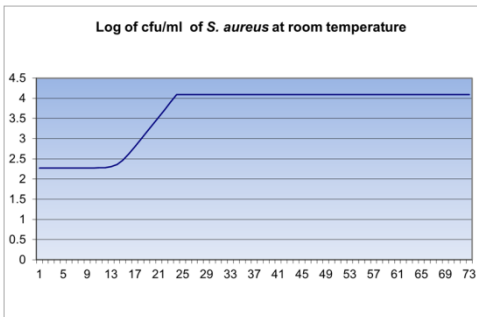


Participatory risk assessment II

- Risk modelling I -

‘Learning Event’ on risk analysis and participatory methods
CSRS, November 28, 2014



Kohei Makita

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(OIE Joint Collaborating Centre for Food Safety)
Joint Appointment Veterinary Epidemiologist at
International Livestock Research Institute (ILRI)



Outline

- Stochastic processes
- Exposure assessment
 - Fault tree
 - Value chain
 - Mixture, separation, growth and inactivation
- Hazard characterization
 - Dose-response

Bayesian inference

Prior belief

Learning from observations

Current knowledge

Prior distribution

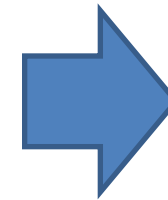
Likelihood function

Posterior distribution

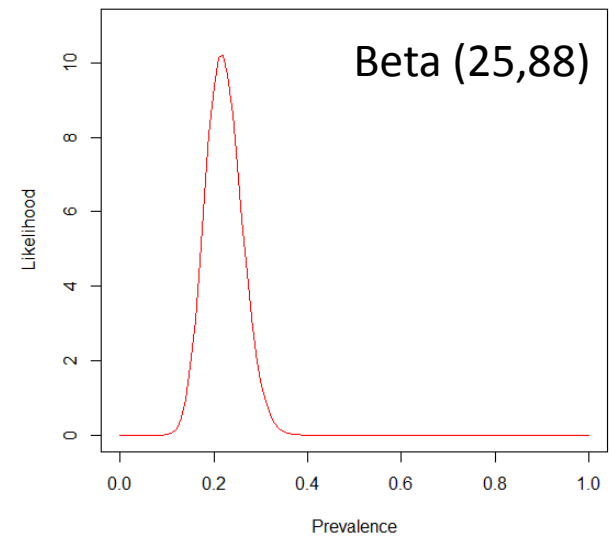
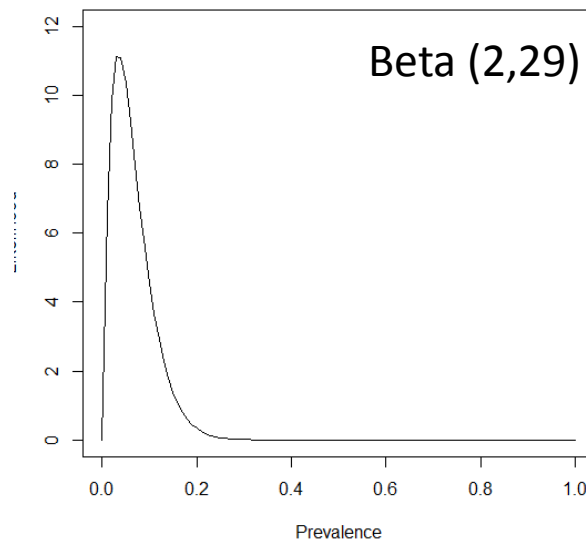
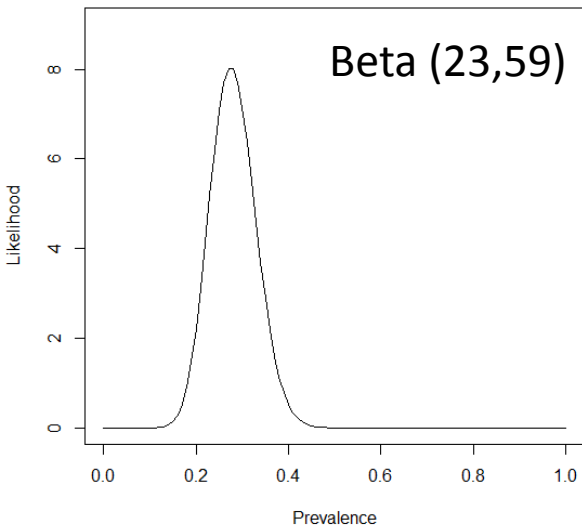
$$\pi(\theta)$$



$$l(X | \theta)$$



$$f(\theta | X)$$



Bayesian inference

Bayes' Theorem

$$P(A_i | B) = \frac{P(B | A_i)P(A_i)}{\sum_{j=1}^n P(B | A_j)P(A_j)}$$

Bayes' Theorem expressed in a different way

$$f(\theta | X) = \frac{\pi(\theta)l(X | \theta)}{\int \pi(\theta)l(X | \theta)d\theta}$$



The denominator normalizes the Posterior distribution to have a total area equal to one.

Bayesian inference

Bayes' Theorem

$$P(A_i | B) = \frac{P(B | A_i)P(A_i)}{\sum_{j=1}^n P(B | A_j)P(A_j)}$$

Bayes' Theorem expressed in a different way

$$f(\theta | X) = \frac{\pi(\theta)l(X | \theta)}{\int \pi(\theta)l(X | \theta)d\theta}$$

So,

$$f(\theta | X) \propto \pi(\theta)l(X | \theta)$$

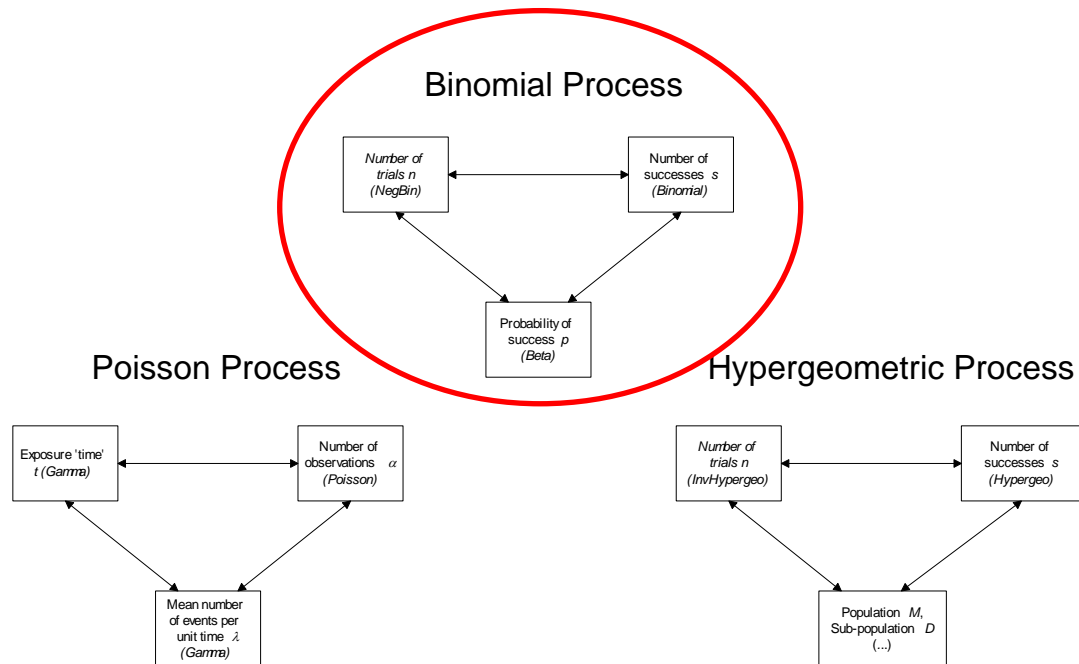
Posterior distribution

Prior distribution

Likelihood function

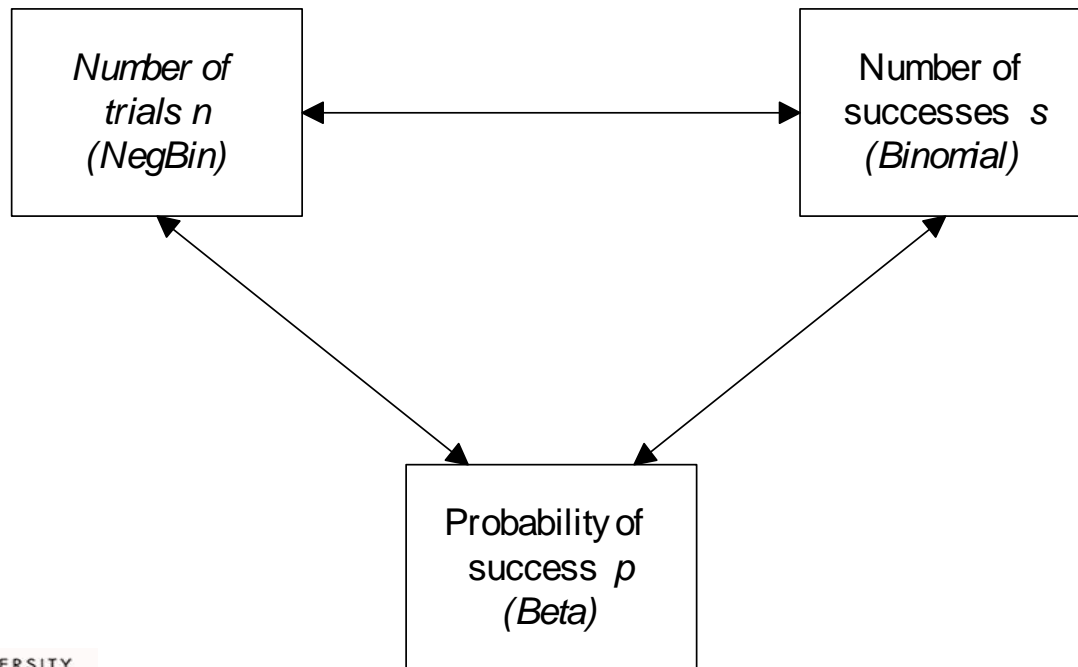
Stochastic processes

- Systems of countable events
- There are three fundamental stochastic processes
 - Binomial process
 - Poisson process
 - Hypergeometric process



Binomial process

- A random counting system where there are;
 - n independent identical trials
 - each one of which has the same probability of success p
 - which produces s successes from n trials



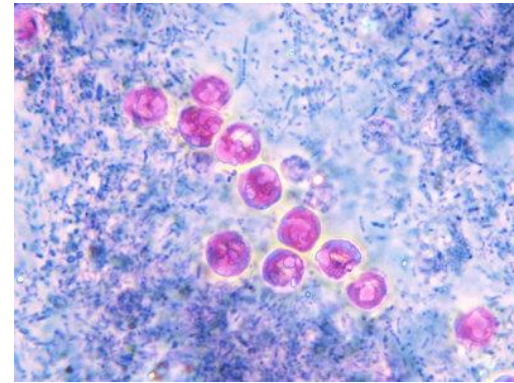
Distributions for the binomial process

- $s = \text{Binomial}(n, p)$
- $n = s + \text{Negbin}(s, p)$ if we know trials stopped in the s^{th} success
- $n = s + \text{Negbin}(s+1, p)$ if don't know trials stopped in the s^{th} success
- $p = \text{Beta}(s+1, n-s+1)$ for a Uniform(0,1) prior
- $p = \text{Beta}(s+a, n-s+b)$ for a Beta(a, b) prior
 - and $\text{Negbin}(1, p) = \text{Geomet}(p)$
 - $\text{Binomial}(1, p) = \text{Bernoulli}(p)$

Exercise for Binomial process

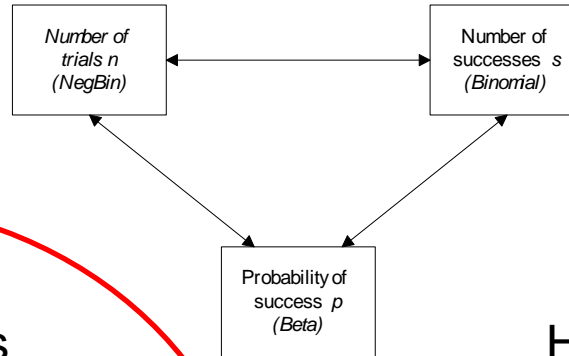
Now start your @Risk

1. 3% of salad in a local restaurant in area A is known to be contaminated with *Cryptosporidium parvum*. When you sample 50 salads, how many of them are contaminated with *C. parvum*?
2. In the area B, a survey on prevalence of *C. parvum* in salad was conducted. Out of 156 samples, 5 were contaminated. What is the prevalence?
3. The probability of attending hospital if infected with *C. parvum* is 80%. We observed 53 patients who visited hospital and diagnosed with *C. parvum* infection in the outbreak last month. How many people were infected?

