The Model-based Approach to Computer-aided Medical Decision Support

Lecture 4: Causal Independence

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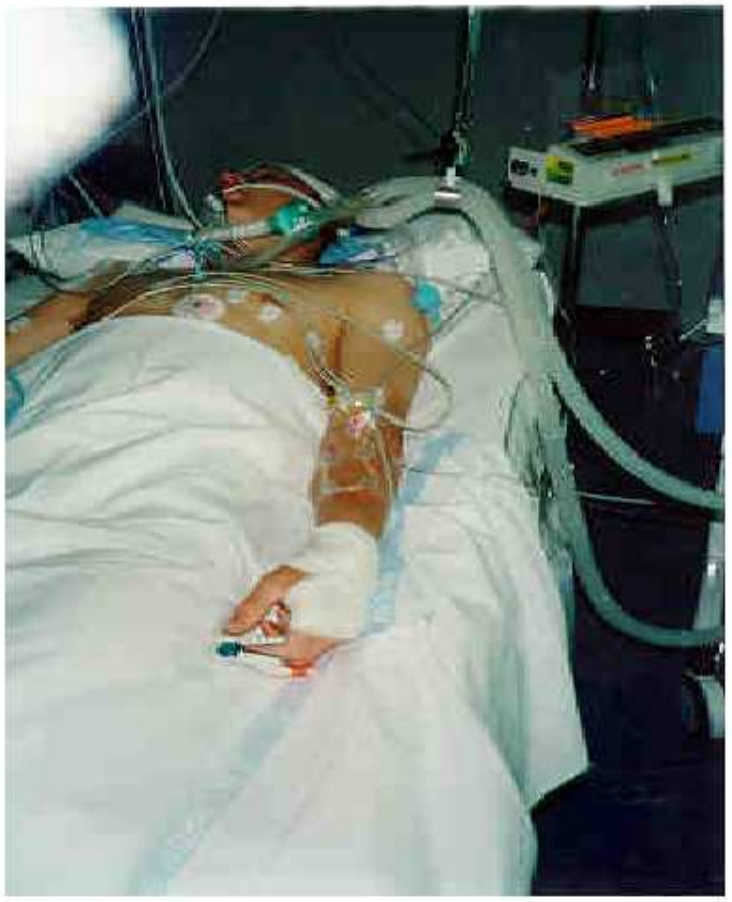
Introduction

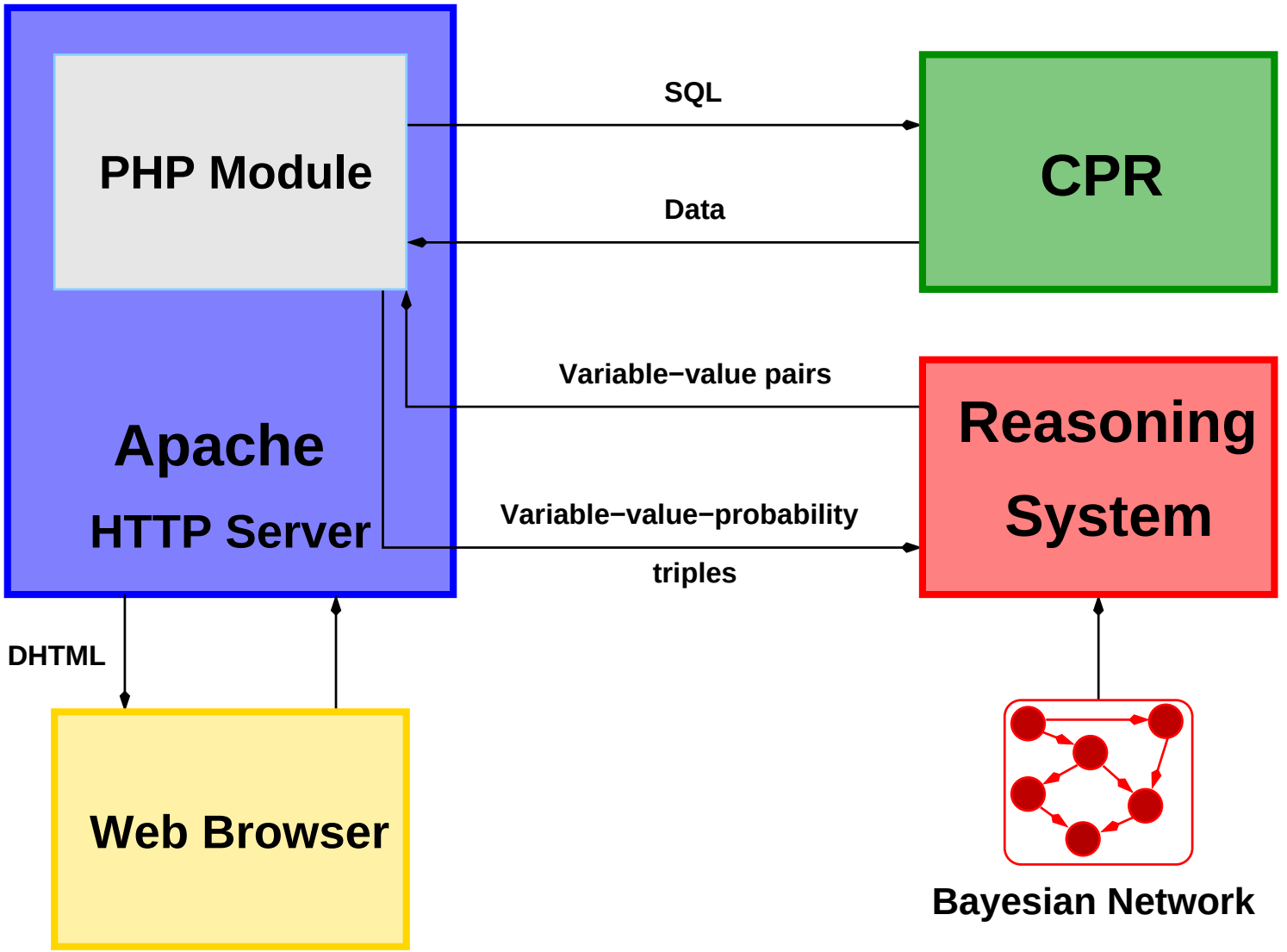
- Clinical decision support, because . . .
  - doctors make more mistakes than you would accept (as a patient)
  - some of their actions are harmful
- Deployment of:
  - probabilistic graphical models
  - logical methods
  - combinations
- Causal modelling for the management of infectious disease (work together with Stefan Visscher) and detection of breast cancer (work with Marina Velikova)

