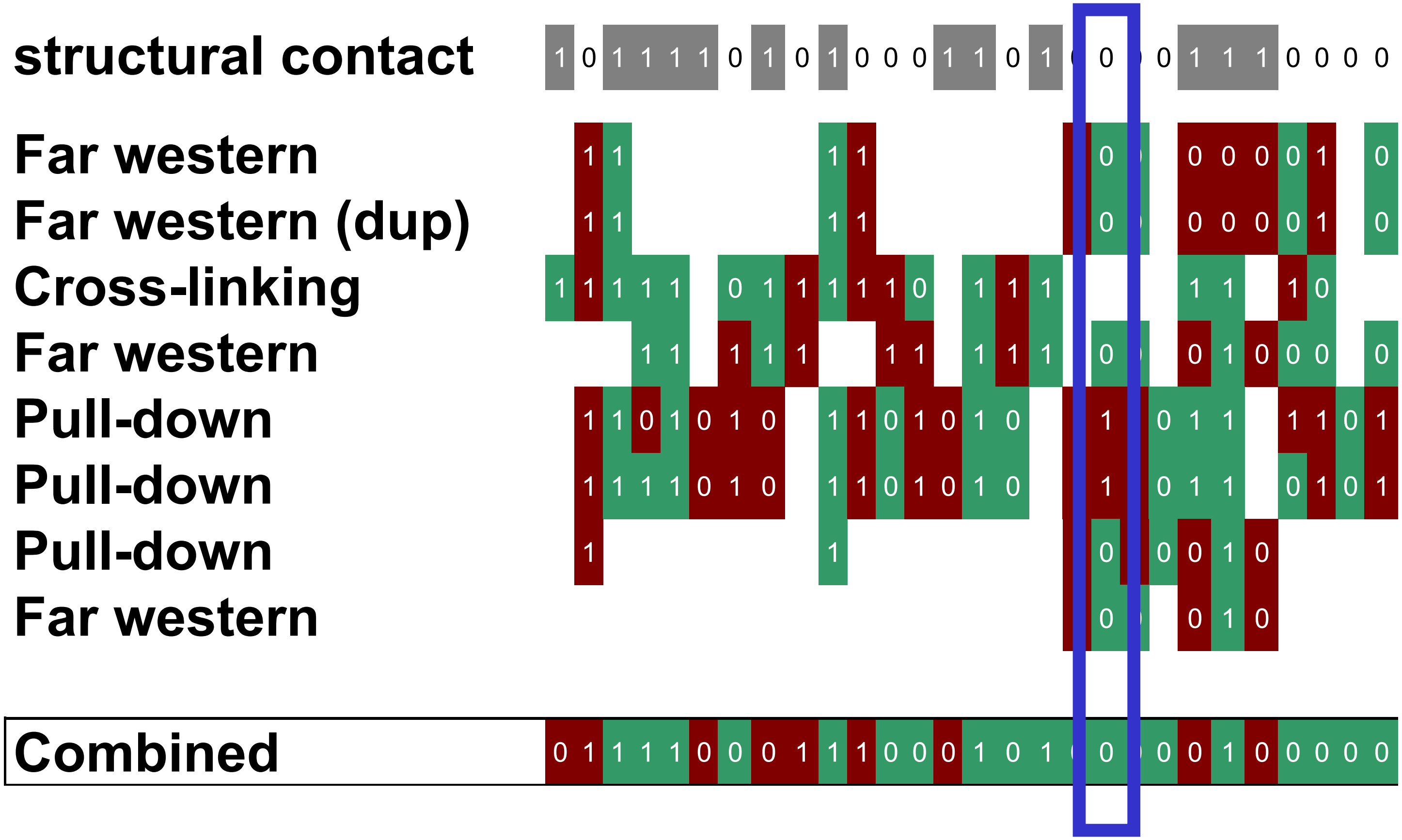
Subunit A	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	11
Subunit B	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	12	12
structural contact	1	0	1	1	1	1	0	1	0	1	0	0	0	1	1	0	1	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Far western		1	1							1	1							1	0	0		0	0	0	0	1		0	0	0															
Cross-linking	1	1	1	1	1		0	1	1	1	1	1	0		1	1	1					1	1		1	0					1														
Far western				1	1		1	1	1			1	1		1	1	1		0	0		0	1	0	0	0		0	0	0	0		0	0	0		0	0	0				0	0	0
Pull-down		1	1	0	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1	1		1	1	0	1	0		0	0	0	0		0	1	0		0	0		0		
Pull-down		1	1	1	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1	1		0	1	0	1	0		0	0	0	0		0	0	0		0	0		0		
Pull-down		1								1								1	0	1	0	0	1	0																					
Far western																		1	0	0		0	1	0																					

