Stochastic Modeling of Chemical Reactions (and more …)

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Outline

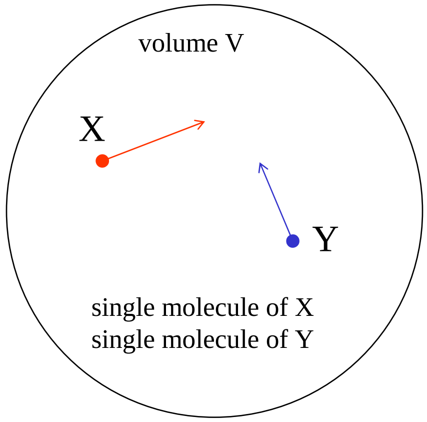
1. Basics behind stochastic modeling of chemical reactions
   (elementary probability $\rightarrow$ stochastic model)
2. BE derivation of Dynkin's formula for Markov processes
   (stochastic model $\rightarrow$ ODEs)
3. Moment dynamics
4. Examples (unconstrained birth-death, African bees, the RPC Island)

BE $\equiv$ back-of-the-envelop
RPC $\equiv$ Rock-paper-scissors

A simple chemical reaction

UCSB

$X + Y \rightarrow Z$



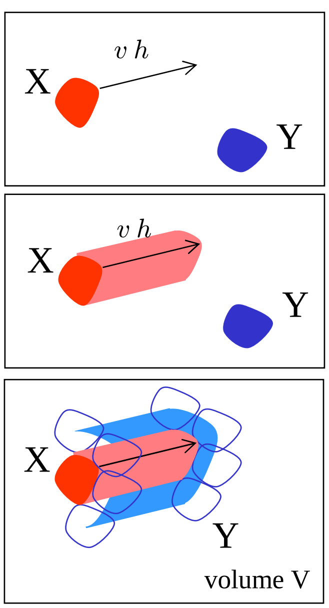
h seconds into future

now

$$\text{Prob(X reacts with Y in interval of time } [0, h] \text{)}$$
$$= \text{Prob (X collides with Y)} \times \text{Prob (X \& Y react once they collide)}$$

Probability of collision (one-on-one)

UCSB



v $\equiv$ velocity of X with respect to Y

$v\,h$ $\equiv$ motion of X with respect to Y in interval $[0, h]$

volume where collision can occur

possible positions for center of Y so that collision will occur

volume = $c\,h$

c depends on the velocity & geometry of the molecules

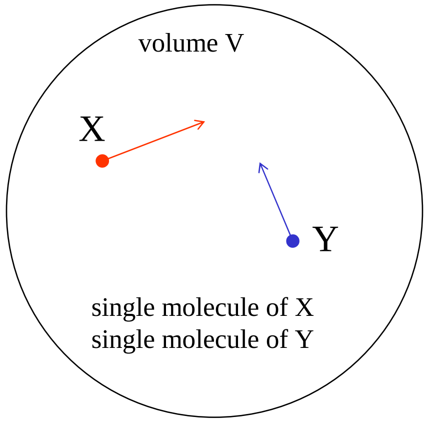
$$\text{Prob(collision)} = \frac{c h}{V}$$

assumes well-mixed solution (Y equally likely to be everywhere)

Probability of reaction (one-on-one)

UCSB

$X + Y \rightarrow Z$



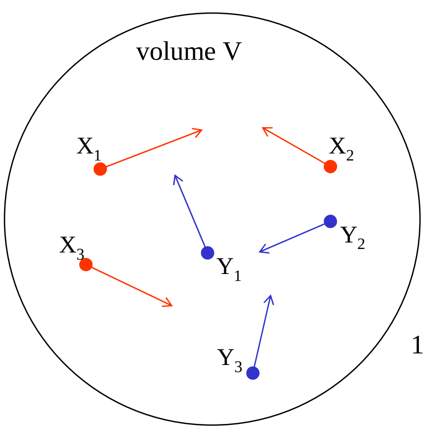
$$\textbf{Prob(X reacts with Y in interval of time } [0, h[\text{)}$$
$$= \text{Prob (X collides with Y)} \times \text{Prob (X \& Y react once they collide)}$$
$$= c\,\text{Prob(X \& Y react once they collide)}\,\frac{h}{V}$$

generally determined experimentally

Probability of reaction (many-on-many)

UCSB

$X + Y \rightarrow Z$



x molecules of X
y molecules of Y

Prob (at least one X reacts with one Y)

$=$ Prob (X_1 reacts with Y_1)
$+$ Prob (X_1 reacts with Y_2)
$\vdots$

terms = # Y molec.

$+$ Prob (X_2 reacts with Y_1)
$+$ Prob (X_2 reacts with Y_2)
$\vdots$

terms = # Y molec.

