Harvard-MIT Division of Health Sciences and Technology HST.950J: Engineering Biomedical Information: From Bioinformatics to Biosurveillance Course Directors: Dr. Isaac Kohane, Dr. Marco Ramoni



Harvard Medical School



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Biomedical Computing

Decision Support Systems November 3rd, 2005

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Decision Support Systems

- * An intelligent system is a computer program able to emulate intelligent performances.
- Computer program:
 - A mechanical (effective) procedure.
- Intelligent performances (pragmatic definition):
 - The performance we expect to require intelligence.
- # Emulate/Simulate:
 - Emulate means to achieve the same objectives.
 - Simulate means to reproduce the same behavior.



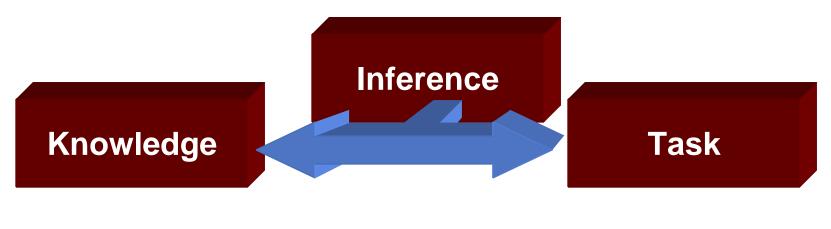


Components

Knowledge: Representation of domain knowledge.

You may regard this knowledge as axioms.

- Inference: Domain independent procedures to handle knowledge in order to achieve these tasks.
 - You may regard these procedures as inference rules.

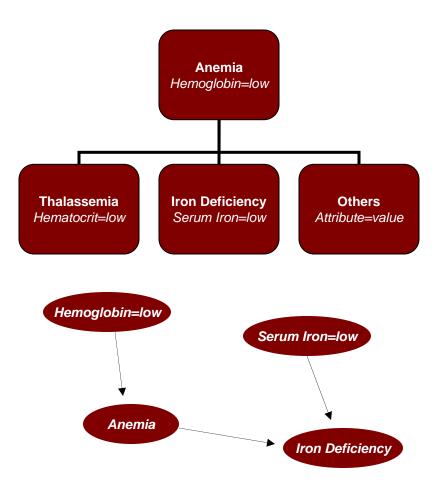






Knowledge Representation

- * Knowledge/Information
 - Knowledge is not just information.
 - Knowledge is structured information.
- Ontology is the structure of the domain knowledge.
 - A classification of medical disorders: a hierarchy prototype definitions.
 - A network of causal relationships and influences.





Inference and Reasoning

- Once knowledge is represented, it must be used.
- Inference: The operation able to draw conclusions.
 Sound: draw only true conclusions.
 - Complete: draw all the true conclusions.
 - The truth, the whole truth, and nothing but the truth.
- Reasoning: Application of inference to knowledge.
 Truth preservative: draw true from true.
 Monotonic: the conclusions drawn are always valid (!).
 - The first 33 theorems of Euclid's Elements are drawn without the Fifth Axiom but they still hold after it.





Problem Solving

Knowledge/inference compilation:

- if (the infection is meningitis)
 (the type is bacterial)
 (therapy is corticosteroids)
 (only circumstatial evidence)
 then
 klebsiella (0.2), e.coli (0.4)
 or pseudomonas (0.1)
- \checkmark Knowledge (1 2 3 5 6) and inference (2).
- ✓ Difficult to acquire, maintain, and update.

Deep systems:

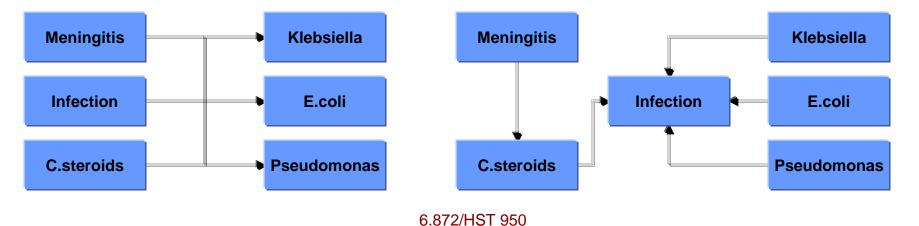
- Knowledge flows in the opposite direction.
- ✓ Inference must reverse this natural path of knowledge.