Problem

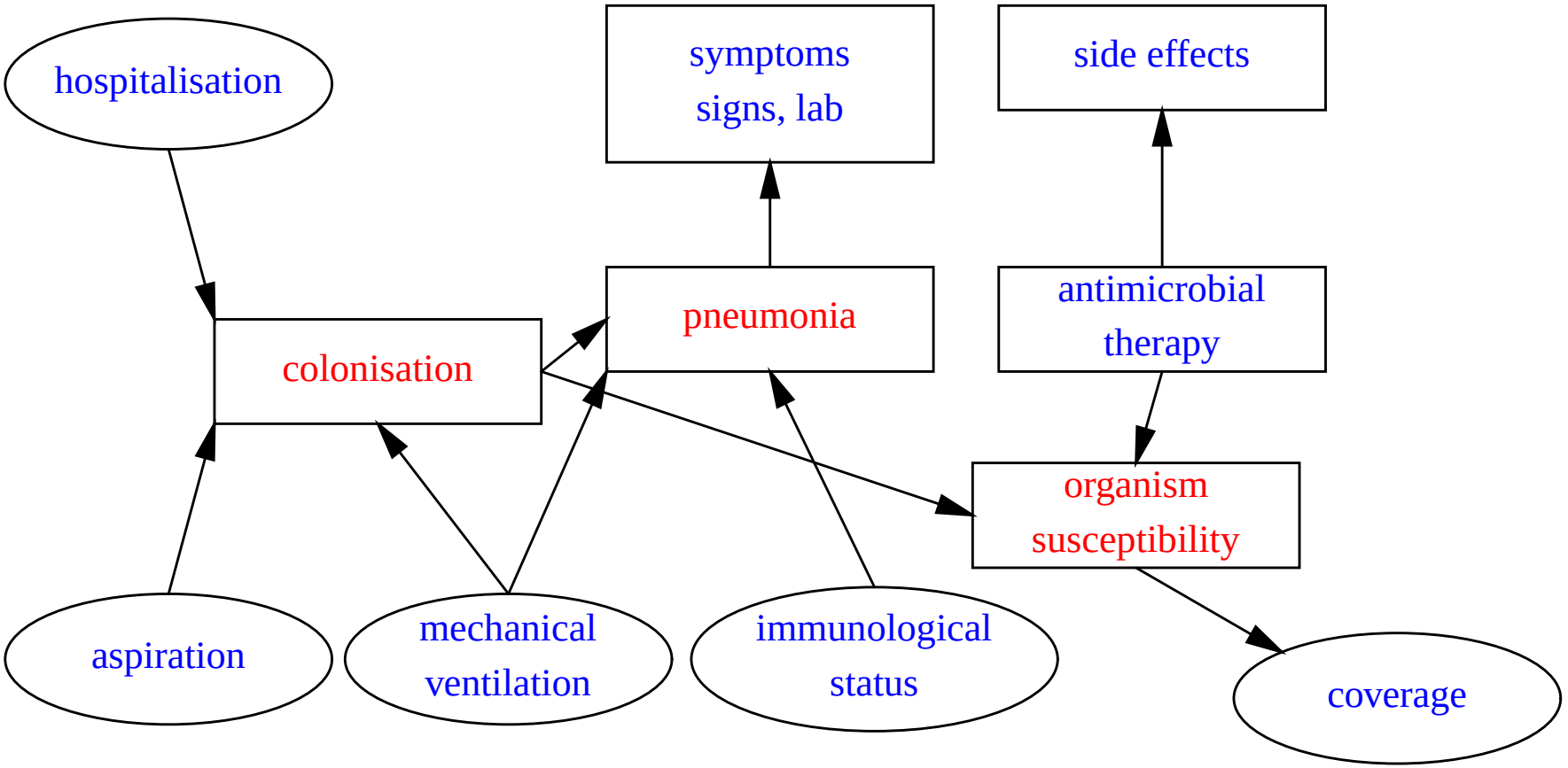


- ICU at Utrecht MC
- Diagnosis and antimicrobial treatment of patients with ventilator-associated pneumonia (VAP)
- About 15-20% of ICU patients develop VAP
- Mortality rate: up to 40%
- Up to 50% of antibiotics in ICUs are prescribed for airway infections

