

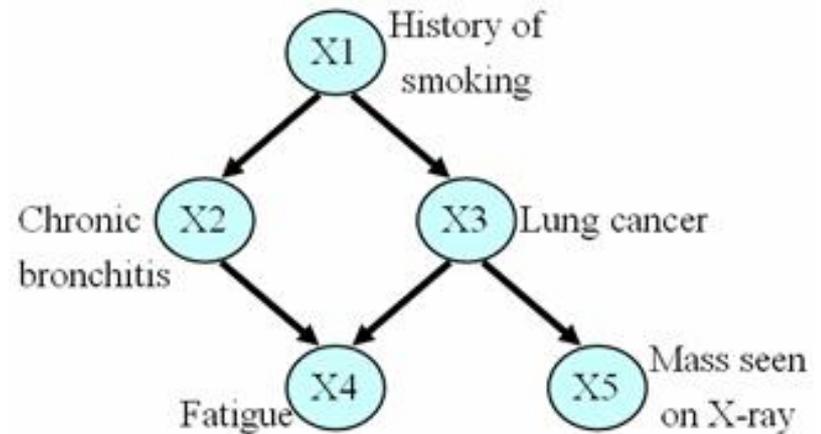
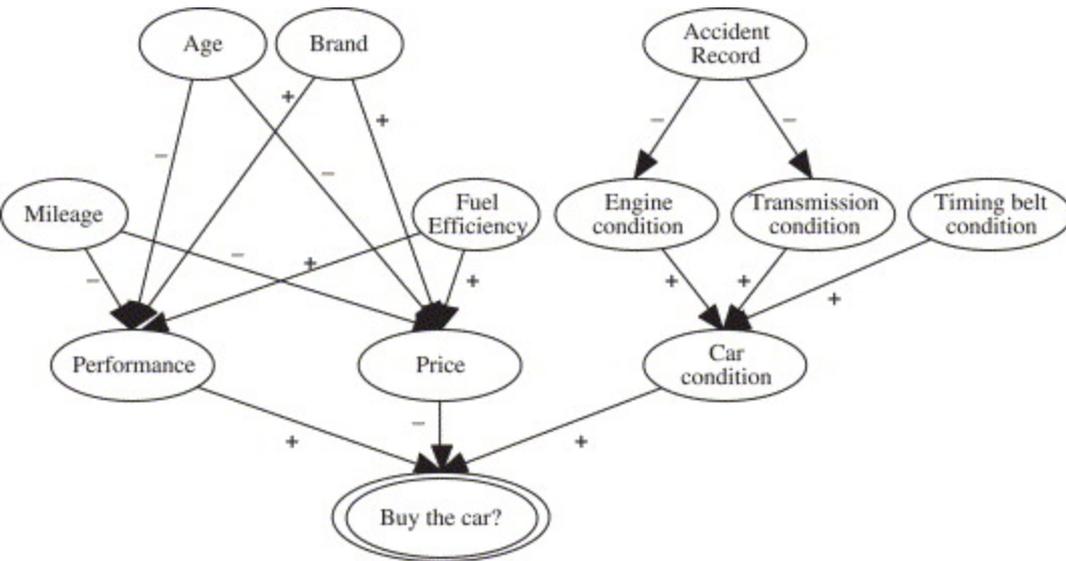
Application of AOP in the Bayesian network ITS framework to assess skin sensitization



The power to transform.