Logical Representation

* Logical knowledge representation (axioms):

 ✓ (meningitis ⇒ corticosteroids) (corticosteroids ⇒ bacterial_infection) (klebsiella ⇒ bacterial_infection) (e.coli ⇒ bacteria_infection) (pseudomonas ⇒ bacterial_infection)





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Logical Reasoning

- Inference rules (e.g. modus [ponendi] ponens)
 - ✓ Metalinguistic inference rules:

✓ Axiom schema:

$$\mathfrak{P}(\alpha \Rightarrow \beta) \land \alpha \Rightarrow \beta$$

- ✓ Example:
 - ☞Axioms:

 \succ (cat \Rightarrow mammal); cat

- Application of the inference rule:
 - \succ cat \Rightarrow mammal
 - cat
 - ∴ mammal



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Example

Axioms

 ✓ (meningitis ⇒ corticosteroids) (corticosteroids ⇒ bacterial_infection) (klebsiella ⇒ bacterial_infection) (e.coli ⇒ bacterial_infection) (pseudomonas ⇒ bacterial_infection)

Observations:

➤ meningitis

Inference

☞meningitis ⇒ corticosteroids ⇒ bacterial_infection

But how do we infer the type of bacteria?





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Limits

Representation of uncertainty:

- How do we represent uncertainty about knowledge?
 - Meningitis may cause brain damage.
- * Abductive inference:
 - ✓ How do we get the bacteria?
 - \succ cat \Rightarrow mammal mammal
 - ∴ cat 🍑
 - > e.coli => bacteria
 - bacteria
 - ∴ e.coli 🍧
- This pattern is called Fallacy of Affirming the Consequent.



Probability

Let's consider our propositions as events:

✓ Probability is a function mapping an event to [0 1].

 $0 \leq p(a) \leq 1$

The probability that tomorrow will rain is 0.4: p(rain)=0.4.

Properties:

Complementation:

$$p(a) + p(\neg a) = 1$$

 $p(\neg a) = 1 - p(a)$

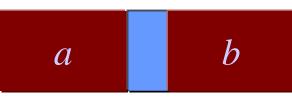
The probability that tomorrow will *not* rain: $p(\neg rain)=0.6$.



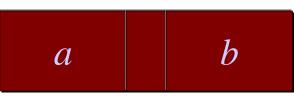
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And and Or

* And (\land) is set intersection: $p(a \land b)$



***** Or (\lor) is set union: $p(a \lor b)$



* If the intersection is empty, the union is the sum: $p(a \land b)=0 \Rightarrow p(a \lor b)=p(a)+p(b)$







Exhaustivity and Exclusivity

Exclusivity: a and b cannot be both true.

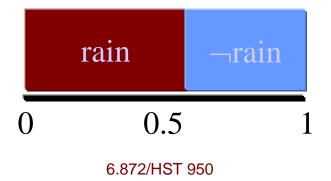
 $p(a \wedge b) = 0$

When it rains, it may never be the case it is not raining.

Exhaustivity: Events exhaust all the possibilities:

p(a) + p(b) = 1

Either it is raining or it is not raining.





Axioms

Axiom 1: $p(a) \ge 0$ \checkmark The probability of an event cannot be negative. Axiom 2: $p(\Omega)=1$ \checkmark The probability of an exhaustive set is 1. $\Im p(rain)+p(\neg rain)=1$ \checkmark This, together with Axiom 1, implies $0 \le p(a) \le 1$. Axiom 3: $p(a \lor b) = p(a)+p(b)$ if $p(a \land b)=0$. \checkmark Theorem: $p(a \lor b) = p(a)+p(b) - p(a \land b)$.