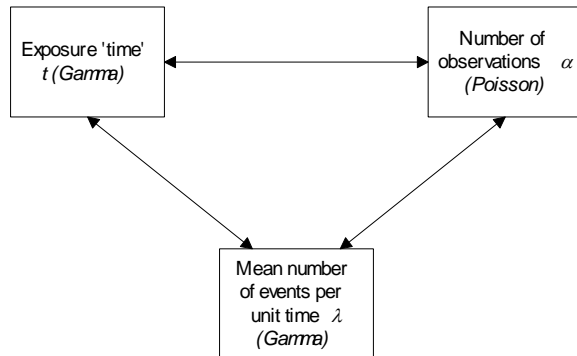


Back to the map...

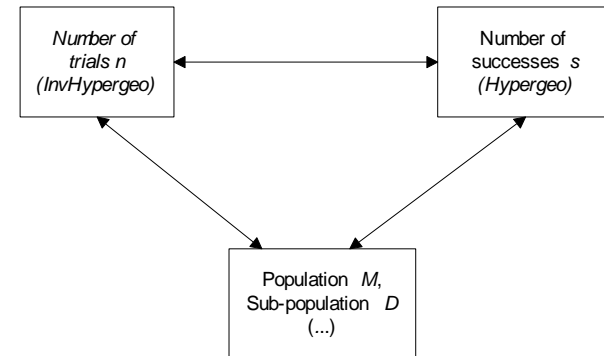
Binomial Process



Poisson Process

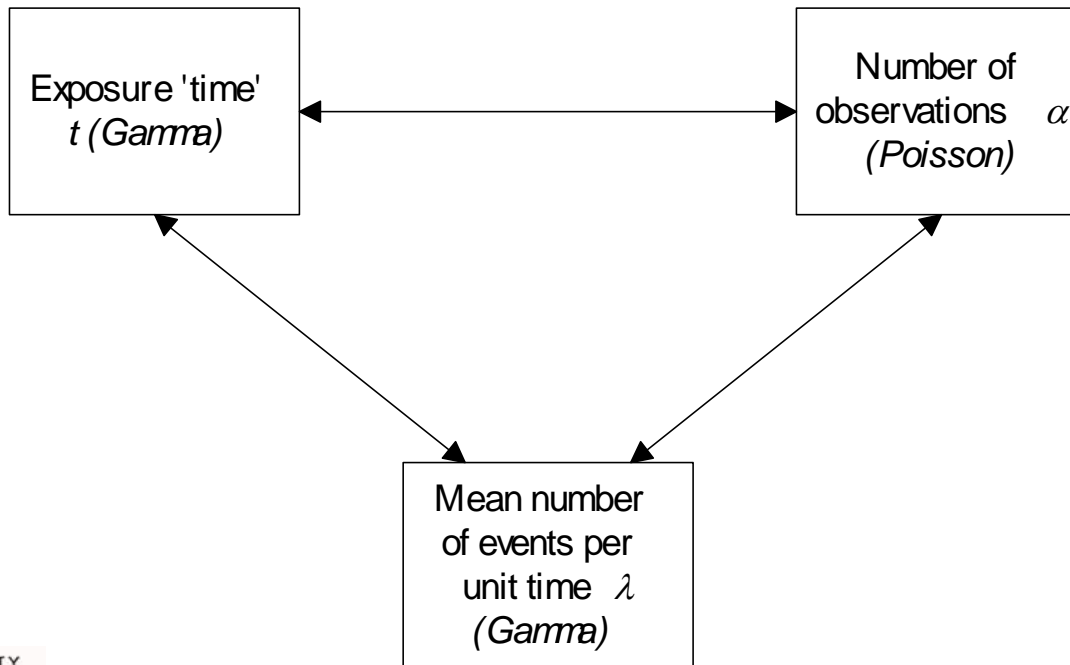


Hypergeometric Process



Poisson process

- There is a continuous and constant opportunity for an event to occur- this is explained by;
 - the number of events that may occur in a period t
 - the amount of “time” one will have to wait to observe α events
 - the average number of events that could occur, λ



Distributions for the Poisson process

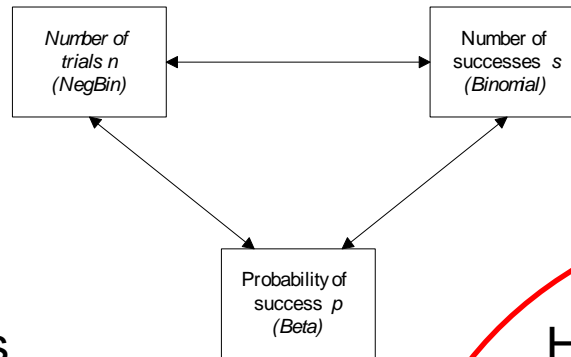
- $\alpha = \text{Poisson}(\lambda * t)$ $P(\alpha=0) = \text{Exp}(-\lambda t)$
- $t = \text{Gamma}(\alpha, \beta)$
 $\beta = 1/\lambda$ (Average time between events)
 i.e. how much time until the next AI outbreak
- $\lambda = \text{Gamma}(\alpha, 1/t)$
 with a $\pi(\lambda) \propto 1/\lambda$ prior
 and $\text{Gamma}(1, \beta) = \text{Expon}(\beta)$

Exercise

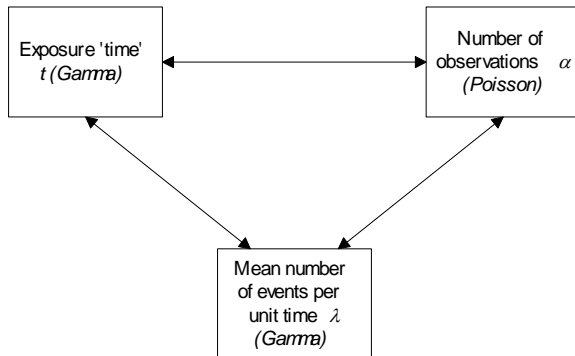
- Food poisoning was reported in a village A for 40 times last 5 years. If food poisoning occurs regardless the season (a constant risk),
 - how many outbreaks would be observed in the next three months?
 - how many months does it take to have the next outbreak since last one (suppose we had an outbreak yesterday)?
- If a bulk of raw milk contains 4 cfu/l of *E. coli* O157:H7,
 - how much milk can you drink before you ingest one *E. coli*?
 - what is the probability that you ingest at least one *E. coli* if you drink 300ml of the milk?

Back to the map...

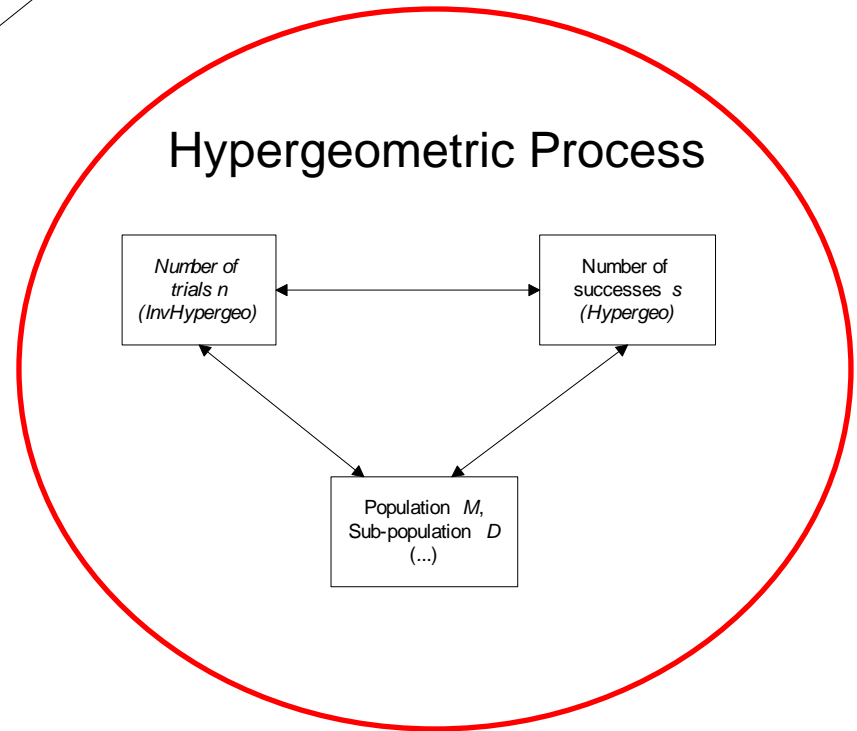
Binomial Process



Poisson Process

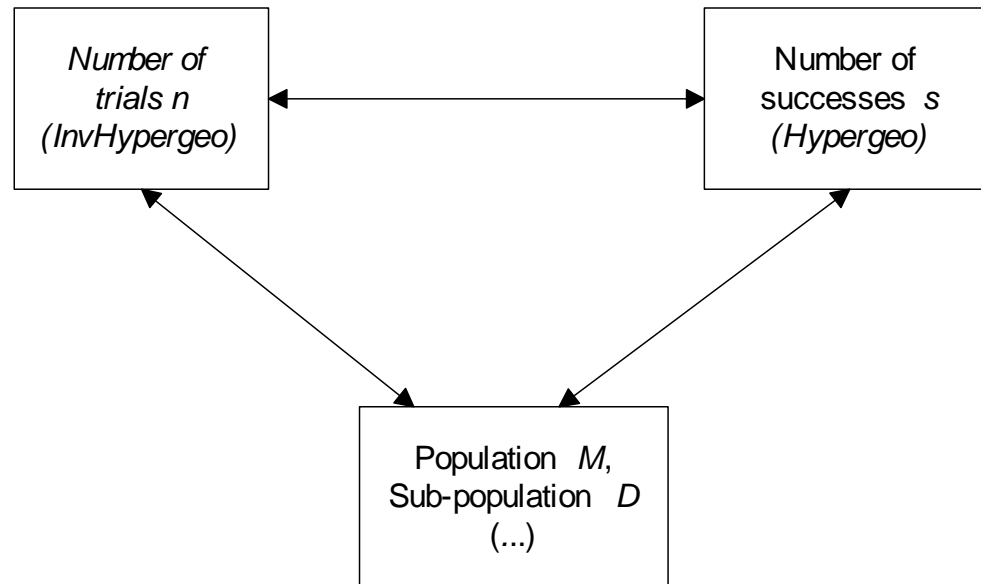


Hypergeometric Process

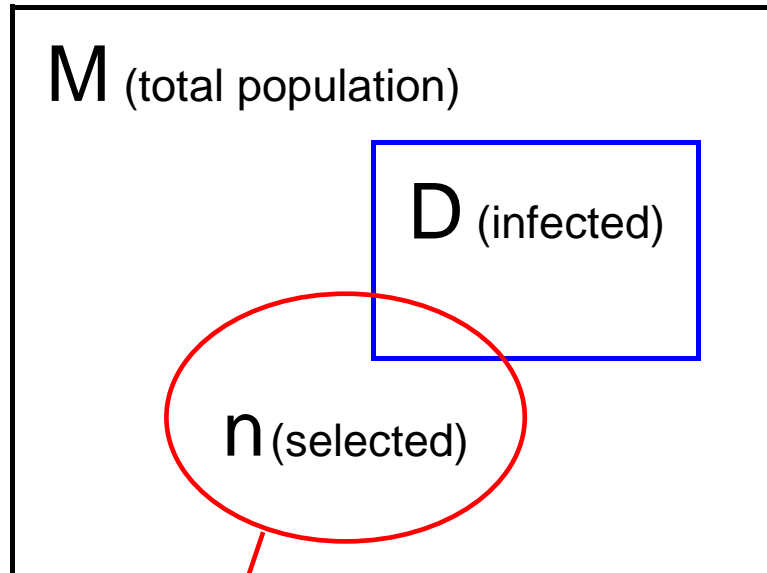


Hypergeometric process

- When the population is not very large compared to the sample (population $< 10 \times$ sample size)
- Out of a group of M individual items, D have a certain characteristic. Randomly picking n items from this group **without replacement**, where each of the M items has the same probability of being selected, is a hypergeometric process.