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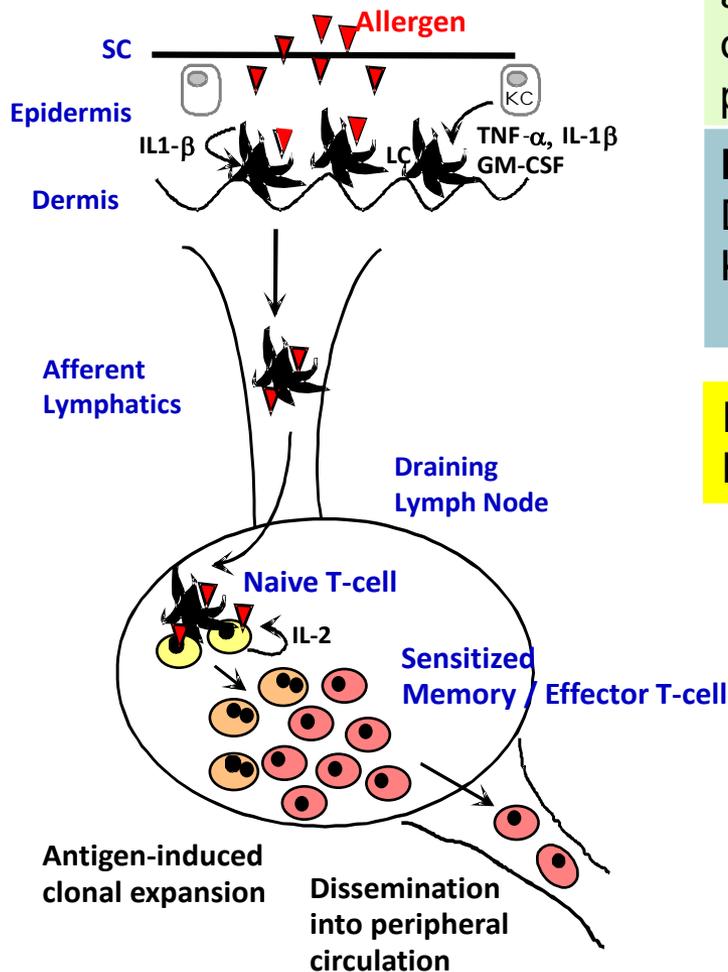
Causal map - directed graphs that represent the cause-effect relations embedded in experts' thinking



Mechanism of Contact Sensitization

LLNA

Sensitization Phase