$$a \qquad b \qquad = \qquad a \qquad \bigcirc \qquad b \qquad = \qquad$$



Variables

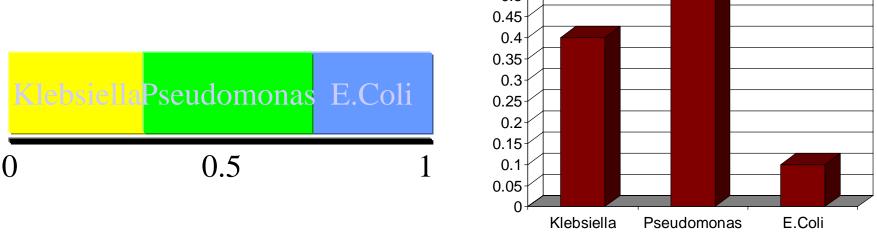
- A variable is a symbol A with a set of J possible values $\{a_1, ..., a_J\}$.
 - \checkmark A state a_{ii} is the assignment of a value to the variable.
 - \checkmark A variable can take just one value at the time.
 - A variable must take at least one value.
 - A variable is a set of exclusive and exhaustive states.
 - The variable Bacteria has values: {klebsiela, e.coli, psedumonas}.
 - There are three states, such as Bacteria= klebsiela.
 - ✓ Our propositions are variables with just two states.
 - The variable Rain can take two values: {true,false}.
 - Rain has two states: Rain=true and Rain=false.





Probability Distribution

- * We can associate a probability value to each state.
- * The set of probabilities associated to a variable is called Probability Distribution.
 - ✓ Since the states are exhaustive, they sum up to 1.
 - ✓ Since the states are exclusive, their intersections are 0.

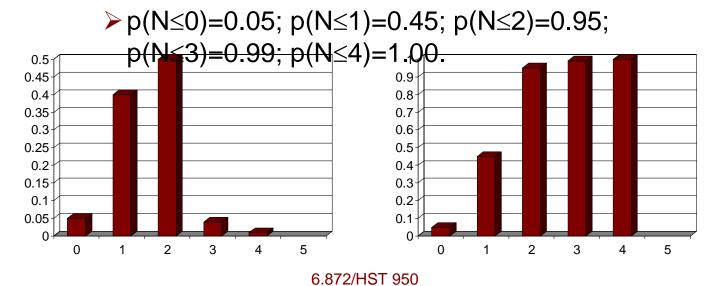






Cumulative Distributions

- * The cumulative distribution is given by the sum of probabilities of some states.
 - The variable N Number of assignments per course.
 - ▶ p(N=0)=0.05; p(N=1)=0.40; p(N=2)=0.50;
 - p(N=3)=0.04; p(N=4)=0.01; p(N≥5)=0.00.
 - The Cumulative Distribution of N.







Joint Probability

Conjunction is represented as joint probability.

 $\begin{array}{ll} \blacktriangleright p(cloudy \land rain) = 0.60 & 1 \\ p(cloudy \land \neg rain) = 0.15 & 2 \\ p(\neg cloudy \land rain) = 0.15 & 3 \\ p(\neg cloudy \land \neg rain) = 0.10 & 4 \end{array}$

Imagine joint events as percentages of days in a year. Note that they sum up to 1.

Inference (marginal probability):



Conditioning

- Modus ponens needs a conditional statement.
- * Inference needs conditional statements but we cannot use standard implication (\Rightarrow) :

 $p(a \Rightarrow b)=0.7 \equiv p(\neg a \lor b)=0.7 \equiv p(b) \le 0.7 \text{ and } p(a) \le 0.3$

- * We need a probabilistic conditioning.
- * Fortunately, we have conditional probability:

$$p(a \mid b) = \frac{p(a \land b)}{p(b)}$$

* It is read the probability of a given b.



Conditional Probability

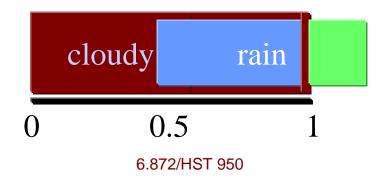
* Conditional probabilities represent the intension:

If it is cloudy it is more likely to rain

- p(rain|cloudy)=0.8; p(¬rain|cloudy)=0.2
- ☞ If it is not cloudy it is more likely not to rain.

▶p(rain|¬cloudy)=0.6; p(¬rain|¬cloudy)=0.4

- The conditional probability is the probability of an event when another event is happening.
- It is a set zoomed in another set.







