

# Multiple-parasites and multiple hosts: What happens when we increase host and parasite diversity?

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# Outline

- Pathogens with multiple hosts 1, CDV
  - Stochastic spatial short-term dynamics
- Hosts with multiple pathogens, CDV and CPV
  - More than SIR + SIR ....
- Pathogens with multiple hosts 2. RPV
  - Dynamics and impact
- Ecosystem level effects of pathogens

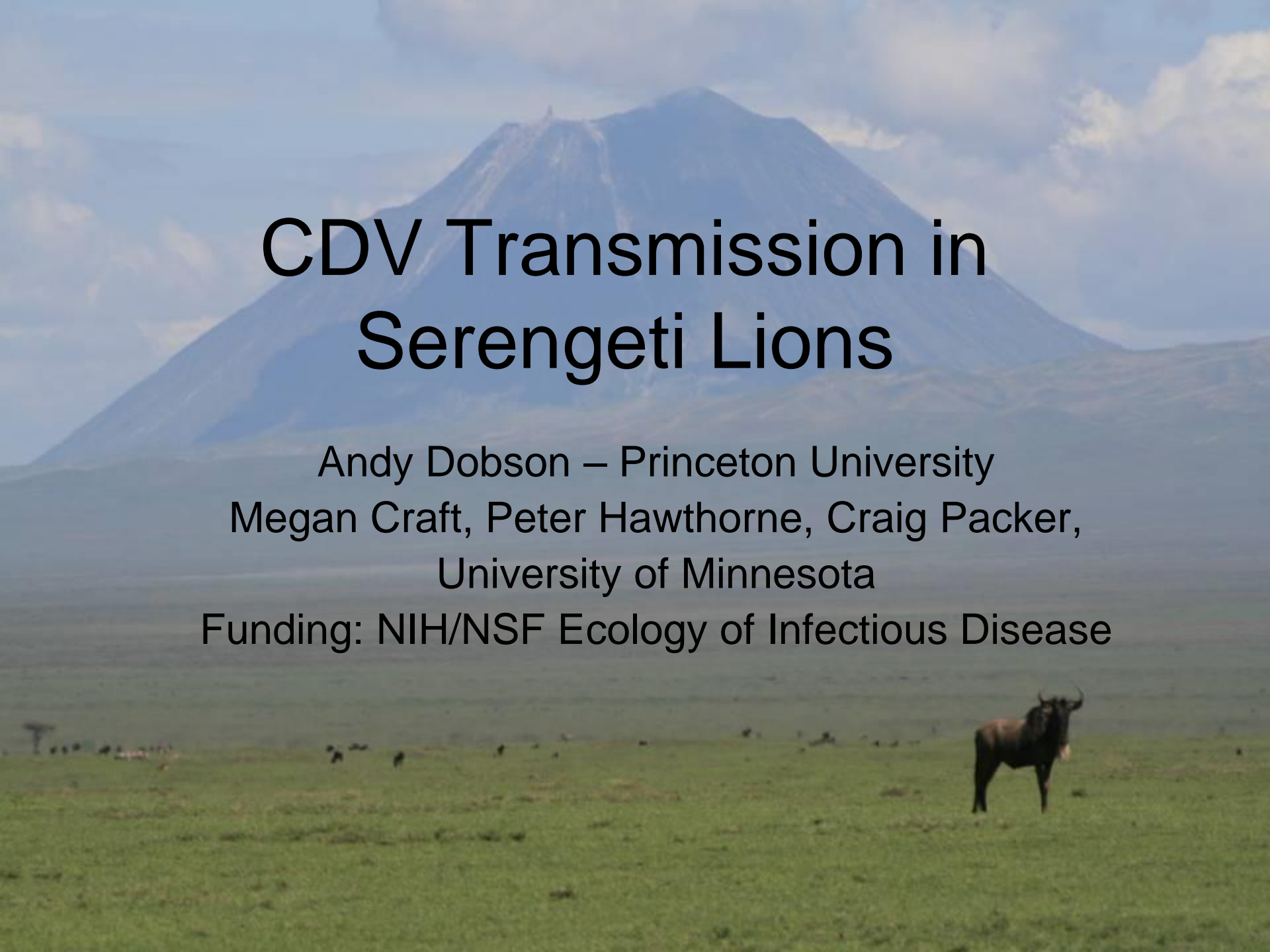


# CDV Transmission in Serengeti Lions

Andy Dobson – Princeton University

Megan Craft, Peter Hawthorne, Craig Packer,  
University of Minnesota

Funding: NIH/NSF Ecology of Infectious Disease









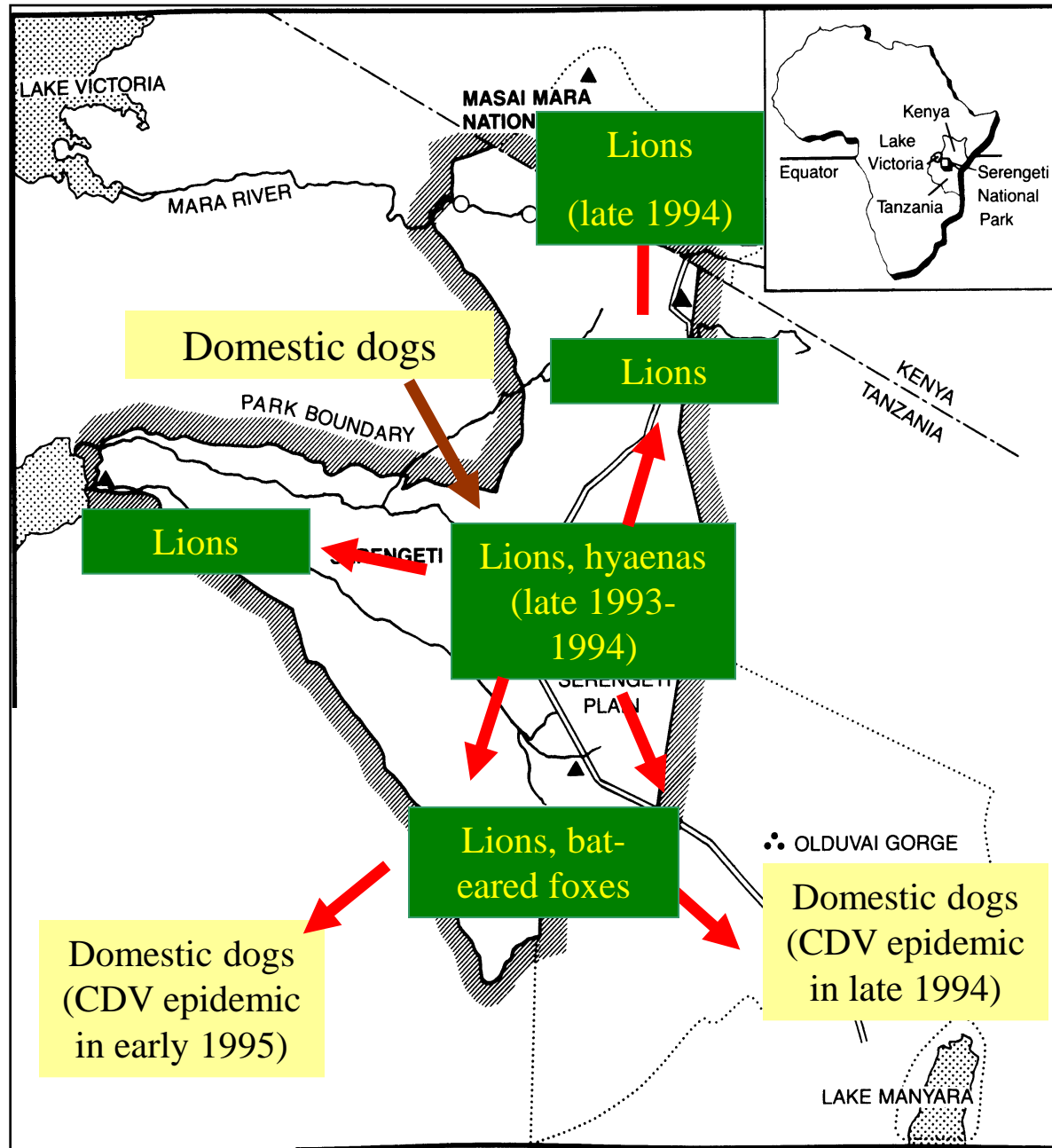


5:33PM  
2/ 3/94

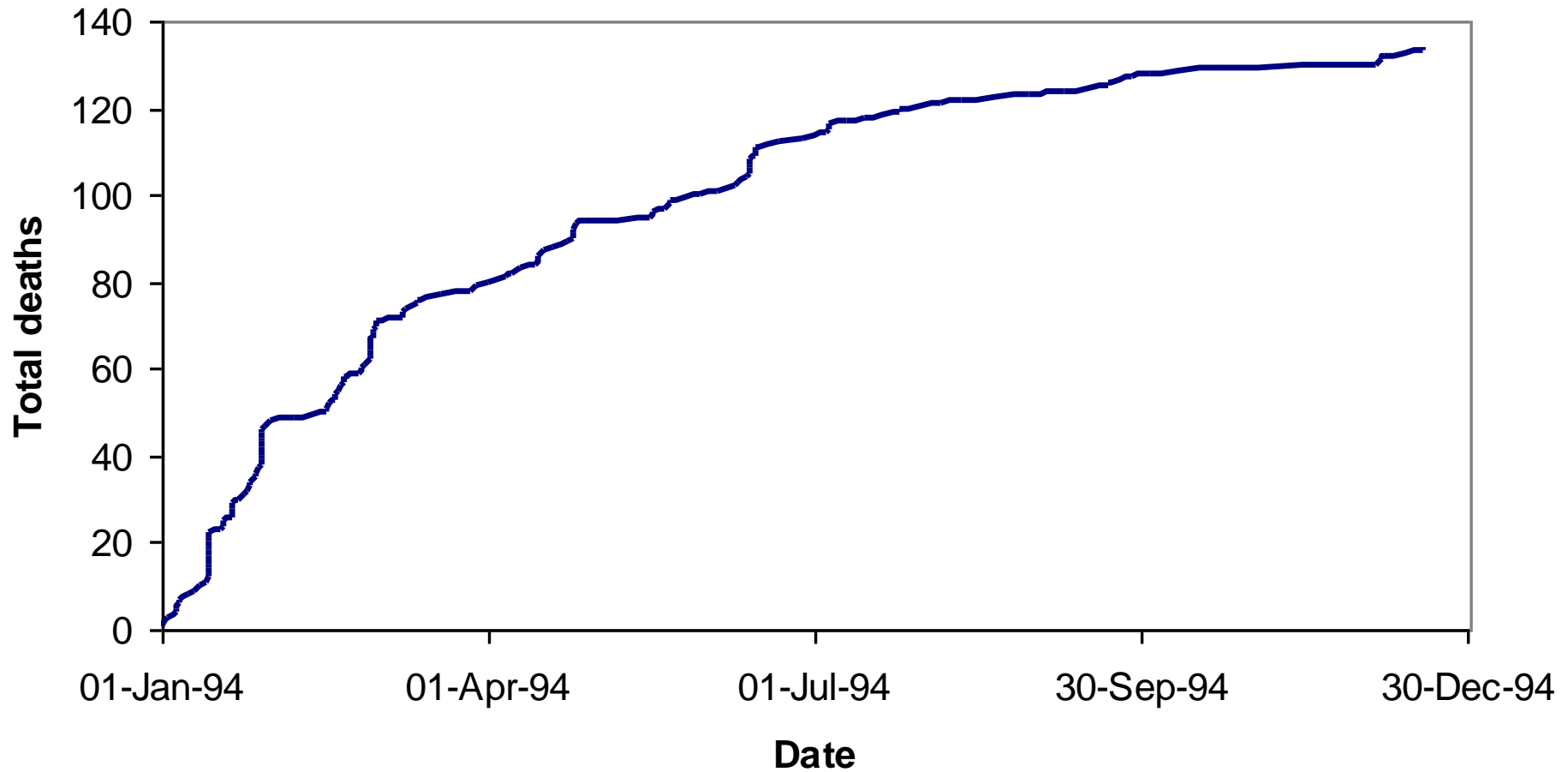
**Ray & Annika Hilborn**



# *Spread of CDV during 1994 epidemic*



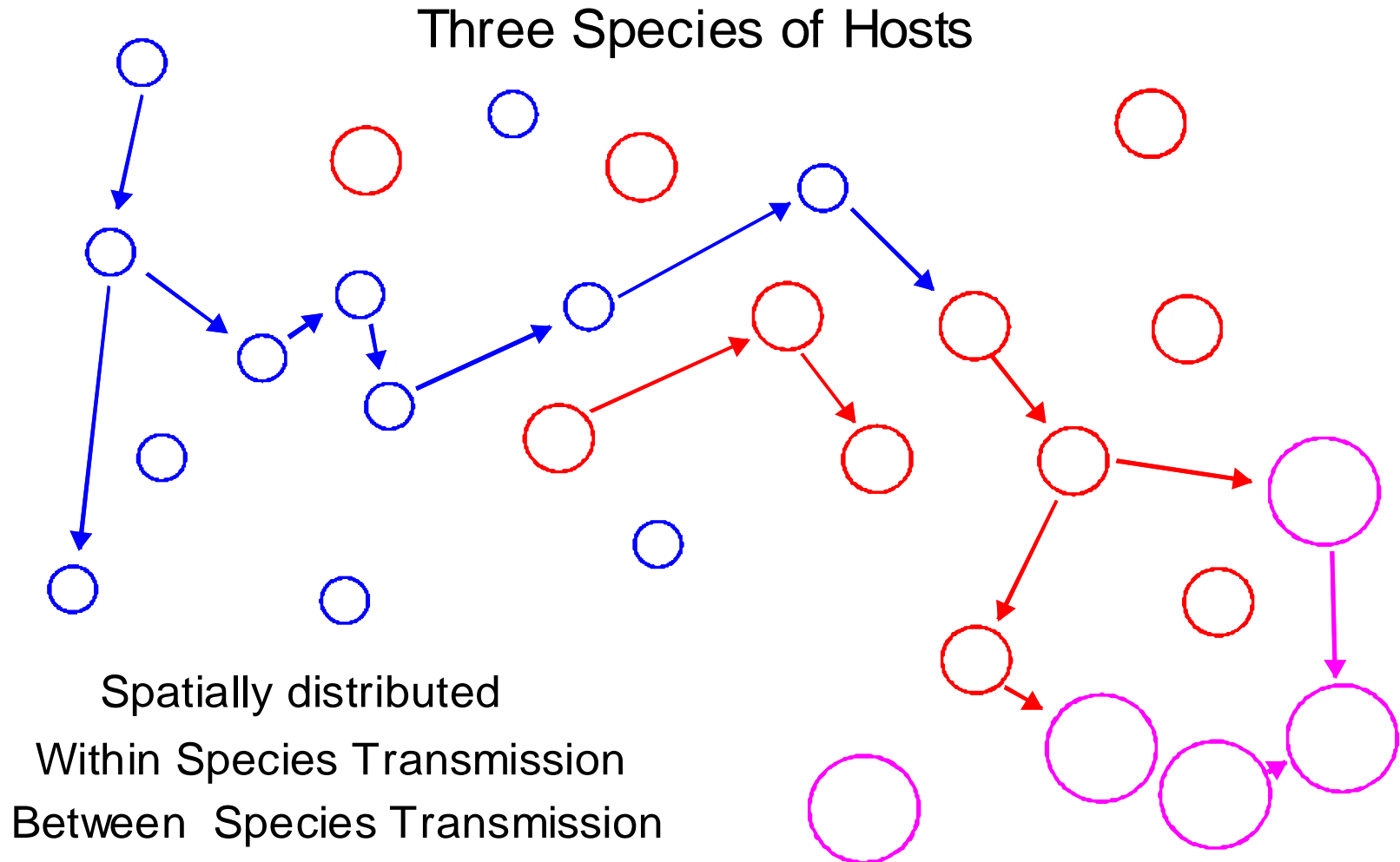