Bioavailability data: Phys-chem properties (Kow, Ws) and kinetic parameters in epidermis from a simulation of exposure in a LLNA test AUC_{120} , C_{free} , serum protein binding (PPB)

Reactivity data

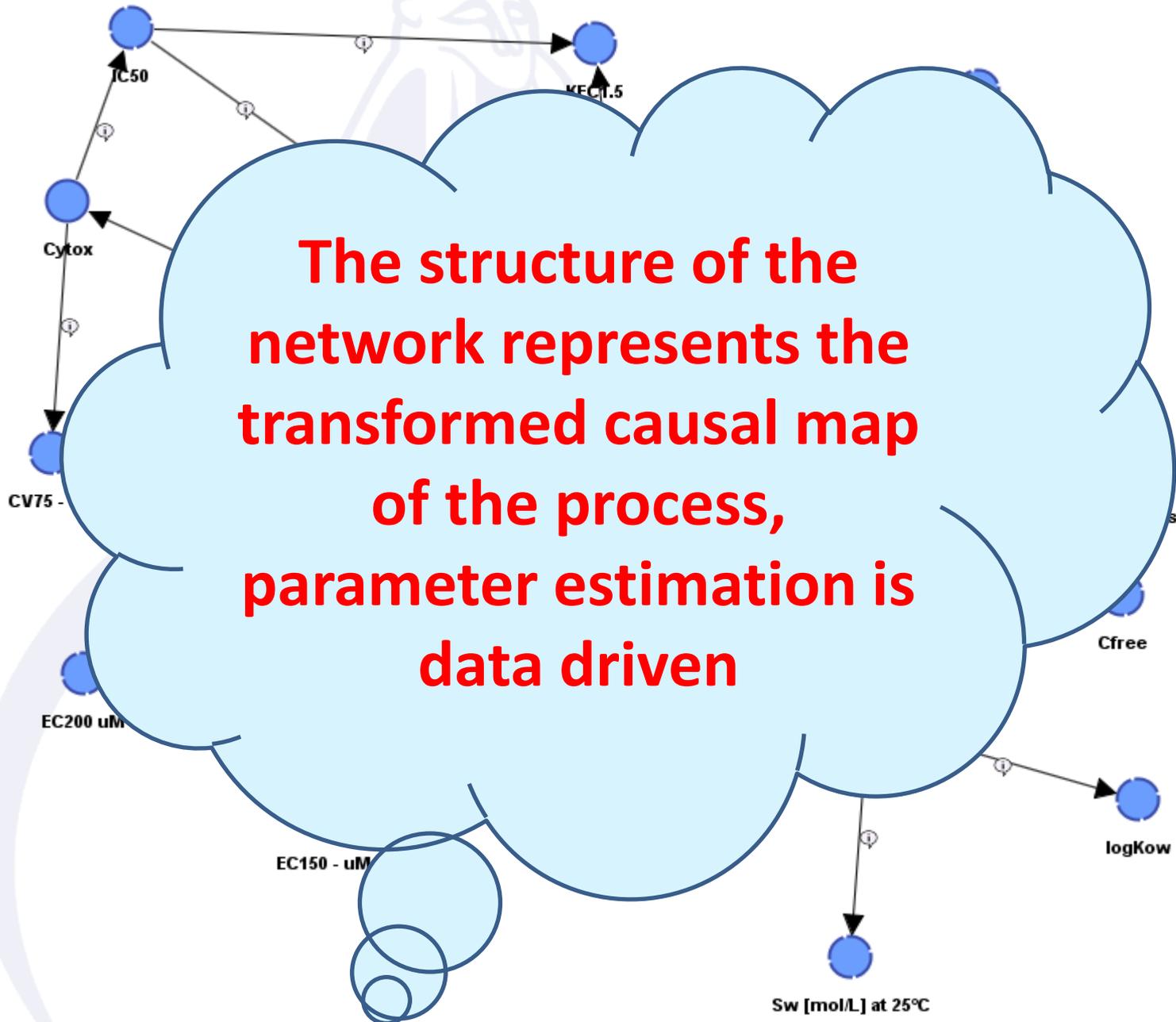
Direct Peptide Reactivity Assay (DPRA)
KeratinoSens Assay (KEC 1.5, KEC3, IC50)