Bayes' Theorem

Bayes' Theorem is the solution to abduction:

$$p(a \mid b) = \frac{p(a \land b)}{p(b)}$$

$$\checkmark \text{ Since } p(a \land b) = p(a \mid b) \times p(b) = p(b \mid a) \times p(a):$$

$$p(b \mid a) = \frac{p(a \mid b) p(b)}{p(a \land b) + p(a \land \neg b)}$$

✓ Invert p(a | b) into the *posterior probability* p(b | a).

$$p(b \mid a) = \frac{p(a \mid b) p(b)}{p(a \mid b) p(b) + p(a \mid \neg b) p(\neg b)}$$

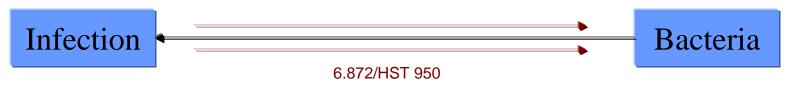


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Exhaustive

* The bacteria are values of a single variable в: \square p(B=k)=0.4; p(B=e)=0.3; p(B=p)=0.3 \square p(I=t|B=k)=.9;p(I=t|B=e)=.8;p(I=t|B=p)=.8 p(I=f|B=k)=.1; p(I=f|B=e)=.2; p(I=f|B=p)=.2Posterior probability p(B=k|l=t) $p(I = t | B = k) \times p(B = k)$ $p(I = t | B = k) \times p(B = k) + p(I = t | B = e) \times p(B = e) + p(I = t | B = p) \times p(B = p)$ $=\frac{0.9\times0.4}{0.9\times0.4+0.8\times0.3+0.8\times0.3}=\frac{0.36}{0.84}=0.428$ $p(B = e | I = t) = \frac{0.24}{0.84} = 0.286$ $p(B = p | I = t) = \frac{0.24}{0.84} = 0.286$ p(B = k | I = t) + p(B = e | I = t) + p(B = p | I = t) = 0.428 + 0.286 + 0.286 = 1

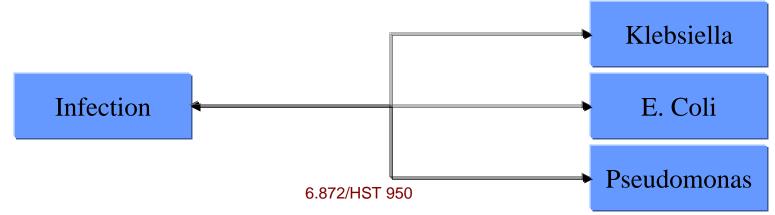




Independent

The bacteria are independent binary variables:

Solution: Transform the antecedents in a single variable: antecedents defines a set of mutually exclusive and exhaustive states and Apply Bayes' Theorem.





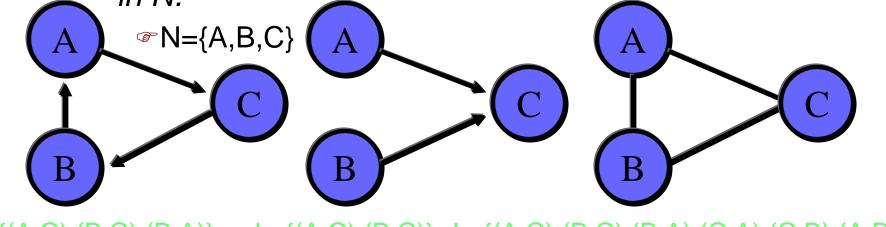


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* A graph (network) G(N,L) is defined by:

- ✓ A finite set $N = \{A, B, ...\}$ of nodes (vertices).
- ✓ A set *L* of links (edges): ordered pair of nodes (*A*,*B*).
- The set L is a subset of all possible pairs of nodes in N.