(Cross validate)

Integrate using naive Bayes classifier

Combined **(Bayesian)**	0	1	1	1	1	0	0	0	1	1	1	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Majority	1	1	1	1	1	0	1	0	1	1	1	0	1	0	1	0	1	1	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Intersection	1	1	1	0	1	0	0	0	1	1	1	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Union	1	1	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	0	1	1	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0

Weighted Voting: the Likelihood Ratio



structural contact	1	0	1	1	1	1	0	1	0	1	0	0	0	1	1	0	1	[illegible]	0	[illegible]	0	1	1	1	0	0	0	0
Far western		1	1							1	1							[illegible]	0	[illegible]		0	0	0	0	1		0
Far western (dup)		1	1							1	1							[illegible]	0	[illegible]		0	0	0	0	1		0
Cross-linking	1	1	1	1	1		0	1	1	1	1	1	0		1	1	1					1	1		1	0		
Far western				1	1		1	1	1			1	1		1	1	1		0	[illegible]		0	1	0	0	0		0
Pull-down		1	1	0	1	0	1	0		1	1	0	1	0	1	0		[illegible]	1	[illegible]	0	1	1		1	1	0	1
Pull-down		1	1	1	1	0	1	0		1	1	0	1	0	1	0		[illegible]	1	[illegible]	0	1	1		0	1	0	1
Pull-down		1								1								[illegible]	0	[illegible]	0	0	1	0				
Far western																		[illegible]	0	[illegible]		0	1	0				
Combined	0	1	1	1	1	0	0	0	1	1	1	0	0	0	1	0	1	[illegible]	0	[illegible]	0	0	1	0	0	0	0	0

Maj. Vote: 0 = round(avg(0 + 0 + 0 + 1 + 1 + 0 + 0)

With weights: **likelihood ratio L** = $L_1 + L_2 + L_3$ …

Predicting Networks via Bayesian Integration: Intuition & Formalism

Derived from
"perceptron model"
R = <w,f> + b

Supervised Classification by Weighted Voting

Simple Vote: $R = f_1 + f_2 + f_3 + ... + f_n$ With f = 1 or -1

If $\begin{cases} R>0; & I \text{ Interact} \\ R<0; & \sim I \text{ No interaction} \end{cases}$

Modify with feature weight:

$$R = w_1 f_1 + w_2 f_2 + w_3 f_3 + ... + w_n f_n = \vec{w} \cdot \vec{f}$$

If has prior knowledge w_0

$$R = \vec{w} \cdot \vec{f} + w_0$$

Classification by Voting

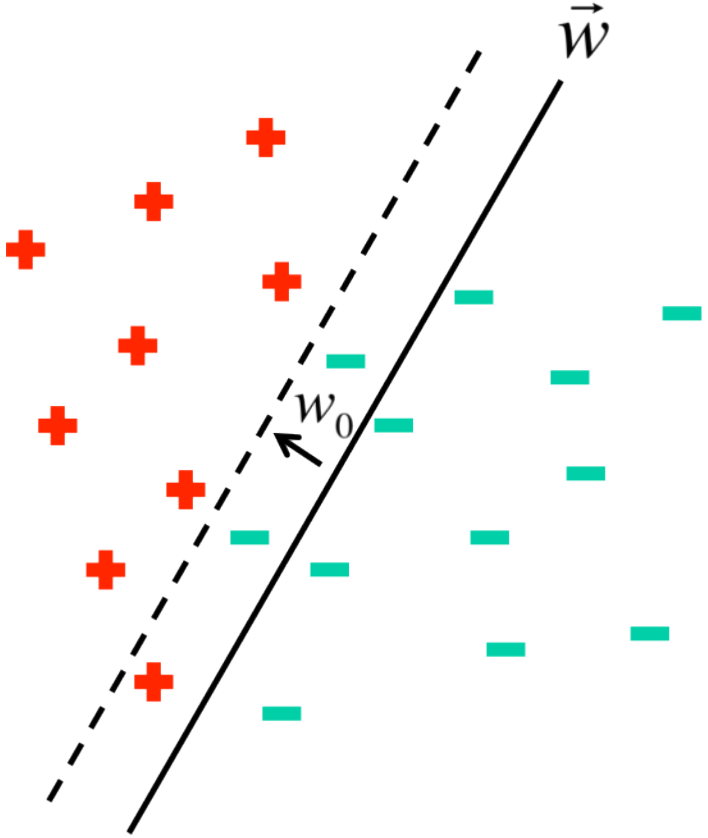
$$R = \vec{w} \cdot \vec{f} + w_0$$

$$w_1 = \log \frac{P(f_1 = 1 \mid I)}{P(f_1 = 1 \mid \sim I)}$$

$$= \log \frac{TP / P}{FR / N}$$

$$w_0 = \log \frac{P}{N}$$ (Estimated from Golden Standard)

On Training Set



Bayes Rule

$$P(Y|X) = \frac{P(X|Y)P(Y)}{P(X)}$$

Which is shorthand for:

$$P(Y = y_i|X = x_j) = \frac{P(X = x_j|Y = y_i)P(Y = y_i)}{P(X = x_j)}$$

[From Mitchell, Machine Learning]

Thus

$$P(I \mid f_1, f_2, f_3, \ldots) = \frac{P(f_1, f_2, f_3, \ldots \mid I) P(I)}{P(f_1, f_2, f_3, \ldots)}$$

Assume Naïve Bayes
(independent)

$$= \frac{P(f_1 \mid I) P(f_2 \mid I) P(f_3 \mid I) \ldots P(I)}{P(f_1, f_2, f_3, \ldots)}$$

$$P(\sim I \mid f_1, f_2, f_3, \ldots) = \frac{P(f_1, f_2, f_3, \ldots \mid \sim I) P(\sim I)}{P(f_1, f_2, f_3, \ldots)}$$

$$= \frac{P(f_1 \mid \sim I) P(f_2 \mid \sim I) P(f_3 \mid \sim I) \ldots P(\sim I)}{P(f_1, f_2, f_3, \ldots)}$$

$$\log\left(\frac{P(I \mid f_1, f_2, f_3, \ldots)}{P(\sim I \mid f_1, f_2, f_3, \ldots)}\right) = \log\left(\frac{P(f_1 \mid I)}{P(f_1 \mid \sim I)} \frac{P(f_2 \mid I)}{P(f_2 \mid \sim I)} \frac{P(f_3 \mid I)}{P(f_3 \mid \sim I)} \ldots \frac{P(I)}{P(\sim I)}\right)$$

$$= \log \frac{TPR_1}{FPR_1} + \log \frac{TPR_2}{FPR_2} + \log \frac{TPR_3}{FPR_3} + .. + \log \frac{P}{N}$$

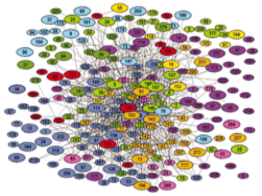
More Bayes Rule

(c) M Gerstein, gerstein.info/talks

$$\log\left(\frac{P(I \mid f_1, f_2, f_3, \ldots)}{P(\sim I \mid f_1, f_2, f_3, \ldots)}\right) = \underset{\substack{\uparrow \\ w_1}}{\log\frac{TPR_1}{FPR_1}} + \underset{\substack{\uparrow \\ w_2}}{\log\frac{TPR_2}{FPR_2}} + \underset{\substack{\uparrow \\ w_3}}{\log\frac{TPR_3}{FPR_3}} + \,..+ \underset{\substack{\uparrow \\ w_0}}{\log\frac{P}{N}}$$