# Serengeti 1994: Overall mortality







# A cartoon of the talk.....







Social, lives in big groups, commutes over large distances





Small family groups that interact only occasionally





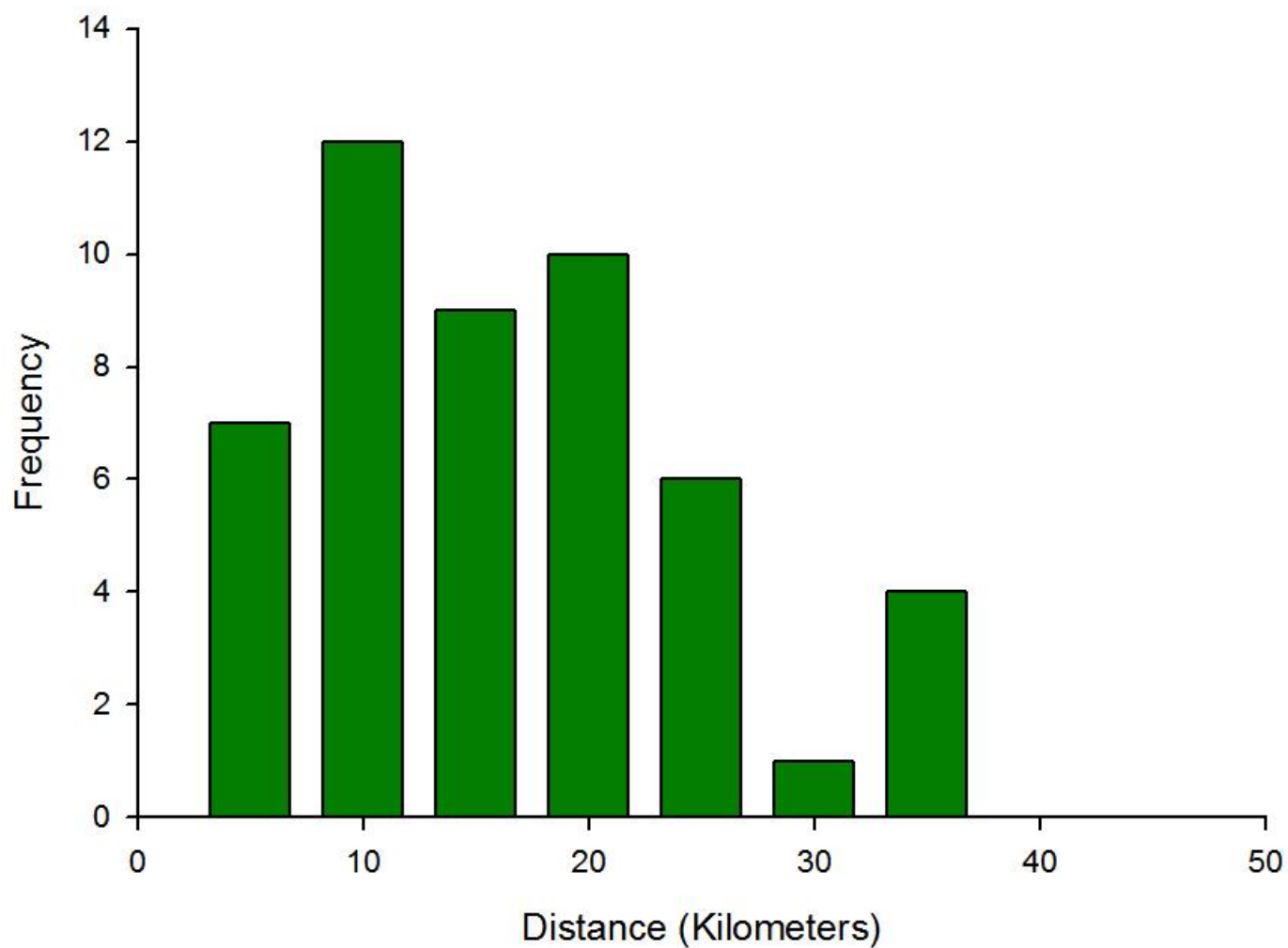
Territorial pairs with young, little between group interactions – scavenge at kills



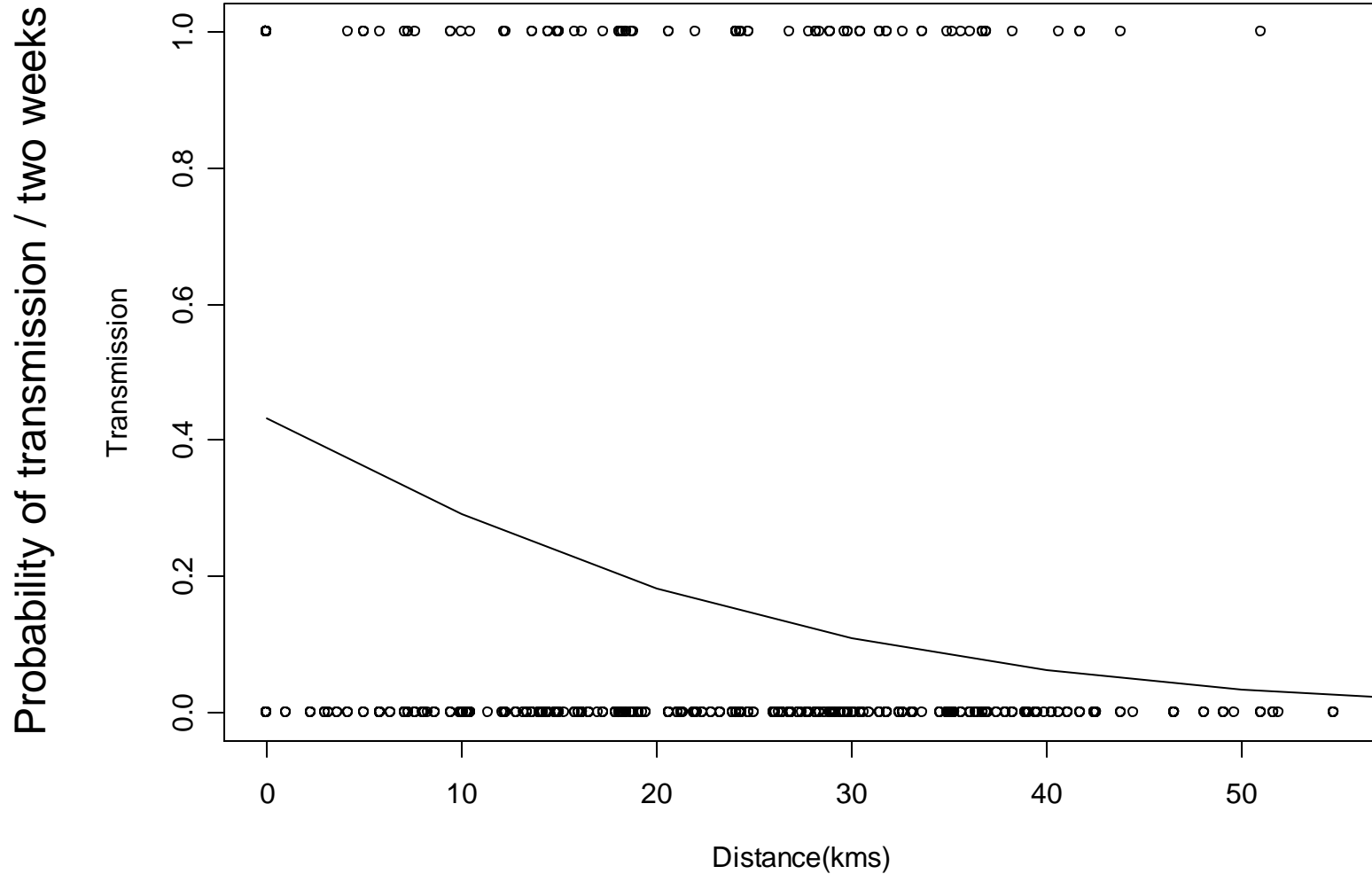
Back to the lions...



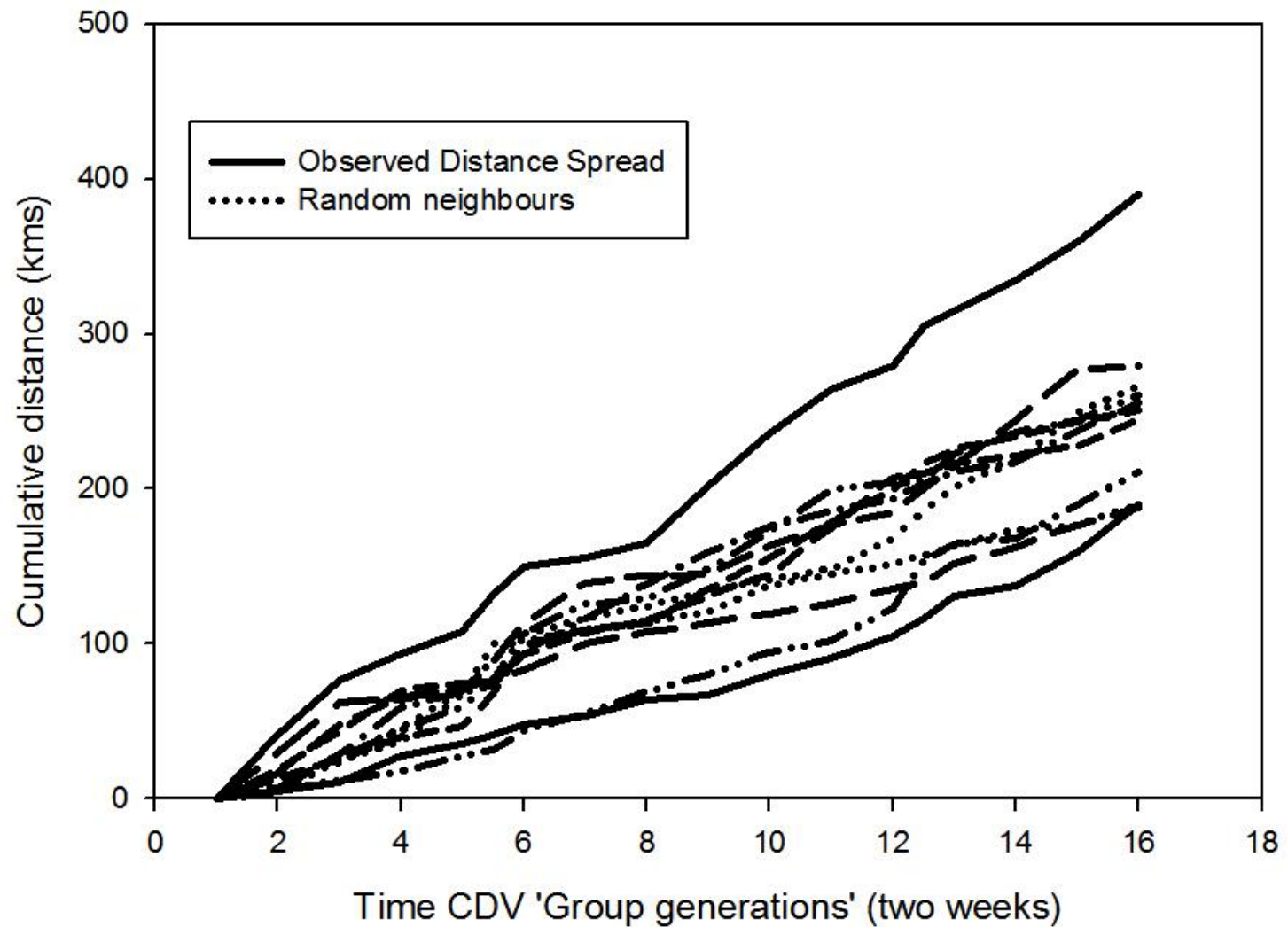
Distances between centrons of adjacent lion prides



# Transmission kernal



## Cumulative Spatial Spread of CDV



Also – only 40% of jumps between adjacent slides

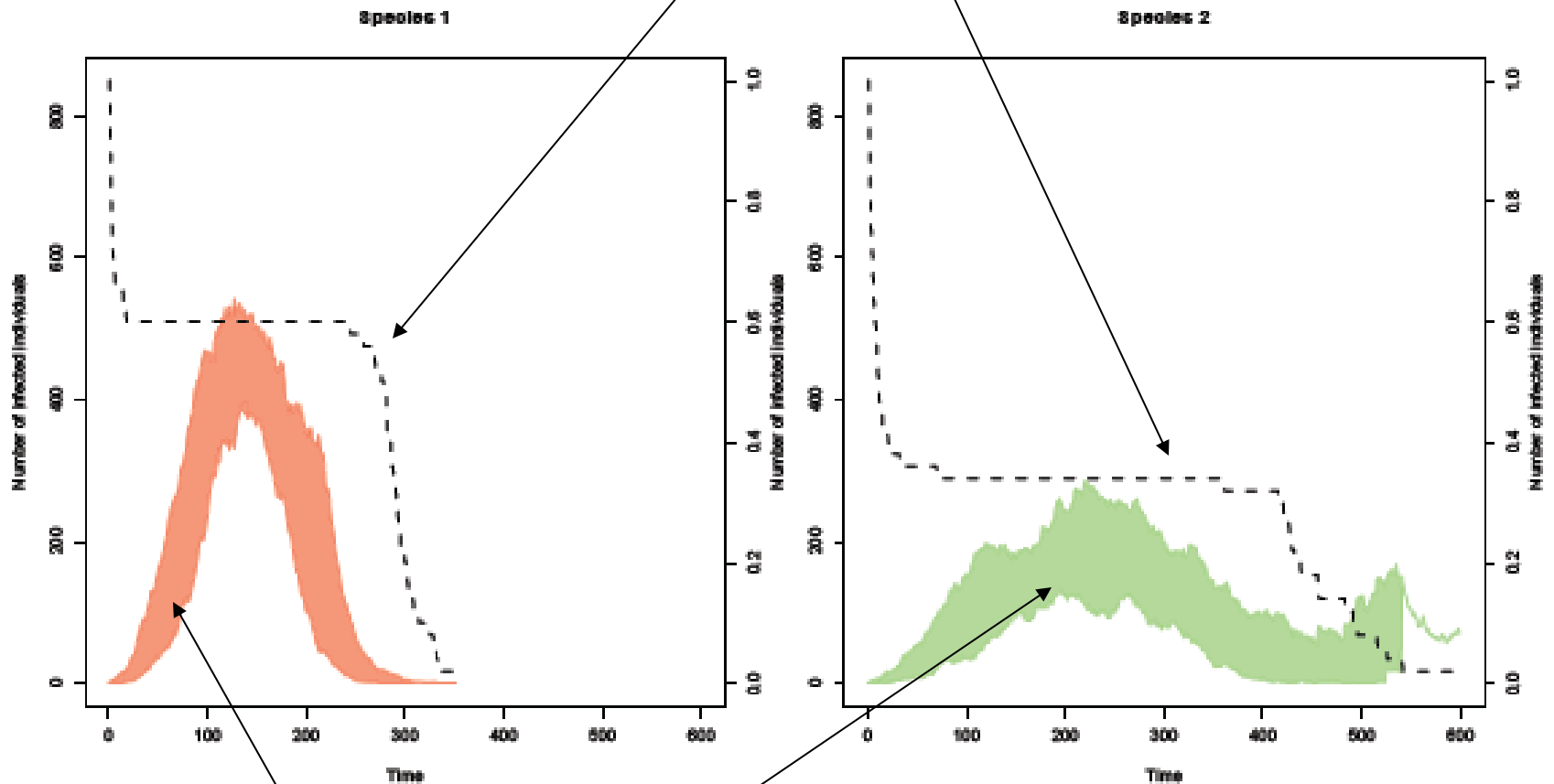


# Make a stochastic spatial model

- Assume the Serengeti is roughly square and contains 25x25 lion territories.
- Assume three types of hosts with different social systems defined by transmission within-in and between territories: lions, hyaenas, jackals
- Look at temporal and spatial properties of epidemic outbreaks in 1, 2, and 3 species.