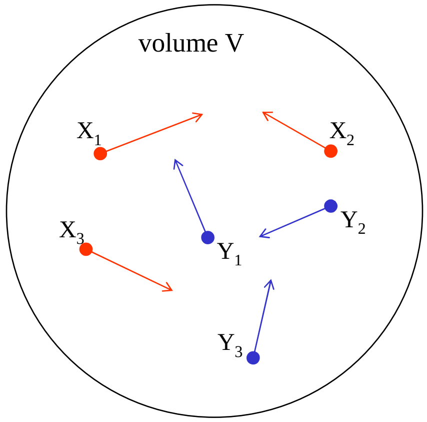
total # terms = # X molec. $\times$ # Y molecules = $x \times y$

1. Assumes small time interval $[0,h]$ so that 2 reactions are unlikely (otherwise double counting)
2. Each term
   Prob (X_i reacts with Y_j)
   is the probability of one-on-one reaction computed before

Probability of reaction (many-on-many)

UCSB

$X + Y \rightarrow Z$



Prob(at least one X reacts with one Y in interval of time $[0, h]$)

$$= \text{Prob } (X_i \text{ collides with } Y_j)\; x\, y$$

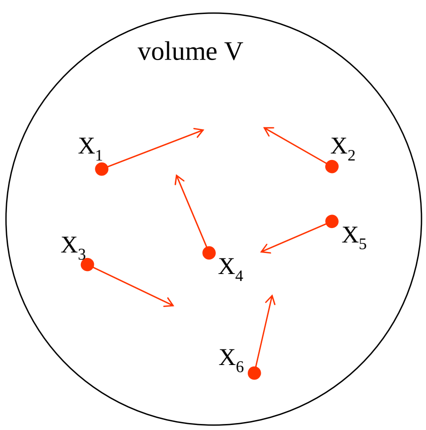
$$= c\,\text{Prob}(X \,\&\, Y \text{ react once they collide})\; \frac{x\, y\, h}{V}$$

generally determined experimentally

Probability of reaction (many-on-many)

UCSB

$X + X \rightarrow Z$



x molecules of X
y molecules of Y

Prob (at least one X reacts with one X)

$= \text{Prob } (X_1 \text{ reacts with } X_2)$
$+ \text{Prob } (X_1 \text{ reacts with } X_3)$
$\vdots$
$+ \text{Prob } (X_1 \text{ reacts with } X_x)$
— # terms = $x - 1$

$+ \text{Prob } (X_2 \text{ reacts with } X_3)$
$+ \text{Prob } (X_2 \text{ reacts with } X_4)$
$\vdots$
— # terms = $x - 2$

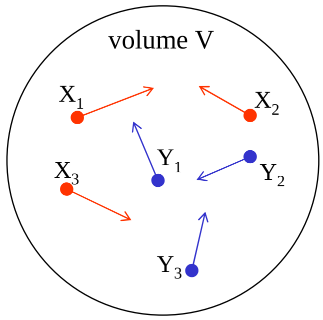
$\vdots$

$+ \text{Prob } (X_{x-1} \text{ reacts with } X_x)$

total # terms = $x \times (x - 1) / 2$

Probability of reaction (many-on-many)

UCSB

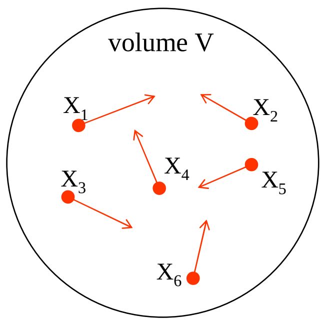


$X + Y \rightarrow ?$

$$\textbf{Prob(one X \& Y react in } [0,h]) = \alpha_1 \frac{x\,y\,h}{V}$$

determined experimentally

propensity functions (recall Brian's talk!)



$2\,X \rightarrow ?$

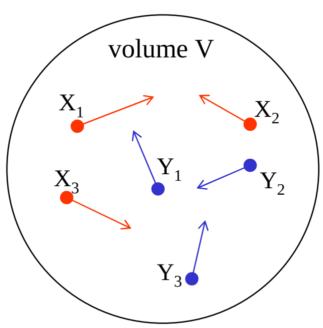
$$\textbf{Prob(two X react in } [0,h]) = \alpha_2 \frac{x(x-1)h}{2V}$$

1. *Covers all "elementary reactions"*
2. *Only valid when h is small*

Questions

UCSB

$X + Y \rightarrow Z$



If we leave system to itself for a while…

Q1: How many molecules of X and Y can we expect to have after some time T ($\gg h$) ?

$\mu_x = E[x] = ?$

$\mu_y = E[y] = ?$

Q2: How much variability can we expect around the average ?

$\sigma_x^2 = E[(x-\mu_x)^2] = E[x^2] - \mu_x^2$?

$\sigma_y^2 = E[(y-\mu_y)^2] = E[y^2] - \mu_y^2$?

Q3: How much correlation between the two variables ?

$C_{xy} = E[(x-\mu_x)(y-\mu_y)] = E[xy] - \mu_x\,\mu_y$?

(e.g., positive correlation $\equiv$ x below mean is generally consistent with y below mean)

Empirical interpretation of averages

$X + Y \to Z$	universe #1	universe #2	universe #3	…
time = 0	$x_1 = x_{init}$ $y_1 = y_{init}$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}$ $y_3 = y_{init}$	…
	(one reaction)	(no reaction)	(no reaction)	
time = h	$x_1 = x_{init}-1$ $y_1 = y_{init}-1$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}$ $y_3 = y_{init}$	…
	(one reaction)	(no reaction)	(one reaction)	
time = 2 h	$x_1 = x_{init}-2$ $y_1 = y_{init}-2$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}-1$ $y_3 = y_{init}-1$	…
	(no reaction)	(one reaction)	(one reaction)	
time = 3 h	$x_1 = x_{init}-3$ $y_1 = y_{init}-3$	$x_2 = x_{init}-1$ $y_2 = y_{init}-1$	$x_3 = x_{init}-2$ $y_3 = y_{init}-2$	…

$$\mathrm{E}[x(T)] = \frac{\sum_{\text{all universes}} x_i(T)}{\#\ \text{universes}} \qquad \mathrm{E}[y(T)] = \frac{\sum_{\text{all universes}} y_i(T)}{\#\ \text{universes}}$$