More Bayes Rule

Predicting Networks via Bayesian Integration: Worked Examples



Likelihood Ratios

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10
Pull-down 1		🟥 1	🟩 1	🟥 0	🟩 1	🟥 0	🟥 1	🟥 0		🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1

Subunits	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5
Subunits	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12
Pull-down 1	🟩 0		🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1		🟥 1	🟥 1	🟩 0	🟥 1	🟩 0	

Subunits	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12
Pull-down 1	🟩 0	🟩 0	🟩 0	🟩 0		🟩 0	🟥 1	🟩 0		🟩 0	🟩 0		🟩 0		

$$L_1 = \frac{p\left(x_1 \mid GSTD+\right)}{p\left(x_1 \mid GSTD-\right)}$$

$$L_0 = \frac{p\left(x_0 \mid GSTD+\right)}{p\left(x_0 \mid GSTD-\right)}$$

Likelihood Ratio
for Feature *f*:

$$L_f \equiv \frac{p\left(x_f \mid GSTD+\right)}{p\left(x_f \mid GSTD-\right)}$$

🟦 GSTD+
⬜ GSTD-
🟩 True
🟥 False

Calculating Likelihood Ratios

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10
Pull-down 1			1	0	1	0		0		1				0	1

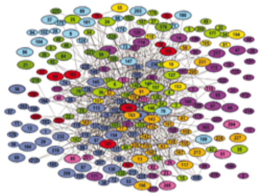
Subunits	2	2	3	3	3	3	3	3	3	5	5	5	5	5	5
Subunits	11	12	5	6	8	9	10	11	12	6	8	9	10	11	12
Pull-down 1							1	1							

Subunits	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12
Pull-down 1															

$$L_1 = \frac{p\left(x_1 \mid GSTD+\right)}{p\left(x_1 \mid GSTD-\right)} = \frac{6/13}{}$$

$$L_0 = \frac{p\left(x_0 \mid GSTD+\right)}{p\left(x_0 \mid GSTD-\right)} = \frac{4/13}{}$$

🟦 GSTD+
⬜ GSTD-
🟩 True
🟥 False



Calculating Likelihood Ratios

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10
Pull-down 1		1	1	0	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1

Subunits	3	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	11	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12
Pull-down 1	1		1	1	0	1	0		0	0	0	0		0	1	0		0	0		0		

$$L_1 = \frac{p\left(x_1 \mid GSTD+\right)}{p\left(x_1 \mid GSTD-\right)} = \frac{6/13}{11/32} = 1.34$$

$$L_0 = \frac{p\left(x_0 \mid GSTD+\right)}{p\left(x_0 \mid GSTD-\right)} = \frac{4/13}{14/32} = 0.70$$

🟦 GSTD+

⬜ GSTD-

🟩 True

🟥 False

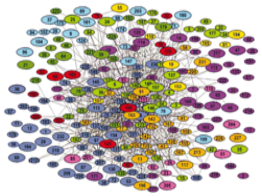
Calculating Likelihood Ratios

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11
Pull-down 1		1	1	0	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1	1
Pull-down 2		1	1	1	1	0	1	0		1	1	0	1	0	1	0		1	1	1	0	1	1
Pull-down 3		1								1								1	0	1	0	0	1
Cross-linking	1	1	1	1	1		0	1	1	1	1	1	0		1	1	1					1	1
Far Western 1		1	1							1	1							1	0	0		0	0
Far Western 2				1	1		1	1	1			1	1		1	1	1		0	0		0	1
Far Western 3																		1	0	0		0	1