# Epidemic outbreaks in viable hosts

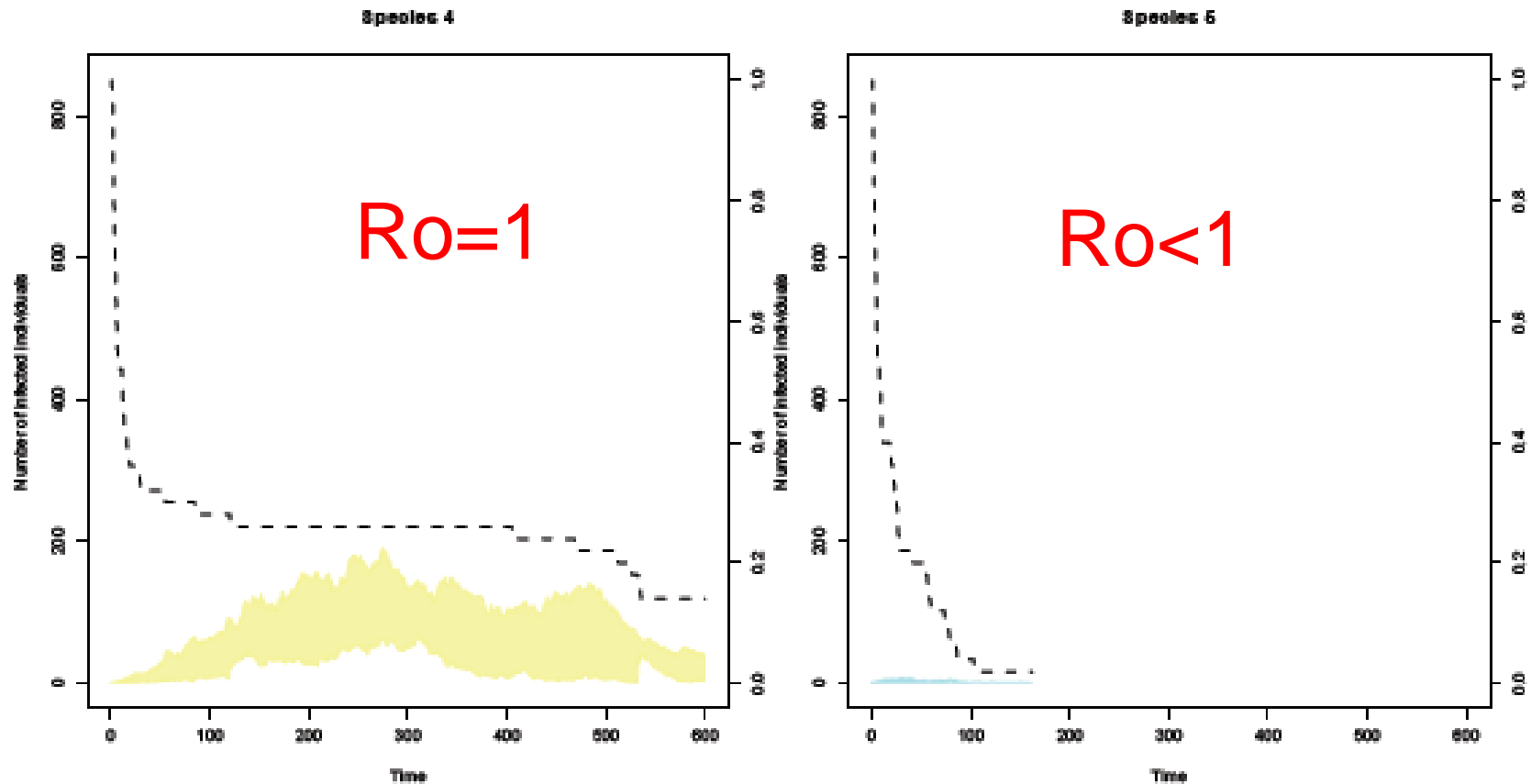
Number of patches containing an infected individual



Number of individuals infected

*50 replicates on 25X25 grid*

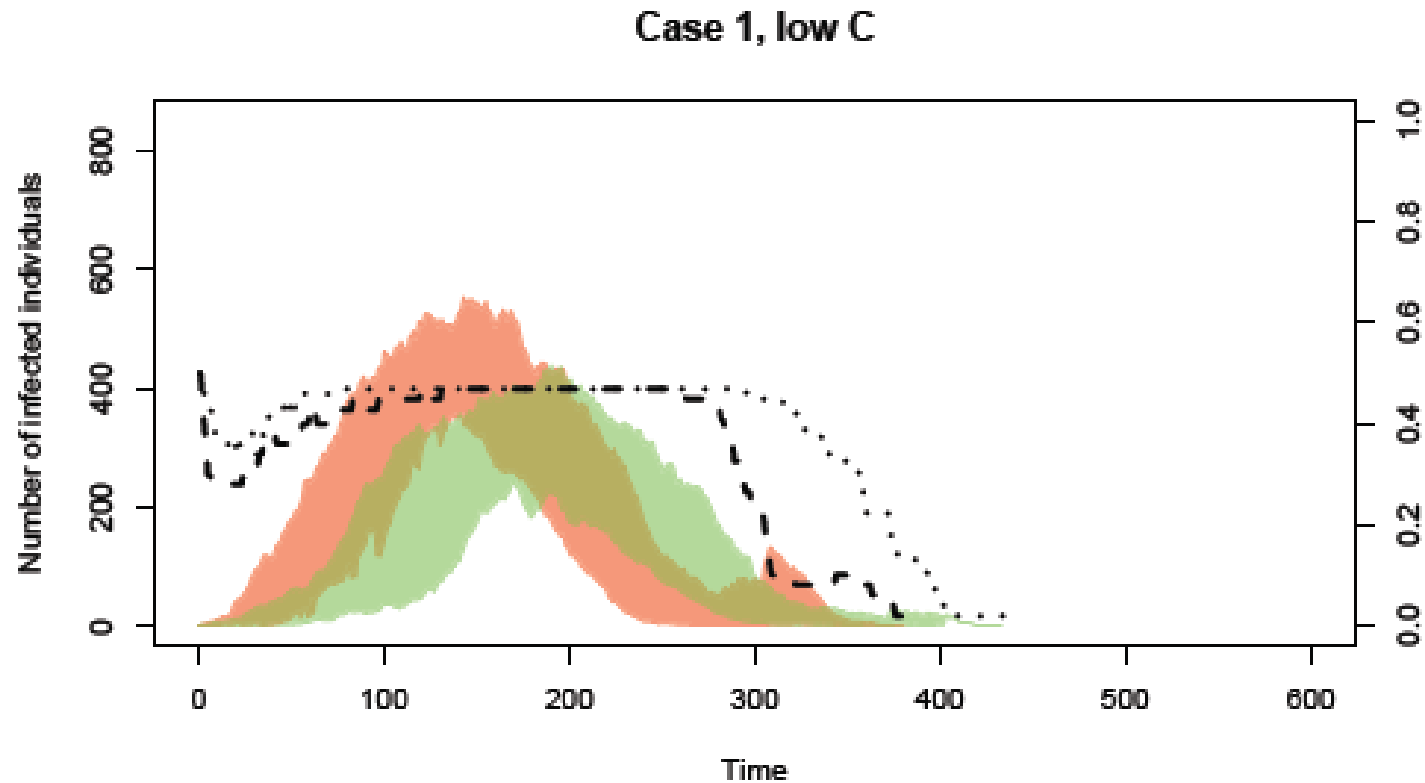
# Epidemics in less viable hosts





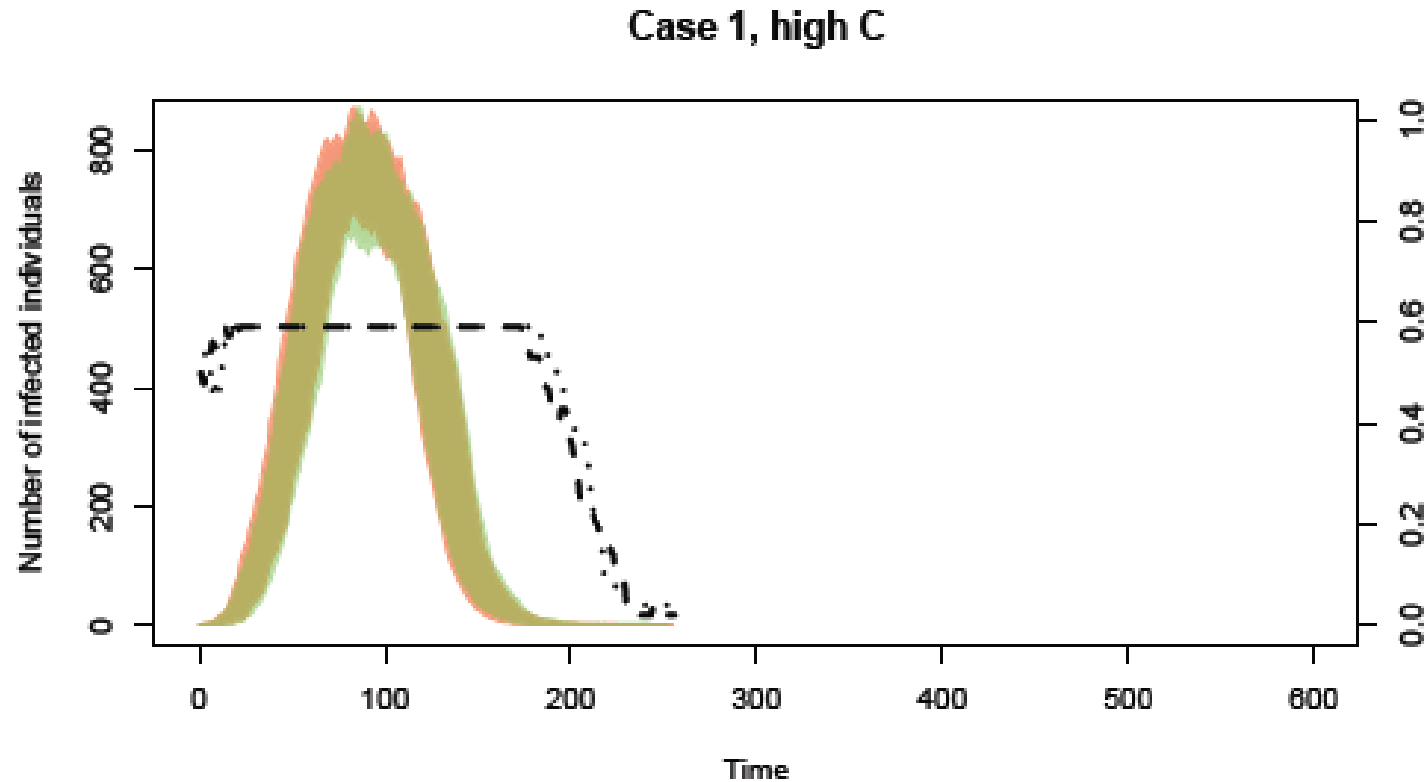
# Mixed Species Epidemics

## 1% between species transmission



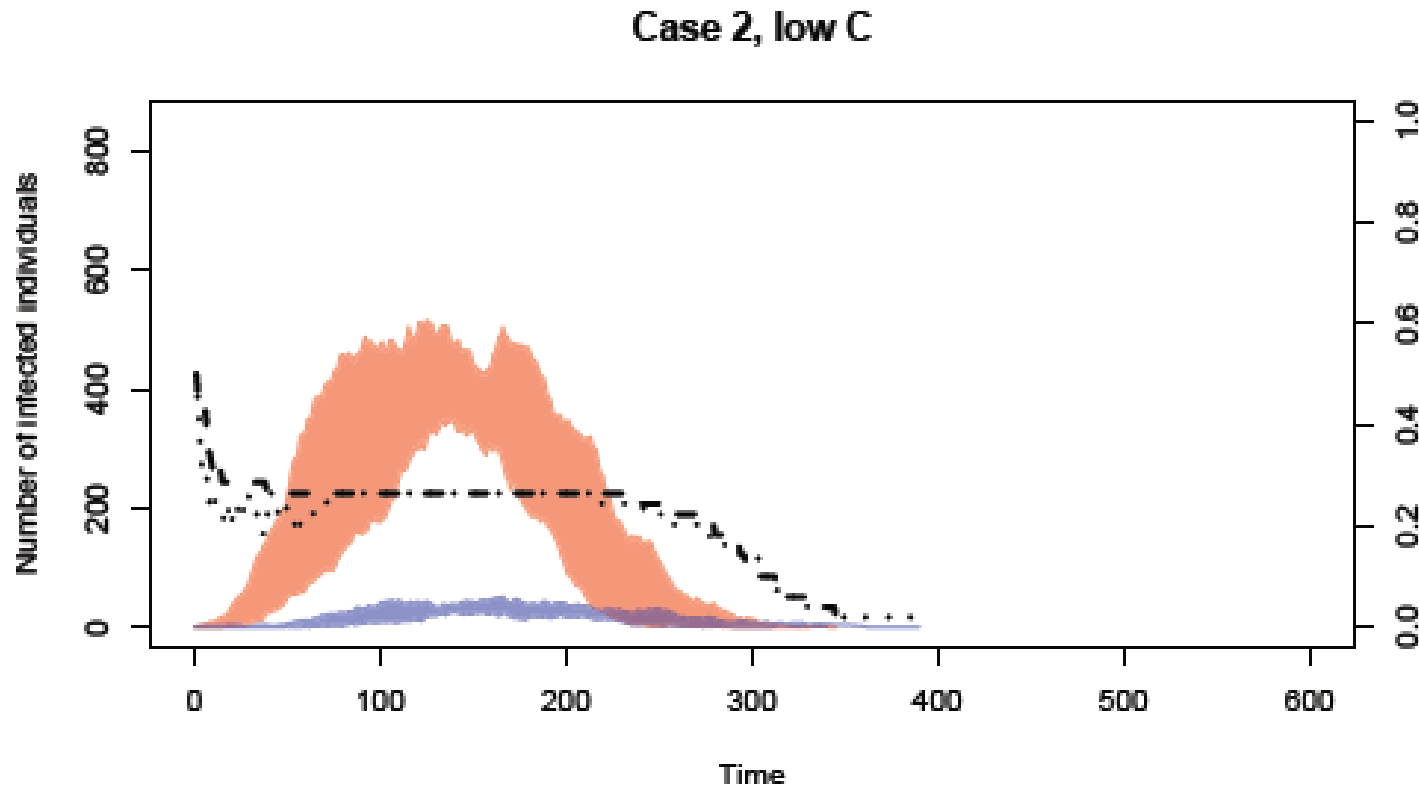
# Mixed Species Epidemics

## 50% between species transmission



# Mixed Species Epidemics

## 1% between species transmission



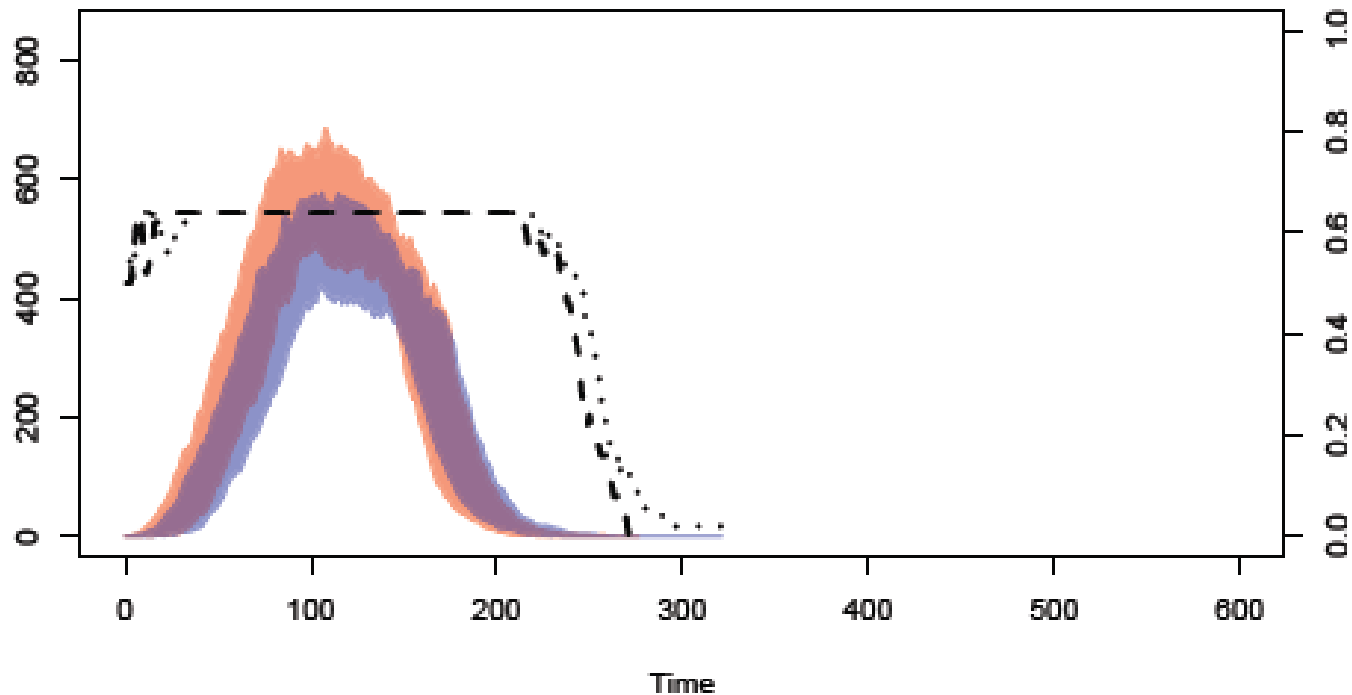
Pathogen can now persist in non-viable host



