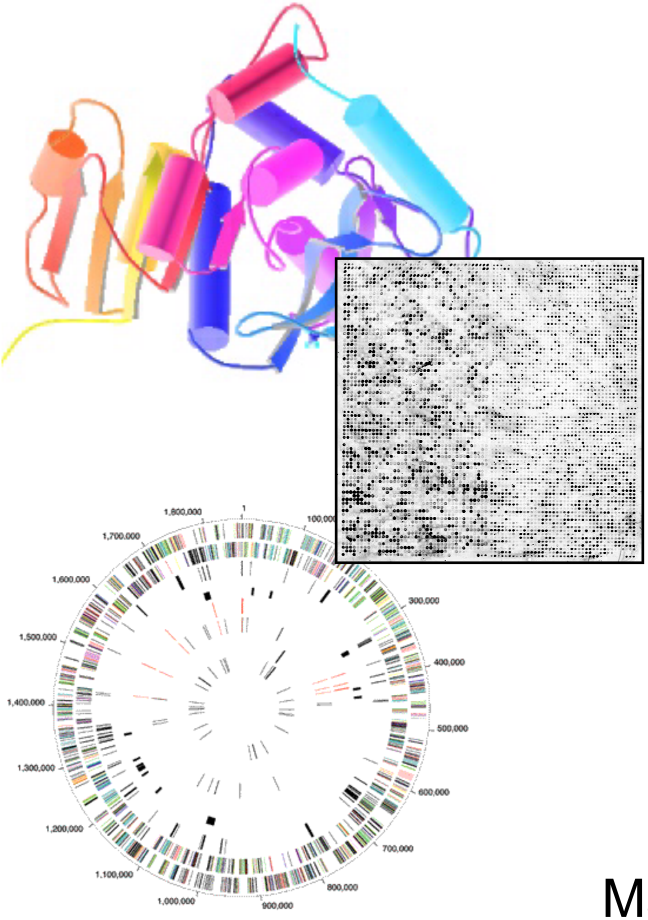
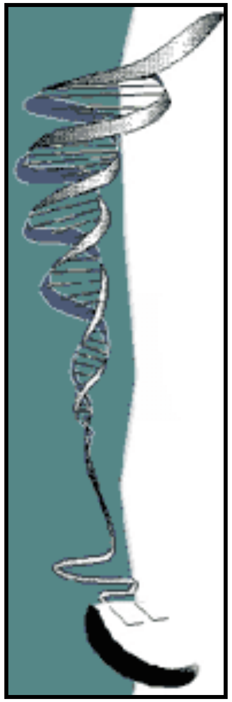
Biomedical Data Science: Predicting Networks





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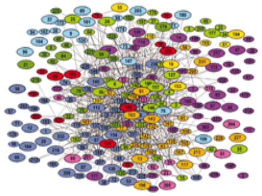
gersteinlab.org/courses/452

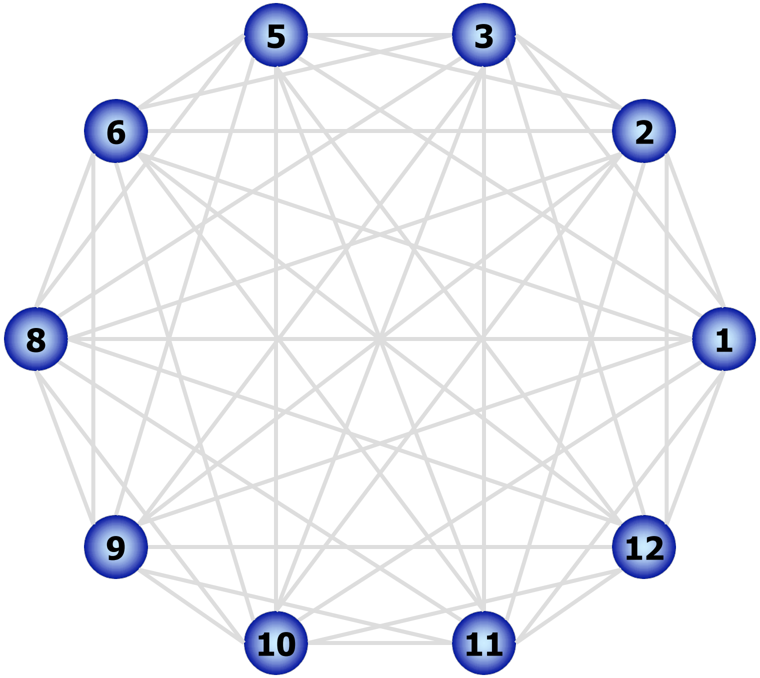
(last edit in Spring '19, pack #11)

