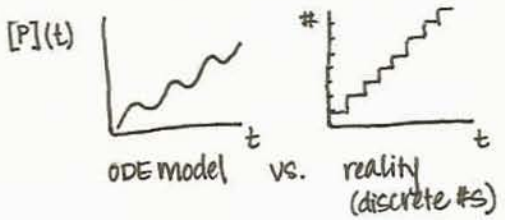
6.581/20.482

LECTURE 25: INFERENCE & STATISTICS

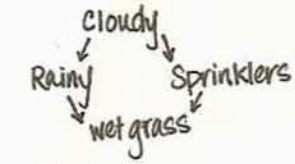
TUESDAY
16 MAY 2006



BAYESIAN NETWORK ANALYSIS

- can only be applied to a directed acyclic graph

Example.



P(C)	T	F
	0.5	0.5

P(S|C)	C=T	C=F
S=T	0.1	0.9
S=F	0.5	0.5

P(R|C)	C=T	C=F
R=T	0.8	0.2
R=F	0.2	0.8

P(W|S,R)	R=T, S=T	R=F, S=T	R=T, S=F	R=F, S=F
W=T	0.99	0.9	0.9	0.0
W=F	0.01	0.1	0.1	1.0

W=T

The chain for probability

$$P(C,S,R,W) = P(C)\cdot P(S|C)\cdot P(R|S,C)\cdot P(W|R,S,C)$$

current model topology → $= P(C)\cdot P(S|C)\cdot P(R|C)\cdot P(W|S,R)$

BAYES THEOREM: $P(A,B) \equiv P(A \cap B)$

$$P(A \cap B) = P(A)P(B|A) = P(B)P(A|B)$$

$$P(S=T|W=T) = \frac{P(S=T,W=T)}{P(W=T)} = \frac{\sum_{C,R} P(C,S=T,R,W=T)}{P(W=T)} = 0.4298$$

$$P(R=T|W=T) = \frac{P(R=T,W=T)}{P(W=T)} = \frac{\sum_{C,S} P(C,S,R=T,W=T)}{P(W=T)} = 0.7079$$

$$P(W=T) = 0.6471$$

Experiments give P(Data)
Models can produce P(Data|Model)
What we want to compare P(Model|Data)

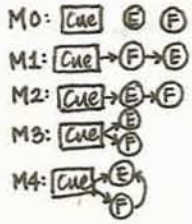
$$P(Model|Data) = \frac{P(Data|Model)P(Model)}{P(Data)}$$

$$Score_i = \log P(Model_i|Data)$$
$$= \log P(Data|Model_i) + \log P(Model_i) - \log P(Data)$$

(prior knowledge about system; constant across all models)

Sachs, Gifford, Jaakkola, Sorger, & Lauffenburger
http://www.stke.org/cgi/content/full/sigtrans;2002/148/pl1

Stimulates (cue) – fibronectin (fn)
(F) Focal Adhesion Kinase
(E) Extracellular signal-related kinase
Experiment was carried out twice



	score Data Set I	Data Set II	(fold-change)
M0:	−50.5 (2)	−60.8	(1700)
M1:	−42.8* (1)	−58.0	(104)
M2:	−43.8 (3)	−57.6	(73)
M3:	−44.3 (4)	−55.6	(10)
M4:	−44.3 (4)	−53.4*	(1)

Simulation of Reaction Kinetics:

Continuous vs Stochastic (ODE)

$$\frac{d\vec{x}}{dt} = f(\vec{x},\vec{u})$$

Alternative framework

$$\vec{y} = \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_M \end{bmatrix}$$ ← # of molecules of species 1

Think about dynamics as:
1) System remains unchanged for time τ
2) System will change by a single chemical reaction, μ

Let $P(\tau,\mu)\delta\tau$ = probability that $\vec{y}$ at time t will evolve such that no reaction occurs in $(t,t+\tau)$, but that the next reaction occurs in $(t+\tau, t+\tau+\delta\tau)$ and, it is Reaction μ ≡ reaction probability density function

μ ∈ discrete list of reactions

$$= \underbrace{P_0(\tau)}_{\text{probability that waiting time is } \tau} \cdot \underbrace{a_\mu d\tau}_{\text{probability that } \mu \text{ is the reaction}}$$

It is shown that

$$P(\tau,\mu) = a_\mu e^{-a_0\tau} \quad \text{for } 0 \le \tau < \infty \text{ \& } \mu \in \{1,\ldots,M\}$$

where

$$a_0 = \sum_{i=1}^{M} a_i$$ ← individual reaction propensities

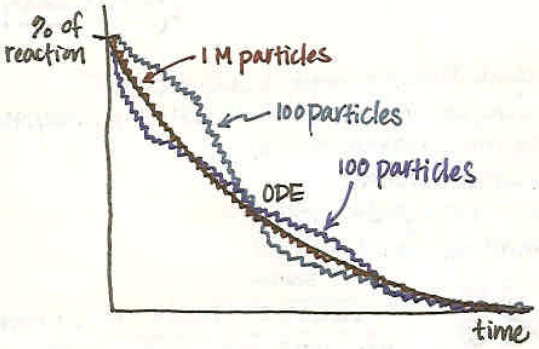
$$a_\mu = h_\mu c_\mu$$ ← reaction rate; ← # of collision types

DT Gillespie J. Phys Chem 81. 2340-61 (1977)
J. Phys Chem 115. 1716-33 (2001)

Pick 2 random numbers R_1 & R_2 uniformly on [0,1]

$$\tau = \frac{1}{a_0}\ln\frac{1}{R_1}$$

Select μ such that $\sum_{i=1}^{\mu-1} a_i < R_2 a_0 < \sum_{i=1}^{\mu} a_i$


% of reaction
1 M particles
100 particles
100 particles
ODE
time