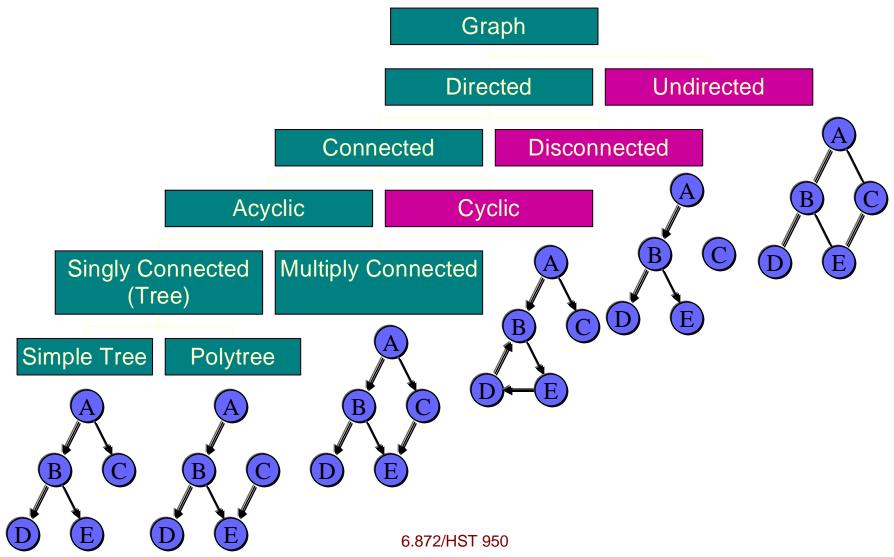


 $L=\{(A,C),(B,C),(B,A)\} L=\{(A,C),(B,C)\} L=\{(A,C),(B,C),(B,A),(C,A),(C,B),(A,B)\}$





Types of Graph





Independence

* Two variables are independent (I(A,B)) if knowing one does not affect our belief in the other:

p(A|B)=p(A)

The conjunction is exactly the Boolean conjunction, since

 $p(A \land B)/p(B) = p(A)$

therefore:

 $p(A \land B) = p(A) \times p(B)$ $p(Rain) = 0.2 \quad p(Sprinkler) = 0.9 \quad p(Rain \land Sprinkler) = 0.18 \quad p(Rain) = 0.2 \quad p(\neg Sprinkler) = 0.11 \quad p(Rain \land \neg Sprinkler) = 0.02 \quad p(\neg Rain) = 0.8 \quad p(Sprinkler) = 0.9 \quad p(\neg Rain \land Sprinkler) = 0.72 \quad p(\neg Rain) = 0.8 \quad p(\neg Sprinkler) = 0.11 \quad p(\neg Rain \land \neg Sprinkler) = 0.11 \quad p(\neg Rain \land \neg Sprinkler) = 0.08 \quad p(\neg Sprinkler) = 0.11 \quad p(\neg Rain \land \neg Sprinkler) = 0.08 \quad p(\neg Sprinkler) = 0.11 \quad p(\neg Sprinkler) = 0.08 \quad p(\neg Sprinkler) = 0.11 \quad p(\neg Sprinkler)$





Conditional Independence

When two variables are independent given a third, they are said to be conditionally independent.

 $p(A|B \land C) = p(A \land B \land C)/p(B \land C) = p(A|C)$

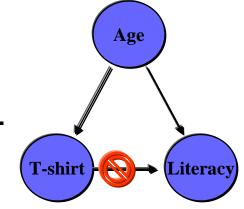
T-shirt size of kids affect their literacy skills. Both T-shirt size and literacy skills depend on age

Literacy					Literacy		
T-shirt	Yes	No	Age	T-shirt	Yes	No	
Small	0.32	0.68	<5	Small	0.3	0.7	
Large	0.35	0.65	<5	Large	0.3	0.7	
			>5	Small	0.4	0.6	
			>5	Large	0.4	0.6	



Bayesian Networks

- Bayesian networks use graphs to capture these statement of conditional independence.
- A Bayesian network (BBN) is defined by a graph: Nodes are stochastic variables.
 Links are dependencies.
 - Absence of a link denotes independence given a parent.
- There are two components in a BBN:
 Qualitative graphical structure.
 Quantitative assessment of probabilities.