Predicting Networks via Bayesian Integration: Problem Motivation



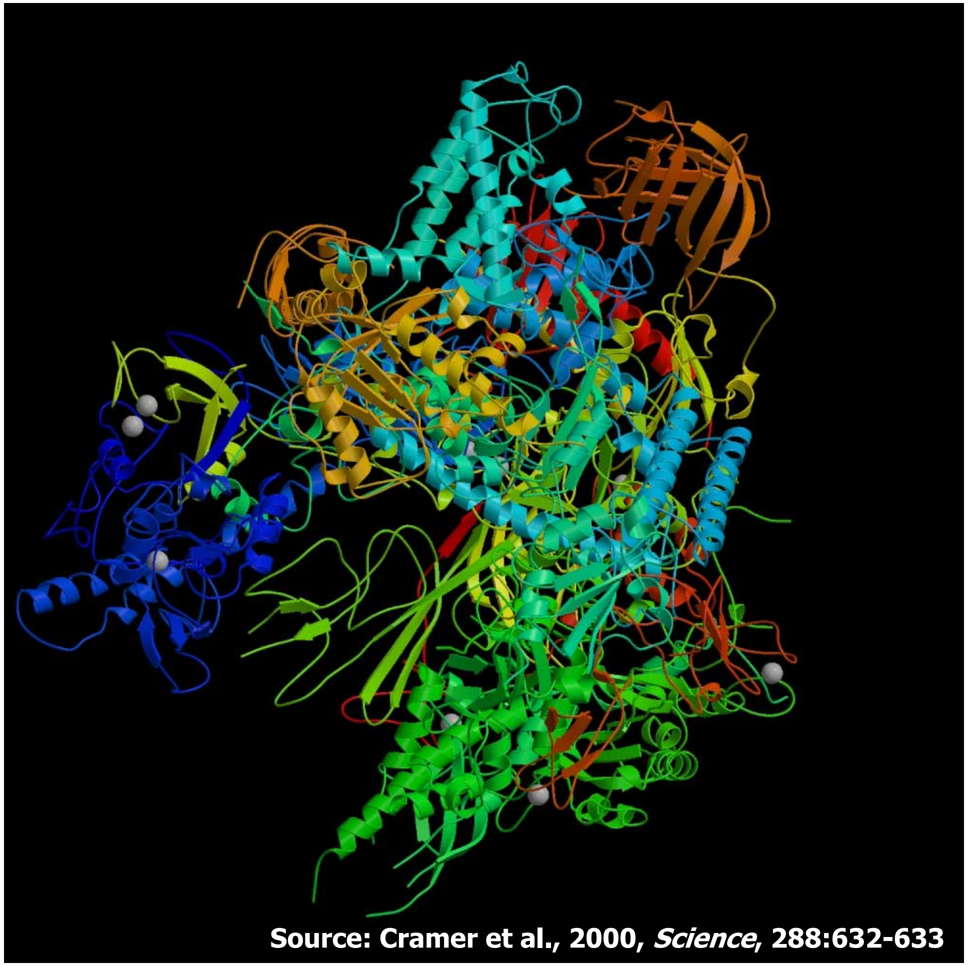
RNA polymerase II: Structure

Which subunits interact? Based on Binding experiments

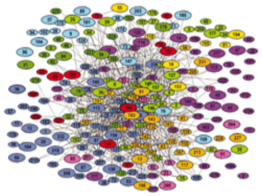


Source: Edwards et al., 2002, *Trends in Genetics*

Compare with Gold Std. Structure



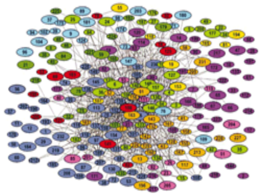
Source: Cramer et al., 2000, *Science*, 288:632-633