Empirical interpretation of averages

$X + Y \to Z$	universe #1	universe #2	universe #3	…
time = 0	$x_1 = x_{init}$ $y_1 = y_{init}$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}$ $y_3 = y_{init}$	…
	(one reaction)	(no reaction)	(no reaction)	
time = h	$x_1 = x_{init}-1$ $y_1 = y_{init}-1$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}$ $y_3 = y_{init}$	…

$$\mathrm{E}[x(h)] = \frac{\sum_{\text{all universes}} x_i(h)}{\#\ \text{universes}}$$
$$= \frac{(x_{init} - 1) \times \#\ \text{univ with one react} + x_{init} \times \#\ \text{univ with no react}}{\text{total}\ \#\ \text{of universes}}$$
$$= \frac{x_{init} \times \text{total}\ \#\ \text{of universes} - 1 \times \#\ \text{univ with one react}}{\text{total}\ \#\ \text{of universes}}$$

Empirical interpretation of averages

$X + Y \to Z$	universe #1	universe #2	universe #3	…
time = 0	$x_1 = x_{\text{init}}$ $y_1 = y_{\text{init}}$	$x_2 = x_{\text{init}}$ $y_2 = y_{\text{init}}$	$x_3 = x_{\text{init}}$ $y_3 = y_{\text{init}}$	…
	(one reaction)	(no reaction)	(no reaction)	
time = h	$x_1 = x_{\text{init}}-1$ $y_1 = y_{\text{init}}-1$	$x_2 = x_{\text{init}}$ $y_2 = y_{\text{init}}$	$x_3 = x_{\text{init}}$ $y_3 = y_{\text{init}}$	…

$$\mathrm{E}[x(h)] = \frac{x_{\text{init}} \times \text{total \# of universes} - 1 \times \text{\# univ with one react}}{\text{total \# of universes}}$$

$$= x_{\text{init}} - 1 \times \frac{\text{\# univ with one react}}{\text{total \# of universes}}$$

initial # of molecules

stoichiometry (change in # molecules due to reaction)

$$\text{Prob(one reaction in } [0,h]) = \alpha \frac{x_{\text{init}}\, y_{\text{init}}\, h}{V}$$

Empirical interpretation of averages

$X + Y \to Z$	universe #1	universe #2	universe #3	…
time = 0	$x_1 = x_{\text{init}}$ $y_1 = y_{\text{init}}$	$x_2 = x_{\text{init}}$ $y_2 = y_{\text{init}}$	$x_3 = x_{\text{init}}$ $y_3 = y_{\text{init}}$	…
	(one reaction)	(no reaction)	(no reaction)	
time = h	$x_1 = x_{\text{init}}-1$ $y_1 = y_{\text{init}}-1$	$x_2 = x_{\text{init}}$ $y_2 = y_{\text{init}}$	$x_3 = x_{\text{init}}$ $y_3 = y_{\text{init}}$	…

$$\mathrm{E}[x(h)] = \frac{x_{\text{init}} \times \text{total \# of universes} - 1 \times \text{\# univ with one react}}{\text{total \# of universes}}$$

$$= x_{\text{init}} - 1 \times \frac{\text{\# univ with one react}}{\text{total \# of universes}}$$

$$\mathrm{E}[x(h)] - x(0) = -1 \times \alpha \frac{x(0)\, y(0)\, h}{V}$$

Empirical interpretation of averages

$X + Y \to Z$	universe #1	universe #2	universe #3	…
time = 0	$x_1 = x_{\text{init}}$ $y_1 = y_{\text{init}}$	$x_2 = x_{\text{init}}$ $y_2 = y_{\text{init}}$	$x_3 = x_{\text{init}}$ $y_3 = y_{\text{init}}$	…
	(one reaction)	(no reaction)	(no reaction)	
time = h	$x_1 = x_{\text{init}}-1$ $y_1 = y_{\text{init}}-1$	$x_2 = x_{\text{init}}$ $y_2 = y_{\text{init}}$	$x_3 = x_{\text{init}}$ $y_3 = y_{\text{init}}$	…

$$\frac{d}{dt}\mathrm{E}[x(t)]_{t=0} \approx \frac{\mathrm{E}[x(h)] - x(0)}{h} = -1 \times \alpha \frac{x(0)\,y(0)}{V}$$

derivative of average at $t = h/2 \approx 0$ (recall that h is very small)

stoichiometry (change in # X molecules due to reaction)

probability of one reaction

Empirical interpretation of averages

$X + Y \to Z$	universe #1	universe #2	universe #3	…
time = 0	$x_1 = x_{\text{init}}$ $y_1 = y_{\text{init}}$	$x_2 = x_{\text{init}}$ $y_2 = y_{\text{init}}$	$x_3 = x_{\text{init}}$ $y_3 = y_{\text{init}}$	…
		⋮		
time = t	$x_1 = ?$ $y_1 = ?$	$x_2 = ?$ $y_2 = ?$	$x_3 = ?$ $y_3 = ?$	…

$$\frac{d}{dt}\mathrm{E}[x(t)] = \mathrm{E}\left[-1 \times \alpha \frac{x(t)\,y(t)}{V}\right]$$

derivative of average

stoichiometry (change in # X molecules due to reaction)