Dendritic cells activation:

hCLAT (EC150, EC200, CV75)

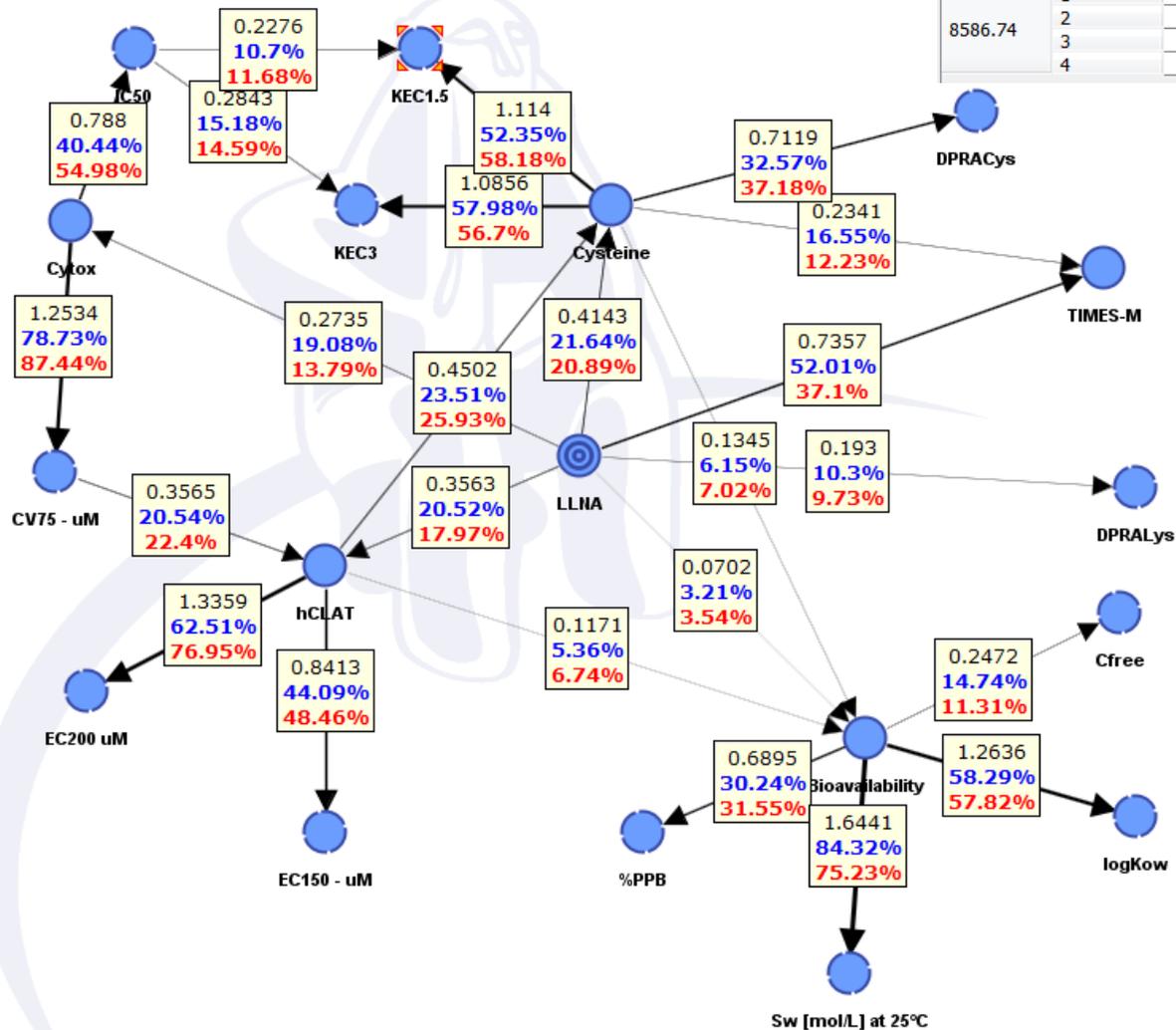
TIMES-M

The structure of the network represents the transformed causal map of the process, parameter estimation is data driven