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																					

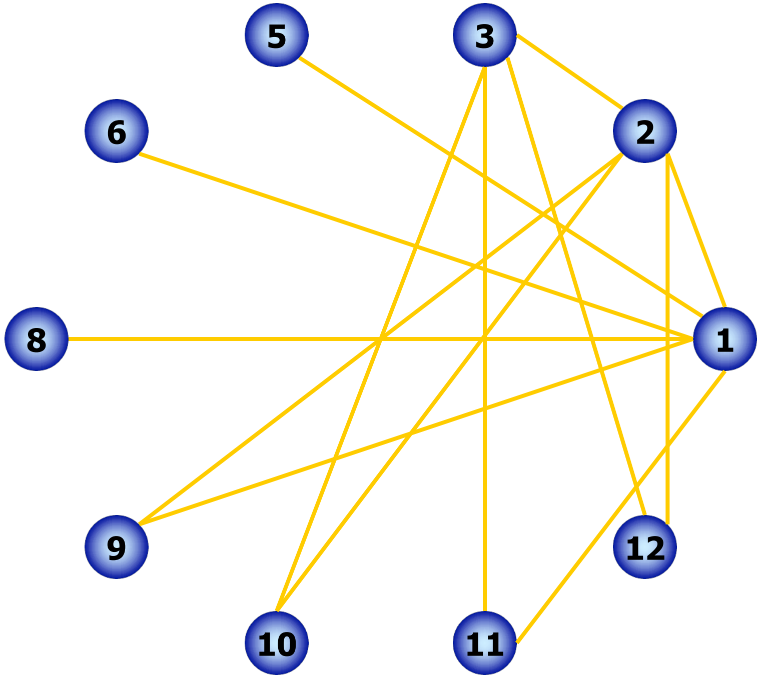
Interaction experiments
before structure was known