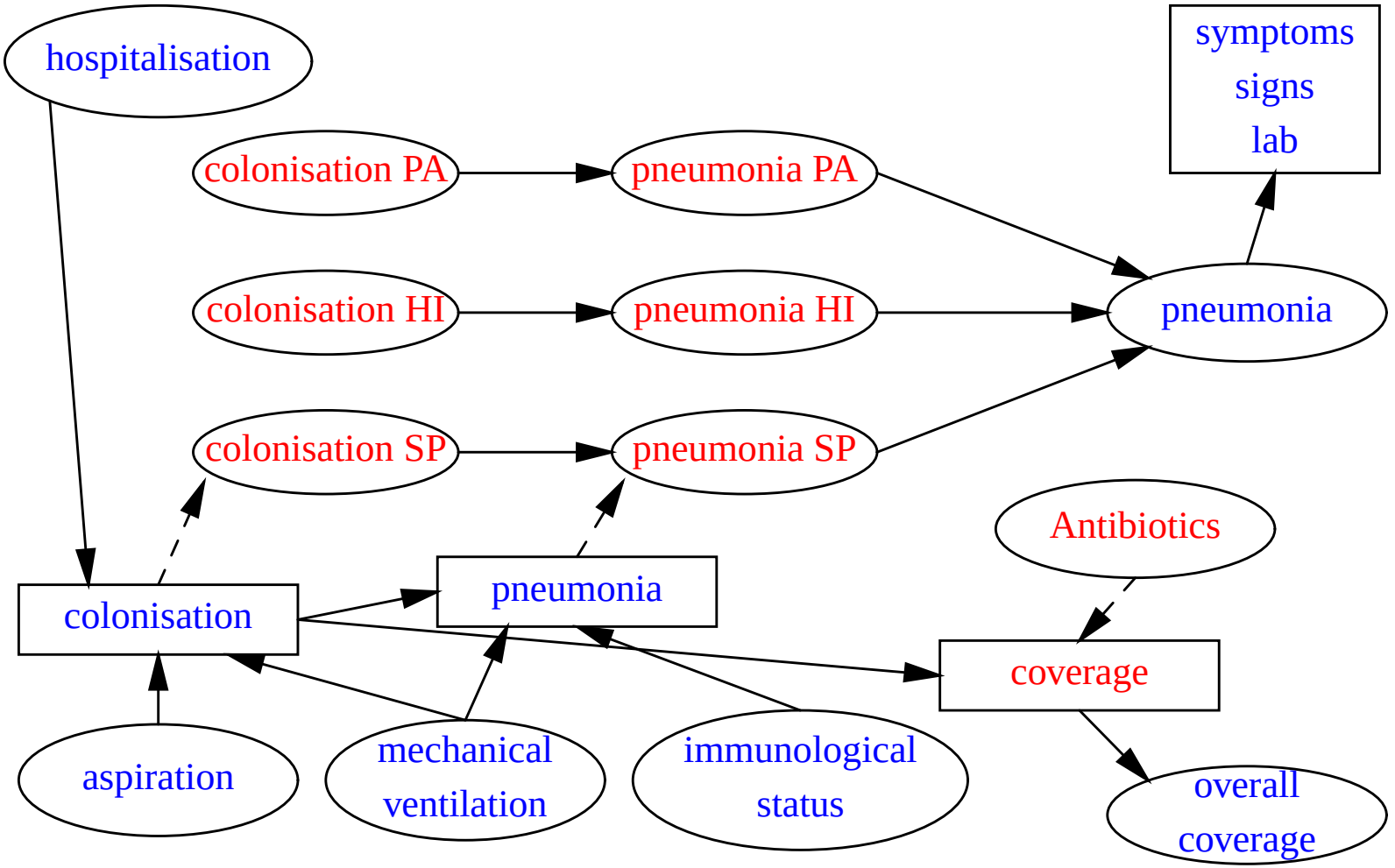
Software Infrastructure



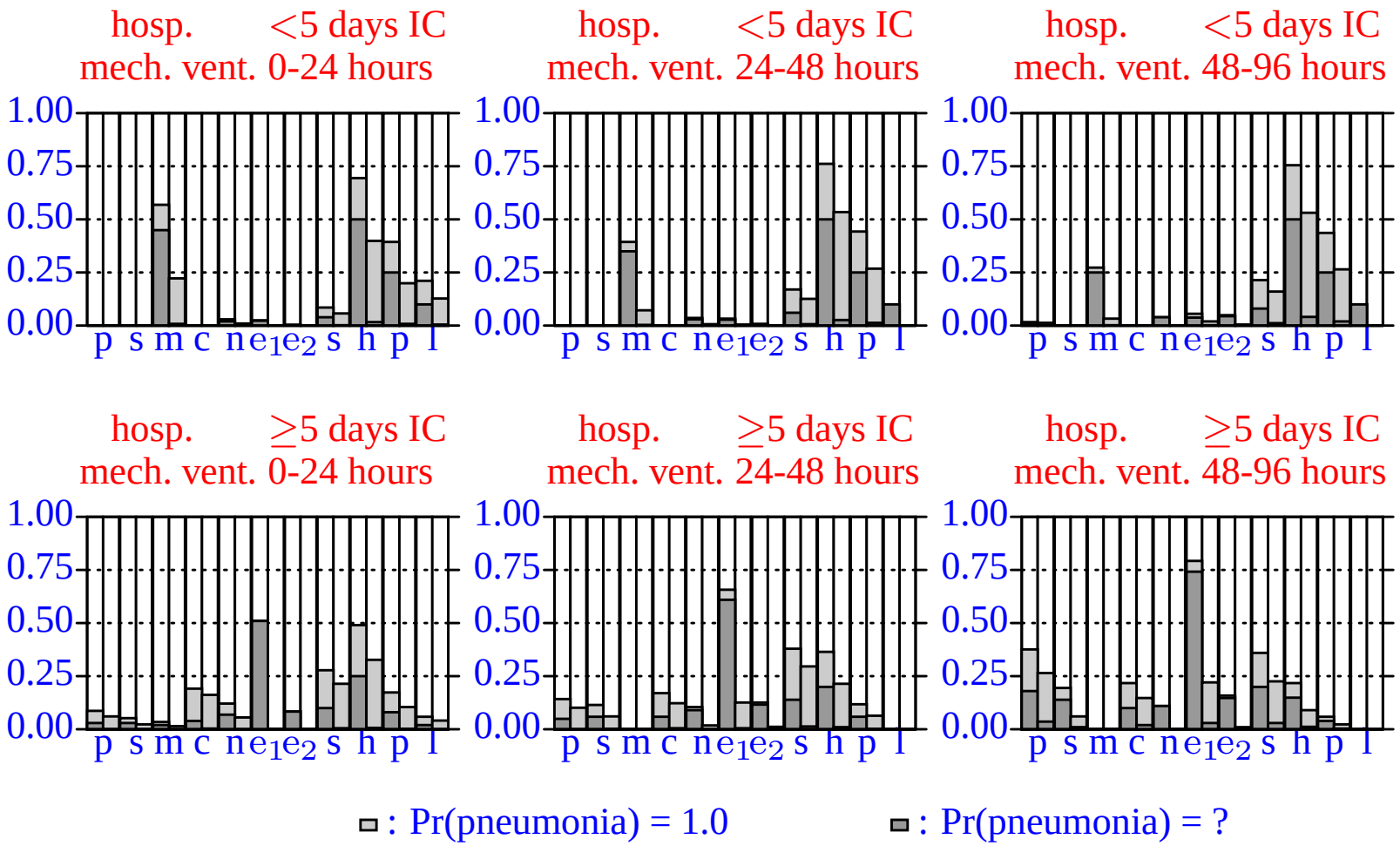
Global Model Pneumonia



Detailed Pneumonia Network



Prediction


hosp. <5 days IC
mech. vent. 0-24 hours
hosp. <5 days IC
mech. vent. 24-48 hours
hosp. <5 days IC
mech. vent. 48-96 hours
hosp. ≥5 days IC
mech. vent. 0-24 hours
hosp. ≥5 days IC
mech. vent. 24-48 hours
hosp. ≥5 days IC
mech. vent. 48-96 hours
1.00
0.75
0.50
0.25
0.00
p s m c n e1 e2 s h p l
: Pr(pneumonia) = 1.0
: Pr(pneumonia) = ?

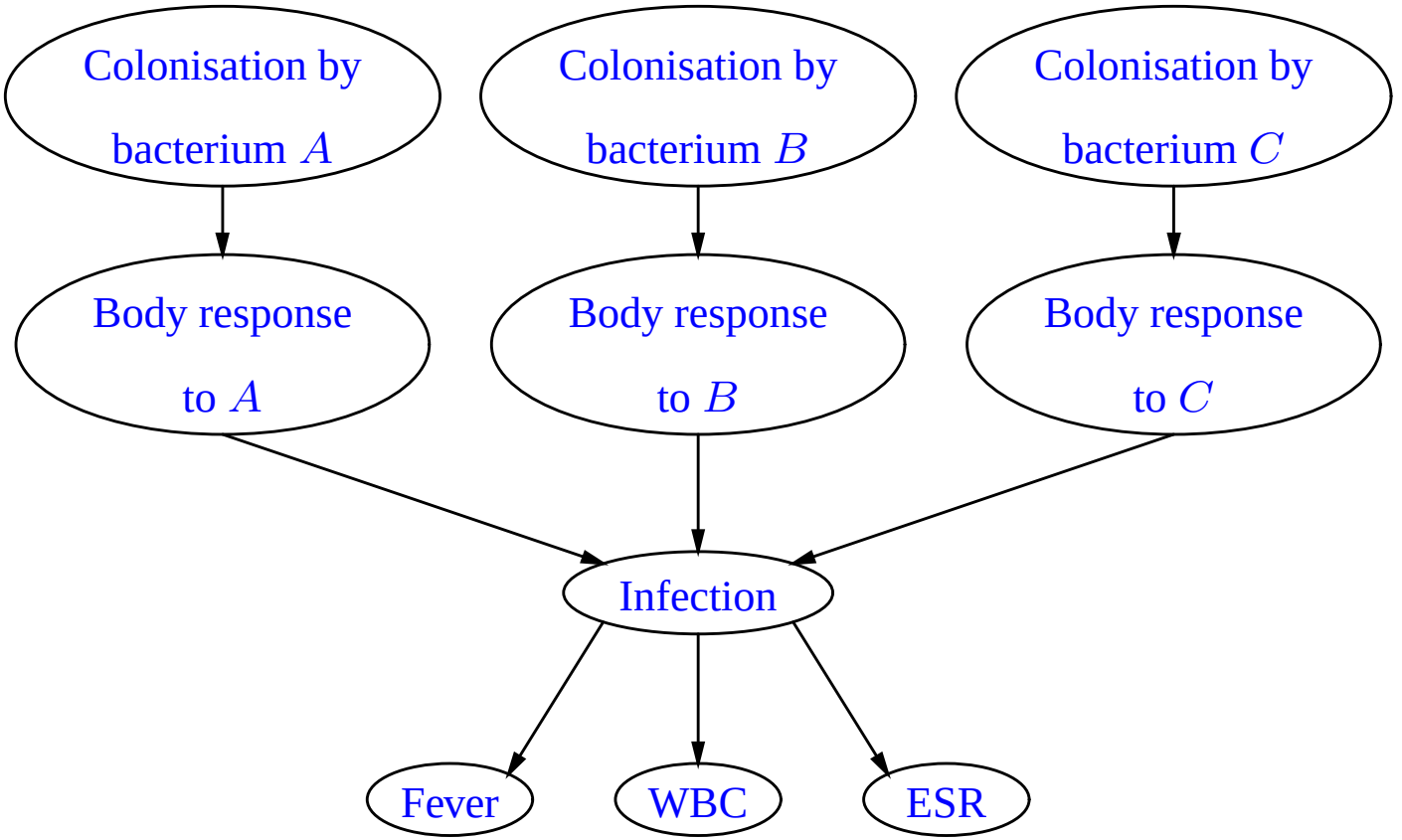
Specification of Interactions

- Compact specification: probability tables

$$P(X_i \mid \text{pa}(X_i))$$

  can still be large even when taking into account independence information
- Easy way to map domain knowledge to entries into a probability table
- Way to use qualitative knowledge about interactions as constraints to probabilistic information
- Might be useful in developing applications

Qualitative Modelling



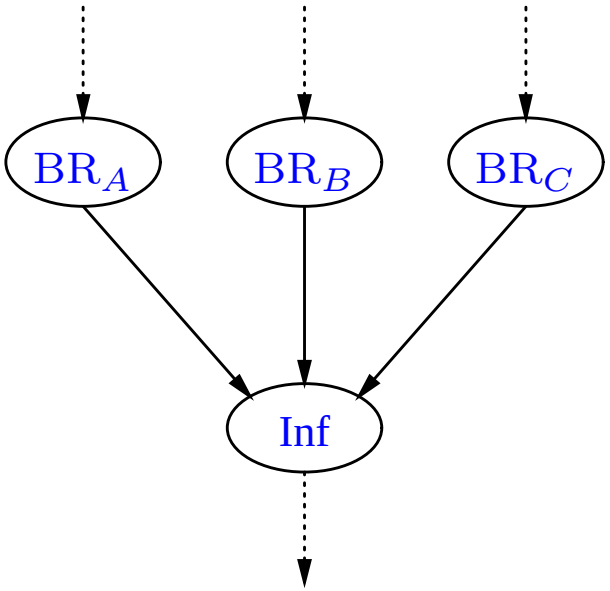
People become colonised by bacteria when entering a hospital, which may give rise to pneumonia

Bayesian-network Modelling

Qualitative Quantitative

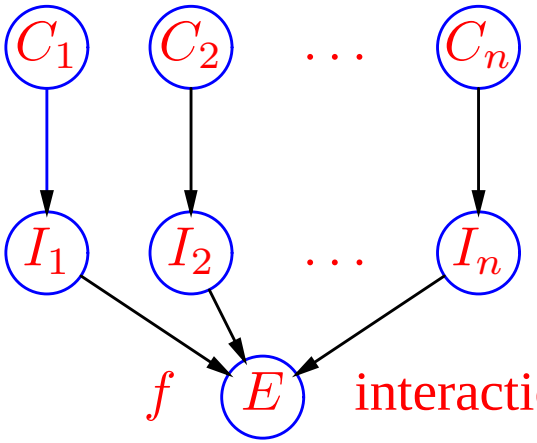
causal modelling *interaction modelling*

Cause $\rightarrow$ Effect $P(\text{Inf} \mid \text{BR}_A, \text{BR}_B, \text{BR}_C)$



	BR_A							
	t				f			
	BR_B				BR_B			
	t		f		t		f	
	BR_C		BR_C		BR_C		BR_C	
Inf	t	f	t	f	t	f	t	f
t	0.8	0.6	0.5	0.3	0.4	0.2	0.3	0.1
f	0.2	0.4	0.5	0.7	0.6	0.8	0.7	0.9