The hypergeometric format



s = number infected from selection

Examples:

- Sampling sheep from an infected flock
- Sampling food from a consignment
- Defective items in a consignment
- Capture-release-recapture surveys

Distributions for the hypergeometric process

- $s = \text{Hypergeo}(n, D, M)$
- $n = s + \text{InvHypgeo}(s, D, M)$
- D, M have no standard distributions
 - Have to be worked out manually (see problems)

Exercise

- In an informal market, Mrs A is selling 100 eggs of which 10 are contaminated with *Salmonella*. You purchased 5 eggs from Mrs A. How many contaminated eggs are included?

Outline

- Stochastic processes
- Exposure assessment
 - Fault tree
 - Value chain
 - Mixture, separation, growth and inactivation
- Hazard characterization
 - Dose-response

Fault tree

- Fault tree is a systematic method for acquiring information about a system

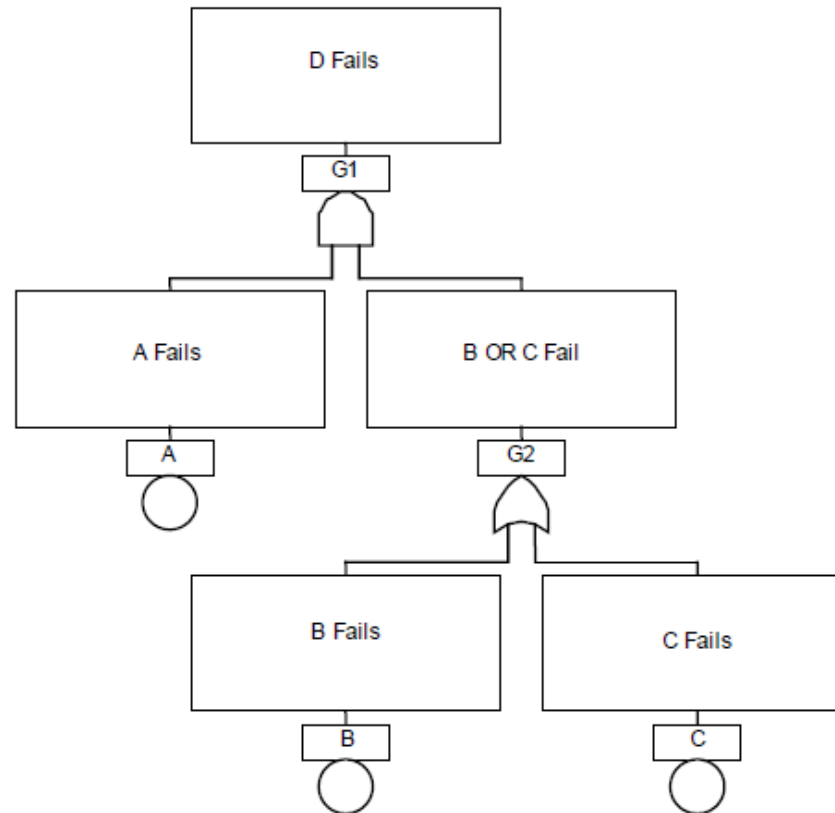


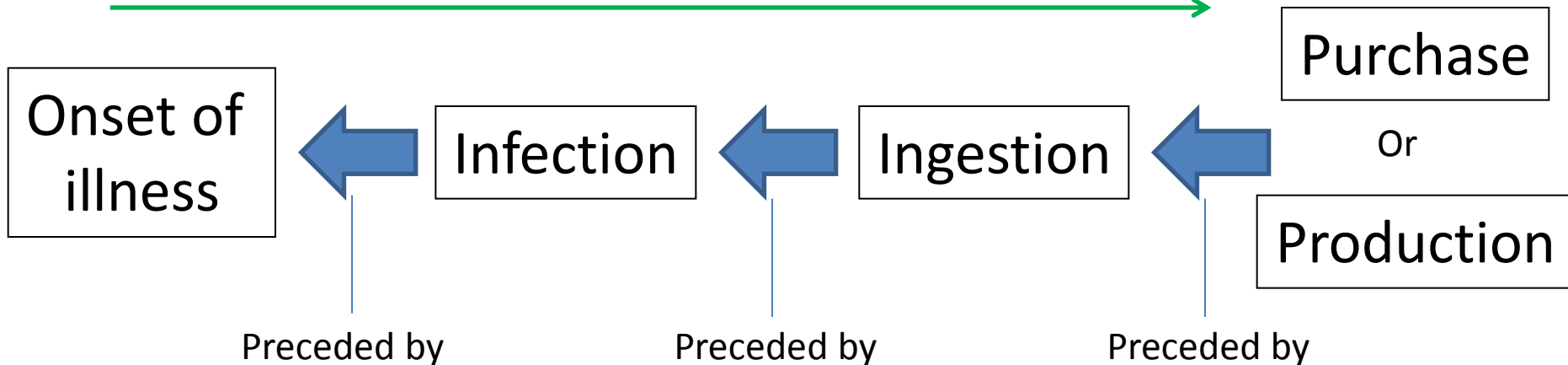
Figure 1-1. A Simplified Fault Tree

Source: NASA. 2002. Fault tree hand book with aerospace applications.

Points of fault tree analysis in food safety

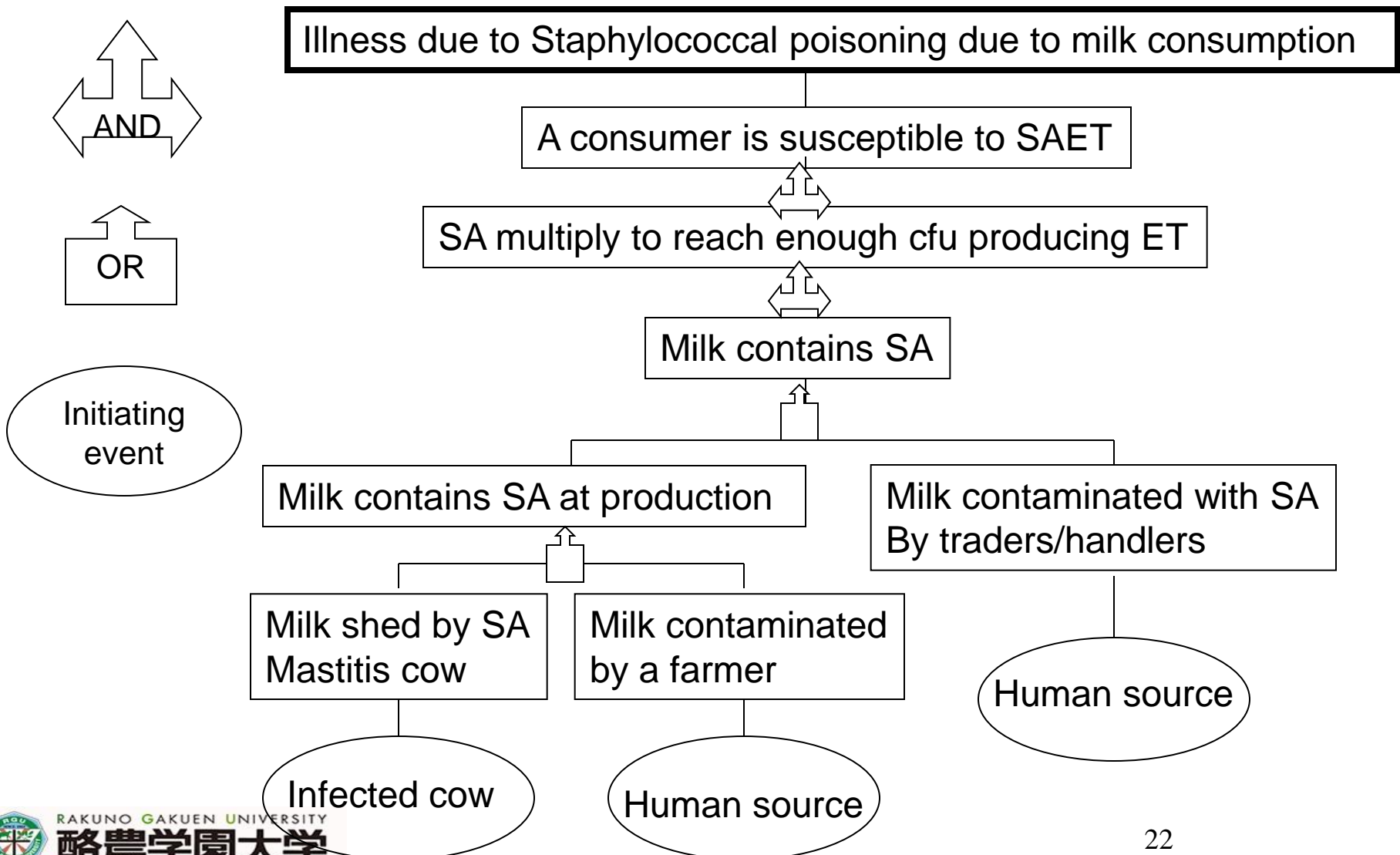
- How the illness can occur

Direction of identification and diagramming →



Risk assessment for staphylococcal poisoning through consumption of informally-marketed milk in Debre Zeit, Ethiopia

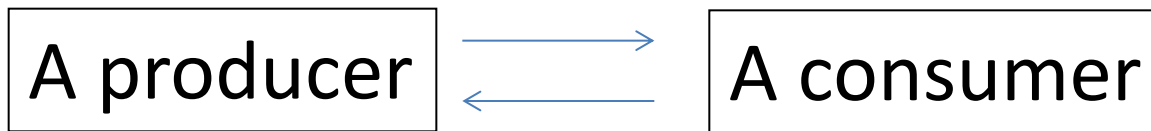
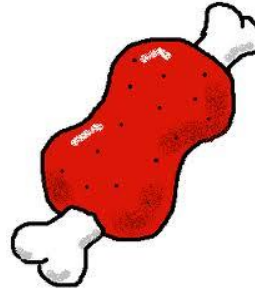
Makita K, Dessisa F *et al.* (2011) International Journal of Food Microbiology



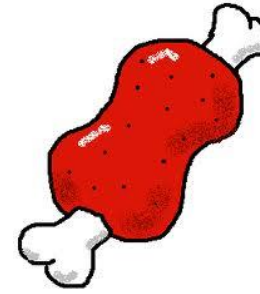
Outline

- Stochastic processes
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Value chain



Value chain



Producers



Middle men



Consumers



Designing a study based on fault tree

- Design a study to collect information on the 'Nodes' identified in fault tree analysis
- 'Nodes' are similar to Critical Control Points (CCPs) in HACCP
- It usually include below segments

Consumer

Retail shop

Middle men

Producer

- In informal markets, marketing systems are sometimes not 'linear', which means unpredictable
- So combination of below techniques are useful
 - Rapid rural appraisal
 - Probabilistic survey using questionnaires
 - Tracing back, tracing forward