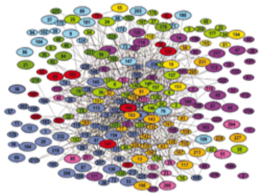


Gold-Standard Positives

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

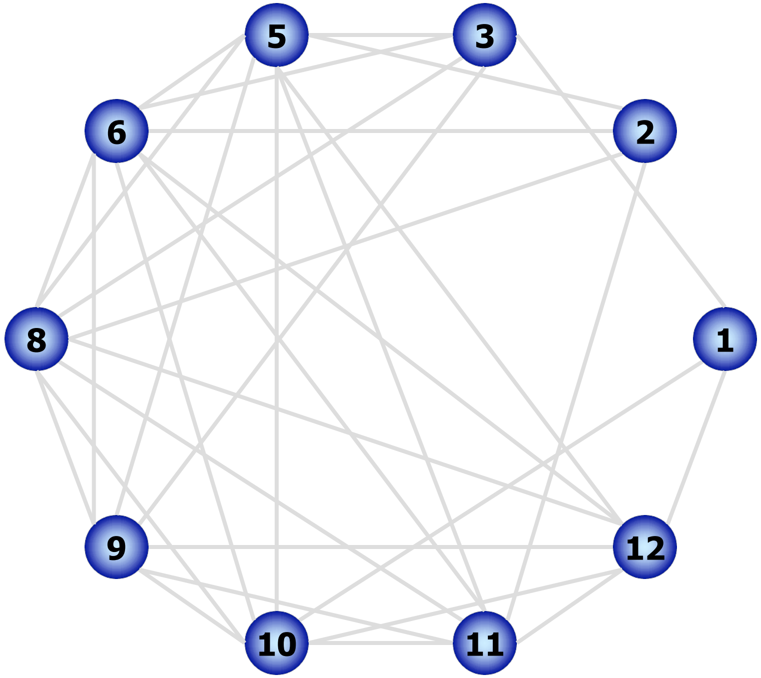


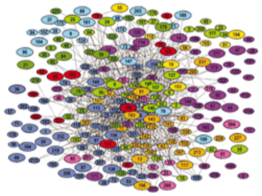


Gold-Standard Negatives

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



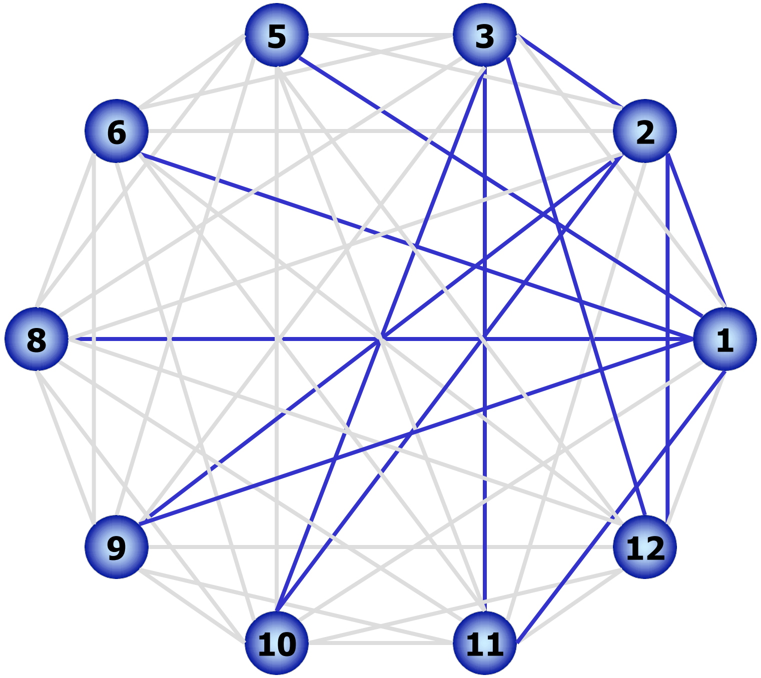


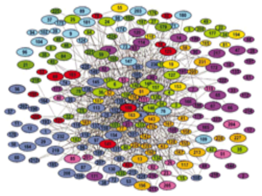
RNA Polymerase II: Gold-Standards

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	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																					

🟦	GSTD+
⬜	GSTD-
🟩	True
🟥	False

Re-drawn in a different color scheme

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																					

Integrate using naive Bayes classifier

(Cross validate)

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	0	0	0	0	1	1	1	0	0	0	0
Far western		1	1							1	1							[illegible]	0	0		0	0	0	0	1		0
Far western (dup)		1	1							1	1							[illegible]	0	0		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	0		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	0		0	1	0				
Combined	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

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

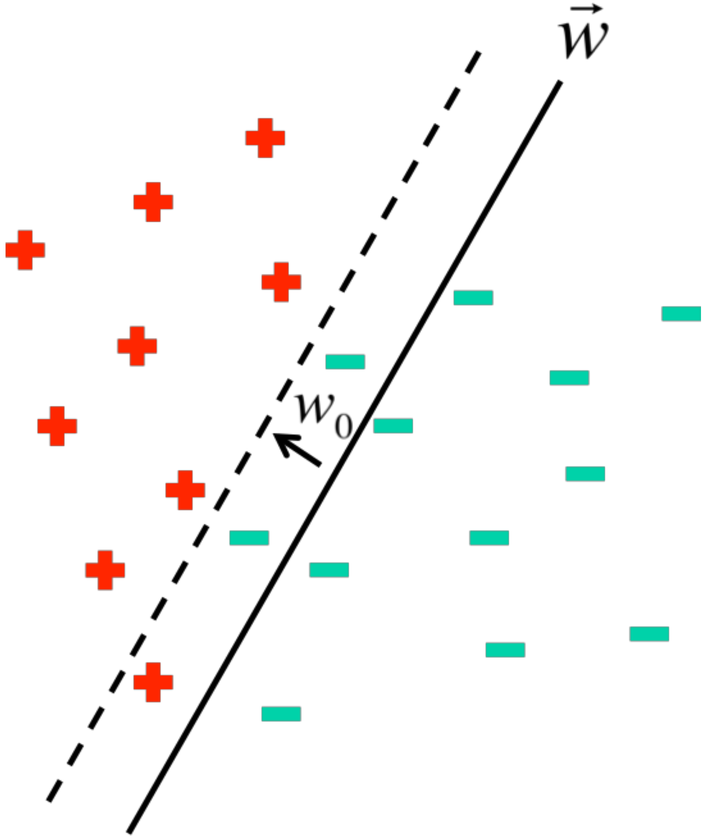
$$R = \vec{w} \cdot \vec{f} + w_0$$

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

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

$$w_0 = \log \frac{P}{N}$$ (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

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

Assume Naïve Bayes (independent)

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

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

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

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

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

More Bayes Rule

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

More Bayes Rule

Estimating Probabilities

- We have so far estimated $P(X=x \mid Y=y)$ by the fraction $n_{x|y}/n_y$, where n_y is the number of instances for which $Y=y$ and $n_{x|y}$ is the number of these for which $X=x$
- This is a problem when n_x is small
    - ◊ E.g., assume $P(X=x \mid Y=y)=0.05$ and the training set is s.t. that $n_y=5$. Then it is highly probable that $n_{x|y}=0$
    - ◊ The fraction is thus an underestimate of the actual probability
    - ◊ It will dominate the Bayes classifier for all new queries with $X=x$

$$\frac{\#\text{ count with feature i in GS+}}{\#\text{ count with feature i in GS-}} = \frac{TPR_i}{FPR_i}$$

m-estimate

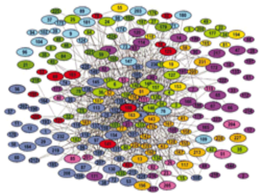
- Replace $n_{x|y}/n_y$ by:

$$\frac{n_{x|y} + mp}{n_y + m}$$

Dummy Counts

- Where p is our prior estimate of the probability we wish to determine and m is a constant
  - Typically, $p = 1/k$ (where k is the number of possible values of X)
  - m acts as a weight (similar to adding m virtual instances distributed according to p)