Causal Independence



conditional independence

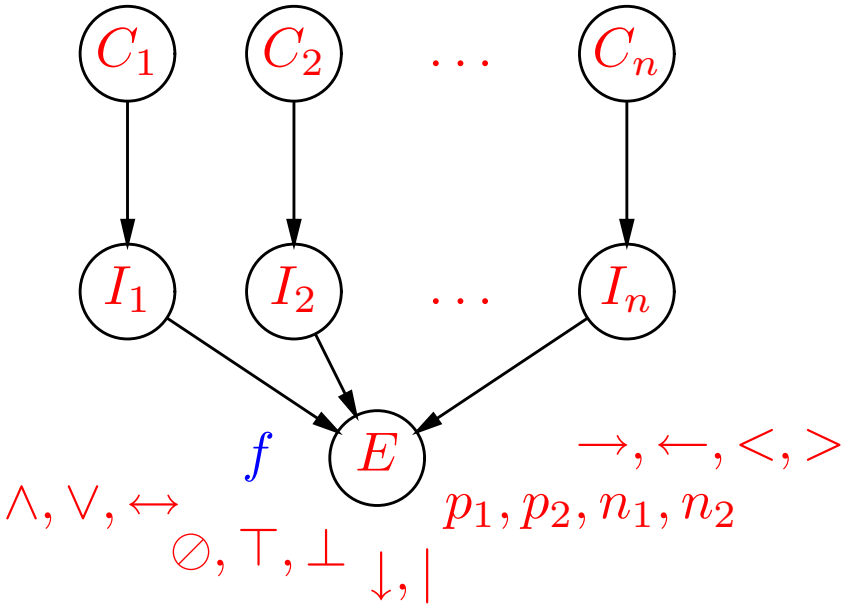
interaction function

$$P(e \mid C_1, \ldots, C_n) = \sum_{I_1,\ldots,I_n} P(e \mid I_1, \ldots, I_n)$$

$$\times \prod_{k=1}^{n} P(I_k \mid C_k) = \sum_{f(I_1,\ldots,I_n)=e} \prod_{k=1}^{n} P(I_k \mid C_k)$$

Note: $P(i_k \mid \bar{c}_k) = 0$ – absent causes don't contribute

Boolean Interaction



- Commutative, associative: $\wedge$, $\vee$, $\leftrightarrow$, $\oslash$, $\top$, $\bot$
- Commutative, non-associative: $\downarrow$, $|$
- Non-commutative, associative: p_1, p_2, n_1, n_2
- Non-commutative, non-associative: $\rightarrow$, $\leftarrow$, $<$, $>$

Symmetric Boolean Functions

Order of arguments doesn't matter; defined in terms of exact function e_k:

$$f(I_1, \ldots, I_n) = \bigvee_{k=0}^{n} e_k(I_1, \ldots, I_n) \wedge \gamma_k$$

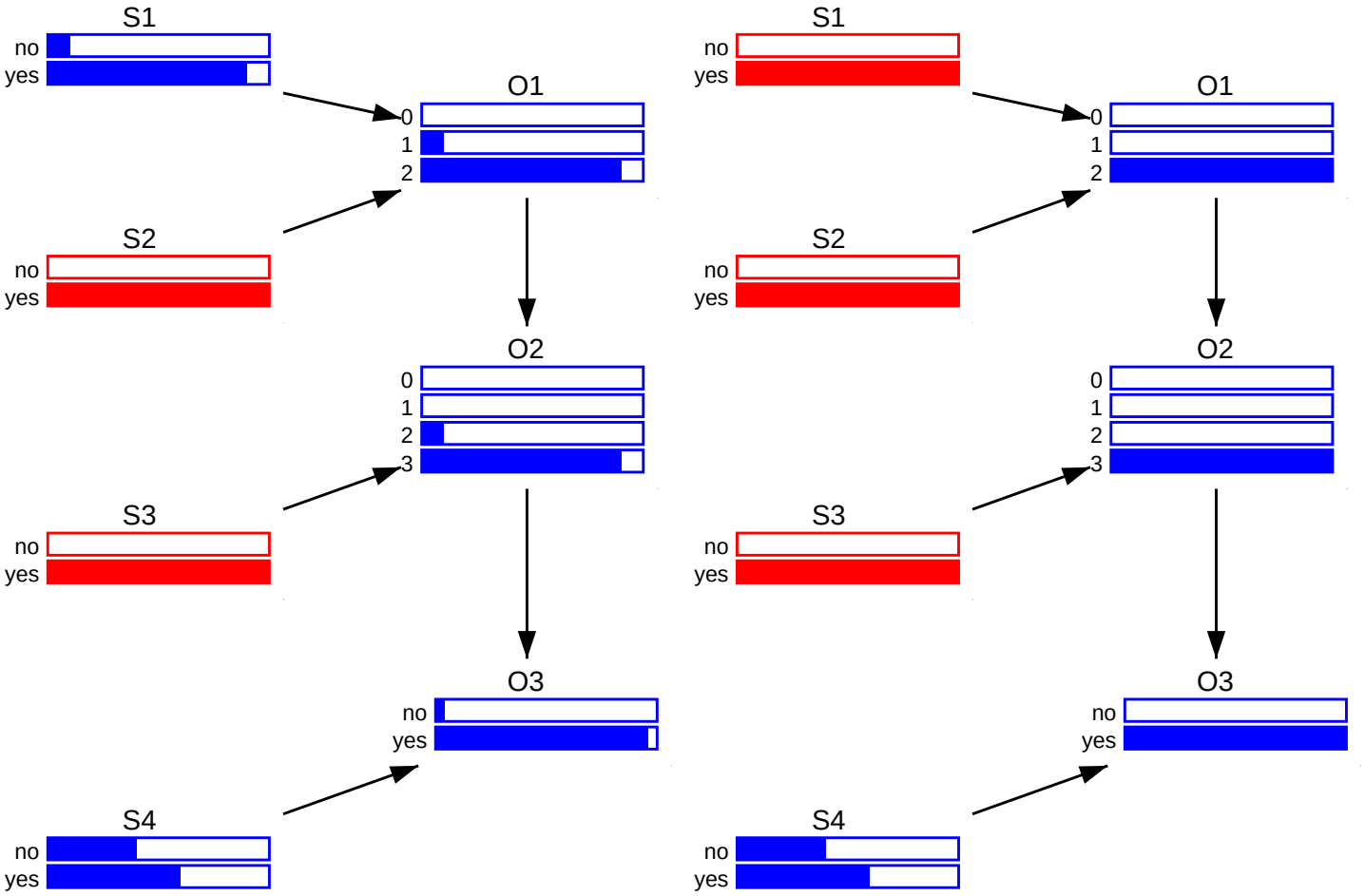
where γ_k are Boolean constants only dependent of the function f

Example: threshold function τ_l:

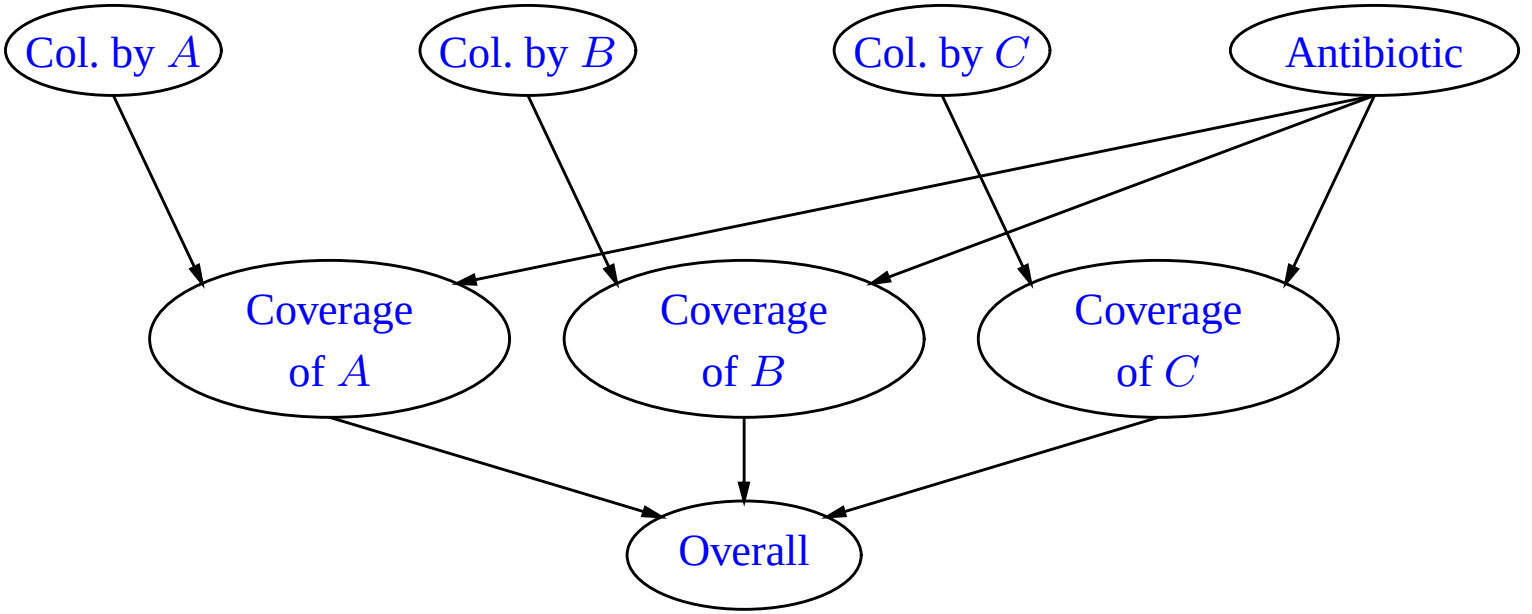
$$\tau_l(I_1, \ldots, I_n) = \bigvee_{k=l}^{n} e_k(I_1, \ldots, I_n)$$