Categorizing actors

- Retail shops or middle men can be categorized even further
- In terms of risk modeling, it is important to have separate 'branches' to predict behavior more precisely
- Examples are shown in the next slide

Actors in informal milk sales in Kampala, Uganda



Shop with a bulk cooler



Shop with a small refrigerator



Boiling centre



Trader with cans on a bicycle



Roadside vendor



Roadside vendor

- Plus milk retail shop without refrigerator and dairy farmers selling at farms

Probabilistic survey

- Random selection of either small administrative units or shops or farmers in a probabilistic manner
- Collect quantitative information (e.g. number of shops, farmers, quantity of sales)
- Divide the quantity with sampling fraction in order to estimate the total amounts of sales in the study area

Probabilistic survey

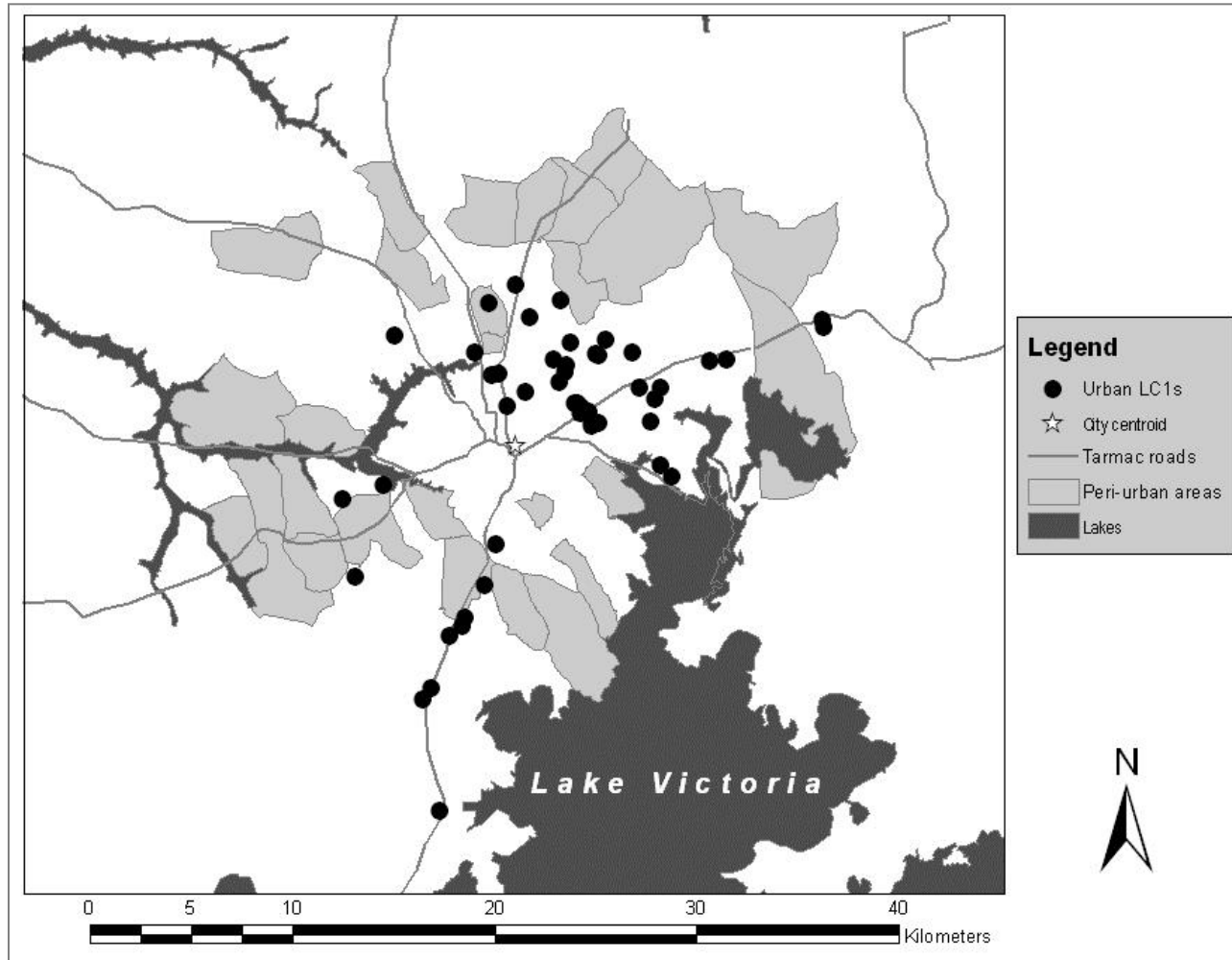


Fig.1. Map of Kampala showing the locations of 48 urban LC1s studied. Areas highlighted are peri-urban parishes.

Source: Makita K. (2009). PhD Thesis.
The University of Edinburgh

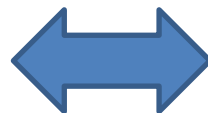
Field survey – Importance of diagnostic tests

Nyama-choma in Tanzania



My bitter experience in *Campylobacter* risk assessment...

<1st survey for prevalence>
High prevalence using
culture without rigorous
identification



<2nd survey for MPN>
Low prevalence using PCR
after culturing

Tracing forward and/or backward

- Wholesale shops, abattoirs and markets identified in RRAs and interviews need to be trucked in order to complete the value chains
- Interviews at such 'hubs' will give you the information on the chains after the 'hubs'
- Tracking will fill the 'gaps' of quantitative information of sales

Tracing forward and/or backward

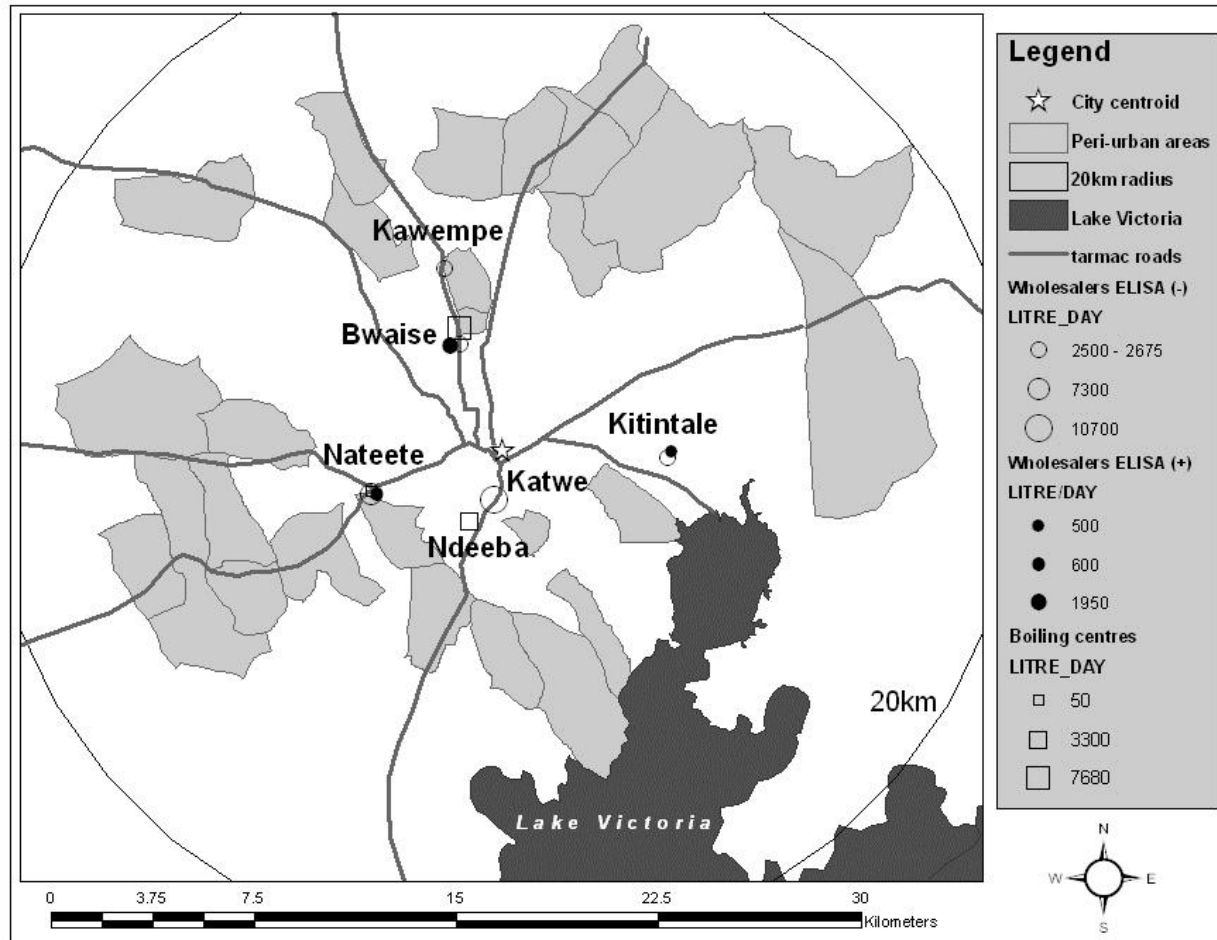


Fig. 2. Spatial distributions of wholesale milk shop centres and milk boiling centres in Kampala

Source: Makita K. (2009). PhD Thesis.
The University of Edinburgh

Tracing forward and/or backward

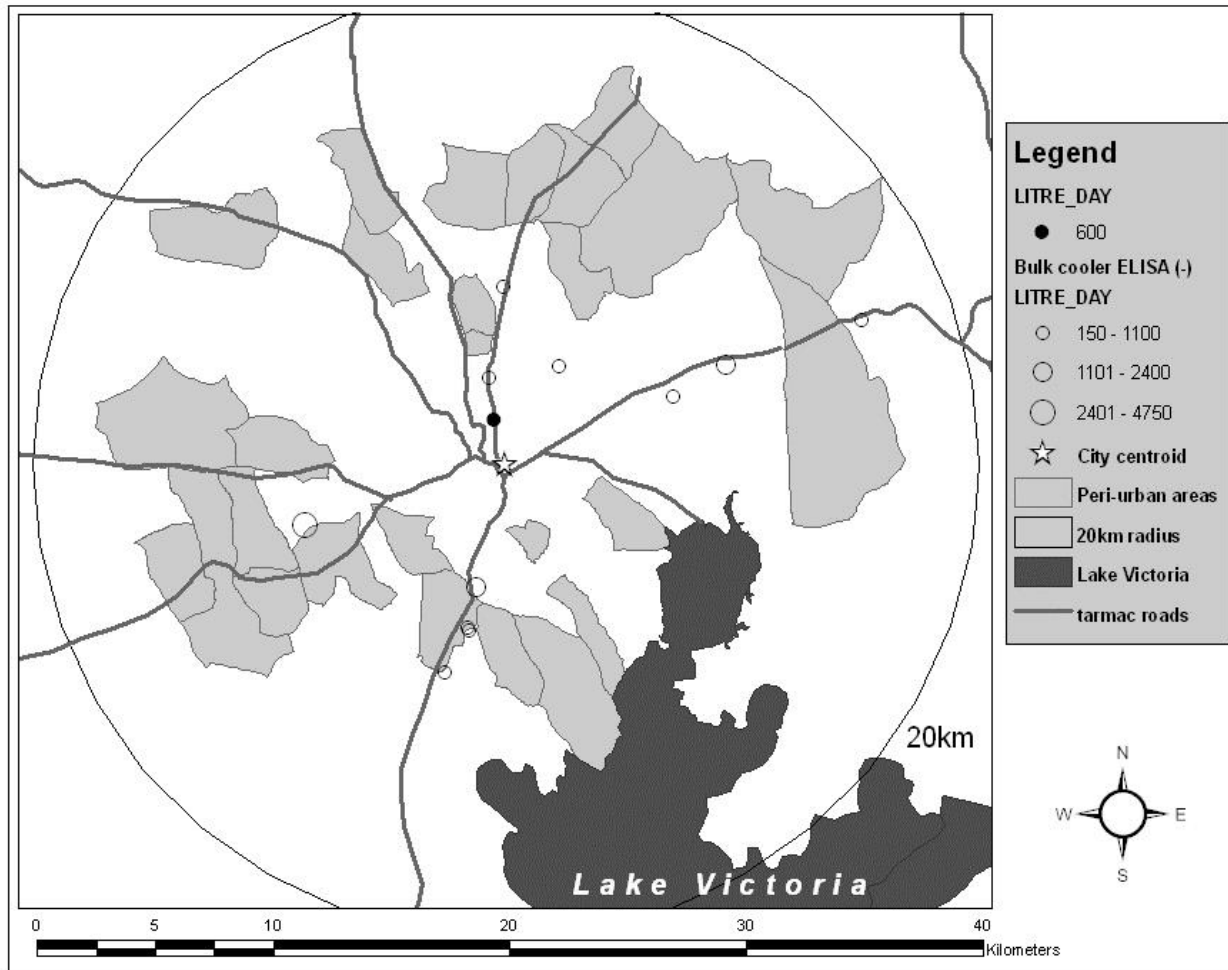


Fig. 3. Spatial distributions of milk shops with a bulk cooler.