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		

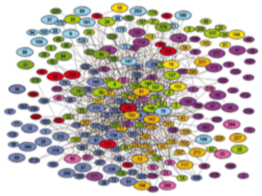
$$L_1 = \frac{p(x_1 \mid GSTD+)}{p(x_1 \mid GSTD-)}$$

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

Likelihood Ratio
for Feature *f*:

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

🟦 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	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	12
Pull-down 1			1	0	1	0		0		1				0	1							1	1	

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

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

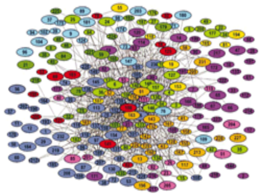
$$L_0 = \frac{p\left(x_0 \mid GSTD+\right)}{p\left(x_0 \mid GSTD-\right)} = \frac{4/13}{}$$

🟦 **GSTD+**

⬜ **GSTD-**

🟩 **True**

🟥 **False**



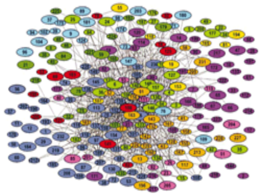
Calculating Likelihood Ratios

Subunits	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	3	3	3	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		

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

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

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

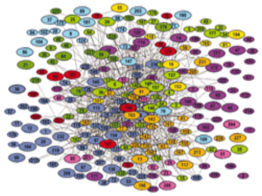


Calculating Likelihood Ratios

Subunits	🟨 1	1	🟨 1	🟨 1	🟨 1	🟨 1	1	🟨 1	1	🟨 2	2	2	2	🟨 2	🟨 2	2	🟨 2	3	3	3	3	🟨 3	🟨 3	🟨 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																					

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 🟩

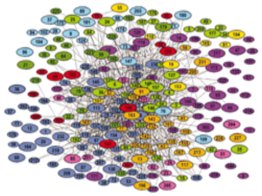
Subunits	2 ⬜	2 🟨	3 ⬜	3 ⬜	3 ⬜	3 ⬜	3 🟨	3 🟨	3 🟨	5 ⬜	5 ⬜	5 ⬜	5 ⬜	5 ⬜	5 ⬜
Subunits	11 ⬜	12 🟨	5 ⬜	6 ⬜	8 ⬜	9 ⬜	10 🟨	11 🟨	12 🟨	6 ⬜	8 ⬜	9 ⬜	10 ⬜	11 ⬜	12 ⬜
Pull-down 1	0 🟩		1 🟥	1 🟥	1 🟥	0 🟩	1 🟩	1 🟩		1 🟥	1 🟥	0 🟩	1 🟥	0 🟩	
Pull-down 2	0 🟩		1 🟥	1 🟥	1 🟥	0 🟩	1 🟩	1 🟩		0 🟩	1 🟥	0 🟩	1 🟥	0 🟩	
Pull-down 3			1 🟥	0 🟩	1 🟥	0 🟩	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
Subunits	🟨 2	⬜ 3	🟨 5	🟨 6	🟨 8	🟨 9	⬜ 10	🟨 11	⬜ 12	🟨 3	⬜ 5	⬜ 6	⬜ 8	🟨 9	🟨 10
	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
Majority	🟩 1	🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟥 1	🟥 0	🟥 1	🟩 1	🟥 1	🟩 0	🟥 1	🟥 0	🟩 1
Intersection	🟩 1	🟥 1	🟩 1	🟥 0	🟩 1	🟥 0	🟩 0	🟥 0	🟥 1	🟩 1	🟥 1	🟩 0	🟩 0	🟥 0	🟩 1
Union	🟩 1	🟥 1	🟩 1	🟩 1	🟩 1	🟥 0	🟥 1	🟩 1	🟥 1	🟩 1	🟥 1	🟥 1	🟥 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
	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
Majority	🟩 0	🟩 1	🟥 1	🟩 0	🟩 0	🟩 0	🟥 0	🟩 1	🟥 0	🟩 0	🟥 1	🟩 0	🟩 0	🟩 0	🟩 0
Intersection	🟩 0	🟩 1	🟥 1	🟩 0	🟩 0	🟩 0	🟥 0	🟥 0	🟥 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0
Union	🟥 1	🟩 1	🟥 1	🟥 1	🟥 1	🟩 0	🟩 1	🟩 1	🟥 0	🟥 1	🟥 1	🟩 0	🟥 1	🟩 0	🟩 0