Decomposition by Counting

Threshold function τ_3:



Qualitative Modelling

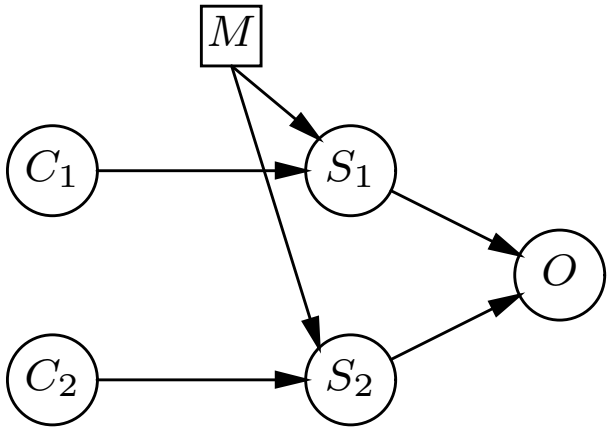


By antibiotic treatment M clinicians try to cover O at most 2 of the bacteria giving rise to pneumonia

$$P(O \mid C_1, \ldots, C_n, M)$$

Overall Susceptibility

$$P_{\tau_k}(o|C_1,\ldots,C_n,M) = \sum_{k\leq l\leq n} \sum_{e_l(S_1,\ldots,S_n)} \prod_{j=1}^{n} P(S_j \mid C_j, M)$$



- C_j: causal factor j
- S_j susceptibility to medication
- M: treatment by antimicrobial medication
- O: overall outcome

Various Models

Conditional probability distributions: $P(S_j \mid C_j, M)$

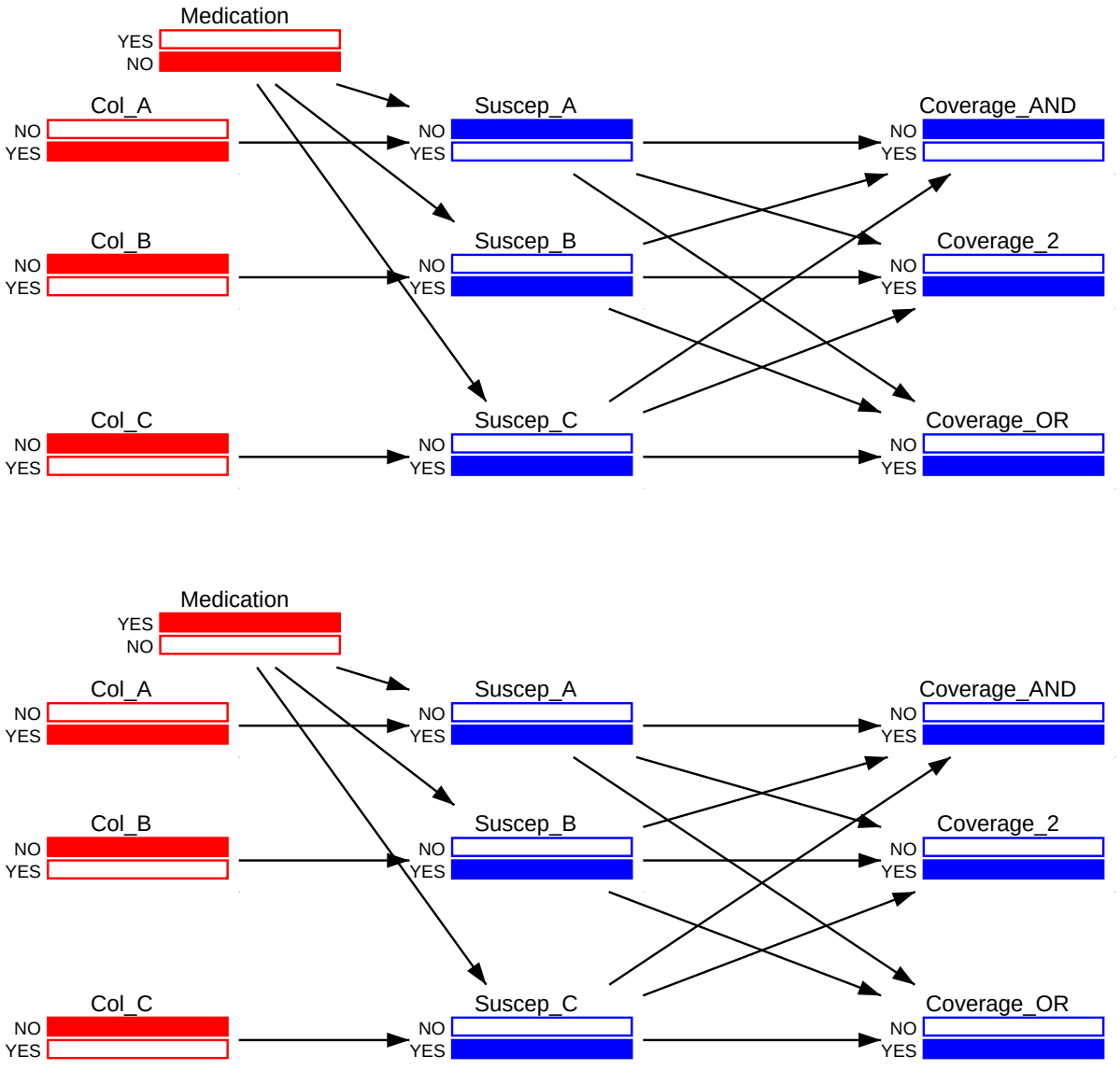
- susceptibility I model:

$$P(s_j \mid C_j, M) = \begin{cases} 0 & \text{if } C_j = \text{yes}, M = \text{no} \\ 1 & \text{otherwise} \end{cases}$$

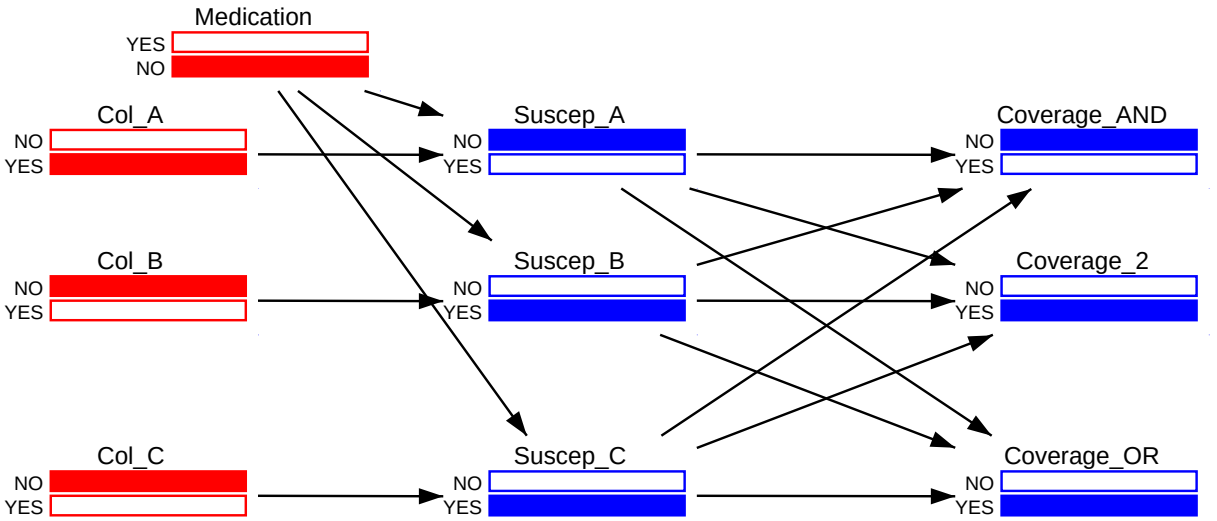
- susceptibility II model: $P(s_i \mid \neg c_i, \neg m) = 1$, whereas $P(s_i \mid \neg c_i, m) = 0$
- susceptibility III model:

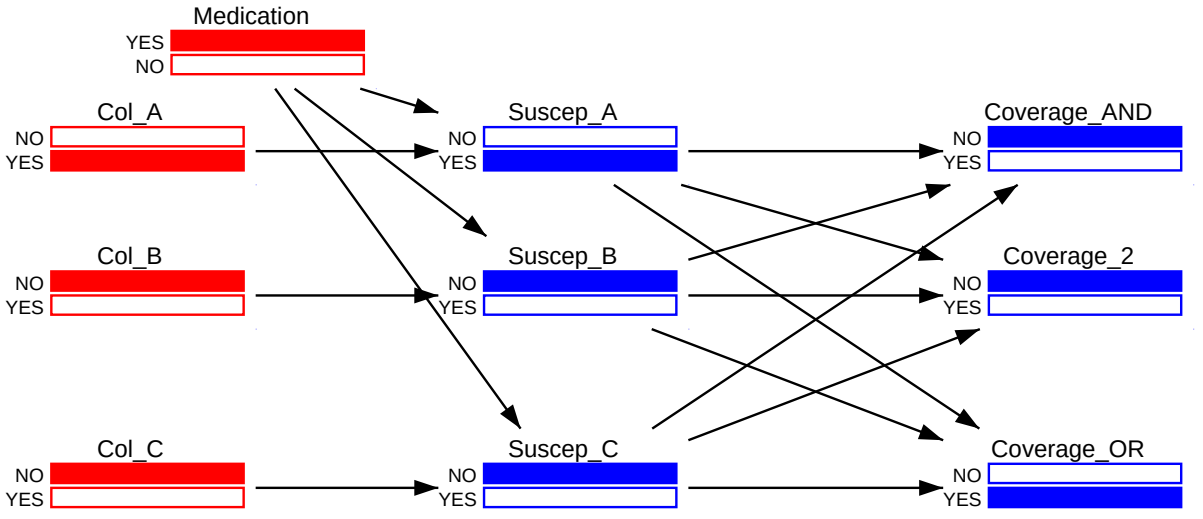
$$P(s_j \mid C_j, M) = \begin{cases} 1 & \text{if } C_j = \text{yes}, M = \text{yes} \\ 0 & \text{otherwise} \end{cases}$$