Subunits	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12
Pull-down 1		1	1	0	1	0		0	0	0	0		0	1	0		0	0		0		
Pull-down 2		0	1	0	1	0		0	0	0	0		0	0	0		0	0		0		
Pull-down 3	0																					
Cross-linking		1	0					1														
Far Western 1	0	0	1		0	0	0															
Far Western 2	0	0	0		0	0	0	0		0	0	0		0	0	0				0	0	0
Far Western 3	0																					

Pull-down 1	$L1 = (6/13) / (11/32)$	$= 1.34$	$L0 = (4/13) / (14/32)$	$= 0.70$
Pull-down 2	$L1 = (7/13) / (9/32)$	$= 1.91$	$L0 = (2/13) / (16/32)$	$= 0.31$
Pull-down 3	$L1 = (2/13) / (3/32)$	$= 1.64$	$L0 = (2/13) / (2/32)$	$= 2.46$
Cross-linking	$L1 = (10/13) / (7/32)$	$= 3.52$	$L0 = (0/13) / (3/32)$	$= 0$
Far Western 1	$L1 = (2/13) / (4/32)$	$= 1.23$	$L0 = (3/13) / (6/32)$	$= 1.23$
Far Western 2	$L1 = (6/13) / (5/32)$	$= 2.95$	$L0 = (2/13) / (17/32)$	$= 0.29$
Far Western 3	$L1 = (1/13) / (1/32)$	$= 2.46$	$L0 = (2/13) / (2/32)$	$= 2.46$

- 🟦 GSTD+
- ⬜ GSTD-
- 🟩 True
- 🟥 False



Data Integration: ROC-Curve

Subunits	🟨 1	⬜ 1	🟨 1	🟨 1	🟨 1	🟨 1	⬜ 1	🟨 1	⬜ 1	🟨 2	⬜ 2	⬜ 2	⬜ 2	🟨 2	🟨 2
Subunits	🟨 2	⬜ 3	🟨 5	🟨 6	🟨 8	🟨 9	⬜ 10	🟨 11	⬜ 12	🟨 3	⬜ 5	⬜ 6	⬜ 8	🟨 9	🟨 10
Pull-down 1		🟥 1	🟩 1	🟥 0	🟩 1	🟥 0	🟥 1	🟥 0		🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1
Pull-down 2		🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟥 1	🟥 0		🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1
Pull-down 3		🟥 1								🟩 1					
Cross-linking	🟩 1	🟥 1	🟩 1	🟩 1	🟩 1		🟩 0	🟩 1	🟥 1	🟩 1	🟥 1	🟥 1	🟩 0		🟩 1
Far Western 1		🟥 1	🟩 1							🟩 1	🟥 1				
Far Western 2				🟩 1	🟩 1		🟥 1	🟩 1	🟥 1			🟥 1	🟥 1		🟩 1
Far Western 3															
	3.52	18.2	11.1	13.9	26.6	0.22	0	2.25	10.4	18.2	11.1	2.25	0	0.22	26.6
Combined (Bayes)	🟥 1	🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟩 0	🟥 0	🟥 1	🟩 1	🟥 1	🟩 0	🟩 0	🟥 0	🟩 1

Subunits	⬜ 2	🟨 2	⬜ 3	⬜ 3	⬜ 3	⬜ 3	🟨 3	🟨 3	🟨 3	⬜ 5	⬜ 5	⬜ 5	⬜ 5	⬜ 5	⬜ 5
Subunits	⬜ 11	🟨 12	⬜ 5	⬜ 6	⬜ 8	⬜ 9	🟨 10	🟨 11	🟨 12	⬜ 6	⬜ 8	⬜ 9	⬜ 10	⬜ 11	⬜ 12
Pull-down 1	🟩 0		🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1		🟥 1	🟥 1	🟩 0	🟥 1	🟩 0	
Pull-down 2	🟩 0		🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1		🟩 0	🟥 1	🟩 0	🟥 1	🟩 0	
Pull-down 3			🟥 1	🟩 0	🟥 1	🟩 0	🟥 0	🟩 1	🟥 0						
Cross-linking	🟥 1	🟩 1					🟩 1	🟩 1		🟥 1	🟩 0				
Far Western 1			🟥 1	🟩 0	🟩 0		🟥 0	🟥 0	🟥 0	🟩 0	🟥 1		🟩 0	🟩 0	🟩 0
Far Western 2	🟥 1	🟩 1		🟩 0	🟩 0		🟥 0	🟩 1	🟥 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0
Far Western 3			🟥 1	🟩 0	🟩 0		🟥 0	🟩 1	🟥 0						
	2.25	10.4	12.7	5.52	3.68	0.53	19.5	132	2.16	0.52	0	0.22	0.91	0.08	0.36
Combined (Bayes)	🟩 0	🟩 1	🟥 1	🟩 0	🟩 0	🟩 0	🟩 1	🟩 1	🟥 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0