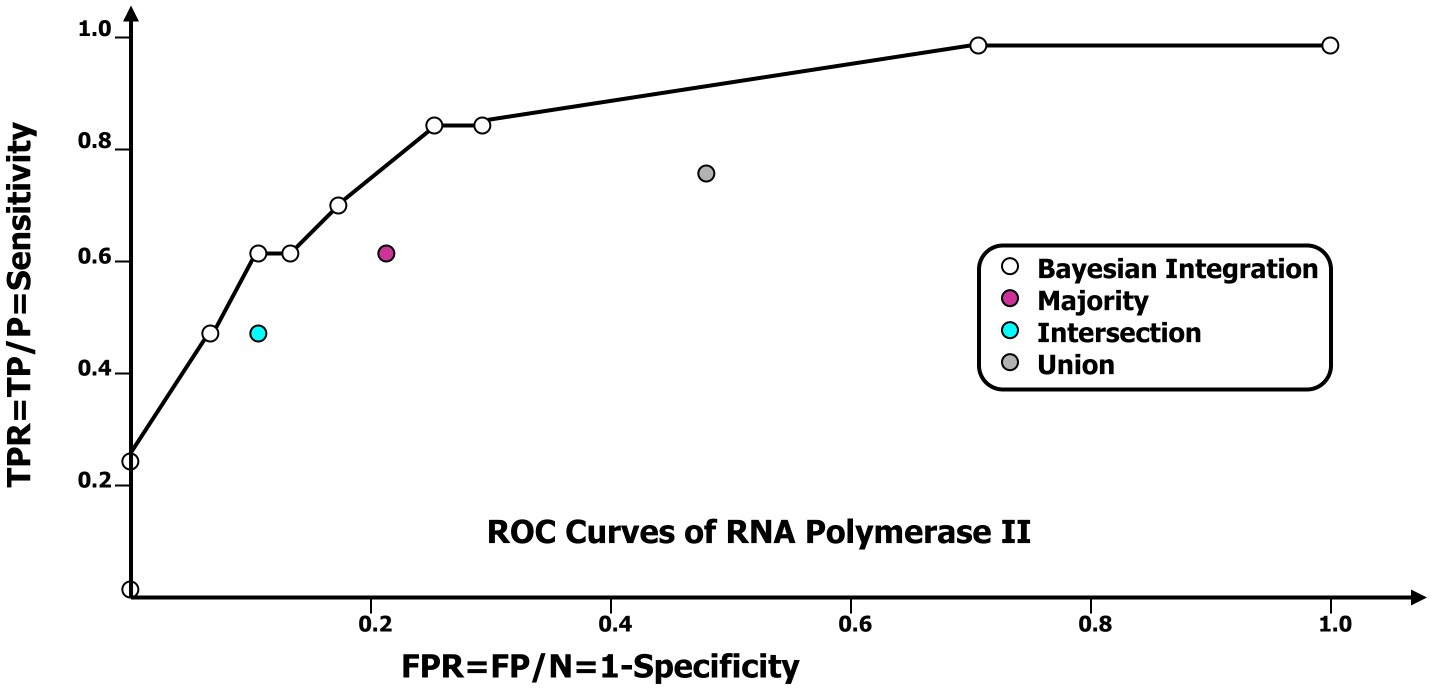
Subunits	⬜ 6	⬜ 6	⬜ 6	⬜ 6	⬜ 6	⬜ 8	⬜ 8	⬜ 8	⬜ 8	⬜ 9	⬜ 9	⬜ 9	⬜ 10	⬜ 10	⬜ 11
Subunits	⬜ 8	⬜ 9	⬜ 10	⬜ 11	⬜ 12	⬜ 9	⬜ 10	⬜ 11	⬜ 12	⬜ 10	⬜ 11	⬜ 12	⬜ 11	⬜ 12	⬜ 12
	0.22	0.22	0.06	0.06	0.29	0.22	0.12	0.06	0.29	0.22	0.22	0	0.06	0.29	0.29
Combined (Bayes)	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0
Majority	🟩 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
Union	🟥 1	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟥 1	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0	🟩 0

🟦 **GSTD+**

⬜ **GSTD-**

🟩 **True**

🟥 **False**



ROC Curves of RNA Polymerase II

Predicting Networks via Bayesian Integration: Features Correlation

Correlations between similar features

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
Far western		1	1							1	1							1	0	0		0	0	0	0	1		0
Far western (dup)		1	1							1	1							1	0	0		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	0		0	1	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
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
Pull-down		1								1								1	0	1	0	0	1	0				
Far western																		1	0	0		0	1	0				
Combined	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