probability of one reaction

Empirical interpretation of averages

UCSB

$X + Y \to Z$	universe #1	universe #2	universe #3	…
time = 0	$x_1 = x_{init}$ $y_1 = y_{init}$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}$ $y_3 = y_{init}$	…
	(one reaction)	(no reaction)	(no reaction)	
time = h	$x_1 = x_{init}-1$ $y_1 = y_{init}-1$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}$ $y_3 = y_{init}$	…

$$\mathrm{E}[x(h)^2] = \frac{\sum_{\text{all universes}} x_i(h)^2}{\#\text{ universes}}$$

$$= \frac{(x_{init}-1)^2 \times \#\text{ univ with one react} + x_{init}^2 \times \#\text{ univ with no react}}{\text{total }\#\text{ of universes}}$$

$$= x_{init}^2 + \left((x_{init}-1)^2 - x_{init}^2\right) \times \frac{\#\text{ univ with one react}}{\text{total }\#\text{ of universes}}$$

initial value

change due to a single reaction

$$\mathrm{Prob}(\text{one reaction in } [0,h]) = \alpha \frac{x_{init}\, y_{init}\, h}{V}$$

Empirical interpretation of averages

UCSB

$X + Y \to Z$	universe #1	universe #2	universe #3	…
time = 0	$x_1 = x_{init}$ $y_1 = y_{init}$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}$ $y_3 = y_{init}$	…
	(one reaction)	(no reaction)	(no reaction)	
time = h	$x_1 = x_{init}-1$ $y_1 = y_{init}-1$	$x_2 = x_{init}$ $y_2 = y_{init}$	$x_3 = x_{init}$ $y_3 = y_{init}$	…

$$\mathrm{E}[x(h)^2] = x_{init}^2 + \left((x_{init}-1)^2 - x_{init}^2\right) \times \alpha \frac{x_{init}\, y_{init}\, h}{V}$$

$$\frac{d}{dt}\mathrm{E}[x(t)^2]_{t=0} \approx \left((x(0)-1)^2 - x(0)^2\right) \times \alpha \frac{x(0)\, y(0)}{V}$$

change due to a single reaction

probability of one reaction

cf. with $\frac{d}{dt}\mathrm{E}[x(t)] = \mathrm{E}\left[-1 \times \alpha \frac{x(t)\, y(t)}{V}\right]$

Dynkin's formula for Markov processes

UCSB

$$X + Y \to Z \quad \dashrightarrow \quad \mathrm{Prob}(\text{X \& Y react in } [0,h]) = \alpha \frac{x\,y\,h}{V}$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E}[\psi(x,y)] = \mathrm{E}\left[\Big(\psi(x-1,y-1)-\psi(x,y)\Big)\times \alpha\frac{x\,y}{V}\right]$$

derivative of average — change due to a single reaction — probability of one reaction

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E}[x(t)] = \mathrm{E}\left[-1\times\alpha\frac{x\,y}{V}\right] = -\frac{\alpha}{V}\mathrm{E}[xy]$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E}[x(t)^2] = \mathrm{E}\left[\Big((x-1)^2-x^2\Big)\times\alpha\frac{x\,y}{V}\right] = -\frac{\alpha}{V}\mathrm{E}\left[(2x-1)xy\right]$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E}[x(t)y(t)] = \mathrm{E}\left[\Big((x-1)(y-1)-xy\Big)\times\alpha\frac{x\,y}{V}\right] = -\frac{\alpha}{V}\mathrm{E}\left[(x+y-1)x\,y\right]$$

$$\frac{\mathrm{d}\sigma_x^2(t)}{\mathrm{d}t} = \frac{\mathrm{d}}{\mathrm{d}t}\Big(\mathrm{E}[x(t)^2]-\mathrm{E}[x(t)]^2\Big) = -\frac{\alpha}{V}\mathrm{E}\left[(2x-1)xy\right] + \frac{2\alpha}{V}\mathrm{E}[x]\,\mathrm{E}[xy]$$

Dynkin's formula for Markov processes

UCSB

Multiple reactions: $X + Y \to Z \quad \dashrightarrow \quad \mathrm{Prob}(\text{X \& Y react in } [0,h]) = \alpha_1 \frac{x\,y\,h}{V}$

$$2\,X \to Z + Y \quad \dashrightarrow \quad \mathrm{Prob}(\text{two X react in } [0,h]) = \alpha_2 \frac{x(x-1)h}{2V}$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{E}[\psi(x,y,z)] = \mathrm{E}\Big[\ \Big(\psi(x-1,y-1,z+1)-\psi(x,y,z)\Big)\times\alpha_1\frac{x\,y}{V} + \Big(\psi(x-2,y+1,z+1)-\psi(x,y,z)\Big)\times\alpha_2\frac{x(x-1)}{2V}\Big]$$

derivative of average

change due to one reaction

probability of one reaction

sum over all reactions

A birth-death example

UCSB

$2\,X \to 3\,X$ — 2 molecules meet and reproduce → $\text{Prob}(\text{two X react in } [0,h]) = b\,\frac{x(x-1)}{2}\,h$

$X \to \varnothing$ — 1 molecule spontaneously die → $\text{Prob}(\text{X decays } [0,h]) = d\,x\,h$

$$\frac{d\,E[x]}{dt} = -\left(\frac{b}{2}+d\right)E[x] + \frac{b}{2}E[x^2]$$

$$\frac{d\,E[x^2]}{dt} = -\left(\frac{b}{2}-d\right)E[x] - \left(\frac{b}{2}+2d\right)E[x^2] + b\,E[x^3]$$

$$\frac{d\,E[x^3]}{dt} = -\left(\frac{b}{2}+d\right)E[x] - (b-3d)\,E[x^2] - 3d\,E[x^3] + \frac{3b}{2}E[x^4]$$