Subunits	⬜ 6	⬜ 6	⬜ 6	⬜ 6	⬜ 6	⬜ 8	⬜ 8	⬜ 8	⬜ 8	⬜ 9	⬜ 9	⬜ 9	⬜ 10	⬜ 10	⬜ 12
Subunits	⬜ 8	⬜ 9	⬜ 10	⬜ 11	⬜ 12	⬜ 9	⬜ 10	⬜ 11	⬜ 12	⬜ 10	⬜ 11	⬜ 12	⬜ 11	⬜ 11	⬜ 12
Pull-down 1	🟩 0	🟩 0	🟩 0	🟩 0		🟩 0	🟥 1	🟩 0		🟩 0	🟩 0		🟩 0		
Pull-down 2	🟩 0	🟩 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0		🟩 0	🟩 0		🟩 0		
Pull-down 3															
Cross-linking	🟥 1														
Far Western 1															
Far Western 2	🟩 0		🟩 0	🟩 0	🟩 0		🟩 0	🟩 0	🟩 0				🟩 0	🟩 0	🟩 0
Far Western 3															
	0.22	0.22	0.06	0.06	0.29	0.22	0.12	0.06	0.29	0.22	0.22	0	0.06	0.29	0.29
Combined (Bayes)	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0

$$L(f_1,\ldots,f_n)=L(f_1)\ldots L(f_n)$$

🟦 GSTD+
⬜ GSTD-
🟩 True
🟥 False

"Weighted Voting"

Data Integration: ROC Curve

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	3
Subunits	2	3	5	6	8	9	10	11	12	3	5	6	8	9	10	11	12	5	6	8	9	10	11
	3.52	18.2	11.1	13.9	26.6	0.22	0	2.25	10.4	18.2	11.1	2.25	0	0.22	26.6	2.25	10.4	12.7	5.52	3.68	0.53	19.5	132
Combined (Bayes)	🟥 1	🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟩 0	🟥 0	🟥 1	🟩 1	🟥 1	🟩 0	🟩 0	🟥 0	🟩 1	🟩 0	🟩 1	🟥 1	🟩 0	🟩 0	🟩 0	🟩 1	🟩 1
Majority	🟩 1	🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟥 1	🟥 0	🟥 1	🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1	🟩 0	🟩 1	🟥 1	🟩 0	🟩 0	🟩 0	🟥 0	🟩 1
Intersection	🟩 1	🟥 1	🟩 1	🟥 0	🟩 1	🟥 0	🟩 0	🟥 0	🟥 1	🟩 1	🟥 1	🟩 0	🟩 0	🟥 0	🟩 1	🟩 0	🟩 1	🟥 1	🟩 0	🟩 0	🟩 0	🟥 0	🟥 0
Union	🟩 1	🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟥 1	🟩 1	🟥 1	🟩 1	🟥 1	🟥 1	🟥 1	🟥 0	🟩 1	🟥 1	🟩 1	🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1