(c) M Gerstein, gerstein.info/talks

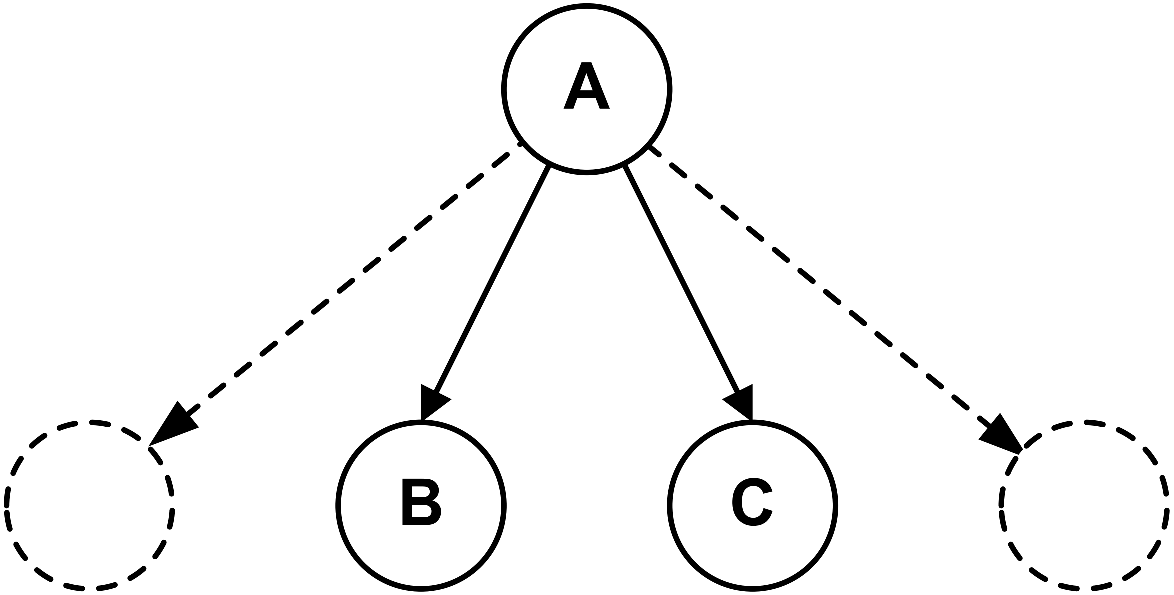
GS	1	0	0	1	1	1	…
F1	1	0	0	1	0	0	...
F2	1	0	0	1	0	0	…
F3	0	0	1	0	1	0	…
F4	0	1	0	0	1	0	…
F5	0	1	0	0	1	0	…
F6	1	0	1	1	0	0	…

Feature Correlation and Fully Connected Bayes

$$w_{4,5} = \log \frac{P(f_4 = 1, f_5 = 1 \mid I)}{P(f_4 = 1, f_5 = 1 \mid \sim I)}$$