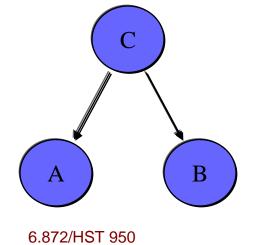
Decomposition

The power of BBNs is to decompose the joint probability distribution using the graphical structure of conditional independence.

$$p(A|B \land C) = p(A|C) \equiv p(A \land B | C) = p(A|C) \times p(B|C)$$

* Therefore, the graphical structure factorizes the joint probability distribution:

$$p(A \land B \land C) = p(A|C) \times p(B|C) \times p(C)$$







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Example

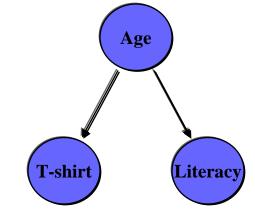
Background knowledge: General rules of behavior.

p(Age=<5)=0.3 p(T-shirt=small| Age=<5)=0.5 p(T-shirt=small|Age=>5)=0.3 p(Literacy=yes|Age=>5)=0.6 p(Literacy=yes|Age=<5)=0.2

Problem: Observation *p*(*T*-*shirt*=*small*)

Solution: The posterior probability distribution of the unobserved nodes given problem: *p*(*Literacy*| *T-shirt=small*) and *p*(*Age*| *T-shirt=small*)

p(Age=<5,T-shirt=small,Literacy=yes) p(Age=<5,T-shirt=small,Literacy=no) p(Age=<5,T-shirt=large,Literacy=yes) p(Age=<5,T-shirt=large,Literacy=no) p(Age=>5,T-shirt=small,Literacy=yes) p(Age=>5,T-shirt=large,Literacy=yes) p(Age=>5,T-shirt=large,Literacy=yes) p(Age=>5,T-shirt=large,Literacy=no)







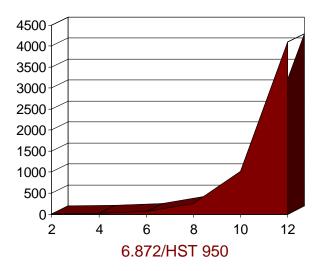
Brute Force

The brute force solution:

 ☆ Compute the Joint Probability Distribution: p(a,b,c,d,e,f,g)= p(a)p(b)p(c|d)p(d|a,b)p(e)p(f|d)p(g|d,e)
 ⊘ Marginalize out the variable of interest:

 $p(d)=\Sigma p(a,b,c,e,f,g)$

- \checkmark Note we have replace \land with ,
- ✓ Cost: we need to sum 2^n probabilities ($2^6 = 64$).





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E

G

F

Knowledge B A ***** Components of a problem: Knowledge: graph and probabilities. Problem: $\varepsilon = \{c \text{ and } g\}.$ C D Solution: p(d|c,g)=?.

Α	p(A) B	p(B)	R	p(E)	Α	B	D	p(D A,B)	D	E	G	p(G D,E)
0	0.3	0	0.6	0	0.1	0	0	0	0.40	0	0	0	0.90
1	0.7	1	0.4	1	0.9	0	0	1	0.60	0	0	1	0.10
	C					0	1	0	0.45	0	1	0	0.70
Α	C	p(C A)	D	R	p(F D)	0	1	1	0.55	0	1	1	0.30
0	0	0.25	0	0	0.80	1	0	0	0.60	1	0	0	0.25
0	1	0.75	0	1	0.20	1	0	1	0.40	1	0	1	0.75
1	0	0.50	1	0	0.30	1	1	0	0.30	1	1	0	0.15
1	1	0.50	1	1	0.70	1	1	1	0.70	1	1	1	0.85



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Method

- In a polytree, each node breaks the graph into two independent graphs and we can deal separatelyε:
 E⁺: evidence coming from the parents (E⁺ = {c}).
 E⁻: evidence coming from the children (E⁻ = {g}).
- ★ Task: p(d|c,g): p(d| E+,E):