# Mixed Species Epidemics

## 50% between species transmission

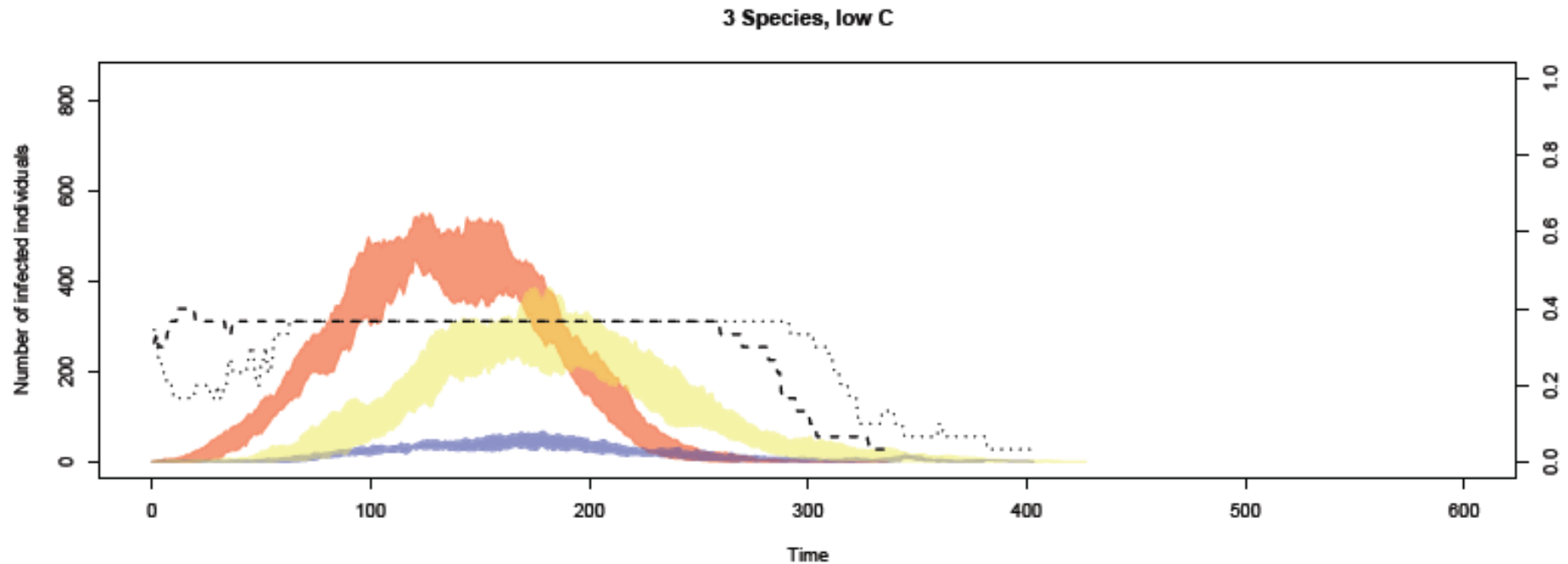
Case 2, high C



Second species can even create epidemic in non-viable species

# Three species epidemics....

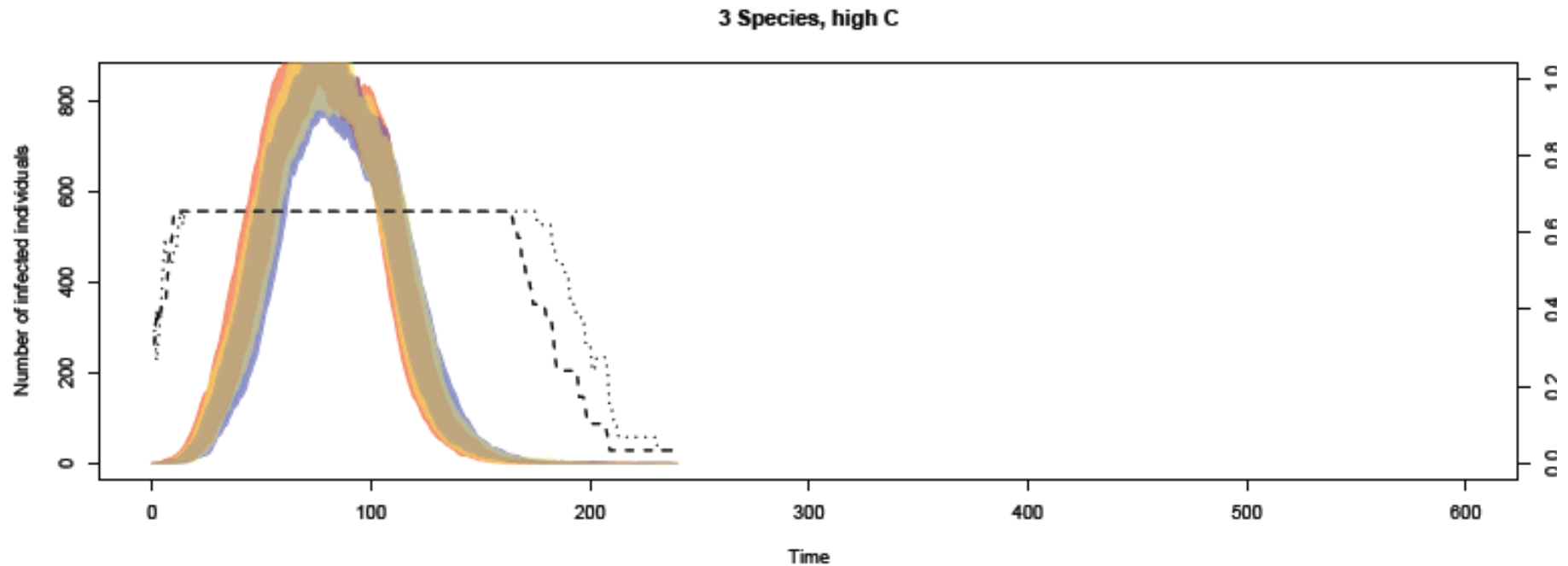
1% between species transmission...



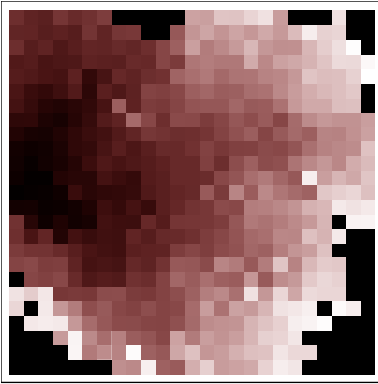


# Three species epidemics....

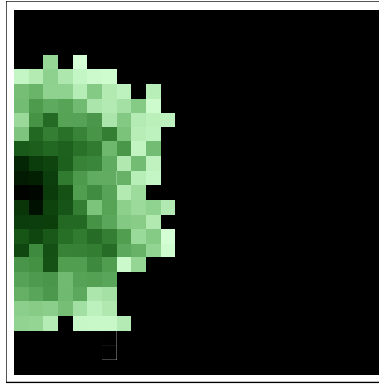
50% between species transmission...



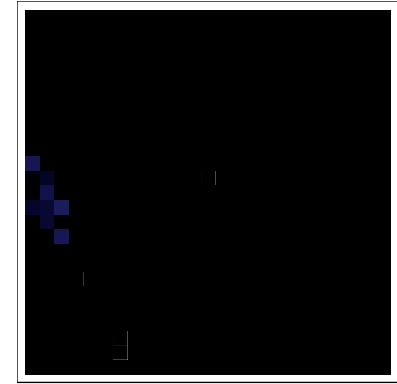
## Spatial Plots: Single Species



Species 1:  
 $R_0$  Local: 1.1  
 $R_0$  Neigh: 1.1

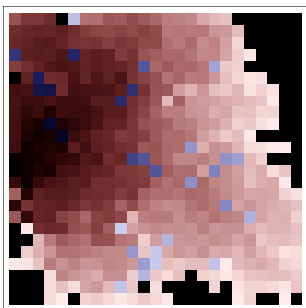


Species 2:  
 $R_0$  Local: 0.5  
 $R_0$  Neigh: 1.7



Species 3:  
 $R_0$  Local: 1.7  
 $R_0$  Neigh: 0.5

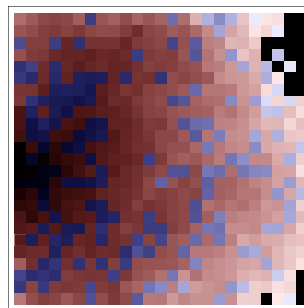
1 & 3,  $C = 0.01$   
Init Inf: 1



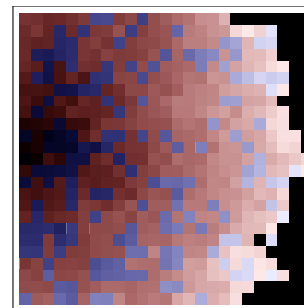
1 & 3,  $C = 0.01$   
Init Inf: 3



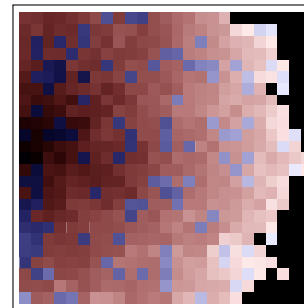
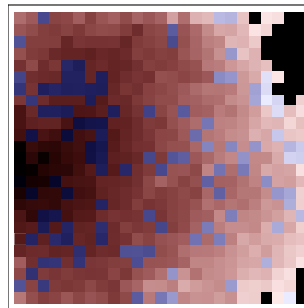
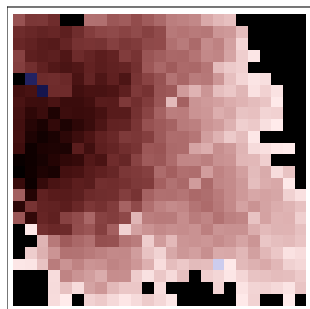
1 & 3,  $C = 0.2$   
Init Inf: 1



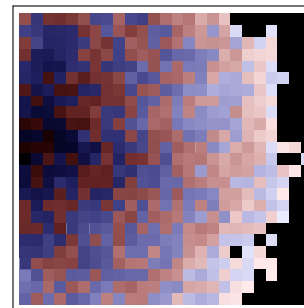
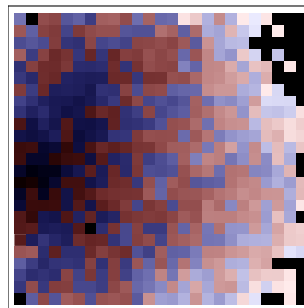
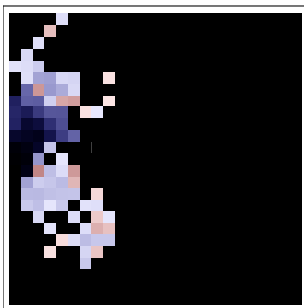
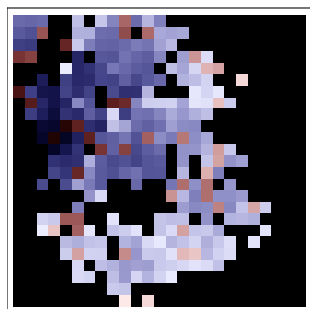
1 & 3,  $C = 0.2$   
Init Inf: 3



First Inf'd  
Spec  
In Cell



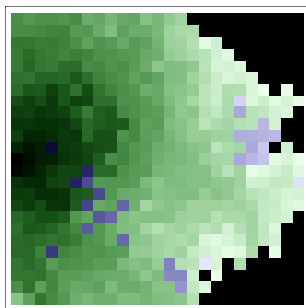
Source of  
inf in 1



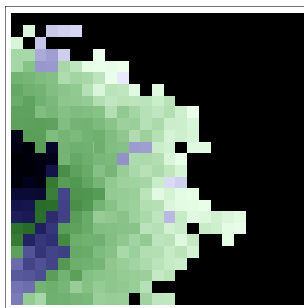
Source of  
inf in 3



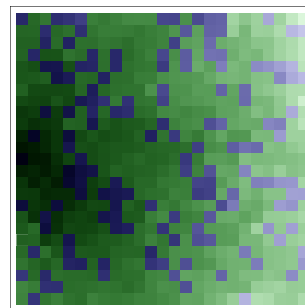
2 & 3,  $C = 0.01$   
Init Inf: 2



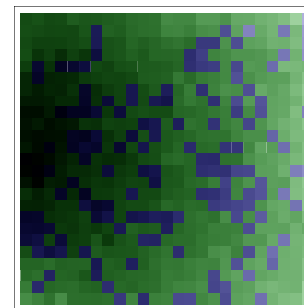
2 & 3,  $C = 0.01$   
Init Inf: 3



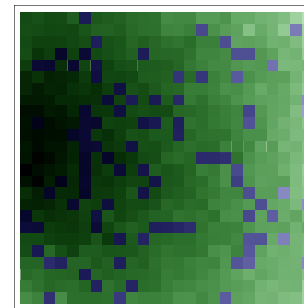
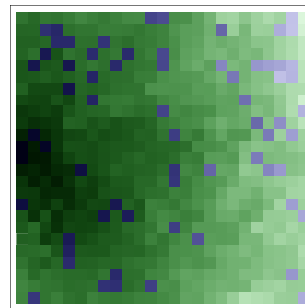
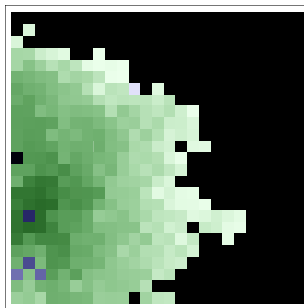
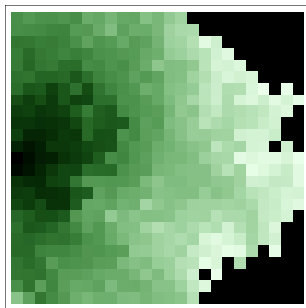
1 & 3,  $C = 0.2$   
Init Inf: 2



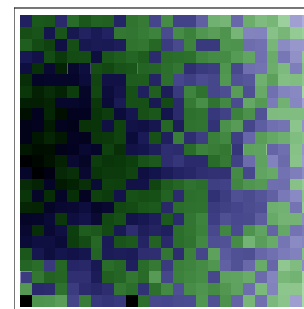
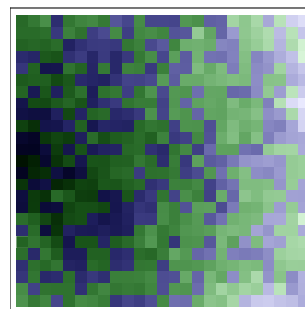
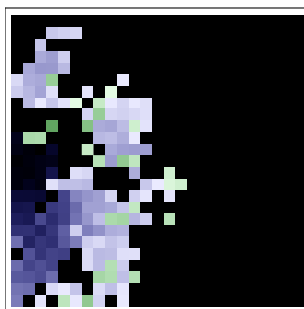
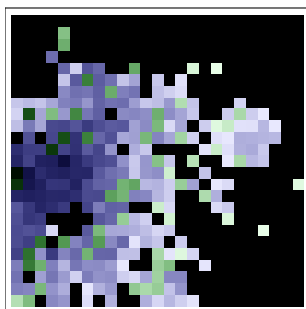
1 & 3,  $C = 0.2$   
Init Inf: 3



First Inf'd  
Spec  
In Cell



Source of  
inf in 2



Source of  
inf in 3

# Conclusions

- The epidemic of CDV in the Serengeti lions likely involved at least two host species.
- Multi-species epidemics have dynamics that are most dependent upon rates of between species transmission
- Single species epidemics spread as waves; multi-species epidemics exhibit jumps if you only study one host species

# Longer term impact of CDV

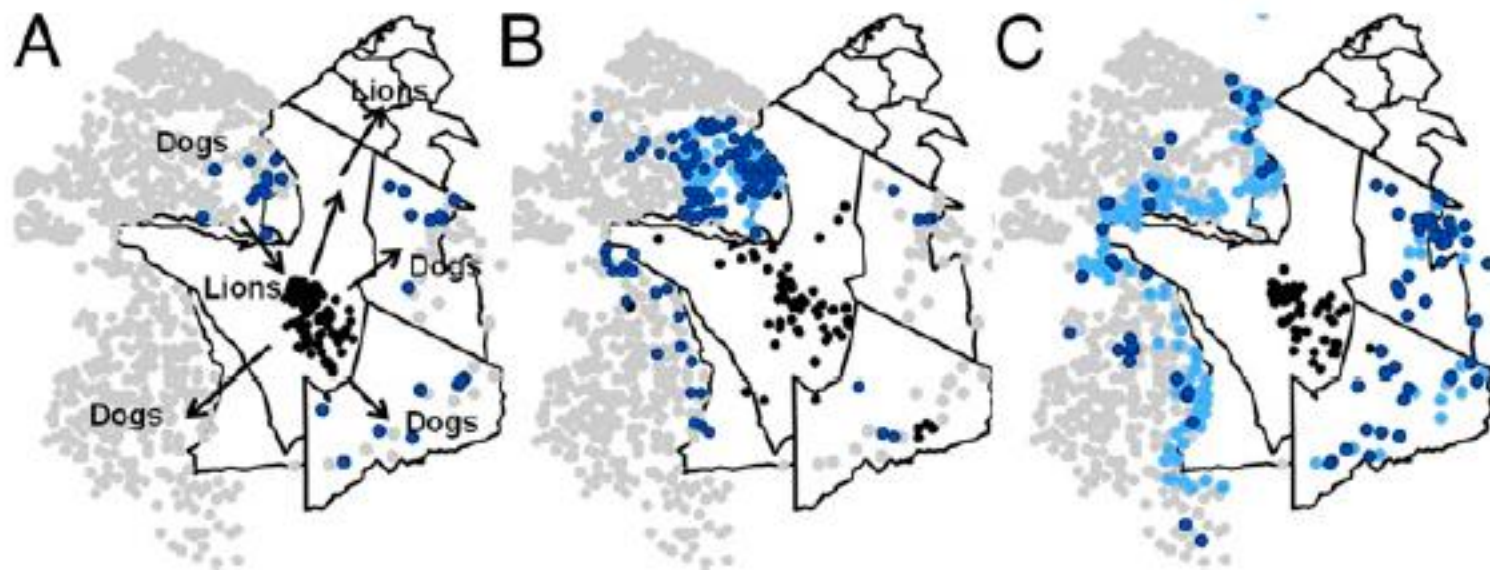
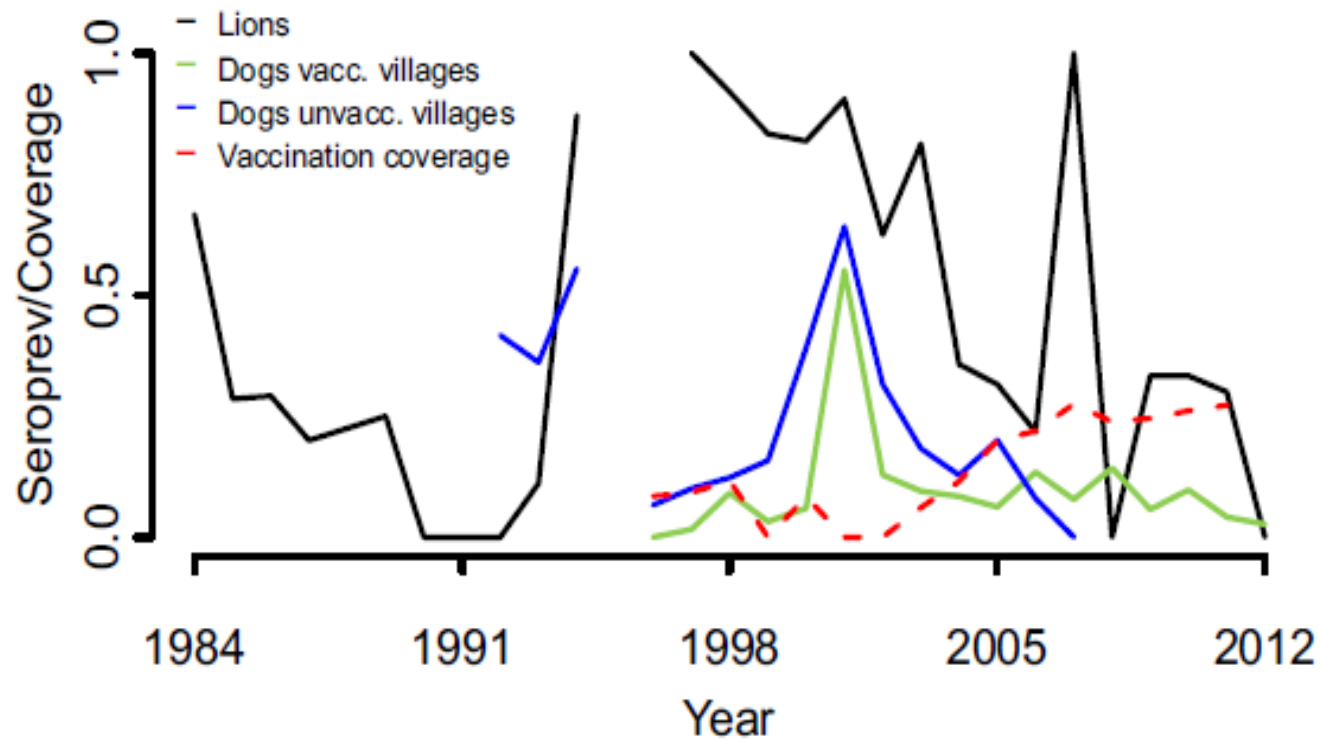