Source: Makita K. (2009). PhD Thesis.
The University of Edinburgh

Tracing forward and/or backward

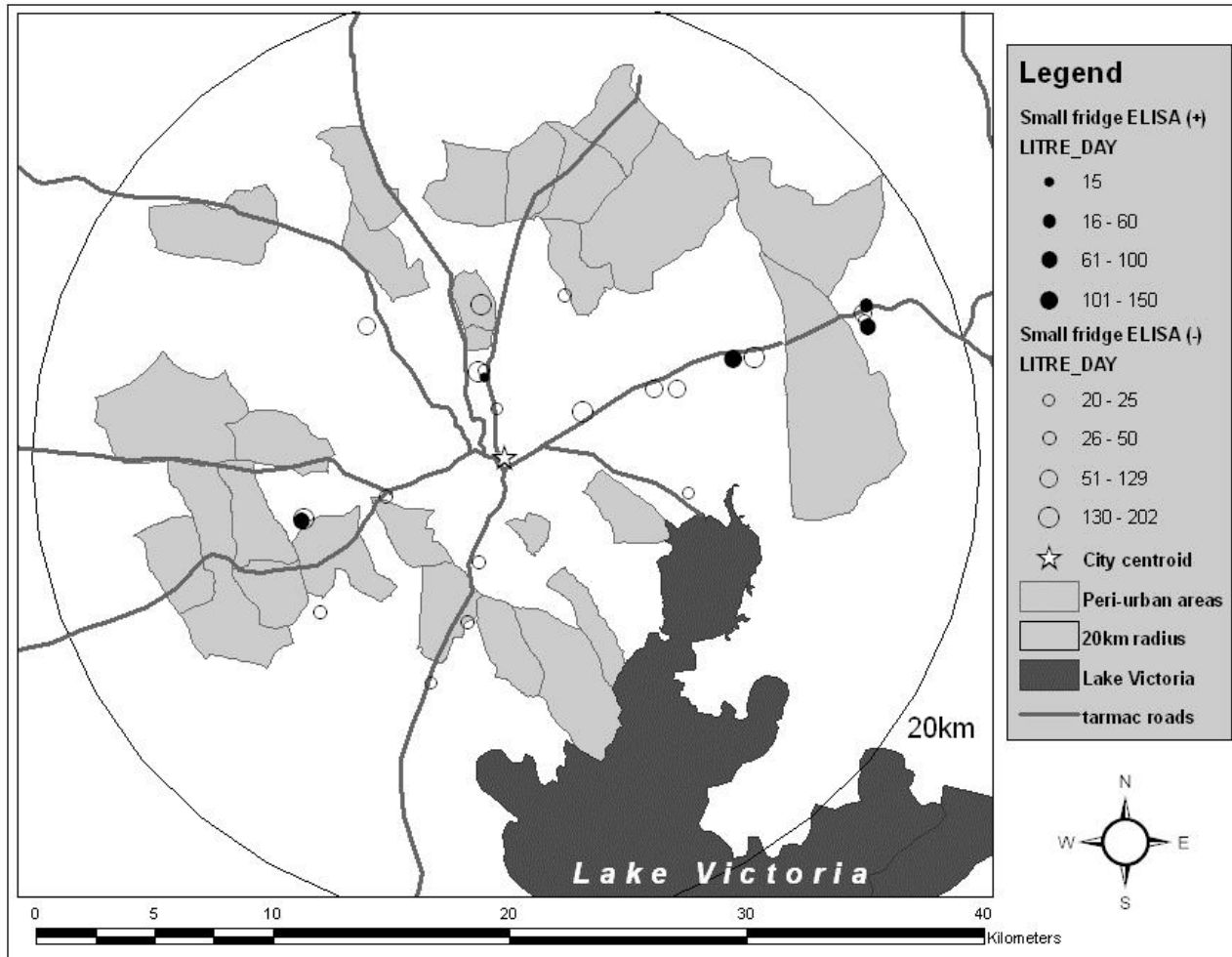
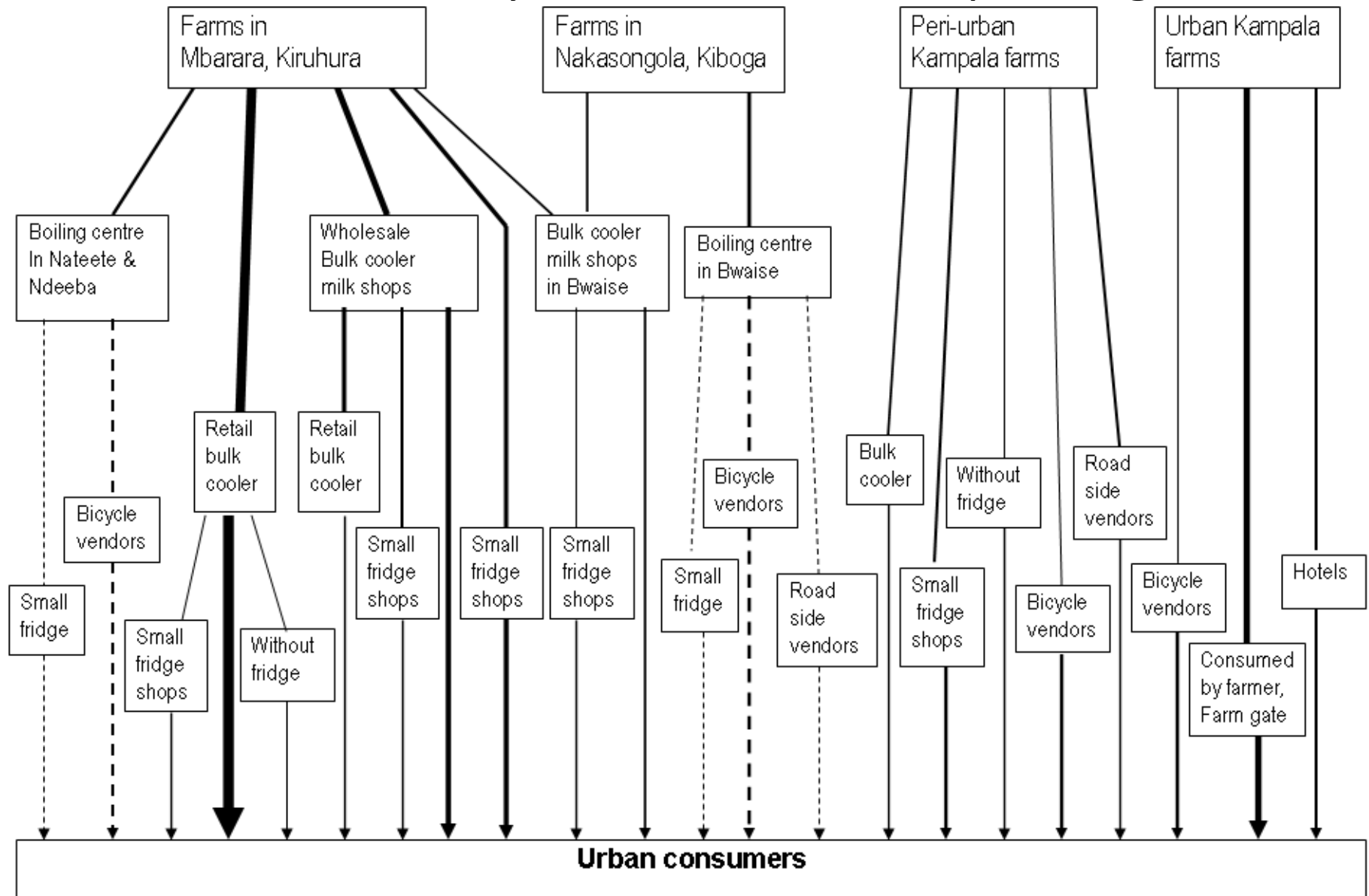


Fig. 4. Spatial distributions of fresh milk shops with a small refrigerator

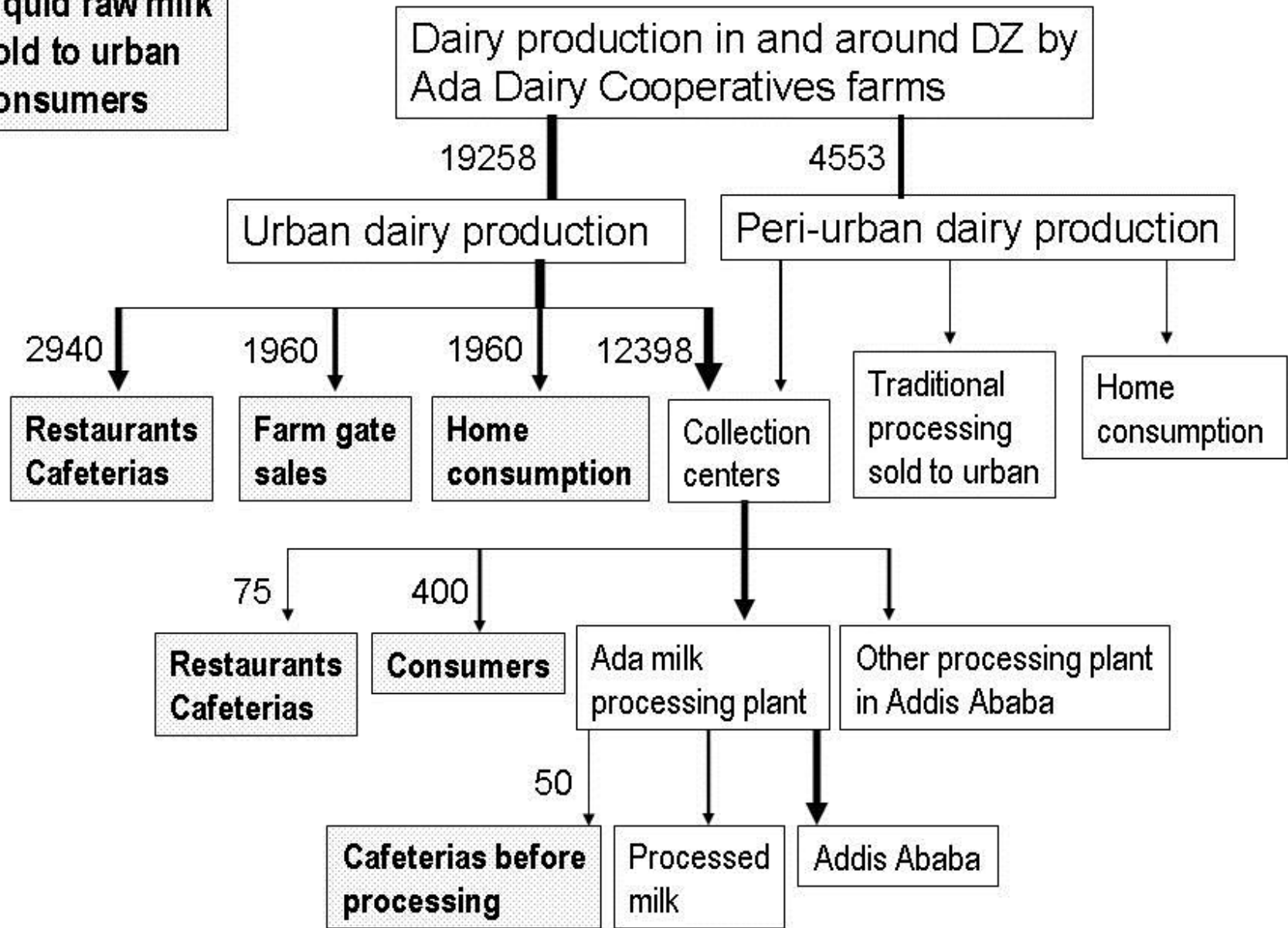
Source: Makita K. (2009). PhD Thesis.
The University of Edinburgh

Quantitative dairy value chain in Kampala, Uganda



Source: Makita K. et al. (2010). How human brucellosis incidence in urban Kampala can be reduced most efficiently? A stochastic risk assessment of informally-marketed milk. PLoS ONE 5 (12): e14188.