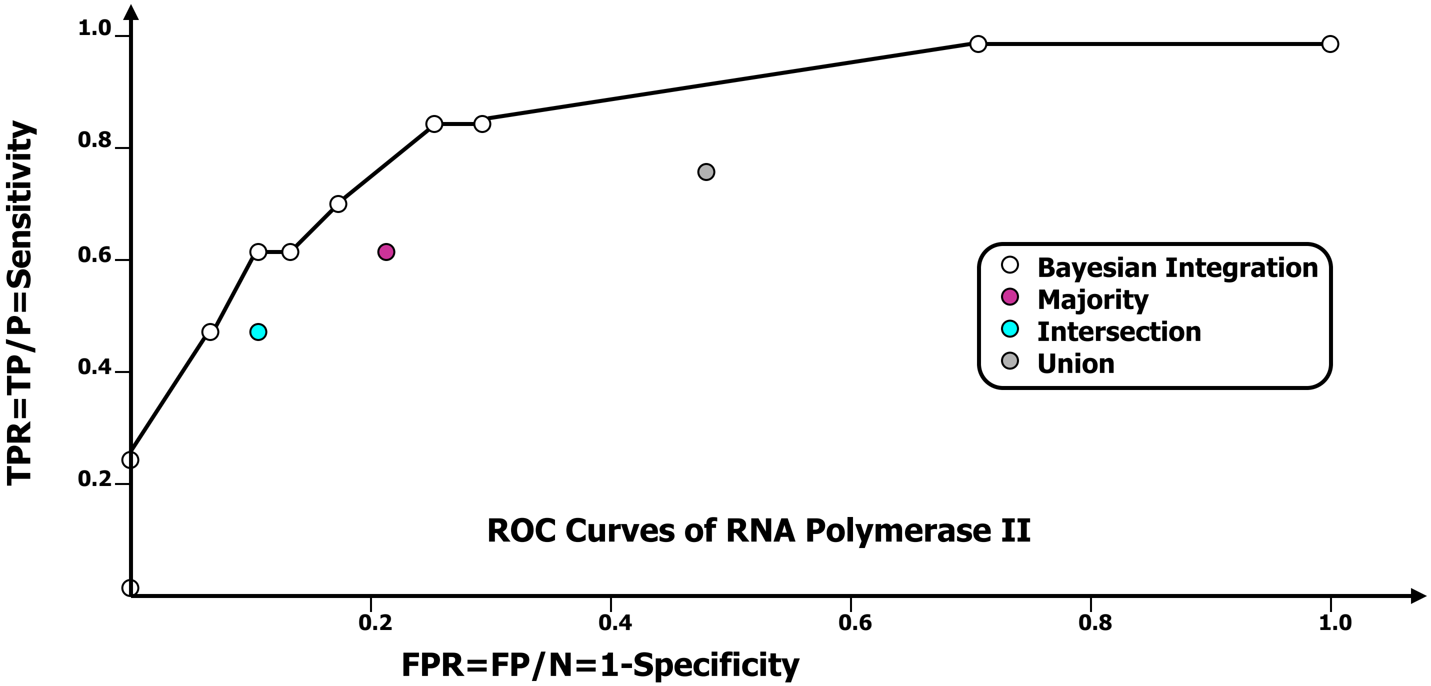
Subunits	3	5	5	5	5	5	5	6	6	6	6	6	8	8	8	8	9	9	9	10	10	12
Subunits	12	6	8	9	10	11	12	8	9	10	11	12	9	10	11	12	10	11	12	11	11	12
	2.16	0.52	0	0.22	0.91	0.08	0.36	0.22	0.22	0.06	0.06	0.29	0.22	0.12	0.06	0.29	0.22	0.22	0	0.06	0.29	0.29
Combined (Bayes)	🟥 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0
Majority	🟥 0	🟩 0	🟥 1	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0
Intersection	🟥 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0
Union	🟥 0	🟥 1	🟥 1	🟩 0	🟥 1	🟩 0	🟩 0	🟥 1	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟥 1	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0

🟦 GSTD+

⬜ GSTD-

🟩 True

🟥 False


TPR=TP/P=Sensitivity
FPR=FP/N=1-Specificity
○ Bayesian Integration
● Majority
● Intersection
● Union
ROC Curves of RNA Polymerase II