Fig. 1. Map of the Serengeti ecosystem (Tanzania). Circles represent human settlements (gray) surrounding the Serengeti National Park, villages/households from which domestic dogs were sampled (dark blue), locations where lions were sampled (black), and villages included in domestic dog vaccination campaigns that were not sampled (pale blue). (A) Arrows indicate the direction of the spread of CDV during the 1994 epidemic as reconstructed by Cleaveland et al. (16). (B) Small-scale domestic dog vaccination campaigns conducted during 1996–2002. (C) Expanded domestic dog vaccination program implemented during 2003–2012.





**Fig. 2.** Annual CDV seroprevalence in Serengeti lions (black) and in non-vaccinated dogs from vaccinated (green) and unvaccinated (blue) villages and regional vaccination coverage (red).

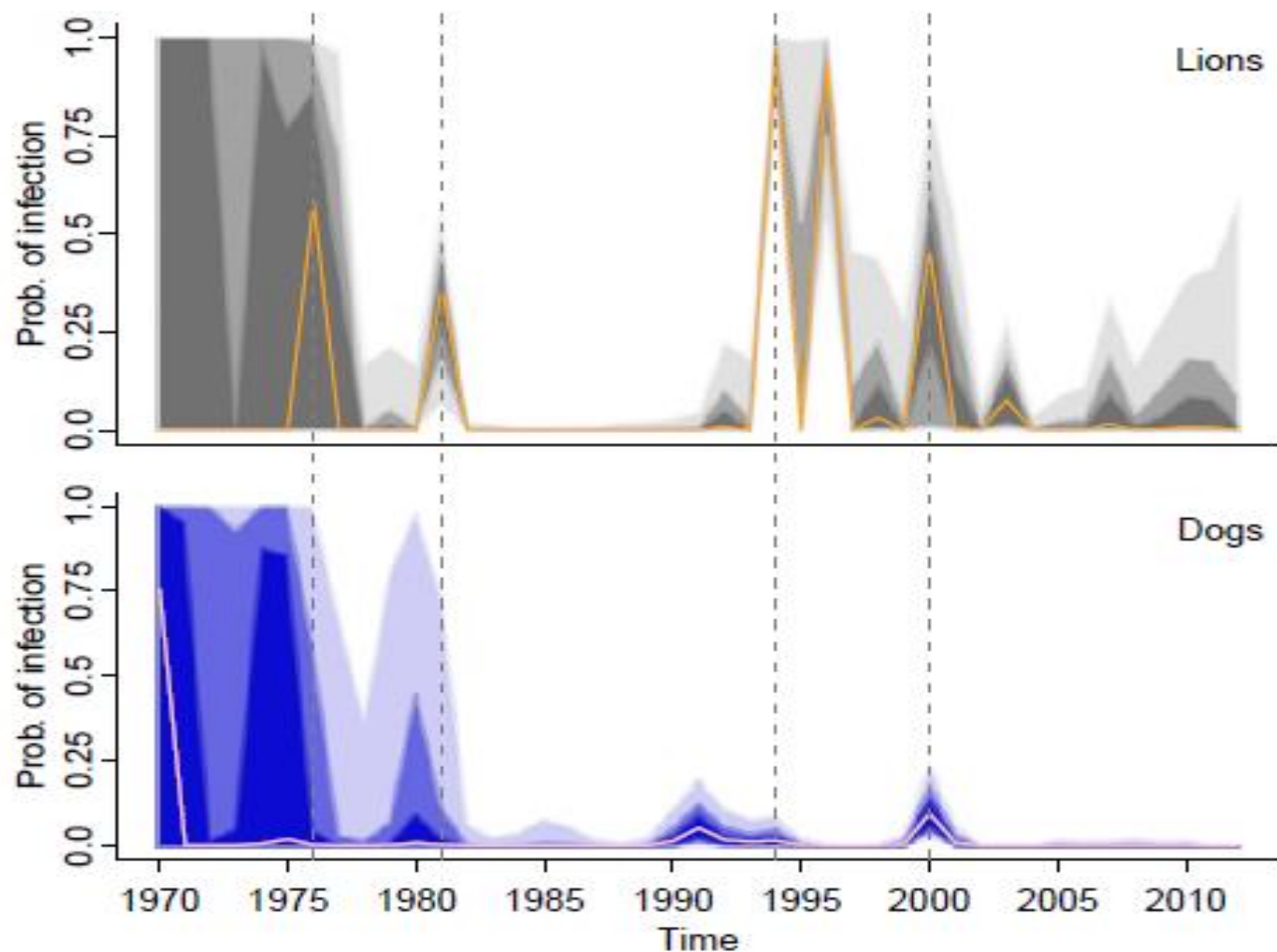
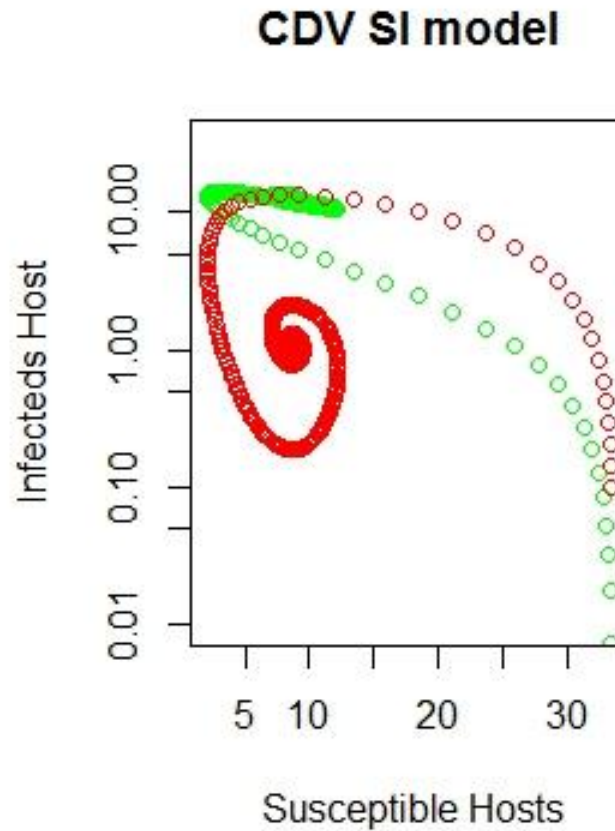
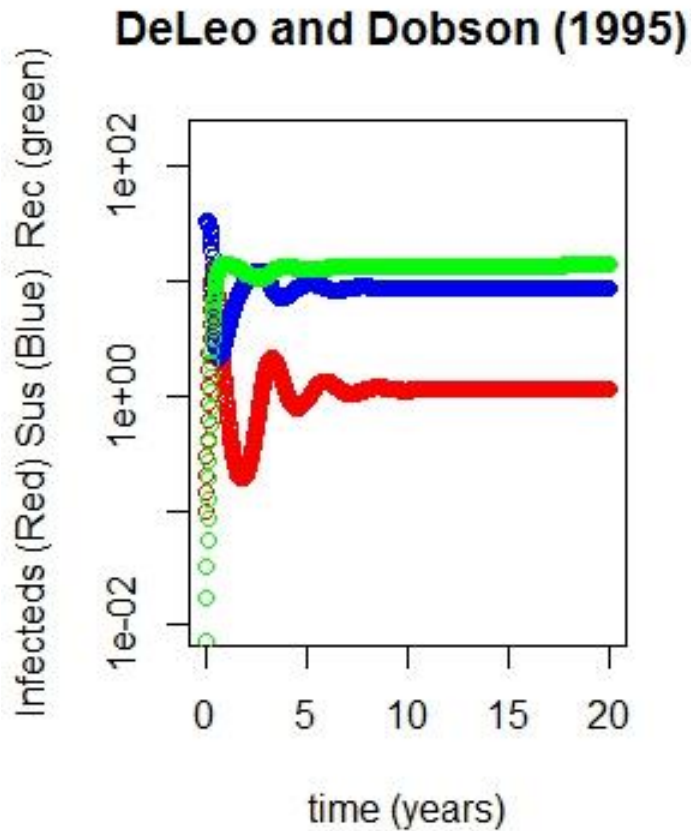


Fig. 3. State-space model estimates of the annual mode probability of CDV infection in lions (orange line, *Upper*) and dogs (pink line, *Lower*). Associated 50%, 75%, and 95% CIs are indicated by light, medium, and dark shading, respectively.

# One host and two parasites

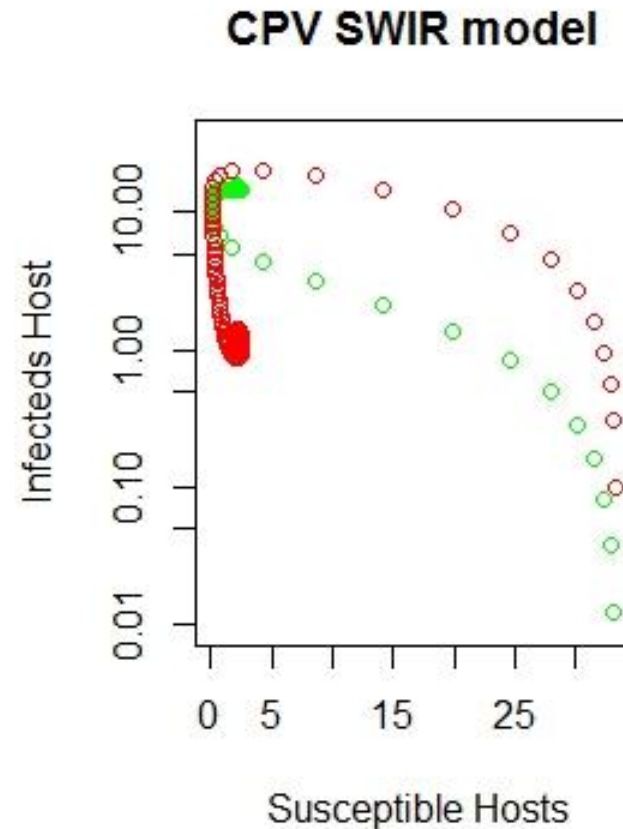
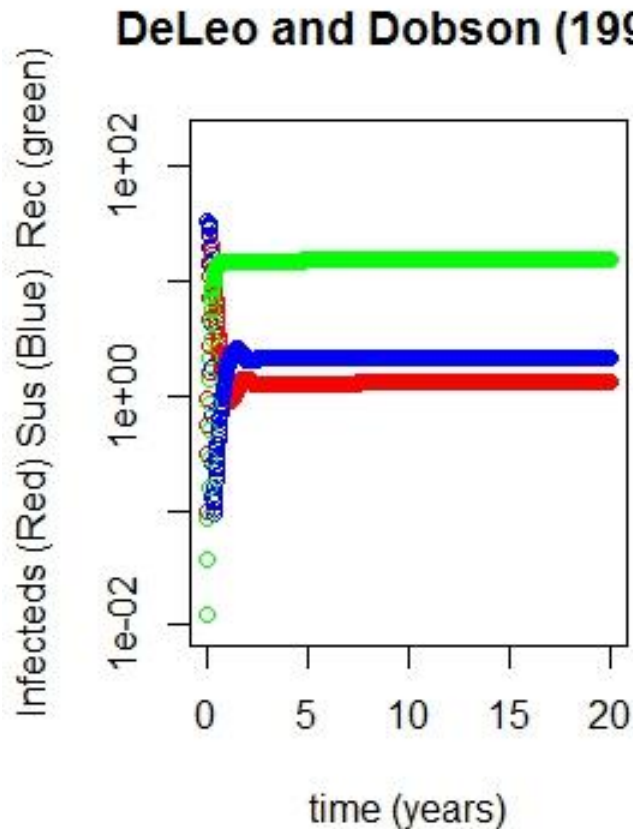
- For the last 10 to 15 years we have been vaccinating dogs against rabies, CDV, canine distemper virus and CPV, canine parvovirus.
- Focused a lot on rabies dynamics
- But what about CDV and CPV
  - CDV – direct transmission, like measles
  - CPV – free-living infective stages
  - Both create high mortality, but also high immunity