Model I, Colonised by 1

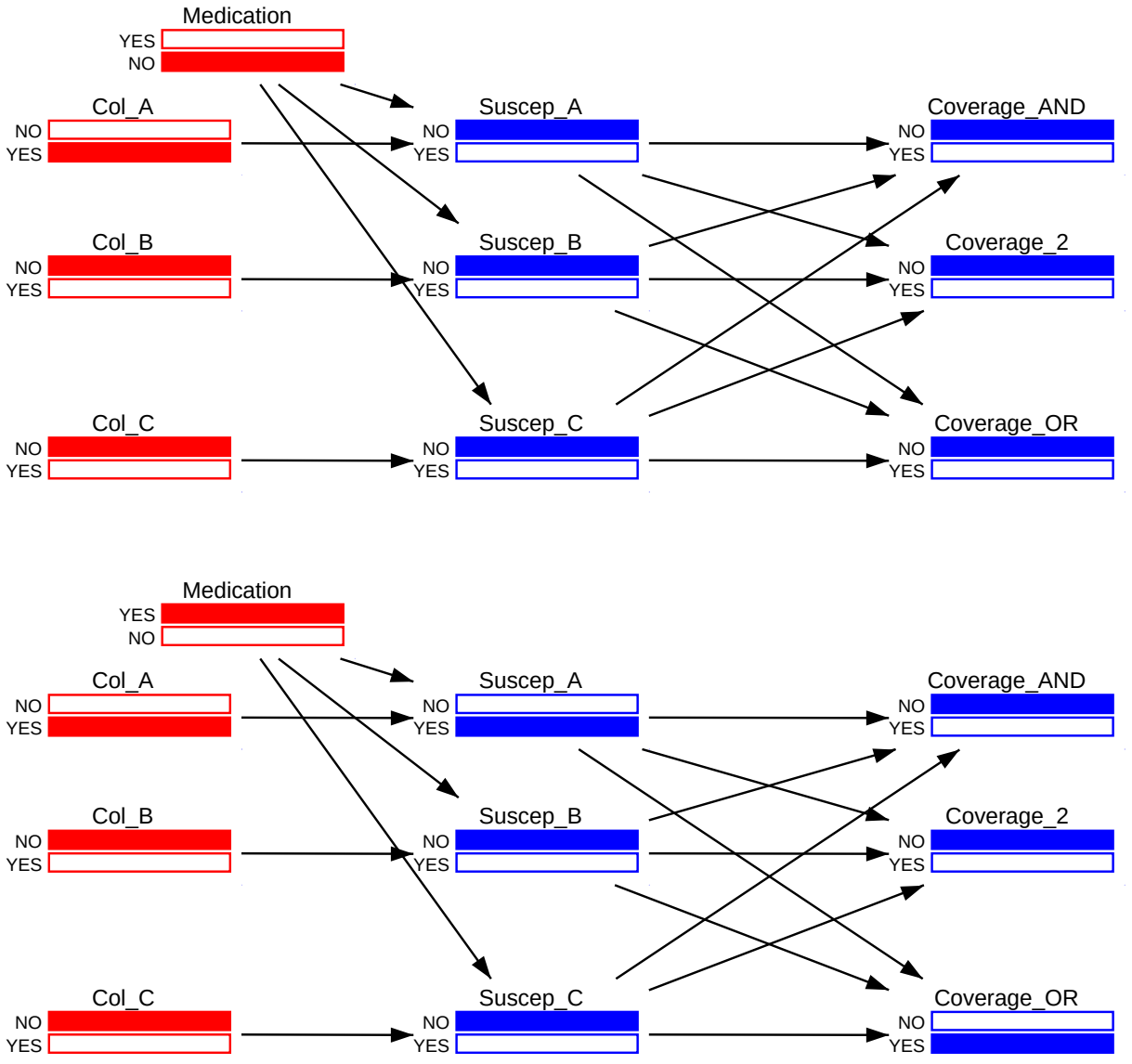


Model II, Colonised by 1

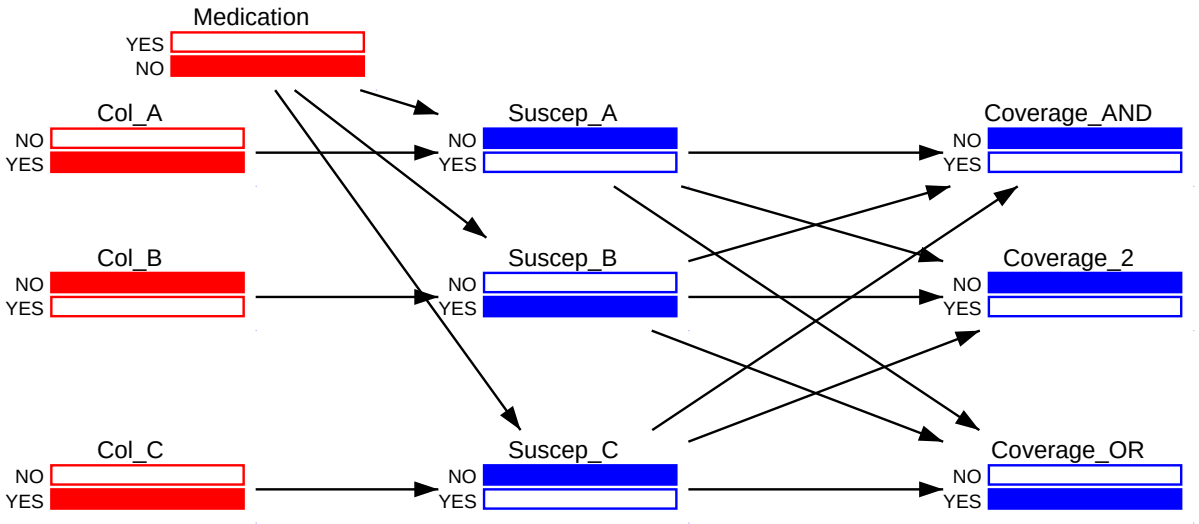


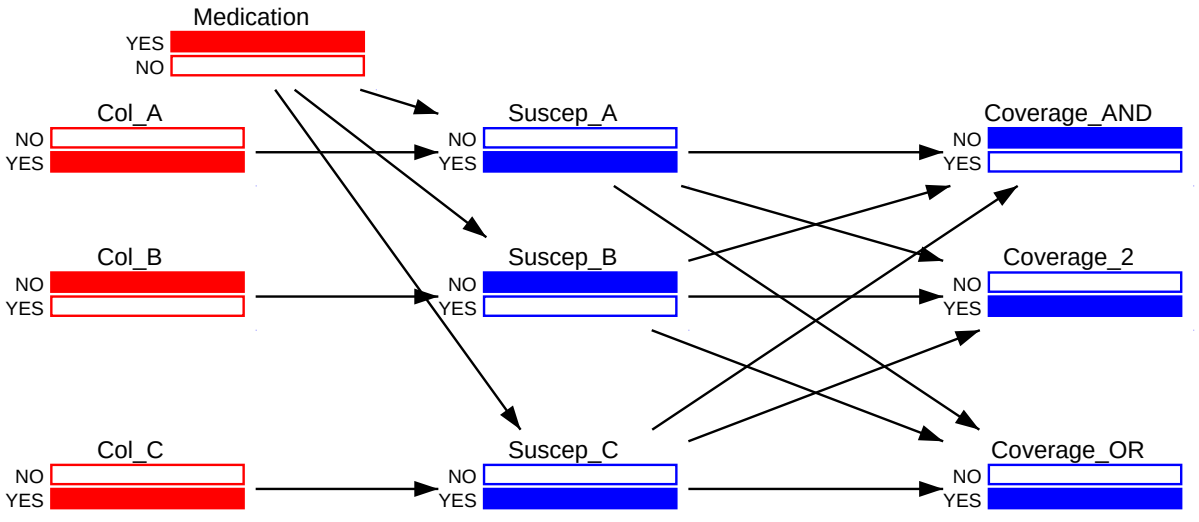


Model III, Colonised by 1



Model II, Colonised by 2





Property

Let $P(E \mid C_1, \ldots, C_n)$ be defined in terms of the Boolean threshold function τ_k using the parameters $P(I_k \mid C_k)$, then:

Theorem: For each k, $0 \leq k \leq n-1$:

$$P_{\tau_k}(e \mid C_1, \ldots, C_n) \geq P_{\tau_{k+1}}(e \mid C_1, \ldots, C_n)$$

Proof:
$P_{\tau_k}(e \mid C_1, \ldots, C_n) + \sum_{e_{k+1}(I_1,\ldots,I_n)} \prod_{j=1}^{n} P(I_j \mid C_j)$
$= P_{\tau_{k+1}}(e \mid C_1, \ldots, C_n)$, and
$\sum_{e_{k+1}(I_1,\ldots,I_n)} \prod_{j=1}^{n} P(I_j \mid C_j) \geq 0$

Predicting Optimal Treatment

153 patients with VAP using the **(SIII,** $k = 1$**)** model

				Antibiotic coverage										
	n	Bac	m	A	B	C	D	E	F	G	H	I	J	K
early	2		13		96					97		100		0
	1	SA	25					94			72	100	72	0
		HI	8	94	99		99					100		0
		SP	3	71	97	65	97					100		0
late	2		33						96			100		0
	1	PA	19				85		91			88		0
		AC	6					92	81			100		0
		Ent1	29				88	89	96			100		0
		Ent2	17					48	98	90		96		0

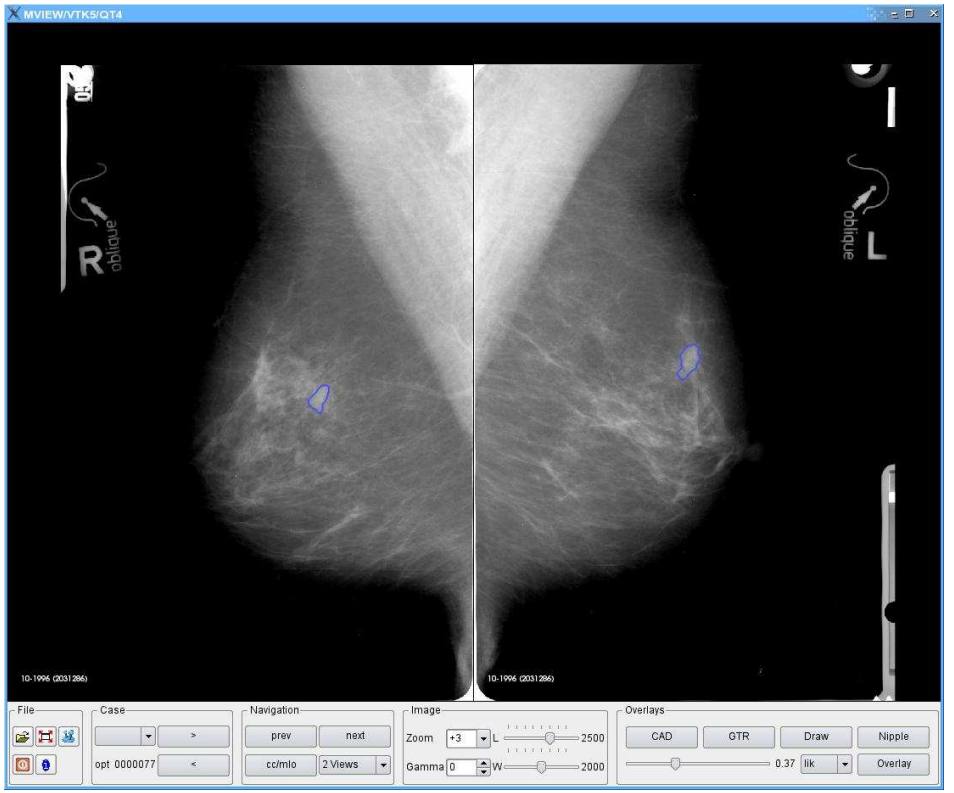
Predicting Optimal Treatment

153 patients with VAP using the **(SIII,** $k = 2$**)** model

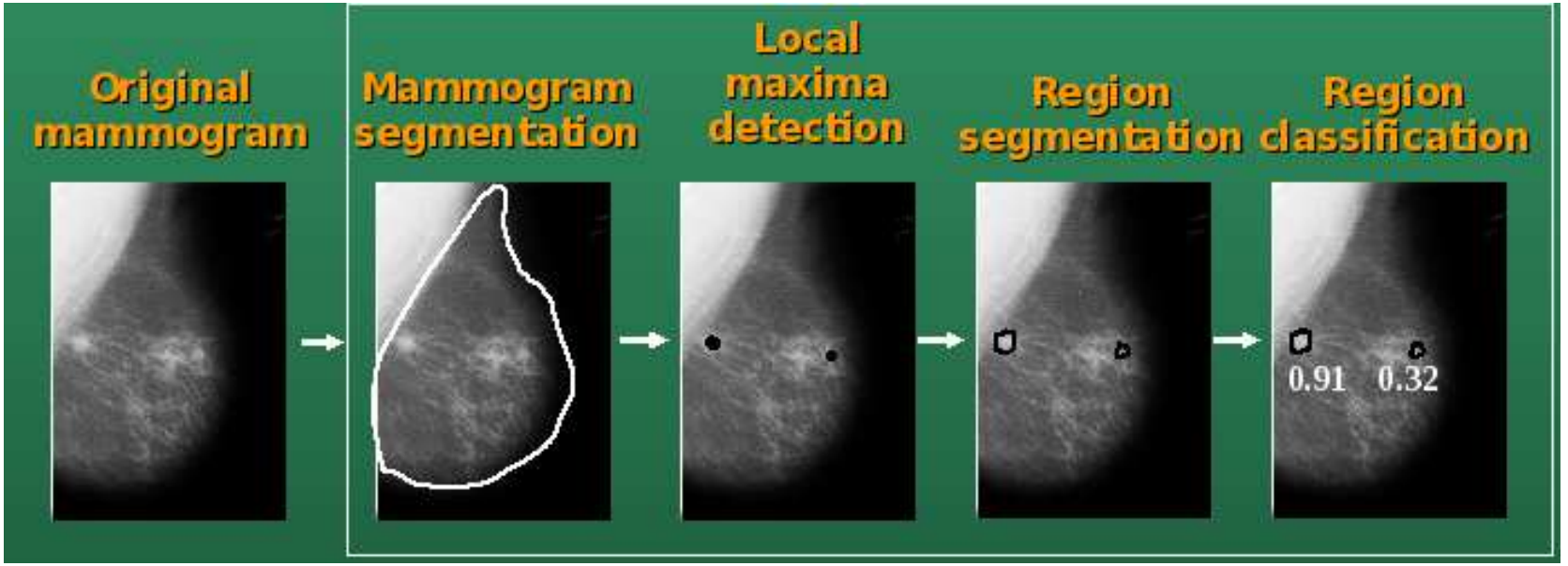
				Antibiotic coverage										
	n	Bac	m	A	B	C	D	E	F	G	H	I	J	K
early	2		13		67					72		85		0
	1	SA	25					42			25	67	28	0
		HI	8	31	34		41					50		0
		SP	3	27	47	0	43					67		0
late	2		33						67			79		0
	1	PA	19				22		26			28		0
		AC	6					13	8			17		0
		Ent1	29				22	10	28			31		0
		Ent2	17					23	40	37		46		0