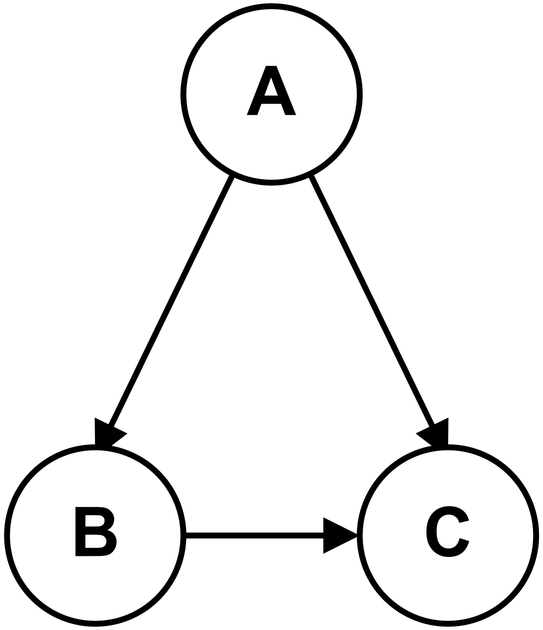
Naive Bayes

$$P(A,B,C) = P(C|A)P(B|A)P(A)$$

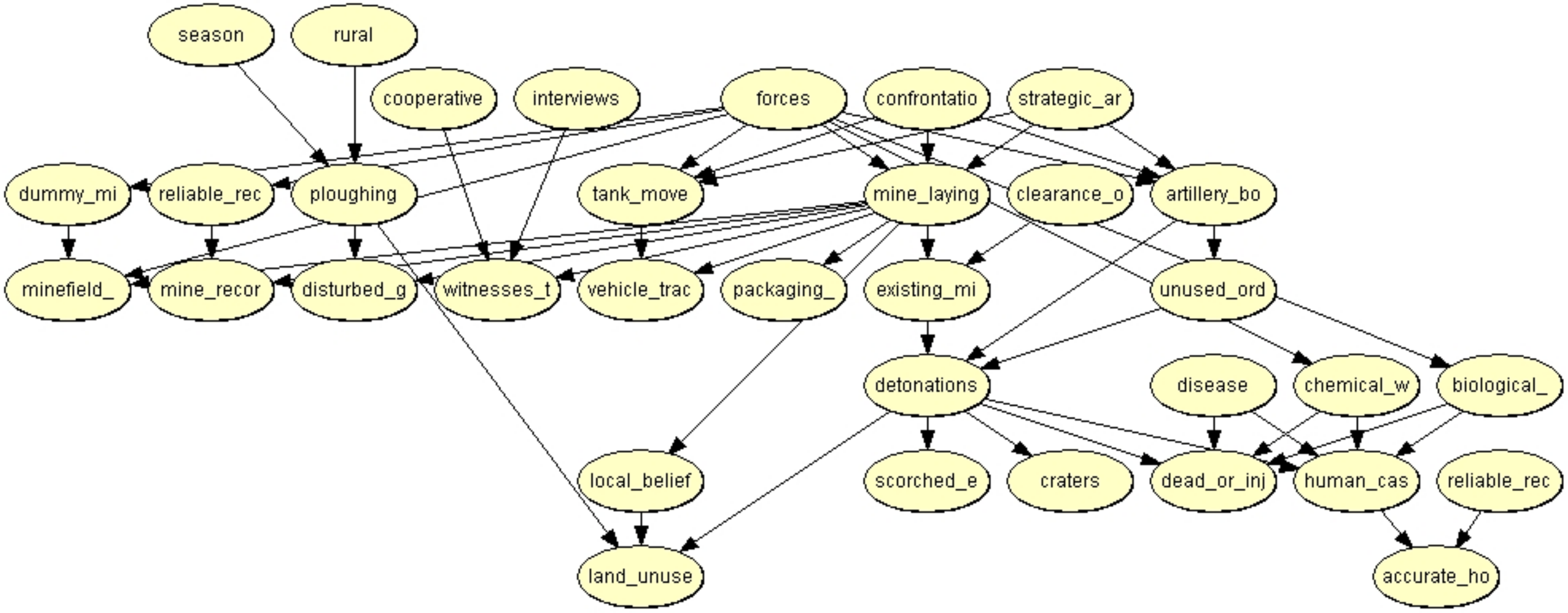


A ‘correct’ factorisation

$$P(A,B,C) = P(C|A,B)P(B|A)P(A)$$



A Typical BBN



Predicting Networks via Bayesian Integration: Real Thing but with a few features

Papers on Predicting Protein Interactions

- A Enright et al. (**1999**) "Protein interaction maps for complete genomes based on gene fusion events." Nature. 402(6757):86-90.
- E Marcotte et al. (1999) "A Combined Algorithm for Genome-Wide Prediction of Protein Function." Nature 402, 83-86 (1999).
- E Marcotte et al. (1999) "Detecting Protein Function & Protein-Protein Interactions from Genome Sequences." Science 285, 751-753
- M Pellegrini et al. (1999) "Assigning protein functions by comparative genome analysis: protein phylogenetic profiles." Proc.Natl. Acad. Sci. 96, 4285-4288.
- R Jansen et al. (2003). "A Bayesian networks approach for predicting protein-protein interactions from genomic data." Science 302: 449-53.
- **I Lee et al. (2004) "A Probabilistic Functional Network of Yeast Genes".** ***Science*** **206: 1555-1558**
- H Yu et al. (2004) "Annotation transfer between genomes: protein-protein interologs and protein-DNA regulogs." Genome Res 14: 1107-18.
- **L Lu et al. (2005) "Assessing the limits of genomic data integration for predicting protein networks." Genome Res 15: 945-53.**
- A Ramani et al. (2005) "Consolidating the set of known human protein-protein interactions in preparation for large-scale mapping of the human interactome." Genome Biology 6:r40.
- Xia et al. (**2006**) "Integrated prediction of the helical membrane protein interactome in yeast." J Mol Biol. 357:339-49