Liquid raw milk sold to urban consumers



Dairy value chain- RRA and interviews

Outline

- Stochastic processes
- Exposure assessment
 - Fault tree
 - Value chain
 - Mixture, separation, growth and inactivation
- Hazard characterization
 - Dose-response

Modular Process Risk Model

Microbial processes

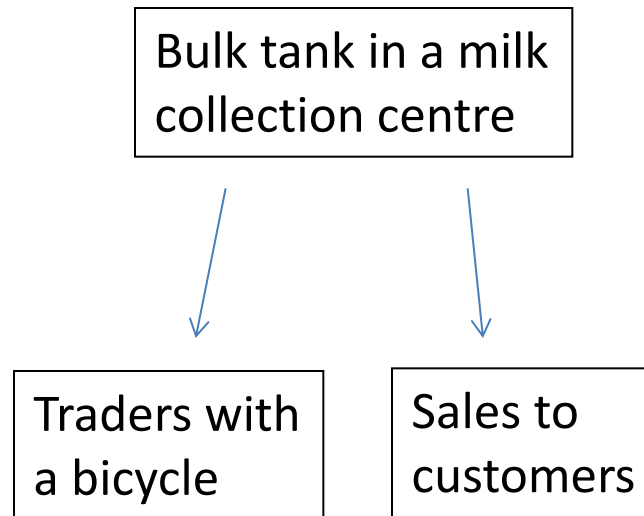
- Growth
- Inactivation

Food handling processes

- Mixing
- Partitioning
- Cutting
- Cross-contamination

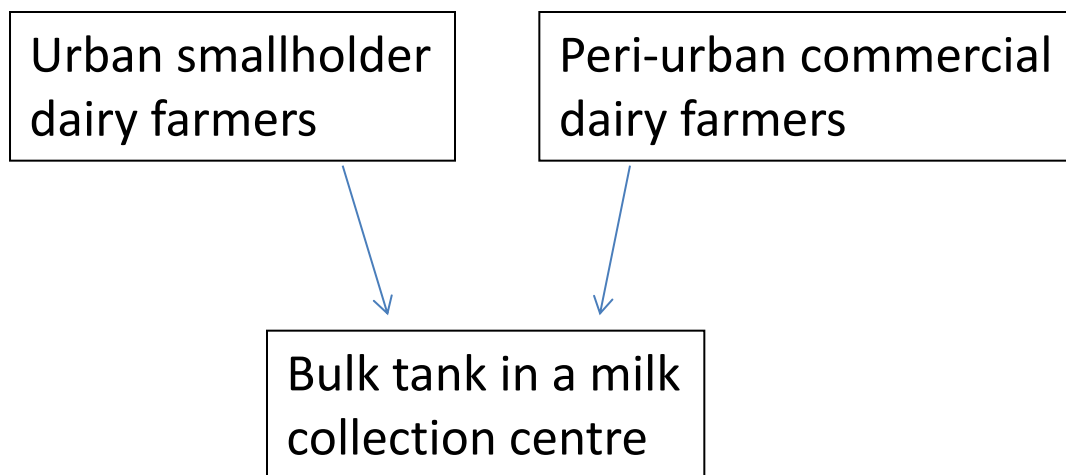
Separation

- Separation in a value chain refers to sales to more than two customers



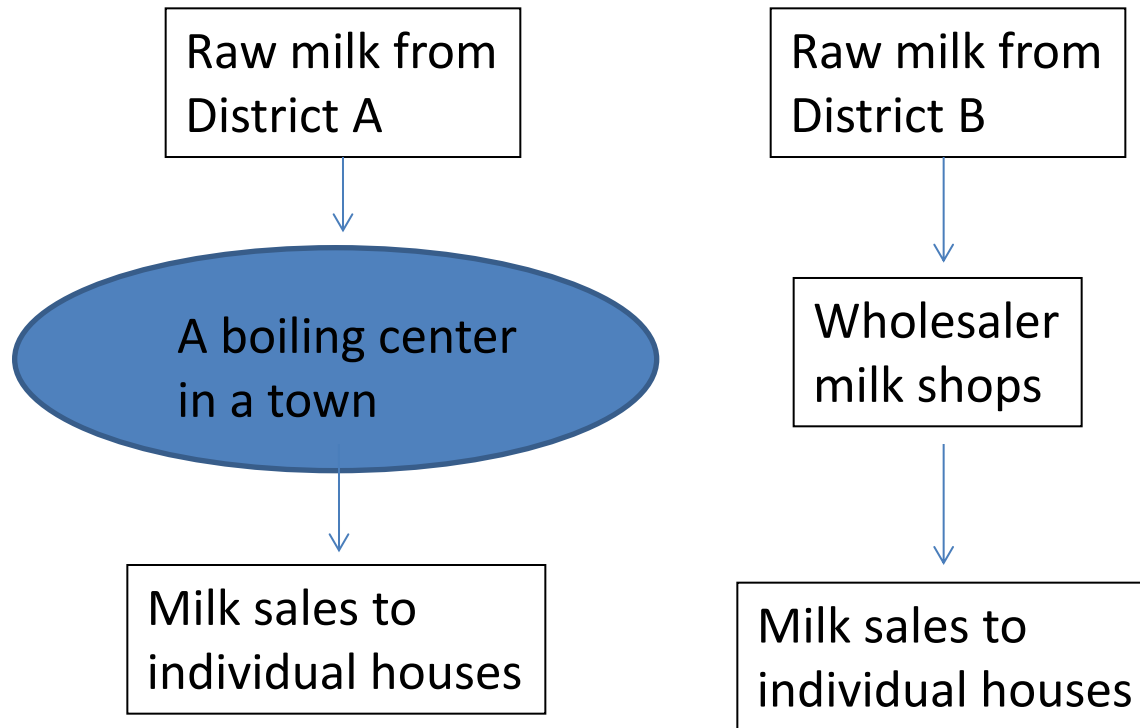
Mixing

- Mixing in a value chain refers to receiving from more than two sources

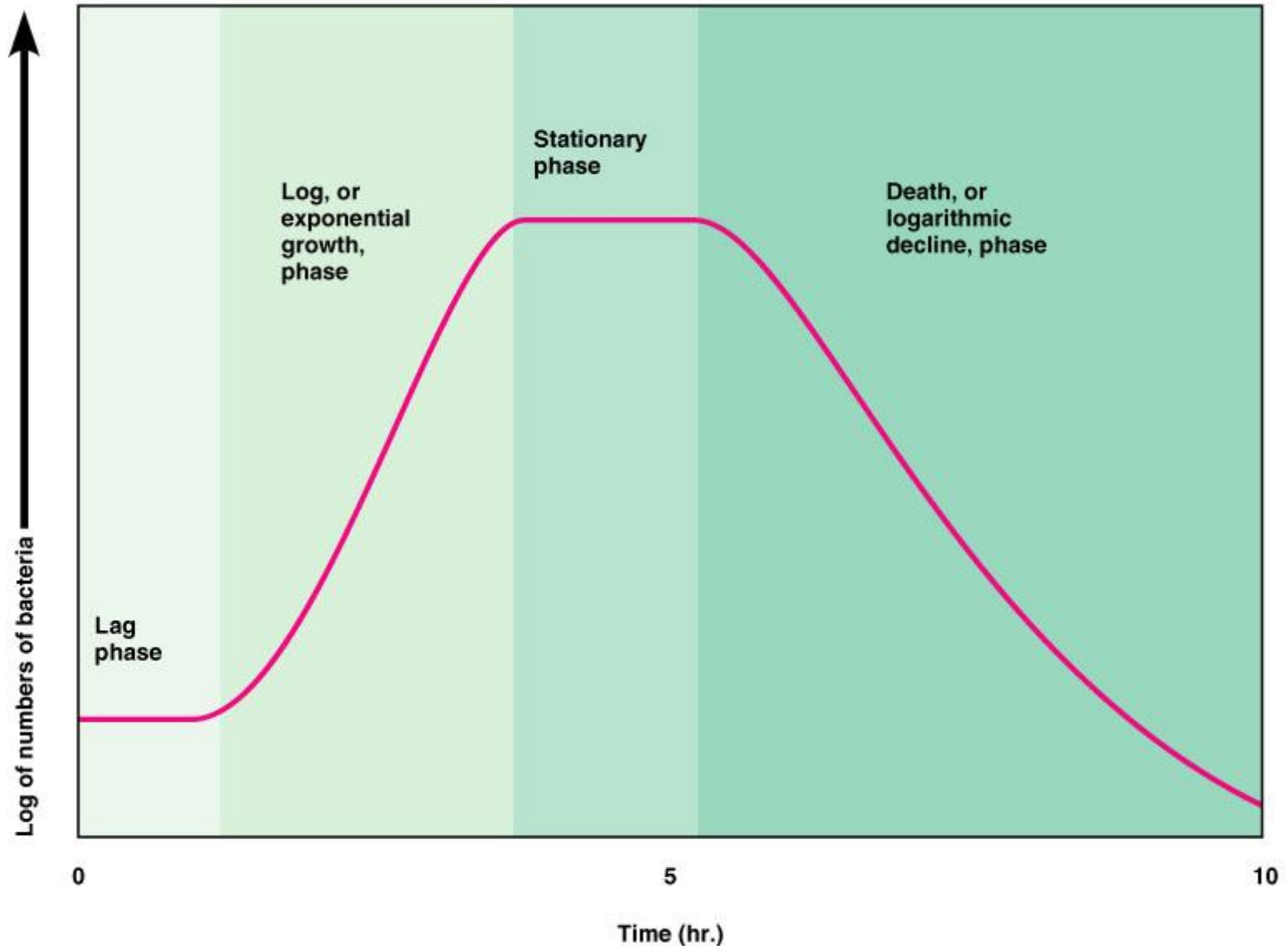


Inactivation

- Inactivation in a value chain usually refers to heat treatment to kill pathogens (note: heat cannot inactivate heat-resistant toxins)



Bacterial growth



Copyright © 2004 Pearson Education, Inc., publishing as Benjamin Cummings.