# Canine distemper by itself

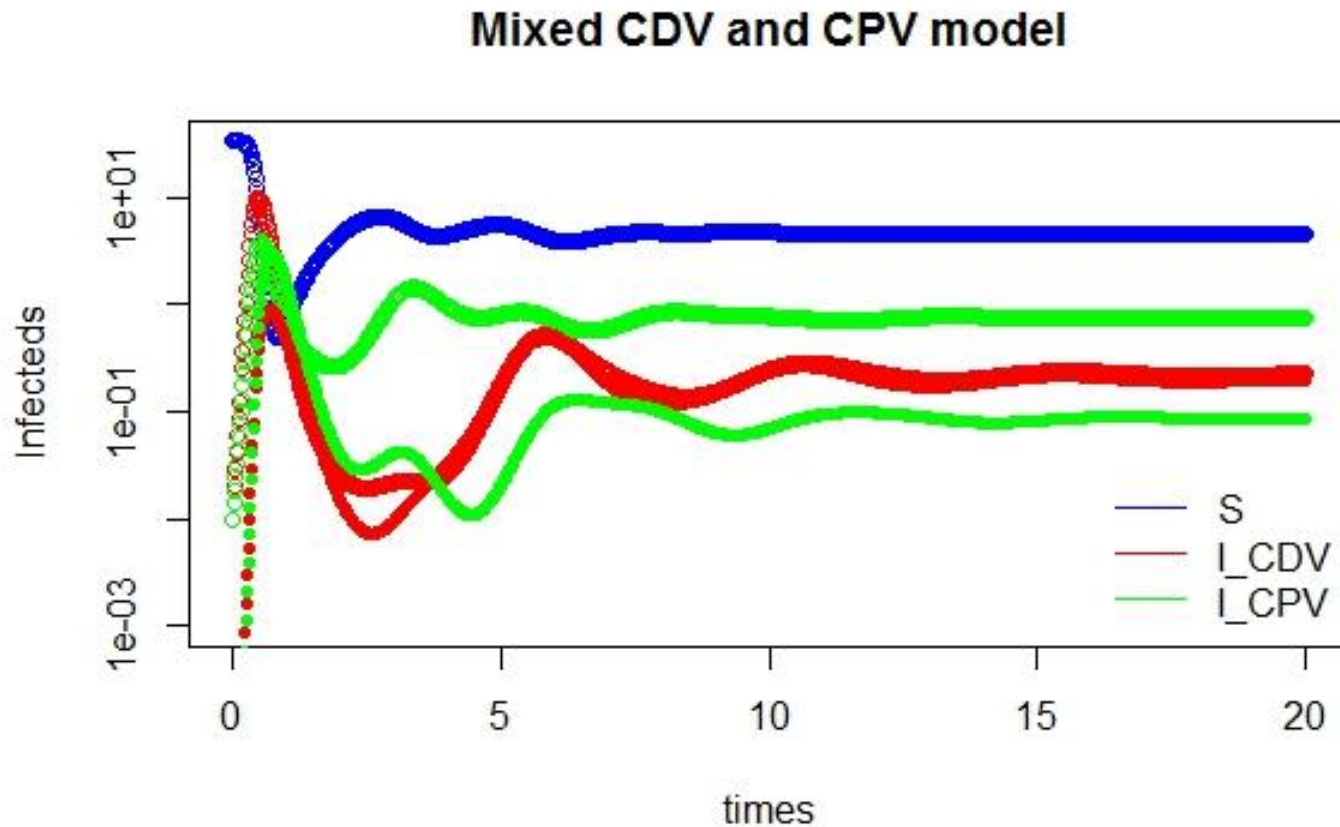




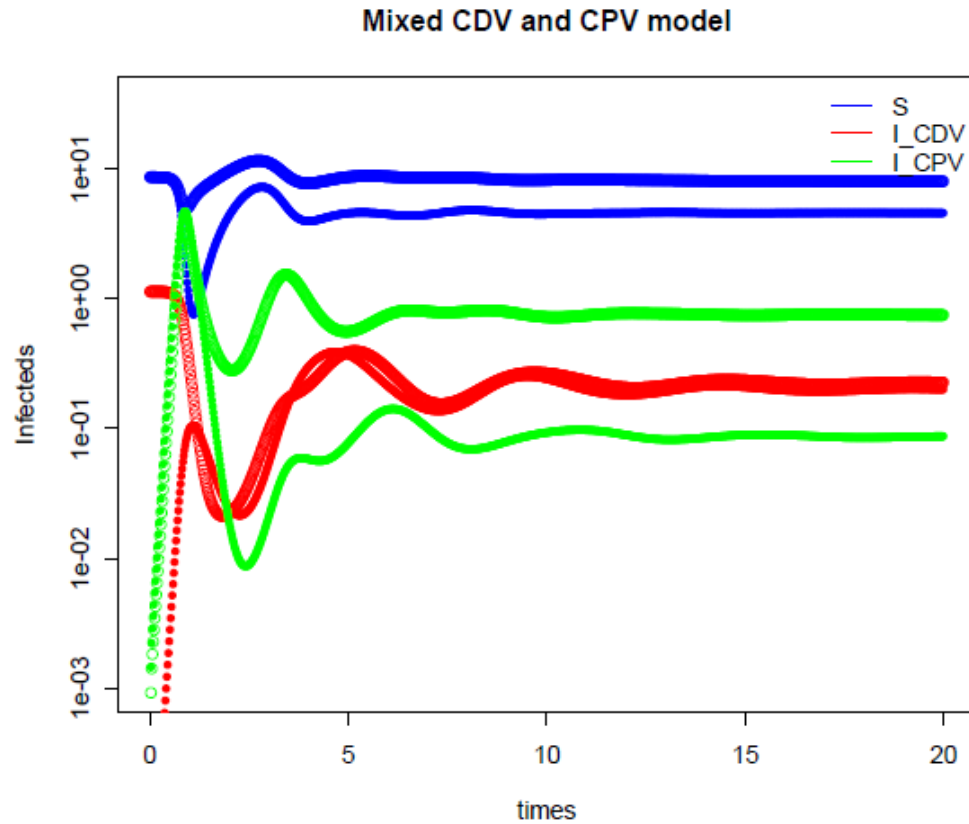
# Canine parvovirus by itself

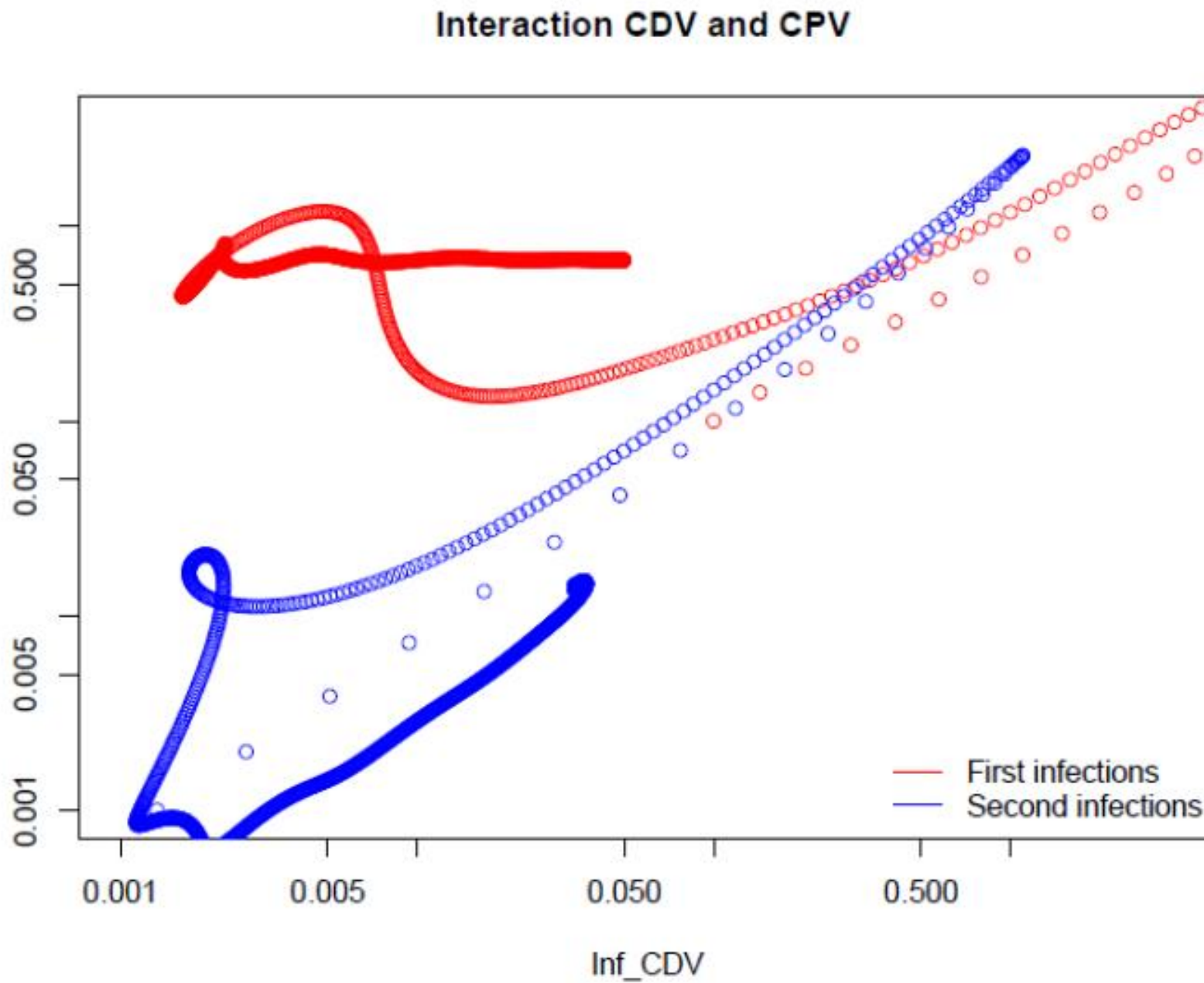


# One host + two pathogens: CDV and CPV



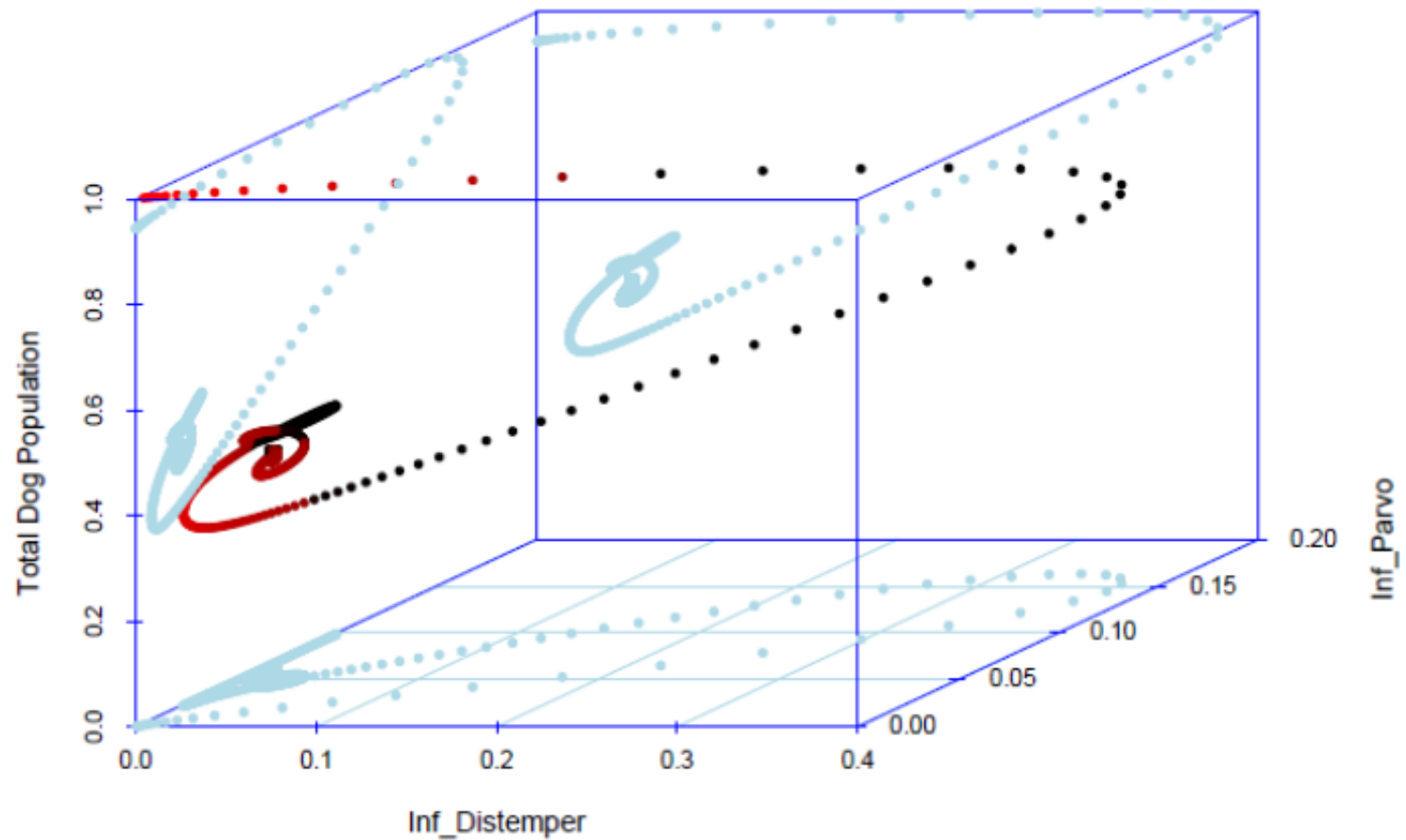
# CDV present; add CPV..