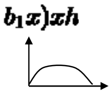
$$\vdots$$

(does not capture finiteness of resources in a natural environment
1. *when x too large reproduction-rate should decrease*
2. *when x too large death-rate should increase)*

African honey bee

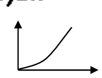
UCSB

$\varnothing \to X$ — 1 honey bee is born → $\text{Prob}(\text{birth in } [0,h]) = (a_1 - b_1 x)\,x\,h$



$X \to \varnothing$ — 1 honey bee dies → $\text{Prob}(\text{death in } [0,h]) = (a_2 + b_2 x)\,x\,h$

Stochastic Logistic model
(different rates than in a chemical reactions, but Dynkin's formula still applies)



$$\frac{d}{dt}E[\psi(x)] = E\Big[\ \big(\psi(x+1)-\psi(x)\big)\times(a_1-b_1x)x + \big(\psi(x-1)-\psi(x)\big)\times(a_2+b_2x)x\Big]$$

$$\frac{d\,E[x]}{dt} = (a_1-a_2)\,E[x] - (b_1+b_2)\,E[x^2]$$

$$\frac{d\,E[x^2]}{dt} = (a_1+a_2)\,E[x] + (2a_1-2a_2-b_1+b_2)\,E[x^2] - 2(b_1+b_2)\,E[x^3]$$

$$\vdots$$

For African honey bees: $a_1 = .3$, $a_2 = .02$, $b_1 = .015$, $b_2 = .001$ [Matis et al 1998]

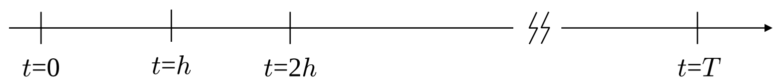
Predicting bee populations

UCSB

$\varnothing \to X$ 1 honey bee is born $(a_1 - b_1 x)x$

$X \to \varnothing$ 1 honey bee dies $(a_2 + b_2 x)x$

$$\frac{d\,E[x]}{dt} = (a_1 - a_2)\,E[x] - (b_1 + b_2)\,E[x^2]$$
$$\frac{d\,E[x^2]}{dt} = (a_1 + a_2)\,E[x] + (2a_1 - 2a_2 - b_1 + b_2)\,E[x^2] - 2(b_1 + b_2)\,E[x^3]$$
$$\vdots$$



$x(0) = x_{\text{init}}$ $E[x(h)]$ $E[x(2h)]$

$x(0)^2 = x_{\text{init}}^2$

$\frac{d\,E[x(0)]}{dt}$ (needs $E[x(0)]$ & $E[x(0)^2]$)

$\frac{d\,E[x(h)]}{dt}$ (needs $E[x(h)]$ & $E[x(h)^2]$)

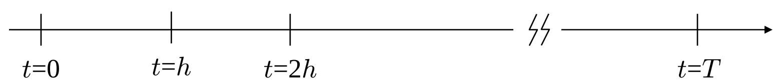
Predicting bee populations

UCSB

$\varnothing \to X$ 1 honey bee is born $(a_1 - b_1 x)x$

$X \to \varnothing$ 1 honey bee dies $(a_2 + b_2 x)x$

$$\frac{d\,E[x]}{dt} = (a_1 - a_2)\,E[x] - (b_1 + b_2)\,E[x^2]$$
$$\frac{d\,E[x^2]}{dt} = (a_1 + a_2)\,E[x] + (2a_1 - 2a_2 - b_1 + b_2)\,E[x^2] - 2(b_1 + b_2)\,E[x^3]$$
$$\vdots$$



$x(0) = x_{\text{init}}$ $E[x(h)]$ $E[x(2h)]$

$x(0)^2 = x_{\text{init}}^2$ $E[x(h)^2]$

$x(0)^3 = x_{\text{init}}^3$

Predicting bee populations

UCSB

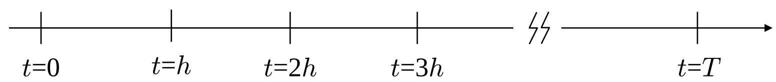
$\varnothing \rightarrow \mathrm{X}$ 1 honey bee is born $(a_1 - b_1 x)x$

$\mathrm{X} \rightarrow \varnothing$ 1 honey bee dies $(a_2 + b_2 x)x$

$$\frac{\mathrm{d}\,\mathrm{E}[x]}{\mathrm{d}t} = (a_1 - a_2)\,\mathrm{E}[x] - (b_1 + b_2)\,\mathrm{E}[x^2]$$

$$\frac{\mathrm{d}\,\mathrm{E}[x^2]}{\mathrm{d}t} = (a_1 + a_2)\,\mathrm{E}[x] + (2a_1 - 2a_2 - b_1 + b_2)\,\mathrm{E}[x^2] - 2(b_1 + b_2)\,\mathrm{E}[x^3]$$

$$\vdots$$



$x(0) = x_{\text{init}}$	$\mathrm{E}[x(h)]$	$\mathrm{E}[x(2h)]$	$\mathrm{E}[x(3h)]$
$x(0)^2 = x_{\text{init}}^2$	$\mathrm{E}[x(h)^2]$	$\mathrm{E}[x(2h)^2]$	
$x(0)^3 = x_{\text{init}}^3$	$\mathrm{E}[x(h)^3]$		
$x(0)^3 = x_{\text{init}}^4$			