Mathematical modeling of growth

- Several models exist
 - Logistic model
 - Michaelis-Menten model
 - Modified Gompertz model (Gibson *et al.*, 1987)
 - Baranyi model (Baranyi and Roberts, 1994)
 - Modified logistic model (Fujikawa *et al.*, 2003)
- Several factors affect on bacteria growth- careful choice from literature is required
 - Temperature
 - pH
 - Water activity (aW)
 - Salinity

Contamination- a survey

| | Isolation of <i>S aureus</i> | Boiling before sales |
|-------------------------------|------------------------------|----------------------|
| Milk collection centre (n=25) | 18 (70.4%) | 0 |
| Dairy farm (n=170) | 74 (43.6%) | 0 |

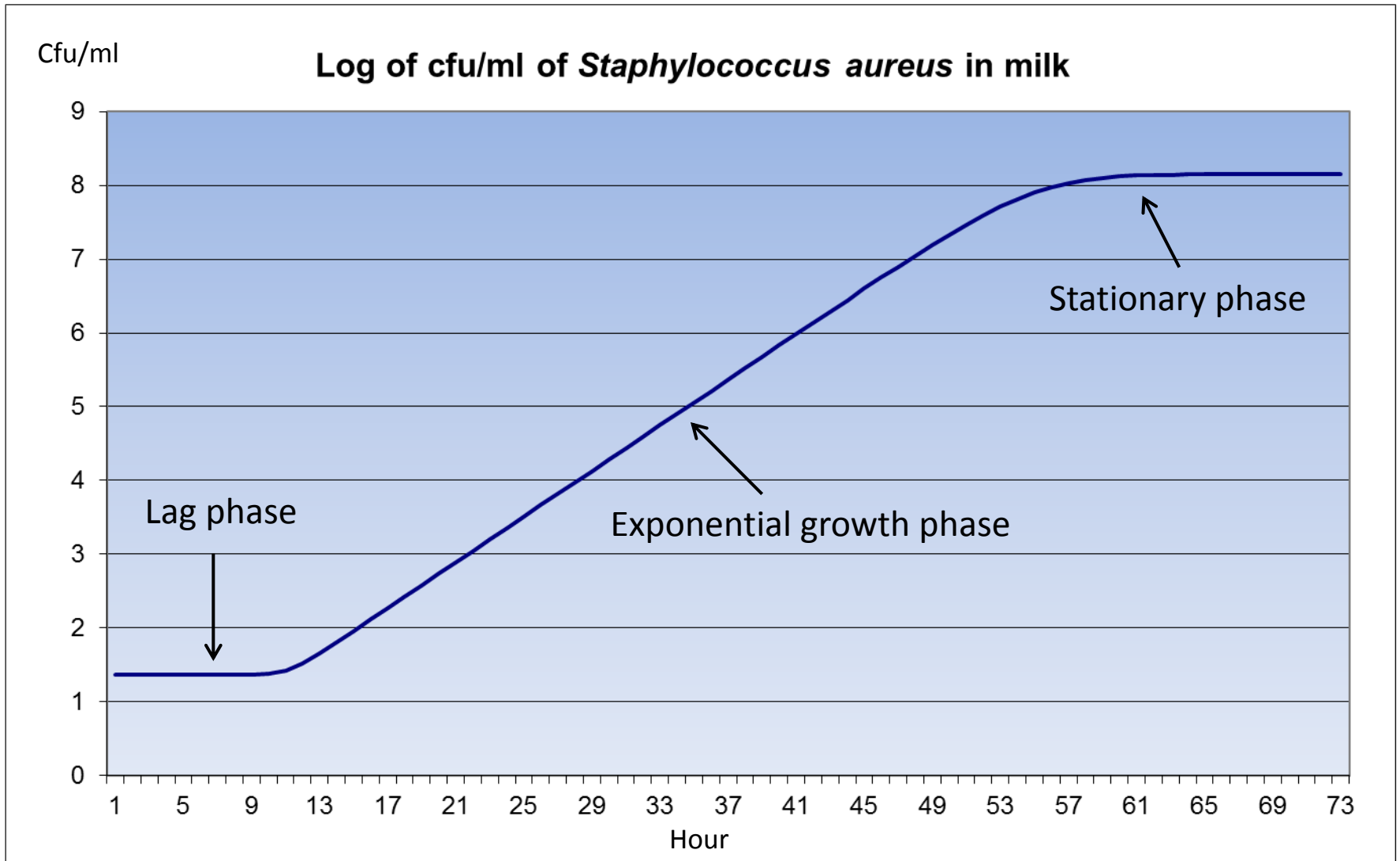


Risk mitigation by consumers -participatory and interviews

| | Boil milk before consumption | Percentage |
|----------------------------------|------------------------------|------------|
| Dairy farming households (n=170) | 116 | 68.2 |
| Consumers (n=25) | 16 | 64.0 |

Example:

Fujikawa and Morozumi (2006)
modified logistic model



Example

Growth of *Staphylococcus aureus* in milk

- Mathematical model of *S. aureus* growth in milk
 - Modified logistic model reported by Fujikawa and Morozumi (2006)
 - Experts say it also applies to meats

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{N_{\max}}\right)\left\{1 - \left(\frac{N_{\min}}{N}\right)^c\right\}$$

Where N is population of a microorganism at time t

r is rate constant or maximum specific rate of growth

N_{\min} is minimum cell concentration and set as slightly lower value than initial concentration N_0

N_{\max} is maximum concentration at stationary phase: $10^{8.5}$ cfu/ml

c is an adjustment factor – **variability of growth speed**: 4.7 ± 1.1

$r^{0.5} = 0.0442T - 0.239$

Where T is temperature in Celsius

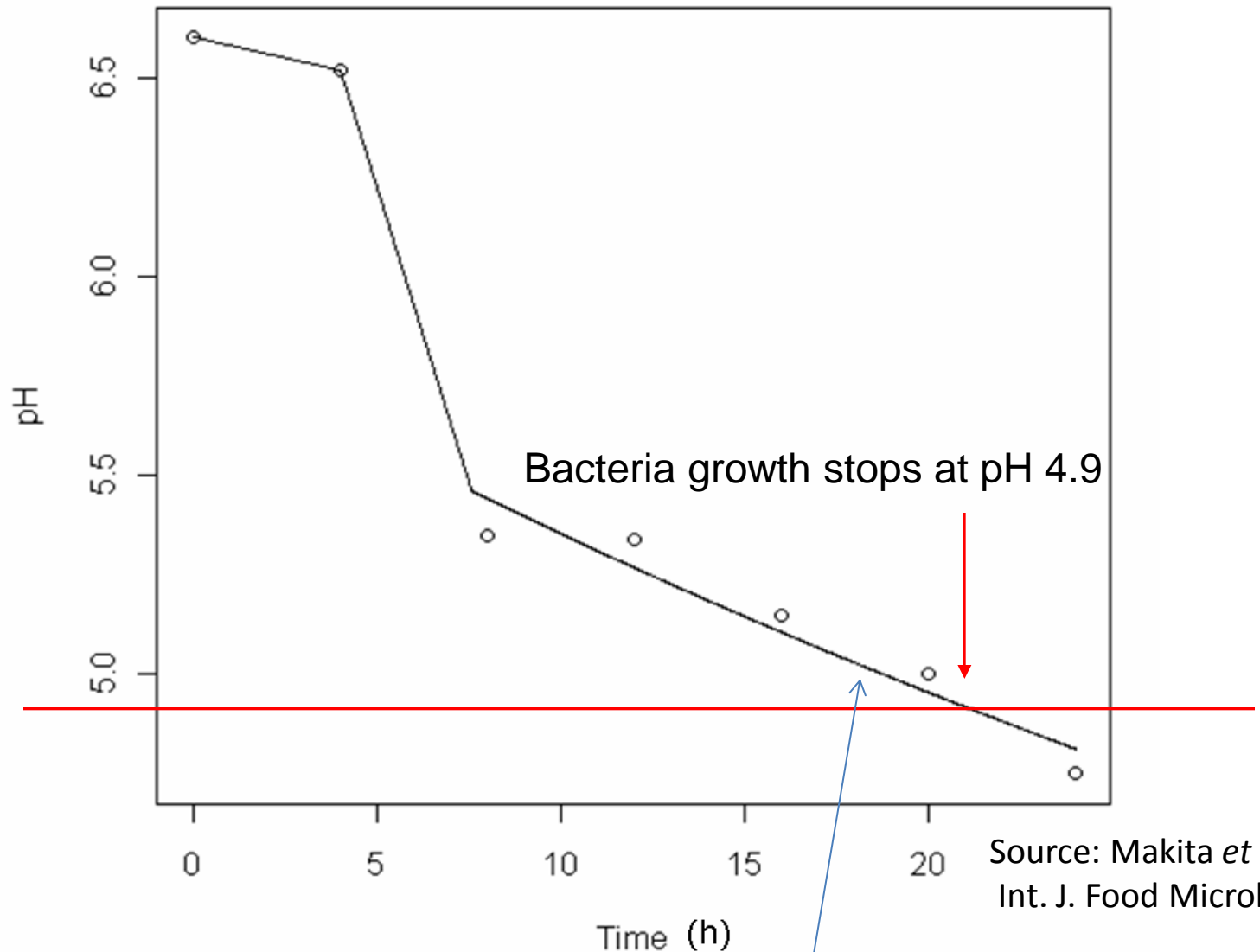
Modeling growth in @Risk



| Time(h) | Log N (D15) | r (E15) | dN/dt (F15) |
|---------|---------------------------------|-----------------------|--|
| 0 | $=N_0$ | $=(0.0442*T-0.239)^2$ | $=E16*10^{(D16)}*(1-10^{(D16)/10^{(Nmax)}})*(1-(Nmin/10^{(D16)})^c)$ |
| 1 | $=\text{LOG}10(10^{(D16)}+F16)$ | $=(0.0442*T-0.239)^2$ | $=E17*10^{(D17)}*(1-10^{(D17)/10^{(Nmax)}})*(1-(Nmin/10^{(D17)})^c)$ |
| 2 | $=\text{LOG}10(10^{(D17)}+F17)$ | $=(0.0442*T-0.239)^2$ | $=E18*10^{(D18)}*(1-10^{(D18)/10^{(Nmax)}})*(1-(Nmin/10^{(D18)})^c)$ |
| 3 | $=\text{LOG}10(10^{(D18)}+F18)$ | $=(0.0442*T-0.239)^2$ | $=E19*10^{(D19)}*(1-10^{(D19)/10^{(Nmax)}})*(1-(Nmin/10^{(D19)})^c)$ |