 $\swarrow p(d| E^+, E^-) = k \pi(d) \lambda(d)$

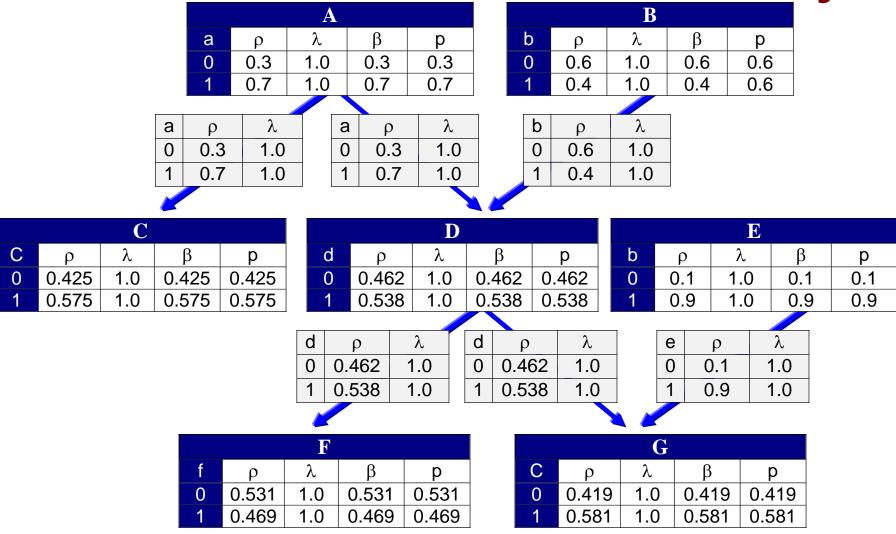
A B C D E F G





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Summary

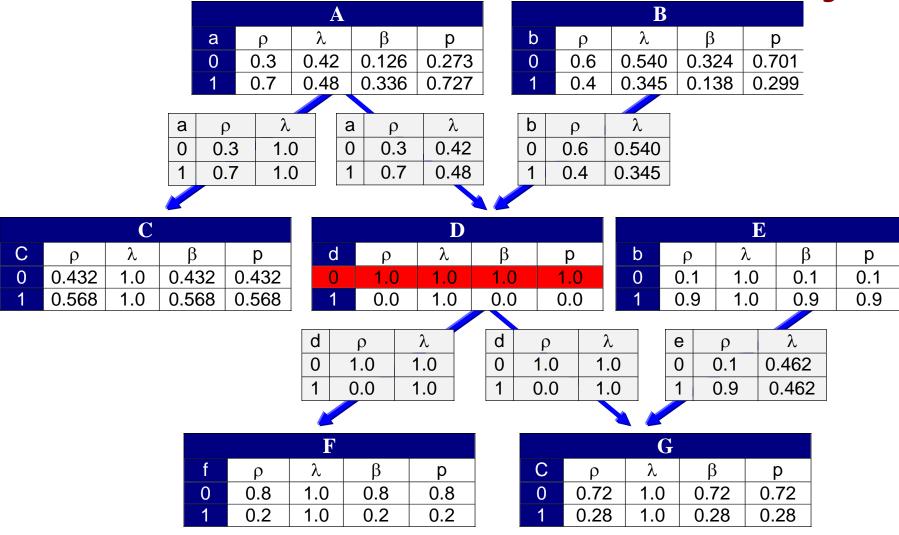






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Summary

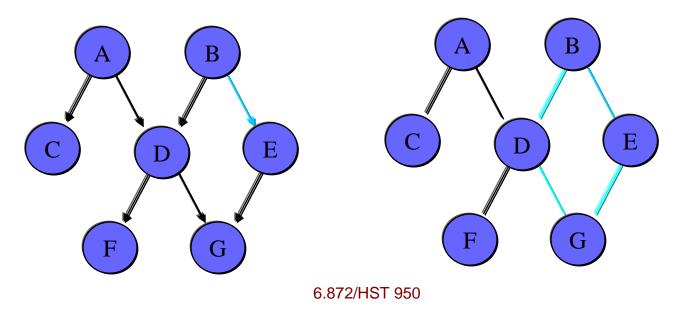




Multiply Connected BBN

When the BBN is a Multiply connected graph

The associated undirected graph contains a loop. Each node does not break the network in two parts. Information may flow through more than one paths. Pearl's Algorithm is no longer applicable.







