Statistical analysis in risk assessment of chemicals

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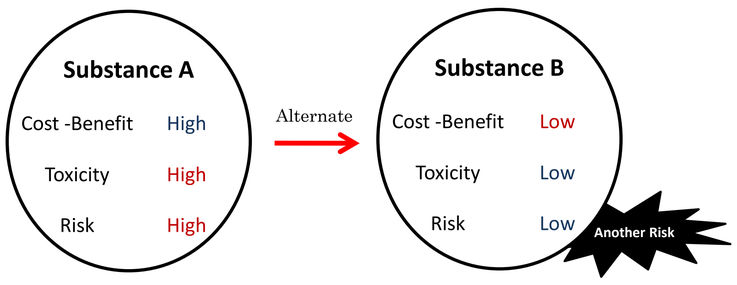
OUTLINE

Our aim is to construct a statistical model and the inference algorithm that provide a theoretical proof for the risk assessment of chemicals. In this talk, we introduce a graphical modeling that is suitable for the representation of the causal relations with uncertainty. It becomes better combining existing statistical tools such as EM-algorism, latent variables and so on. Our approach is challenging, but substantial progress can be made.

Risk Trade-off of Chemicals

Once we find toxicity of the substance A, ….



Another risk may offset the reduction in the target risk

Risk Trade-Off

In order to promote appropriate assessment and management of chemical risks, it is necessary to construct the evaluation system which makes it possible to quantify and compare the risk of the substance and its alternative.

Statistical Tools

We use a graphical model to describe the relativity among the markers.

Extensions

EM algorithm is a technique for analysing the data with missing value.

EM Algorithm

Incomplete Data

Substance	Sex	Dose	Effect
A	雄	0ppm	0
A	雄	400ppm	0
A	雌	NA	1
A	NA	2000ppm	1
A	雄	400ppm	NA
B	NA	100ppm	NA
…	…	…	…
Z	雌	2000ppm	1

Complete Data

Substance	Sex	Dose	Effect
A	雄	0ppm	0
A	雄	400ppm	0
A	雌	1000ppm	1
A	雄	2000ppm	1
A	雄	400ppm	0
B	雌	2000ppm	1
…	…	…	…
Z	雌	2000ppm	1

Parameter Estimation

MODEL (Association)

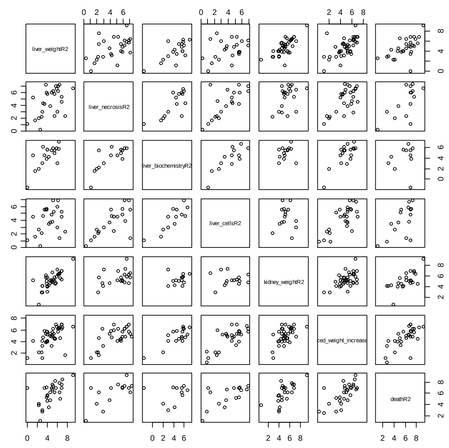
Data Update

The optimal model is set for the incomplete problem.

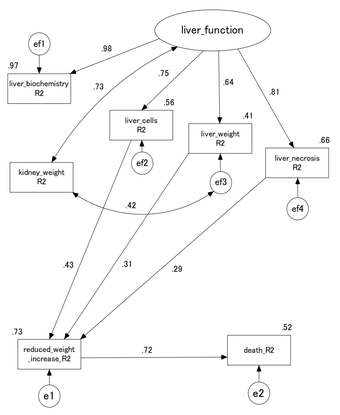
Results

The followings are some analytical Results for the chemical toxicity effect of liver and Kidney by rat's oral ingestion.

1. Scatter Plot



2. Latent Model (AIC=58.453)



Pass-Coefficient

			MLE	S.D.	Test Statistics	Prob.
Liver_necro.R2	<---	Liver function	1.559	.262	5.947	***
Liver_cellR2	<---	Liver function	1.303	.249	5.242	***
Liver_weightR2	<---	Liver function	1.109	.229	4.849	***
Weight_Inc.R2	<---	Liver_cellR2	.422	.123	3.417	***
Weight_Inc.R2	<---	Liver_weightR2	.303	.106	2.849	.004
Weight_IncR2	<---	Liver_necro.R2	.259	.120	2.158	.031
Liver_bioc.R2	<---	Liver function	2.050	.287	7.139	***
DeathR2	<---	Weight_Inc.R2	.750	.123	6.119	***

Covariance

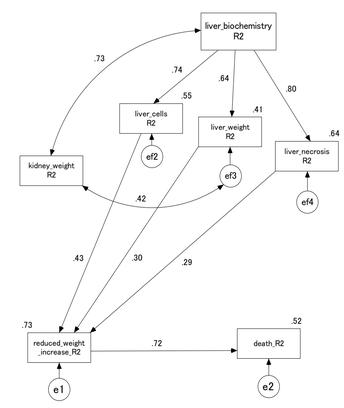
			MLE	S.D.	Test Statistics	Prob.
Kidney_weightR2	<-->	ef3	.859	.319	2.696	.007
Kidney_weightR2	<-->	Liver_function	1.120	.201	5.578	***

Variance

	MLE	S.D.	Test Statistics	Prob.
Liver function	1.000			
ef3	1.785	.427	4.179	***
ef2	1.357	.439	3.092	.002
ef4	1.274	.457	2.788	.005
e1	.811	.209	3.881	***
e2	1.532	.377	4.066	***
ef1	.134	.476	.281	.779
Kidney weightR2	2.367	.452	5.240	***

The error variance of the liver biochemistry is not significant. Hence we propose the following model revision.

3. Revision of Model (AIC=56.523)



Pass Coefficient

			MLE	S.D.	Test Statistics	Prob.
Liver_cellsR2	<---	Liver_biocR2	.619	.113	5.456	***
Liver_weightR2	<---	Liver_biocR2	.530	.106	4.991	***
Liver_necrosisR2	<---	Liver_biocR2	.734	.114	6.426	***
Weight_Inc.R2	<---	Liver_cellR2	.423	.121	3.487	***
Weight_Inc.R2	<---	Liver_necrosisR2	.261	.118	2.217	.027
Weight_Inc.R2	<---	Liver_weightR2	.302	.105	2.866	.004
DeathR2	<---	Weight_Inc.R2	.750	.123	6.113	***

Covariance

			MLE	S.D.	Test Statistics	Prob.
Kidney_weightR2	<-->	ef3	.860	.307	2.801	.005
Kidney_weightR2	<-->	Liver_bioc.R2	2.335	.568	4.111	***

Variance

	MLE	S.D.	Test Statistics	Prob.
Liver_biochemistryR2	4.379	1.021	4.289	***
ef3	1.784	.417	4.281	***
ef2	1.383	.425	3.252	.001
ef4	1.350	.424	3.188	.001
e1	.808	.209	3.874	***
e2	1.532	.377	4.066	***
Kidney_weightR2	2.363	.451	5.238	***

Acknowledgment

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