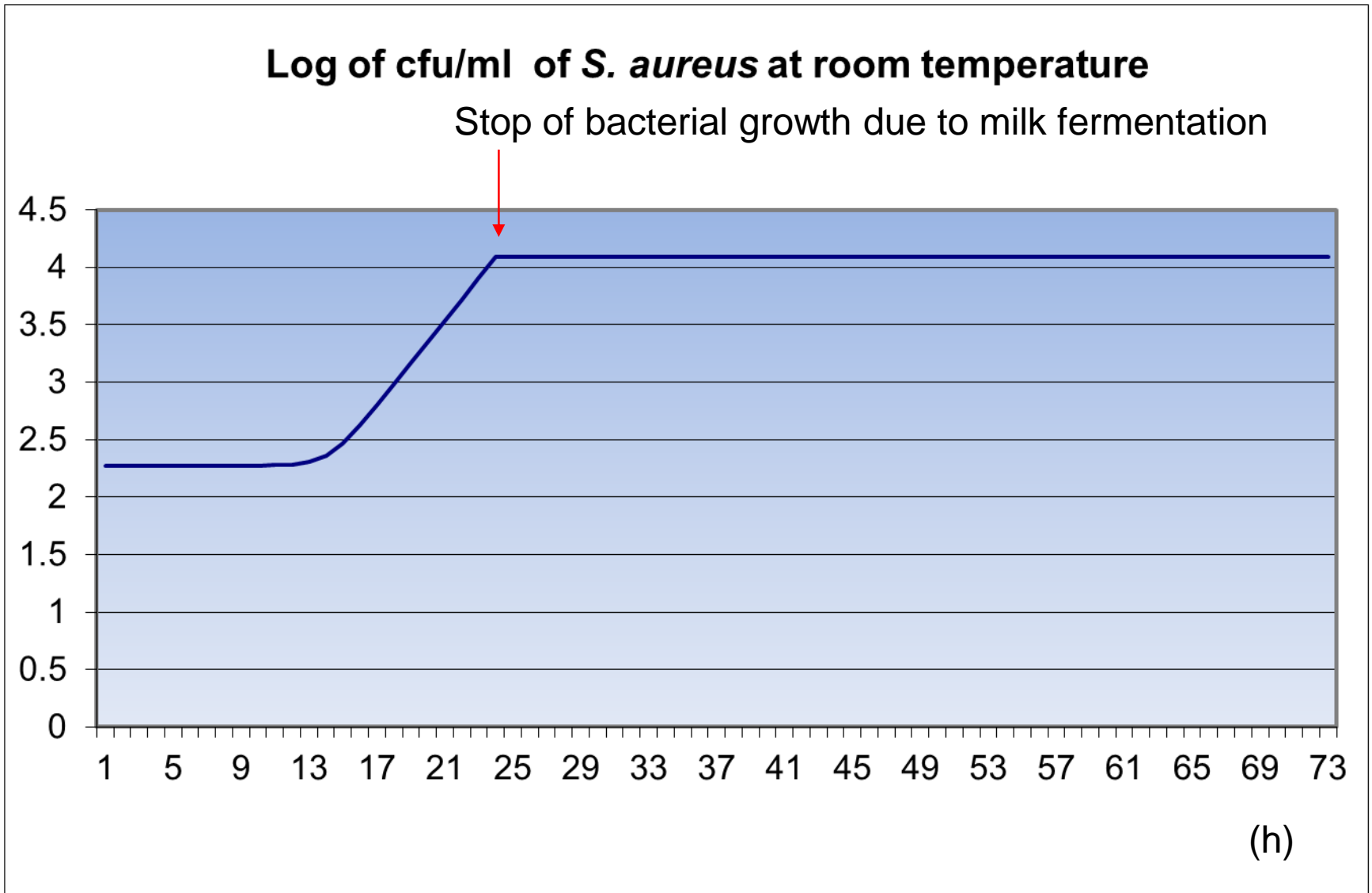
| Time(h) | Log N | r | dN/dt |
|---------|----------|----------|-----------|
| 0 | 0.35916 | 0.234521 | 2.684E-06 |
| 1 | 0.35916 | 0.234521 | 5.837E-06 |
| 2 | 0.359162 | 0.234521 | 1.269E-05 |
| 3 | 0.359164 | 0.234521 | 2.759E-05 |
| 4 | 0.359169 | 0.409327 | 0.000104 |
| 5 | 0.359189 | 0.409327 | 0.000319 |
| 6 | 0.35925 | 0.409327 | 0.000973 |
| 7 | 0.359434 | 0.409327 | 0.002964 |
| 8 | 0.359997 | 0.409327 | 0.009008 |
| 9 | 0.361701 | 0.409327 | 0.027184 |
| 10 | 0.366805 | 0.409327 | 0.080358 |

Risk mitigation by traditional milk fermentation- Modeling using reported data (Gonfa et al., 1999)



$$1/\text{pH} = 0.002 t \text{ (h)} + 1.187 \text{ (df=3, } r^2=0.90, p=0.009)$$

Stop of growth of *S. aureus* in milk by low pH

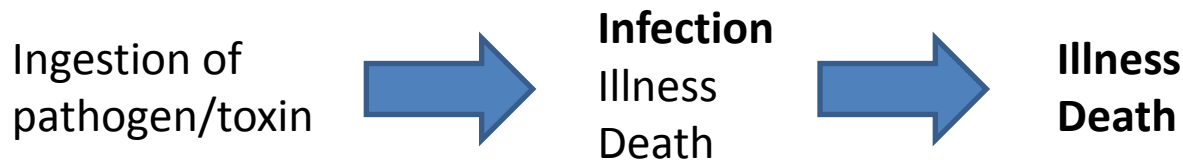


Outline

- Stochastic processes
- Exposure assessment
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Overview

- Here we learn how to model the probability of infection/illness based on how much a person ingests pathogens
- We learn different types of model
- Later we work on an example of campylobacteriosis



The four most common no-threshold DR models

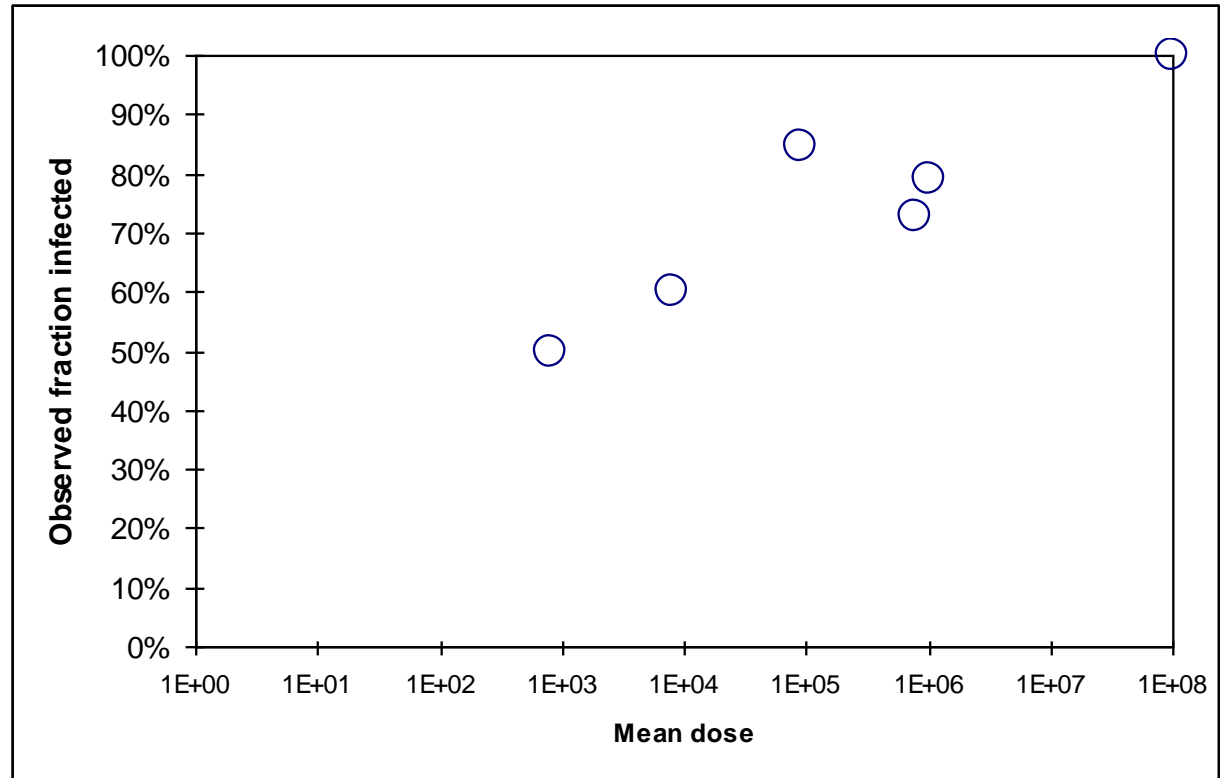
| D-R model | Dose measure | P(effect) |
|------------------|---------------------|---|
| Exponential | Mean dose λ | $= 1 - \exp(-\lambda p)$ |
| Beta-Poisson | Mean dose λ | $\approx 1 - \left(1 + \frac{\lambda}{\beta}\right)^{-\alpha}$ |
| Beta-binomial | Actual dose D | $= 1 - \frac{\Gamma(D + \beta)\Gamma(\alpha + \beta)}{\Gamma(\alpha + \beta + D)\Gamma(\beta)}$ |
| Weibull-gamma | Actual dose D | $= 1 - \left(1 + \frac{D^b}{\beta}\right)^{-\alpha}$ |

Example Applications: *C. jejuni*

Data set for infection

Black RE et al (1988), Experimental *Campylobacter jejuni* infections in humans. J infectious Diseases, **157**(3), 472-479.

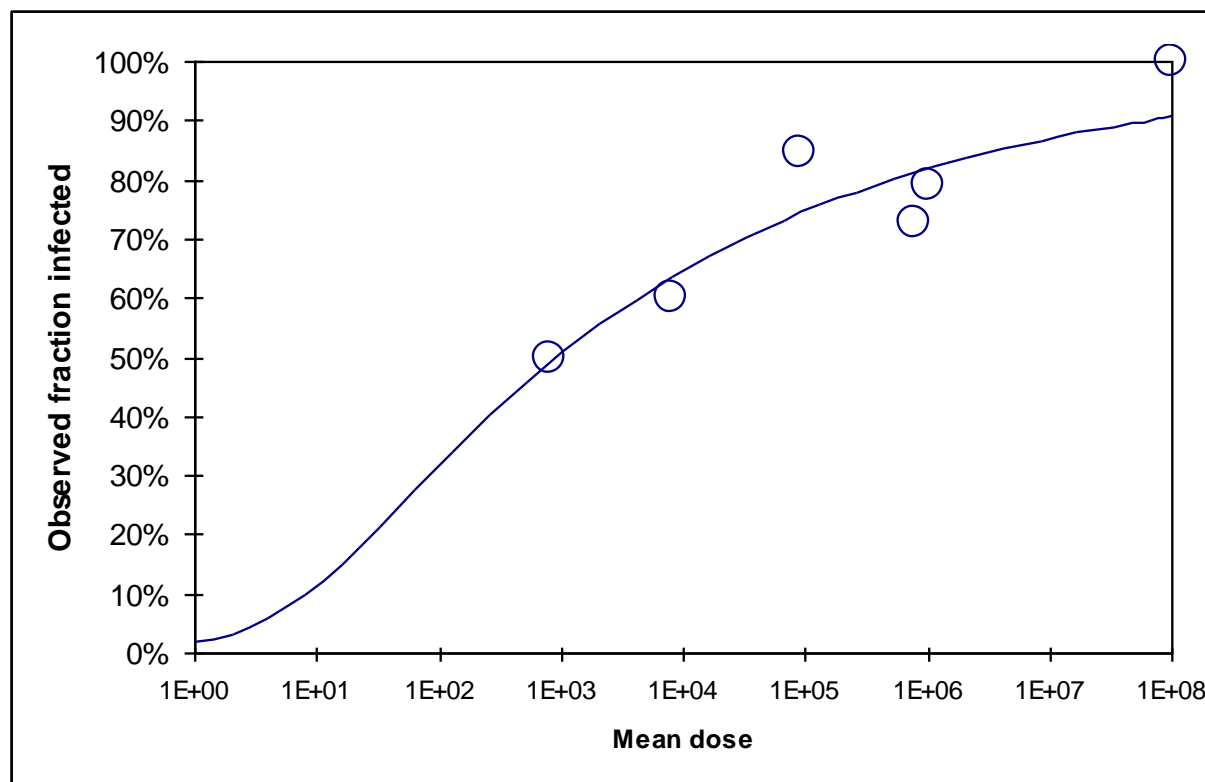
| Mean dose | Tested | Infected |
|-----------------|--------|----------|
| 8×10^2 | 10 | 5 |
| 8×10^3 | 10 | 6 |
| 9×10^4 | 13 | 11 |
| 8×10^5 | 11 | 8 |
| 1×10^6 | 19 | 15 |
| 1×10^8 | 5 | 5 |



Example Applications: *C. jejuni*

Beta-Poisson model. MLE fit has $\alpha = 0.145$, $\beta = 7.589$

| Mean dose | Infected /Tested | B-P MLE probability |
|-----------------|------------------|---------------------|
| 8×10^2 | 5/10 | 49% |
| 8×10^3 | 6/10 | 64% |
| 9×10^4 | 11/13 | 74% |
| 8×10^5 | 8/11 | 81% |
| 1×10^6 | 15/19 | 82% |
| 1×10^8 | 5/5 | 91% |



Questions?

Thank you for your efforts to catch up...