not sustainable if $T \gg h$

Moment truncation

UCSB

$\varnothing \rightarrow \mathrm{X}$ 1 honey bee is born $(a_1 - b_1 x)x$

$\mathrm{X} \rightarrow \varnothing$ 1 honey bee dies $(a_2 + b_2 x)x$

$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{bmatrix}\mathrm{E}[x]\\ \mathrm{E}[x^2]\end{bmatrix} = \begin{bmatrix} a_1 - a_2 & -b_1 - b_2 \\ a_1 + a_2 & 2(a_1 - a_2) - b_1 + b_2 \end{bmatrix}\begin{bmatrix}\mathrm{E}[x]\\ \mathrm{E}[x^2]\end{bmatrix} - \begin{bmatrix} 0 \\ 2(b_1 + b_2)\end{bmatrix}\mathrm{E}[x^3]$$

Moment truncation $\equiv$ Substitute $\mathrm{E}[x^3]$ by a function φ of both $\mathrm{E}[x]$ & $\mathrm{E}[x^2]$

$$\mathrm{E}[x^3] \approx \varphi\big(\mathrm{E}[x], \mathrm{E}[x^2]\big)$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{bmatrix}\mathrm{E}[x]\\ \mathrm{E}[x^2]\end{bmatrix} \approx \begin{bmatrix} a_1 - a_2 & -b_1 - b_2 \\ a_1 + a_2 & 2(a_1 - a_2) - b_1 + b_2 \end{bmatrix}\begin{bmatrix}\mathrm{E}[x]\\ \mathrm{E}[x^2]\end{bmatrix} - \begin{bmatrix} 0 \\ 2(b_1 + b_2)\end{bmatrix}\varphi\big(\mathrm{E}[x], \mathrm{E}[x^2]\big)$$

How to choose $\varphi(\cdot)$?

Option I – Distribution-based truncations

UCSB

$$\frac{d}{dt}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}=\begin{bmatrix}a_1-a_2 & -b_1-b_2\\a_1+a_2 & 2(a_1-a_2)-b_1+b_2\end{bmatrix}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}-\begin{bmatrix}0\\2(b_1+b_2)\end{bmatrix}E[x^3]$$

$$E[x^3]\approx\varphi\big(E[x],E[x^2]\big)$$

Suppose we knew the distribution was {BLANK}, then we could guess $E[x^3]$ from $E[x]$ and $E[x^2]$, e.g.:

Normal $E[x^3]=3E[x^2]\,E[x]-2\,E[x]^3$

Log Normal $E[x^3]=\left(\frac{E[x^2]}{E[x]}\right)^3$

Binomial $E[x^3]=2\frac{(E[x^2]-E[x]^2)^2}{E[x]}-E[x^2]+E[x]^2+3E[x^2]E[x]-2E[x]^3$

Poisson $E[x^3]=E[x]+3E[x^2]\,E[x]-2\,E[x]^3$

or $E[x^3]=E[x^2]-E[x]^2+3E[x^2]\,E[x]-2\,E[x]^3$

*these equalities hold **for every** distribution of the given type*

Option II – Derivative-matching truncation

UCSB

Exact dynamics

$$\frac{d}{dt}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}=\begin{bmatrix}a_1-a_2 & -b_1-b_2\\a_1+a_2 & 2(a_1-a_2)-b_1+b_2\end{bmatrix}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}-\begin{bmatrix}0\\2(b_1+b_2)\end{bmatrix}E[x^3]$$

Truncated dynamics

$$\frac{d}{dt}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\approx\begin{bmatrix}a_1-a_2 & -b_1-b_2\\a_1+a_2 & 2(a_1-a_2)-b_1+b_2\end{bmatrix}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}-\begin{bmatrix}0\\2(b_1+b_2)\end{bmatrix}\varphi\big(E[x],E[x^2]\big)$$

Select φ to minimize derivative errors

$$\frac{d}{dt}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{exact}}-\frac{d}{dt}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{truncated}}$$

$$\frac{d^2}{dt^2}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{exact}}-\frac{d^2}{dt^2}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{truncated}}$$

$$\vdots$$

Option II – Derivative-matching truncation

UCSB

It is possible to find a function φ such that for every initial population x_{init}

$$\frac{d}{dt}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{exact}} = \frac{d}{dt}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{truncated}}$$

$$\frac{\left\| \frac{d^k}{dt^k}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{exact}} - \frac{d^k}{dt^k}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{truncated}} \right\|}{\left\| \frac{d^k}{dt^k}\begin{bmatrix}E[x]\\E[x^2]\end{bmatrix}\Big|_{\text{exact}} \right\|} \lessapprox \frac{c}{x_{\text{init}}^2} \qquad \forall k \geq 2$$

There are a few "universal" φ, e.g.,

$$E[x^3] = \left(\frac{E[x^2]}{E[x]}\right)^3$$

the above property holds
for every set of chemical reactions
(and also for every
stochastic logistic model)

We like Option II …

UCSB

1. Approach does not start with an arbitrary assumption of the population distribution. Distribution should be discovered from the model.
2. Generalizes for high-order truncations:

   It is possible to find a function φ such that for every initial population x_{init}

$$\frac{\left\| \frac{d^k}{dt^k}\begin{bmatrix}E[x]\\E[x^2]\\\vdots\\E[x^n]\end{bmatrix}\Big|_{\text{exact}} - \frac{d^k}{dt^k}\begin{bmatrix}E[x]\\E[x^2]\\\vdots\\E[x^n]\end{bmatrix}\Big|_{\text{truncated}} \right\|}{\left\| \frac{d^k}{dt^k}\begin{bmatrix}E[x]\\E[x^2]\\\vdots\\E[x^n]\end{bmatrix}\Big|_{\text{exact}} \right\|} \lessapprox \frac{c}{x^n{}_{\text{init}}} \qquad \forall k \geq 2$$

smaller and smaller
error as n increases

but two options not incompatible (on the contrary!)