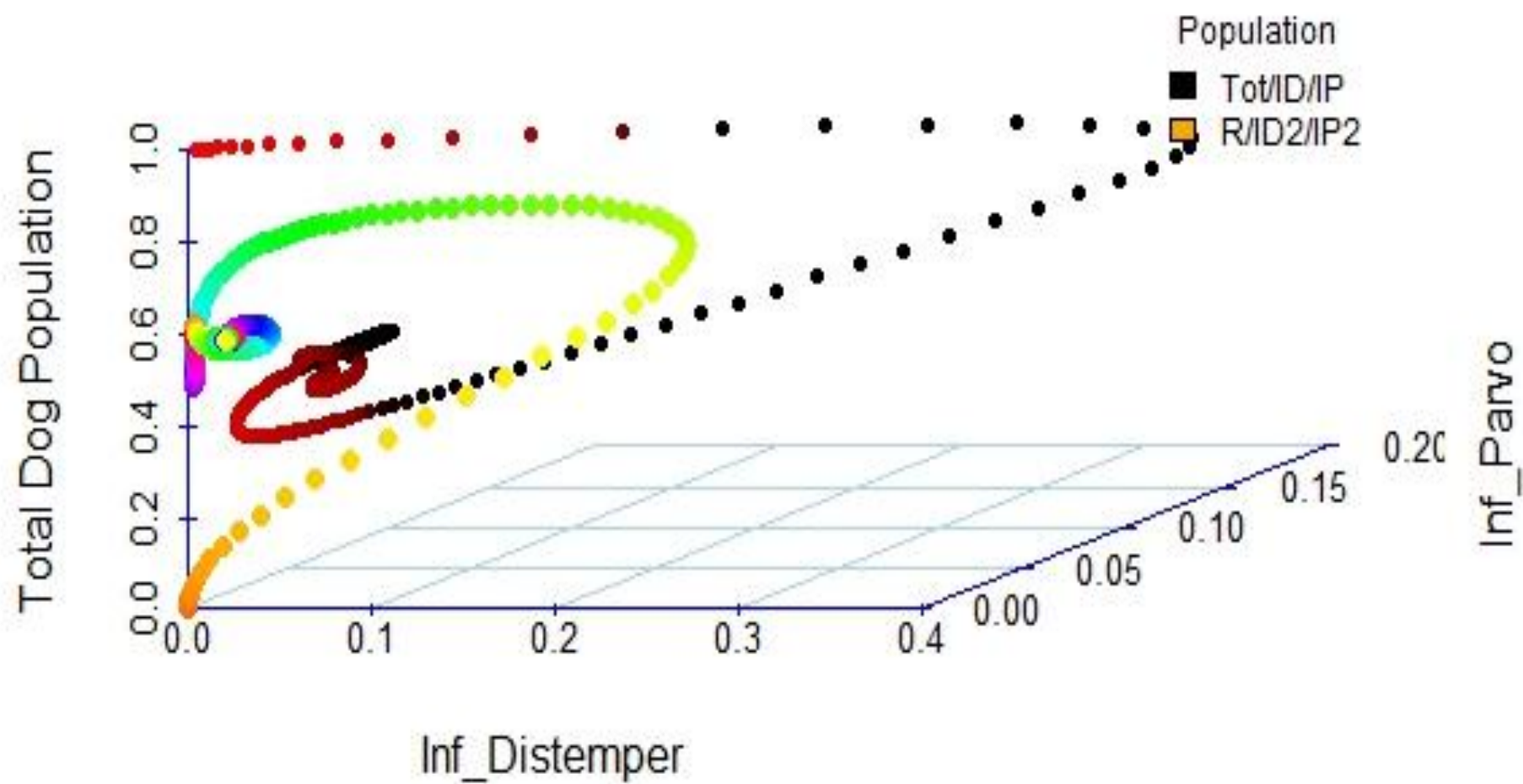




## Two pathogens and a single host: CVD, CPV and Domestic dogs

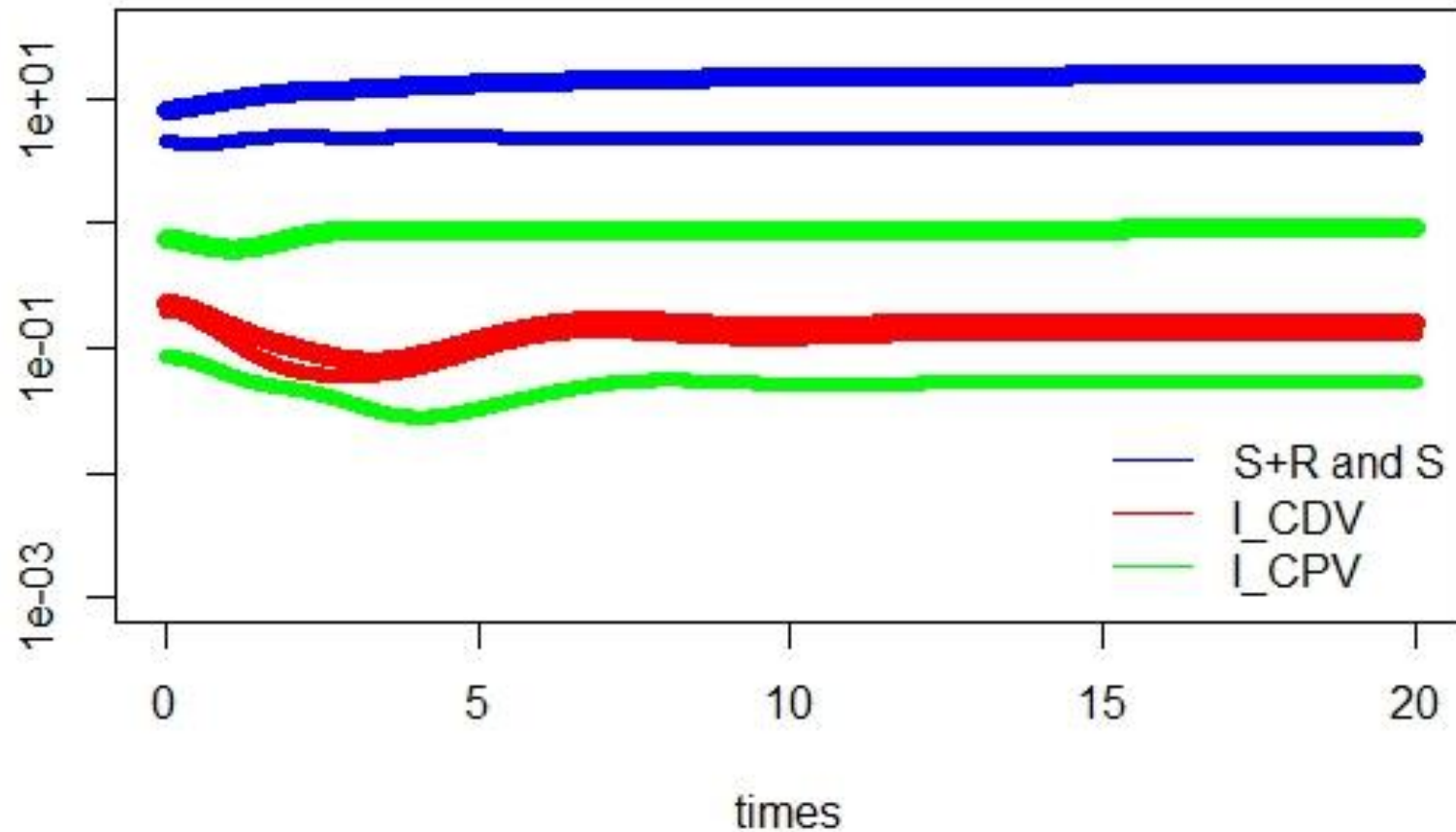


## Mixed CDV & CPV Model

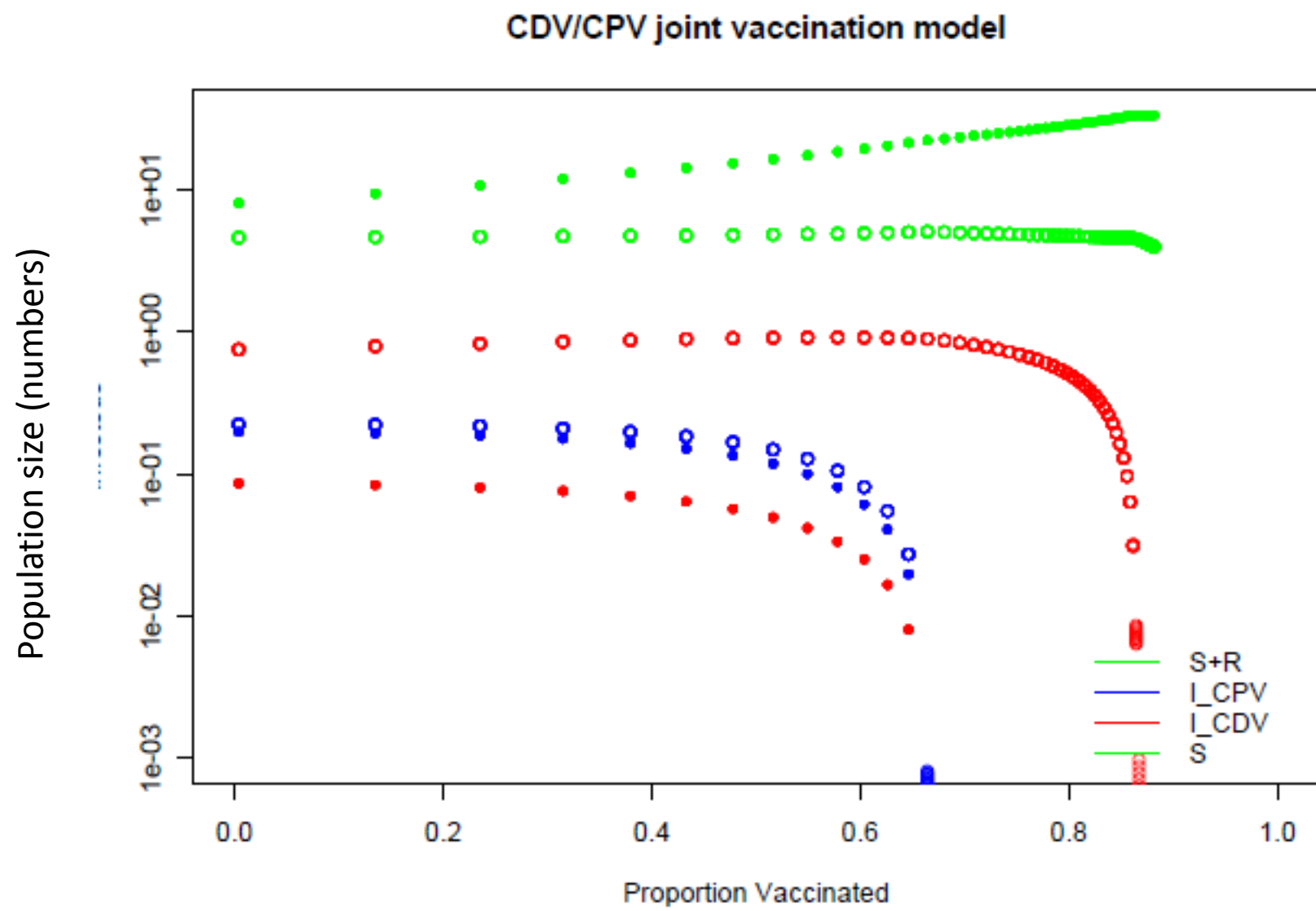


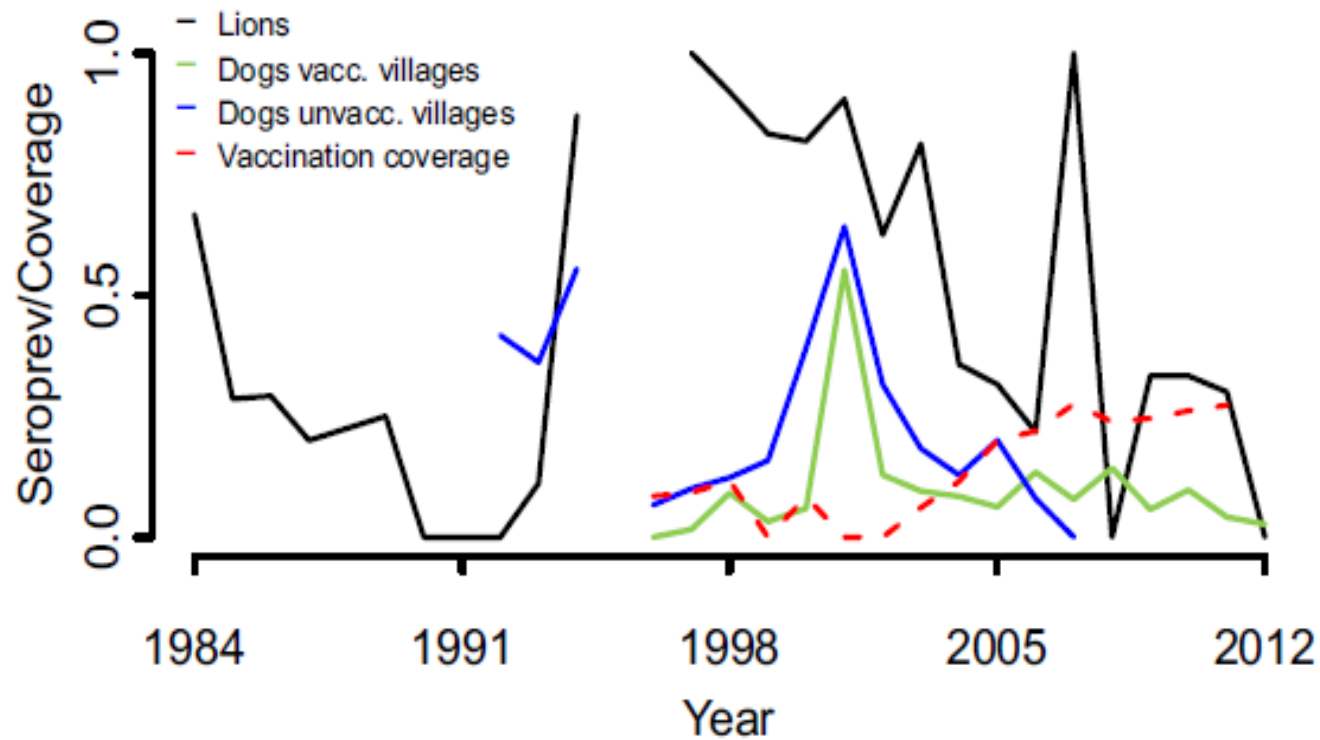
# 25% vaccination ..?

Mixed CDV and CPV model



# Vaccination with two pathogens and a single host (CPV, CDV and dogs)

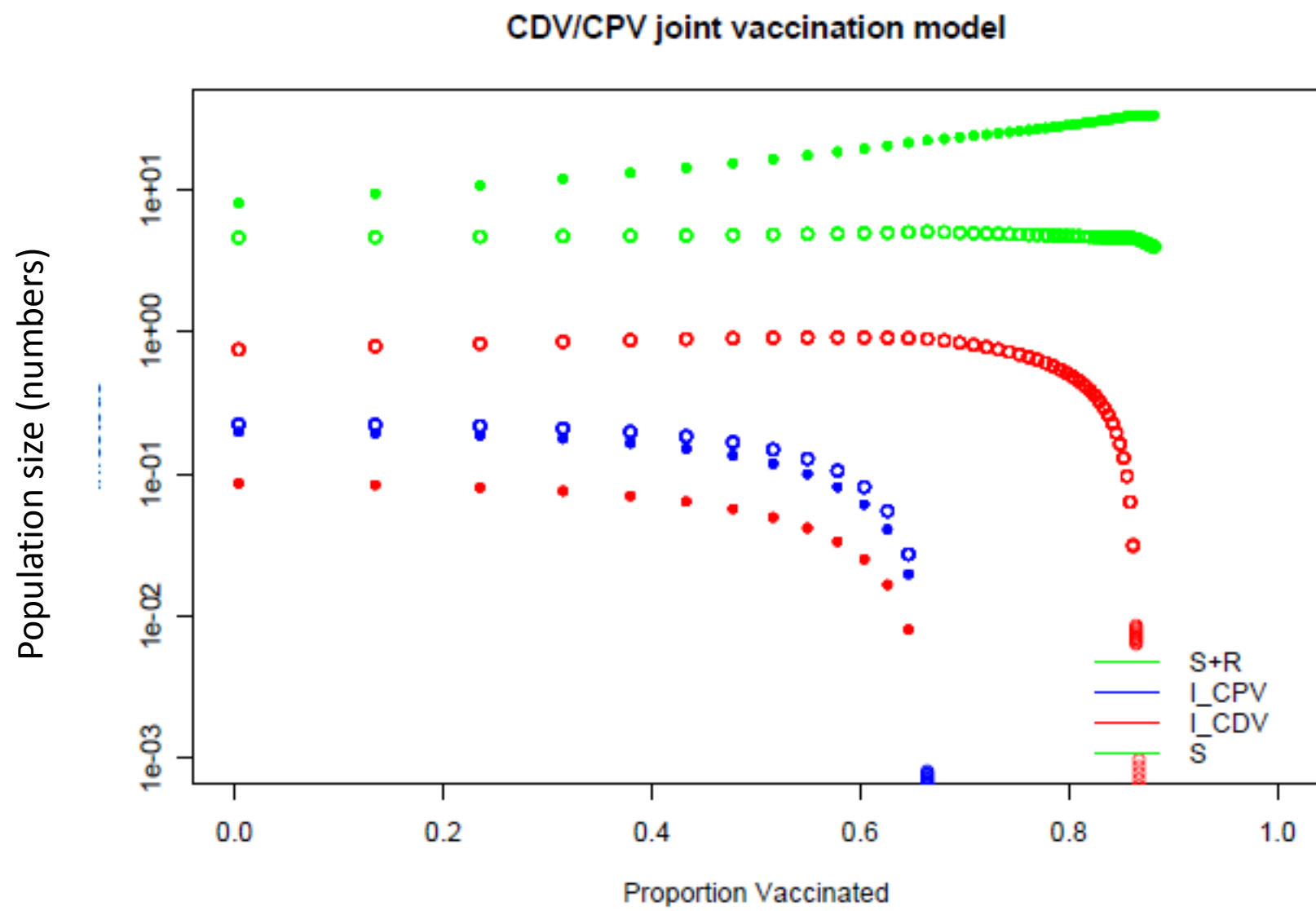




**Fig. 2.** Annual CDV seroprevalence in Serengeti lions (black) and in non-vaccinated dogs from vaccinated (green) and unvaccinated (blue) villages and regional vaccination coverage (red).



# Vaccination with two pathogens and a single host (CPV, CDV and dogs)



## Bottom line here...

- The presence of a second pathogen (and a third, fourth, etc) will change the dynamics away from simple SIR dynamics.
- Keep this in mind when interpreting data (or fitting model) and assuming simple SIR dynamics
- Be particularly cautious when morbilliviruses are involved as 1000x more immuno-compromising than HIV!!!

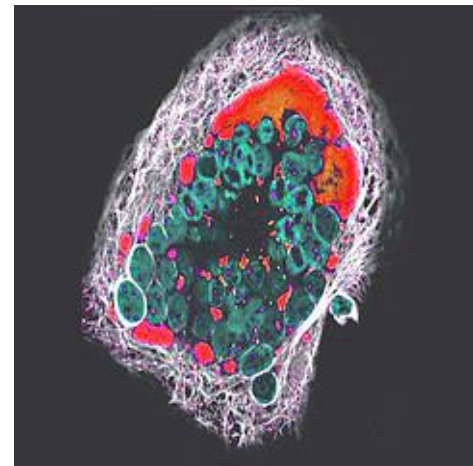


Many thanks to Meggan Craft, Peter Hawthorne, Craig Packer and Serengeti Lion Project and Serengeti Carnivore Disease Project. Funded by NIH/NSF - Ecology of Infectious Diseases.

# Heroes and Villains



Walter Plowright



Rinderpest virus

# Outline of talk

- Brief history of rinderpest and its eradication
- Consequences of eradication – ecosystem level effects
- Worries for the future



# More rinderpest heroes...!

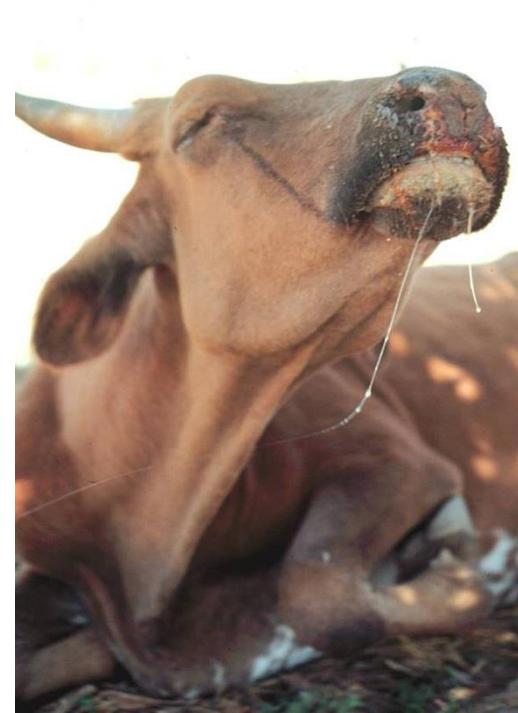


From left to right Michael Baron, Martyn Jeggo, Bill Taylor, Peter Roeder and John Anderson