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Example

A Multiply connected BBN

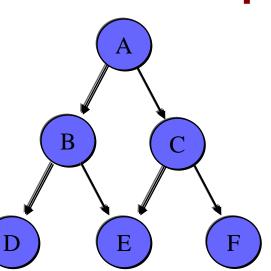
Α	p(A)
0	0.3
1	0.7

Α	B	p(B A)
0	0	0.4
0	1	0.6
1	0	0.1
1	1	0.9

A	С	p(C A)
0	0	0.2
0	1	0.8
1	0	0.50
1	1	0.50

B	D	p(D B)
0	0	0.3
0	1	0.7
1	0	0.2
1	1	0.8

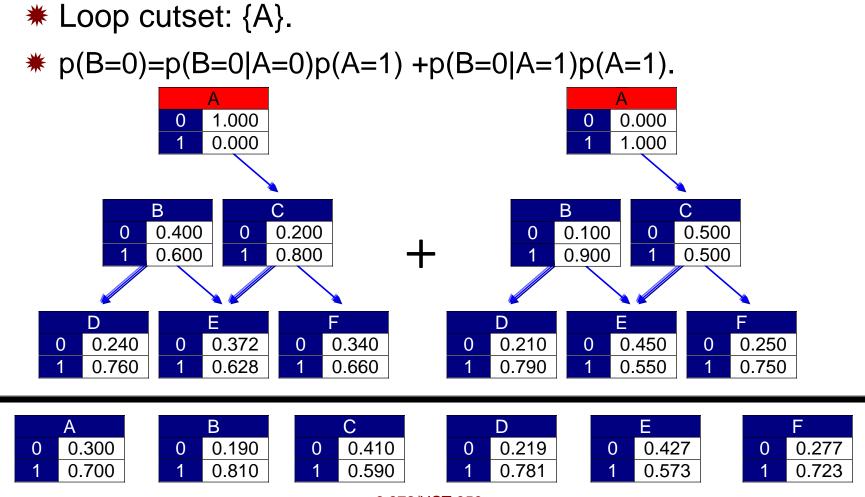
С	F	p(F C)
0	0	0.1
0	1	0.9
1	0	0.4
1	1	0.6



B	С	E	p(E B,C)
0	0	0	0.4
0	0	1	0.6
0	1	0	0.5
0	1	1	0.5
1	0	0	0.7
1	0	1	0.3
1	1	0	0.2
1	1	1	0.8



Conditioning





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Decision Problems

* A Decision Problem has three components:

- ✓ A set of chance variables.
- A set of possible alternative decisions.
- A utility function ranking the possible outcomes.
- * A set of possible decisions is called a strategy
 - An antibiotic is given together vitamins: dosage of antibiotics is one decision, dosage of vitamin another, the strategy identifies the two dosages together.
- * The solution is the strategy that maximizes the expected (value of the) utility. This is called Maximum Expected Utility (MEU) Principle.



Expected Value

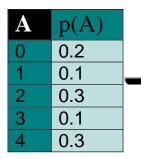
When values are numerical, a BBN can be used to predict the expected value given the evidence:

 $E(A)=\Sigma_i (p(A=a_i) \times a_i)$

that is, the sum of each possible value a_i of A times its probability $p(A=a_i)$ of being assigned to A:

1. Propagate the evidence in the BBN.

2. Apply the formula to calculate expected value.



$$E(A) = (0.2 \times 0) + (0.1 \times 1) + (0.3 \times 2) + (0.1 \times 3) + (0.3 \times 4) = 2.2$$

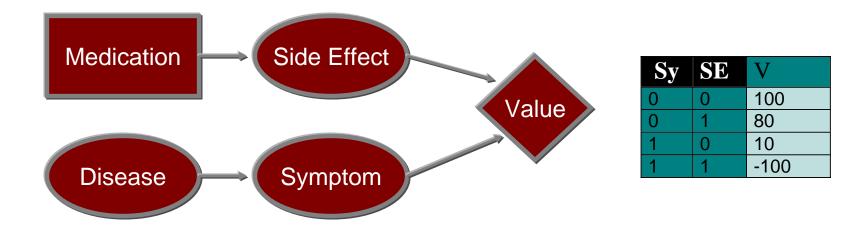




Influence Diagrams

Influence diagram are BBN with 3 kinds of nodes: Chance nodes: stochastic variables (oval) Decision nodes: variables to be set the value (square).

Utility nodes: variables ranking the outcomes.







Making Decisions

* The solution of a decision problem is the decision that maximizes the expected utility, and expected utility is the expected value of a utility node.