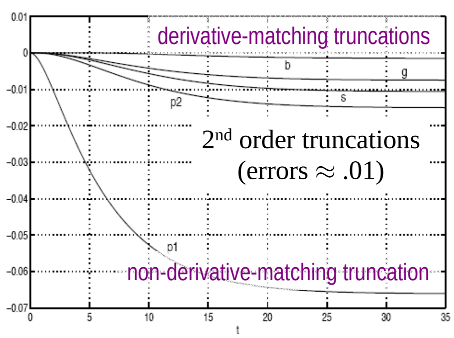
Back to African honey bees

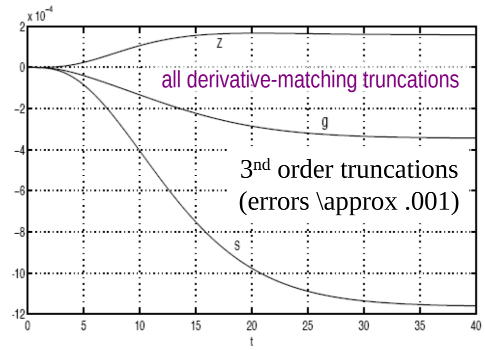
UCSB

$\varnothing \to X$ 1 honey bee is born $(a_1 - b_1 x)x$

$X \to \varnothing$ 1 honey bee dies $(a_2 + b_2 x)x$

Errors in the mean for an initial population of 20 bees





For African honey bees: $a_1 = .3$, $a_2 = .02$, $b_1 = .015$, $b_2 = .001$ [Matis et al 1998]

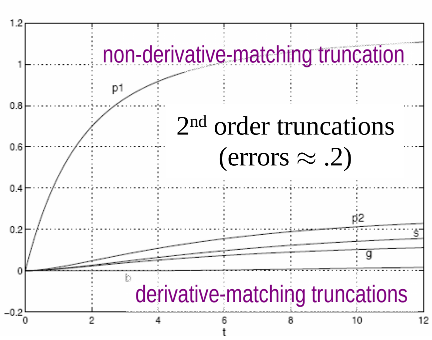
Back to African honey bees

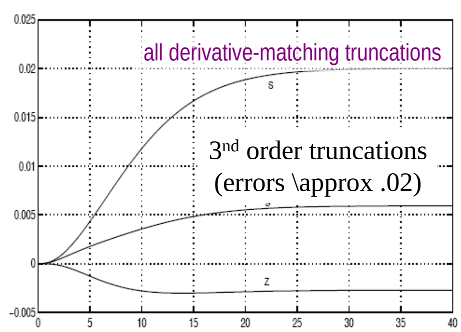
UCSB

$X \to 2X$ 1 honey bee is born $(a_1 - b_1 x)x$

$X \to \varnothing$ 1 honey bee dies $(a_2 + b_2 x)x$

Errors in the variance for an initial population of 20 bees

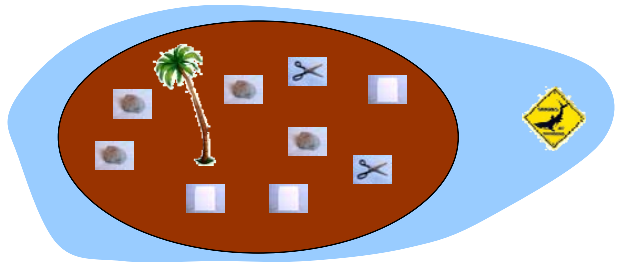




For African honey bees: $a_1 = .3$, $a_2 = .02$, $b_1 = .015$, $b_2 = .001$ [Matis et al 1998]

The Rock-Paper-Scissors island

Each person in the Island has one of three genes
This gene only affects the way they play RPS



Periodically, each person seeks an adversary and plays RPS
Winner gets to have exactly one offspring, loser dies (high-stakes RPS!)

(total population constant)

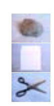
Scenario I: offspring always has same gene as parent
Scenario II: with low probability, offspring suffers a mutation (different gene)

The Rock-Paper-Scissors island

For a well-mixed population, this can be modeled by…

Scenario I: offspring always has same gene as parent

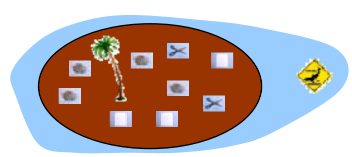
R + P → 2 P	with rate prop. to $r \cdot p$	$r \equiv$ # of
R + S → 2 R	with rate prop. to $r \cdot s$	$p \equiv$ # of
P + S → 2 S	with rate prop. to $p \cdot s$	$s \equiv$ # of



Scenario II: with low probability, offspring suffers a mutation (different gene)

R + P → P + S	with rate prop. to $r \cdot p$
R + S → R + P	with rate prop. to $r \cdot s$
P + S → S + R	with rate prop. to $p \cdot s$
2 R → R + P	with rate prop. to $r \cdot (r-1)/2$
2 R → R + S	with rate prop. to $r \cdot (r-1)/2$
2 P → P + R	with rate prop. to $p \cdot (p-1)/2$
2 P → P + S	with rate prop. to $p \cdot (p-1)/2$
2 S → S + R	with rate prop. to $s \cdot (s-1)/2$
2 S → S + P	with rate prop. to $s \cdot (s-1)/2$

Q: What will happen in the island?