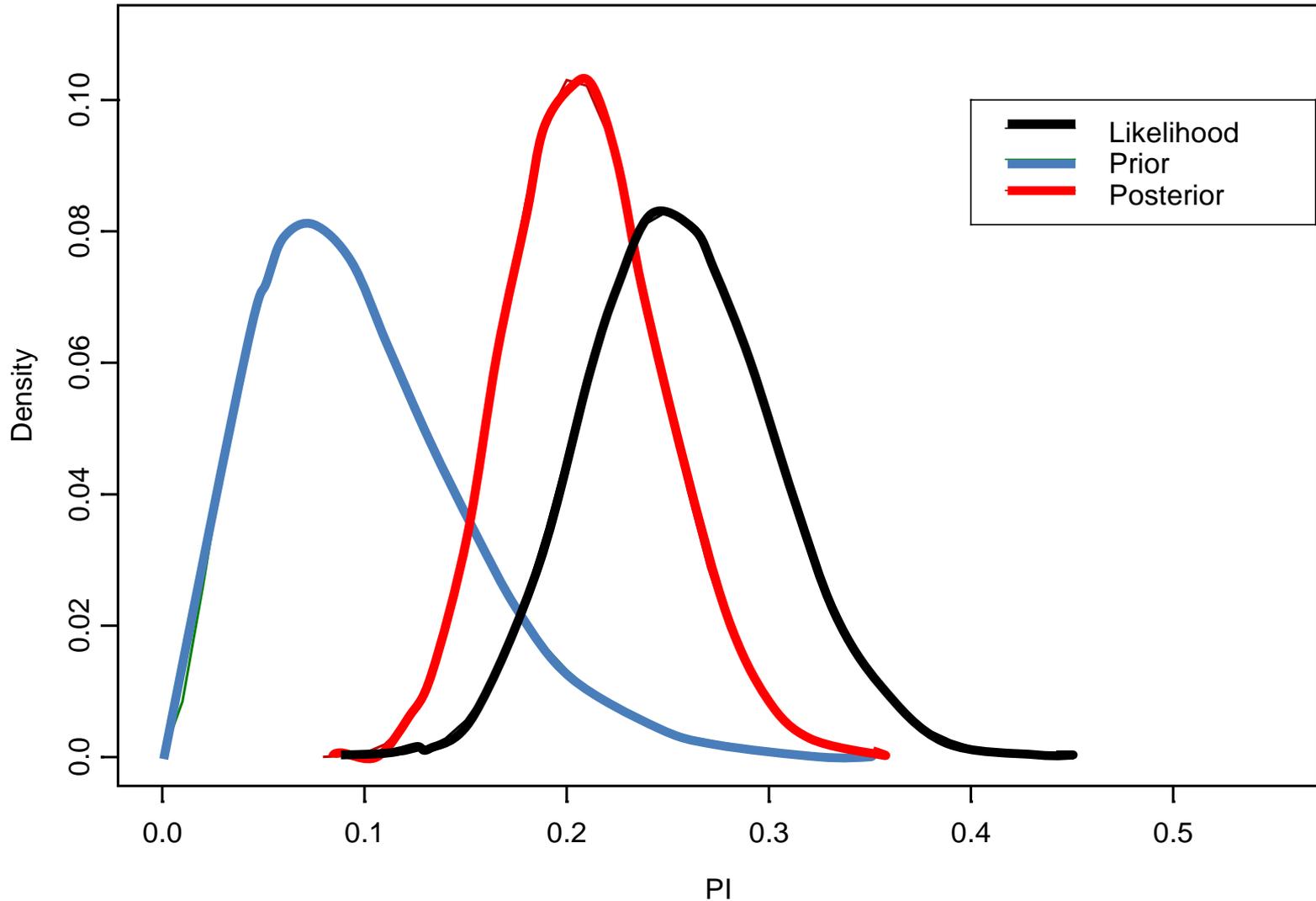


- In black, the mutual information of the arc.
- In blue, the relative mutual information in the direction of the arc.
- In red, the relative mutual information in the opposite direction of the arc.

hCLAT	LLNA	45.819153	59.484303	112.02059	232.44417	1059.1002
525.98236	1	1.176	1.176	1.176	1.176	95.294
	2	0.138	0.138	66.345	11.172	22.207
	3	7.200	28.533	35.644	7.200	21.422
	4	20.000	39.753	39.753	0.247	0.247
2441.1626	1	20.000	20.000	20.000	20.000	20.000
	2	20.000	20.000	20.000	20.000	20.000
	3	97.576	0.606	0.606	0.606	0.606
	4	64.089	28.533	0.089	7.200	0.089
2686.893	1	0.247	0.247	0.247	0.247	99.012
	2	0.247	0.247	59.506	0.247	39.753
	3	0.247	0.247	20.000	0.247	79.259
	4	0.408	33.061	0.408	33.061	33.061
8586.74	1	0.039	0.039	6.277	3.158	90.487
	2	0.073	11.795	11.795	5.934	70.403
	3	5.934	29.377	23.516	0.073	41.099
	4	0.308	0.308	0.308	24.923	74.154



Hypothesis (prior, $P(H)$) \times evidence (likelihood, e) =
Revised hypothesis (posterior, $P(H|e)$)



Decision rules – towards Bayes factor

chemical	LLNA. NonSens	LLNA. Weak	LLNA. Moderate	LLNA. Strong	Most likely	Bayes Factor
Triethanolamine	0.35	0.17	0.40	0.08	M	2
Vinyl acetate	0.01	0.12	0.70	0.16	M	7
Phenol	0.94	0.00	0.04	0.02	NS	48
Benzen 1-methoxy-4-methyl-2-nitro	0.38	0.16	0.37	0.09	NS	1.8
2-Phenoxyethanol	0.54	0.15	0.29	0.02	NS	2.5

Prior : NS=0.28, W=0.23, M=0.28, S=0.20

If you are interested details of ITS-3

- Tue, Aug 26th session IIa – skin sensitization
- Tue, Aug 26th session II-5 – decision making