Image Interpretation

- national breast cancer screening programme
- decision-making under uncertainty
- interpretation of image features in terms of probabilistic graphical models
- from single- to multi-view interpre-tation

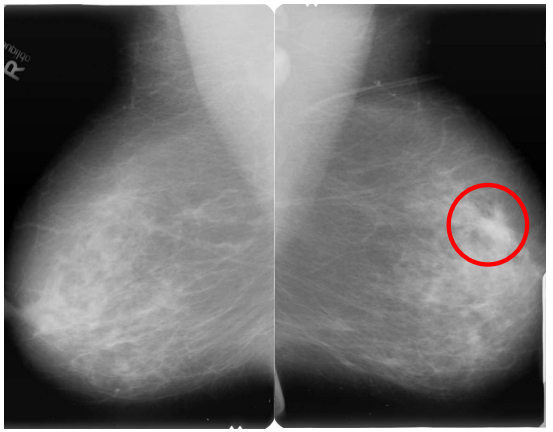


Singleview CAD System

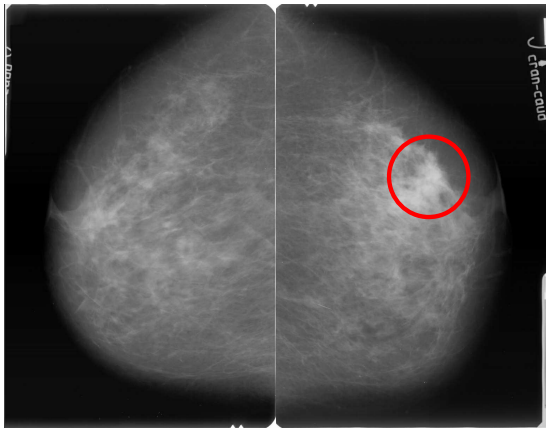


- Region features: contrast, size, location, margin, spiculation, etc.
- Advantage: a good detection rate per image
- Shortcoming: unsatisfactory performance at a patient level because views are treated independently

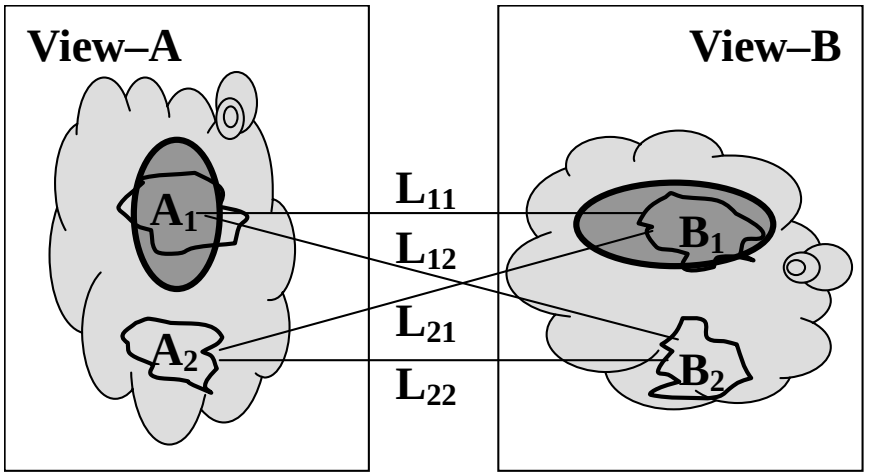
Multiview Interpretation



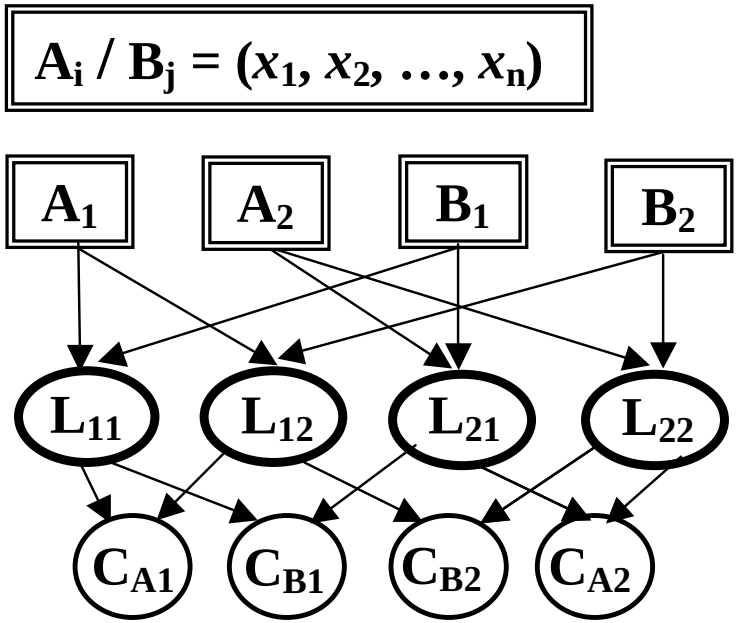
Mediolateral oblique view



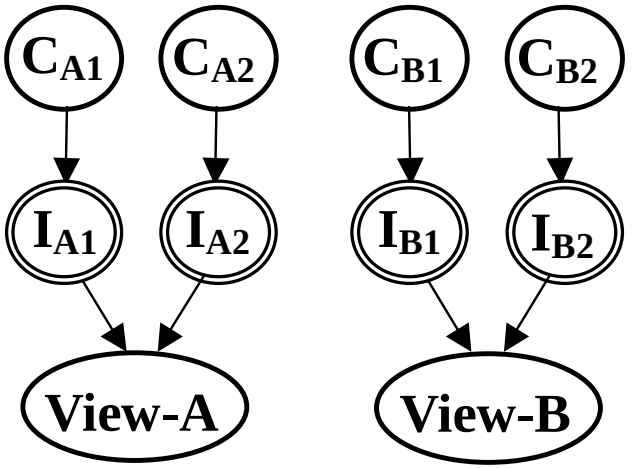
Craniocaudal view



Multiview Bayesian Network



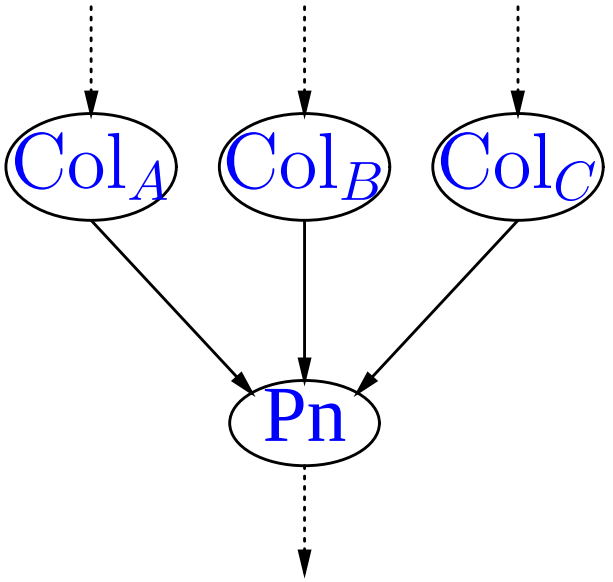
a) **RegNet**



b) **ViewNet**

- Interpretation of regions of interest (real-valued feature vector): logistic regression
- Combination of region and view information: causal independence

Conclusions



Use of modelling approach:

- Select the right qualitative pattern
- Select the right Boolean interaction function
- Fill in arc probabilities $P(I_k \mid C_k)$

Some future work:

- Study learning of interaction functions from data
- Study other interaction patterns

[See: Artificial Intelligence, vol. 163, pp. 233–263, 2005; Artificial Intelligence in Medicine, vol. 46, pp. 251–266, 2009; Physics in Medicine and Biology, vol. 54, pp. 1131–1147, 2008]