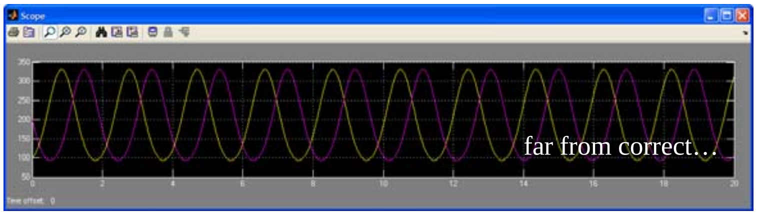


The Rock-Paper-Scissors island

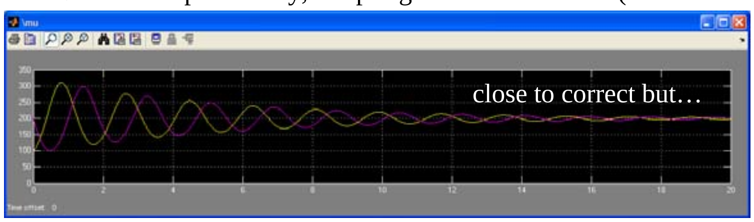
Q: What will happen in the island?
Answer given by a deterministic formulation
(chemical rate equation/Lotka-Volterra-like model)

$r(0) = 100$, $p(0) = 200$, $s(0) = 300$

Scenario I: offspring always has same gene as parent



Scenario II: with low probability, offspring suffers a mutation (1/50 mutations)

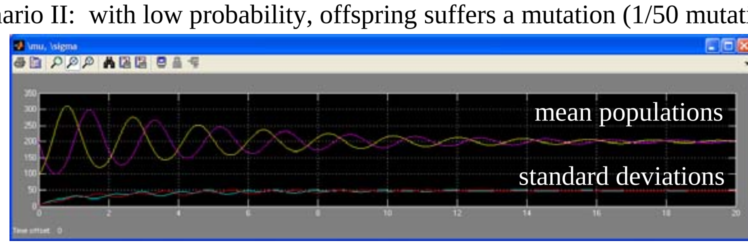


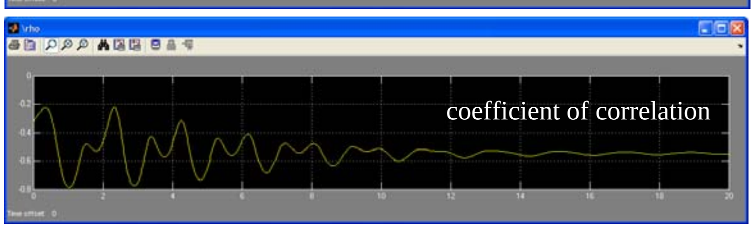
The Rock-Paper-Scissors island

Q: What will happen in the island?
Answer given by a stochastic formulation (2nd order truncation)

$r(0) = 100$, $p(0) = 200$, $s(0) = 300$

Scenario II: with low probability, offspring suffers a mutation (1/50 mutations)





Even at steady state, the populations oscillate significantly with negative coefficient of correlation

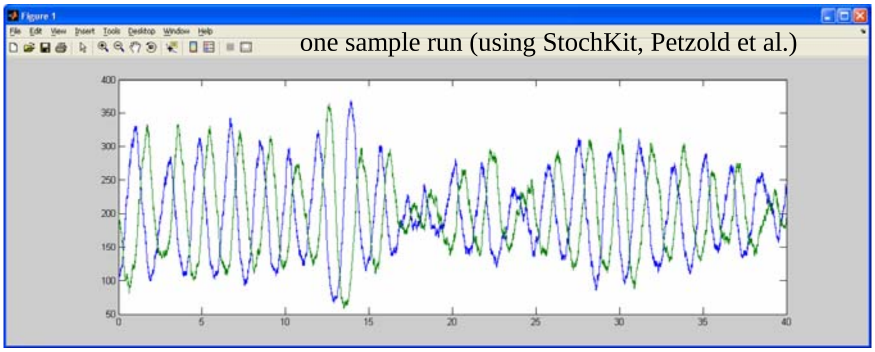
The Rock-Paper-Scissors island

Q: What will happen in the island?

$r(0) = 100$, $p(0) = 200$, $s(0) = 300$

Answer given by a stochastic formulation (2nd order truncation)

Scenario II: with low probability, offspring suffers a mutation (1/50 mutations)



Even at steady state, the populations oscillate significantly with negative coefficient of correlation

What next?

Gene regulation:

$X \to \varnothing$	natural decay of X
Gene_on $\to$ Gene_on + X	protein X produced when gene is on
Gene_on + X $\to$ Gene_off	X binds to gene and inhibits further production of protein X
Gene_off $\to$ Gene_on + X	X detaches from gene and activates production of protein X

(binary nature of gene allows for very effective truncations)

Times to extinction/Probability of extinction:

Sometimes truncations are poorly behaved at times scales for which extinctions are likely
(predict negative populations, lead to division by zero, etc.)

Temporal correlations:

Sustained oscillations are often hard to detected solely from steady-state distributions.