**Rinderpest virus**



**Infected cow**

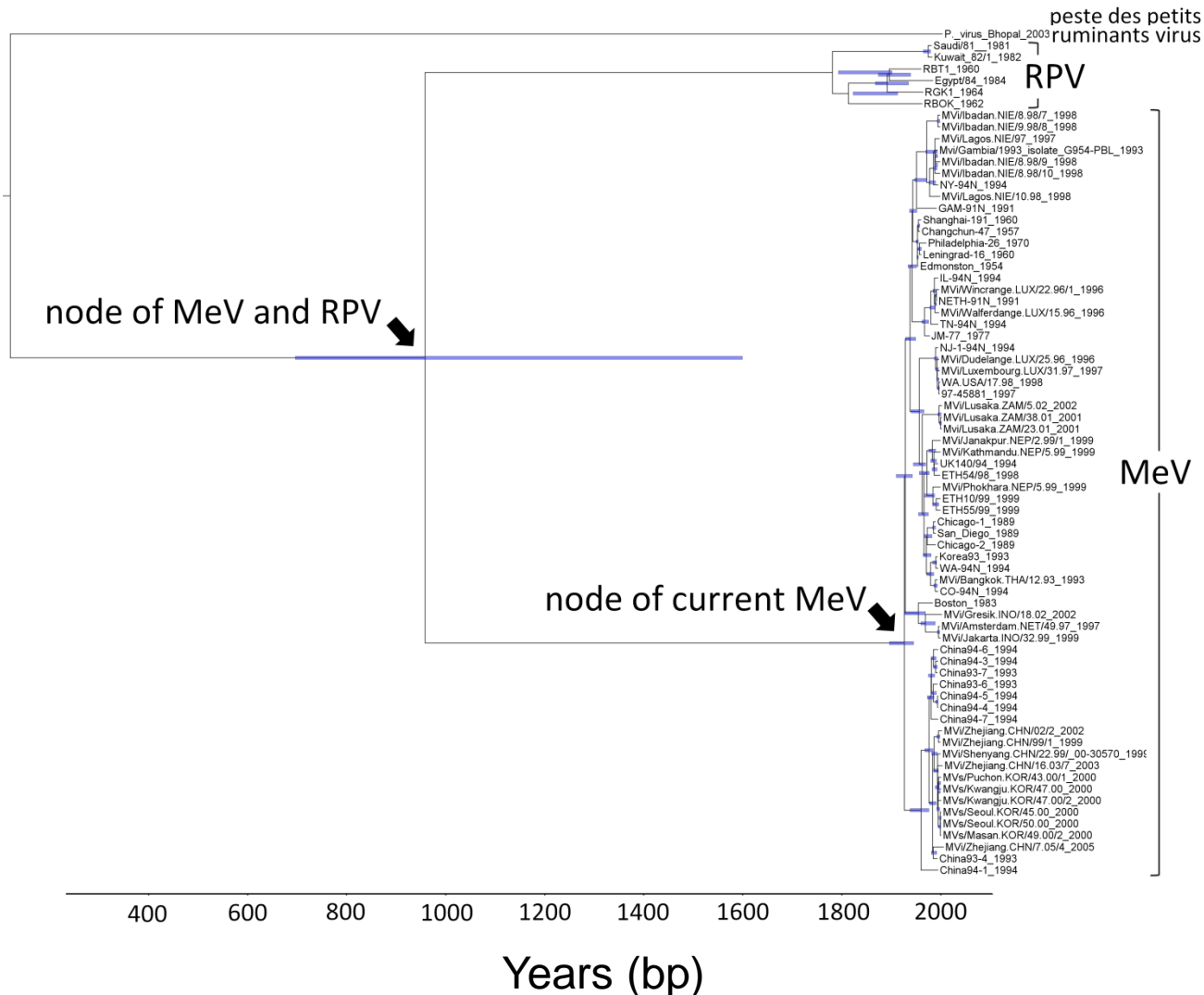


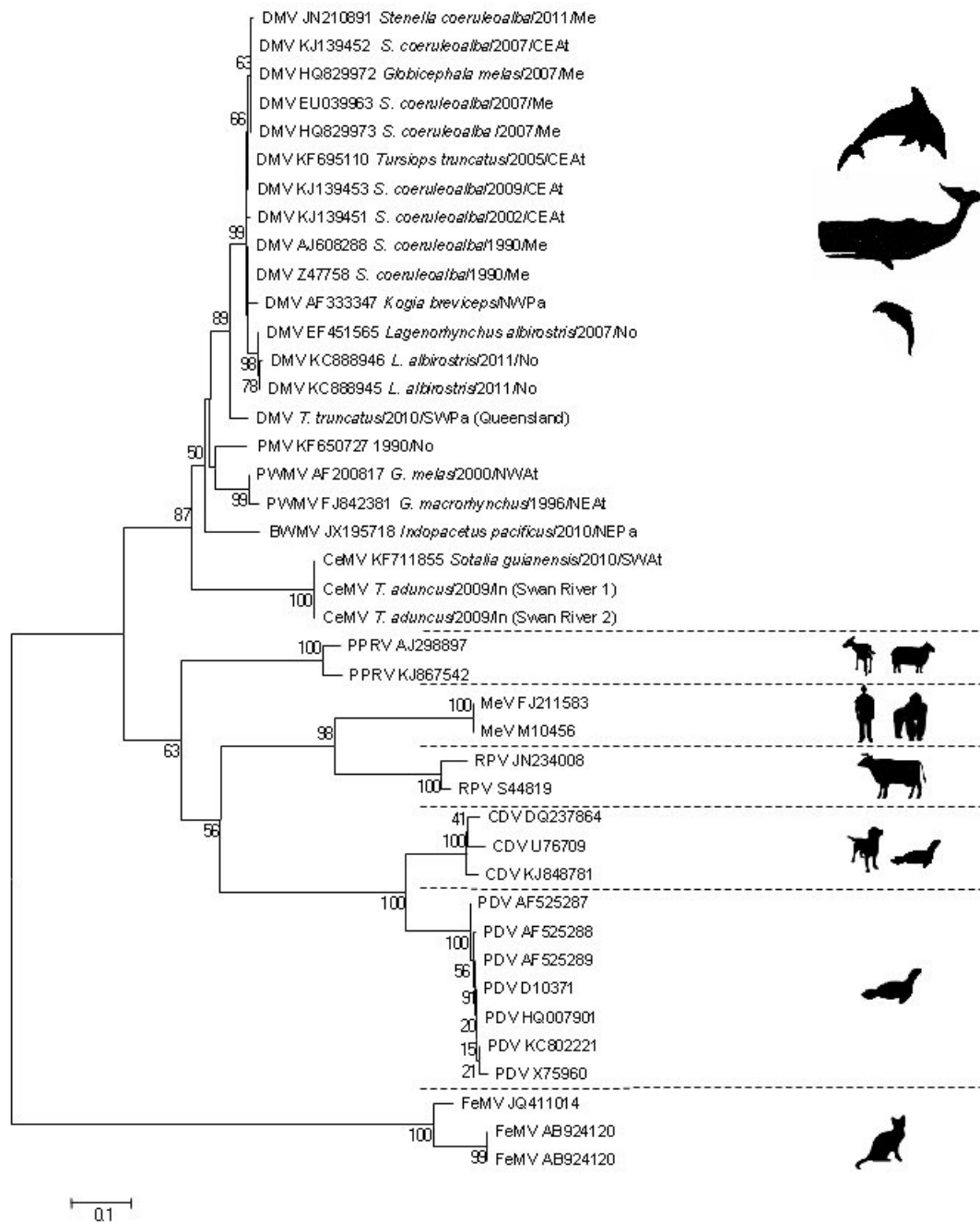




# Split between Rinderpest and Measles

(from Furuse, Suzuki, Oshitani, Virology Journal 2010)









- Early diagnostics and control.

Bernardino Ramazzini had been the first to describe rinderpest, in 1712.<sup>5</sup> He was the principal professor of medicine at the University of Padua. He saw several similarities between rinderpest and smallpox and his views were widely accepted. Giovanni Maria Lancisi, the Pope's personal physician, recommended the slaughter of all infected and exposed animals.<sup>6</sup> This policy was undoubtedly the most logical approach to combat the rinderpest epizootics, but it understandably met with much resistance and was therefore applied only sparingly especially at the beginning; later in the century it would be used successfully in several countries. In others, however, the measures were seen as too drastic and costly; in addition, their strict application required a strong central authority, which was often lacking, as in the United Dutch Provinces for example.

Against this background it was not surprising that attempts were made to apply the inoculation principle to rinderpest, as it was extrapolated to measles by Francis Home a few years later.<sup>7</sup> Both diseases were seen as closely related to smallpox and one attack was known to provide lifelong protection. Several of the most fervent and experienced smallpox inoculators, like Pieter Camper in the Netherlands, became the most enthusiastic promoters of applying the procedure to rinderpest, especially because all attempts to cure the disease had failed; the whole range of the then known drugs used in human medicine had been tried, all to no avail.<sup>8</sup>

- Huygelen (1997) *Medical History* 41: 182-196

### **Initial Inoculations in England and the Netherlands**

The first written report of rinderpest inoculation was published as a letter signed “T.S.” in the November 1754 issue of the *Gentleman’s Magazine*, a journal then widely read by educated people not only in Britain, but also on the Continent. This magazine also actively supported the progress of smallpox inoculation.<sup>9</sup> In this context it was eager to publish letters about the applications of the principle to other diseases. The author of the letter reported that a Mr Dobson, a gentleman of Yorkshire, had inoculated his cattle and had thus preserved nine out of ten of them.<sup>10</sup> In the next issue of the journal, a correction appeared stating that Mr Dobson was very surprised to see his name mentioned in

connection with the procedure. The letter stated that “Mr. Dobson lives in the city of York, and is so far from having any stock of cattle, that he does not even keep a cow”. The real story Dobson had heard, was as follows:

Sir William St. Quintin, of Scampton in Yorkshire, inoculated eight calves, seven of which had the distemper from the inoculation, and recovered, and were afterwards turned into a herd of infected cattle, without being infected a second time; the other case was of an old ox, which was inoculated at Malton, which had the distemper from inoculation, and recovered, and was afterwards turned into a herd of infected cattle, but did not receive the infection a second time. Mr. Dobson had the foregoing account from an eminent physician in Yorkshire, who told him the method of performing the operation, and of treating the beast in distemper, which is as follows: First bleed the beast, and from that time keep him from hay, and all dry meat, till he is quite recovered; and in order to keep his body open, give him scalded bran, or chaff. At the end of three days make an incision in the dewlap, into his wound put a piece of tow, dipped in the morbid matter discharged from the nostrils, or eyes, of an infected beast, then stitch up the wound, and let the tow remain until the symptoms of distemper appear, when the tow must be taken out; after turn the beast out to grass.<sup>11</sup>

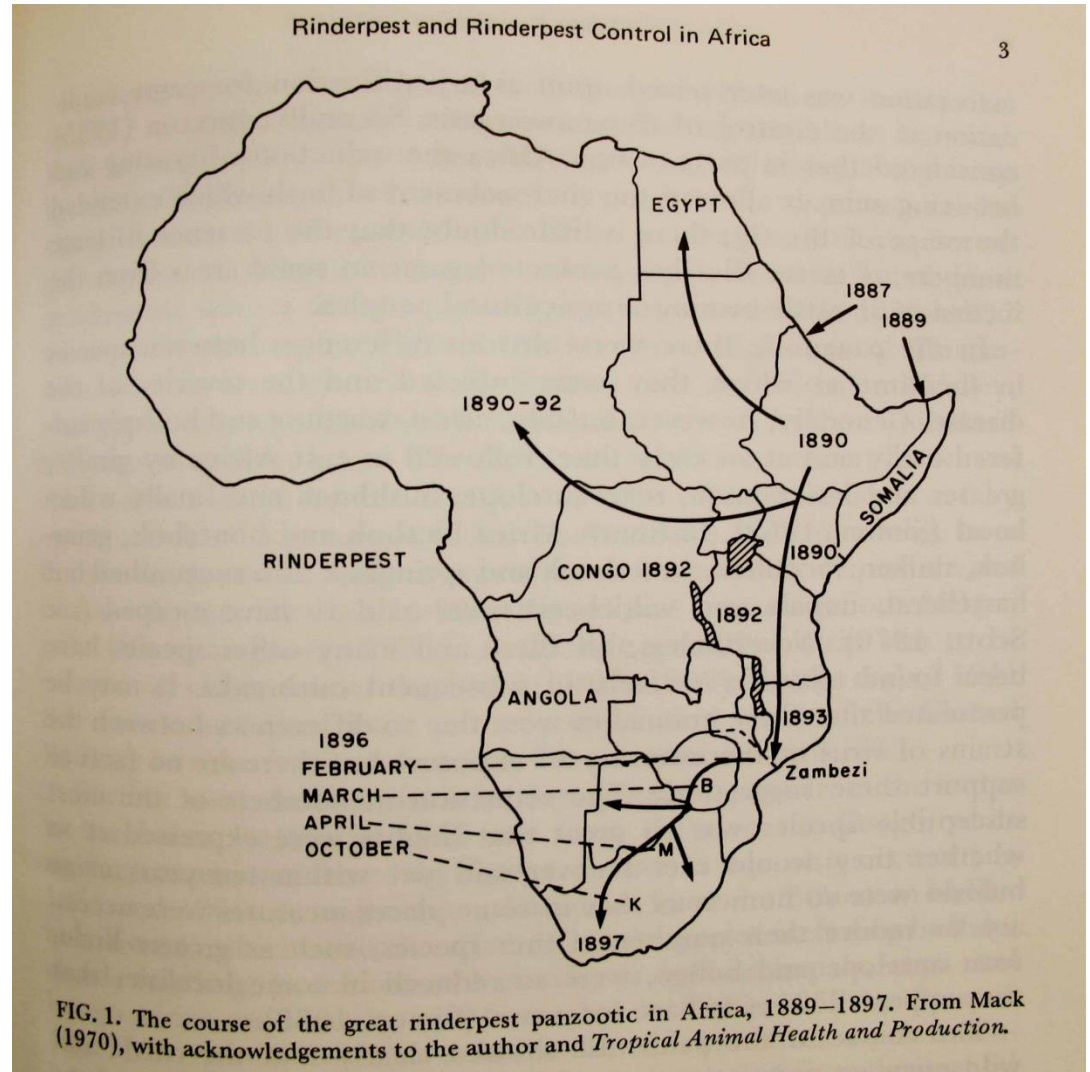
In almost all later literature on rinderpest the first inoculations have been erroneously attributed to Dobson, probably because the second letter went unnoticed; in addition, most authors misspelled his name: “Dodson”. Many also gave the incorrect date of 1744 instead



# Spread of Rinderpest in Africa 1889-1897 (after Mack 1970).

Introduced into Horn of Africa –  
most likely by Italian Army laying  
siege to Gordon in Khartoum.

Easier and faster to transport cattle  
by steamboat – so Sahara no  
longer provided a barrier to cattle  
movement.





Oxen were main power of transport and agriculture in South Africa in 19<sup>th</sup> Century



Around 2.5 million cattle died of rinderpest in South Africa in 1890's (Mack 1970)

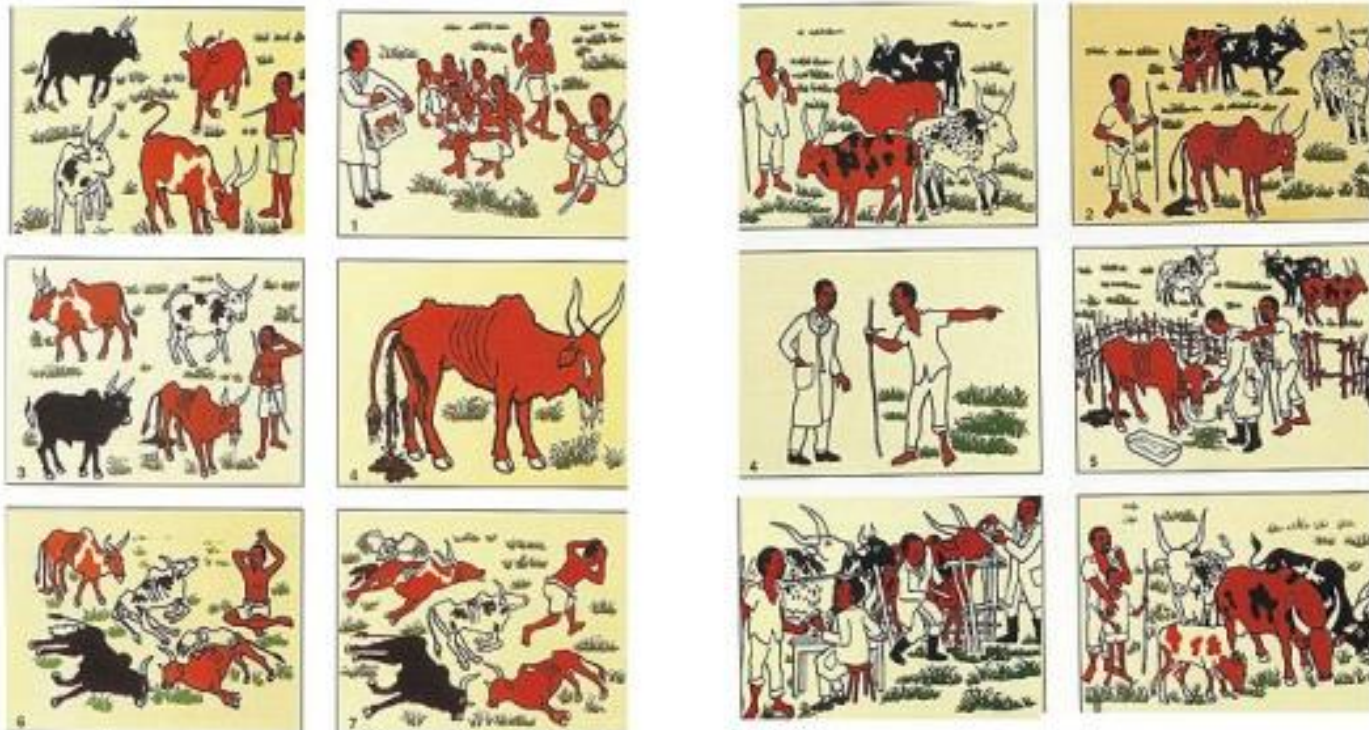
## Walter Plowright

**Walter Plowright**, [CMG](#), [FRS](#)<sup>[1]</sup>, [FRCVS](#) (born 20 July 1923, [Holbeach](#), Lincolnshire – 19 February 2010 London<sup>[2]</sup>) was an English [veterinary scientist](#) who devoted his career to the [eradication](#) of the cattle plague [rinderpest](#). Dr Plowright received the 1999 [World Food Prize](#) for his development of tissue culture rinderpest vaccine (TCRV), the key element in the quest to eliminate rinderpest.<sup>[3]</sup> Rinderpest became the first animal disease to be eliminated worldwide





# Rinderpest eradication programmes: Education



Disease of the 3Ds : discharge, diarrhoea and death



Pan-African Rinderpest Campaigns  
 Attempted to rid Africa of rinderpest;  
 But constant leaking on of infections  
 From middle east and Pakistan

Need to go for global campaign

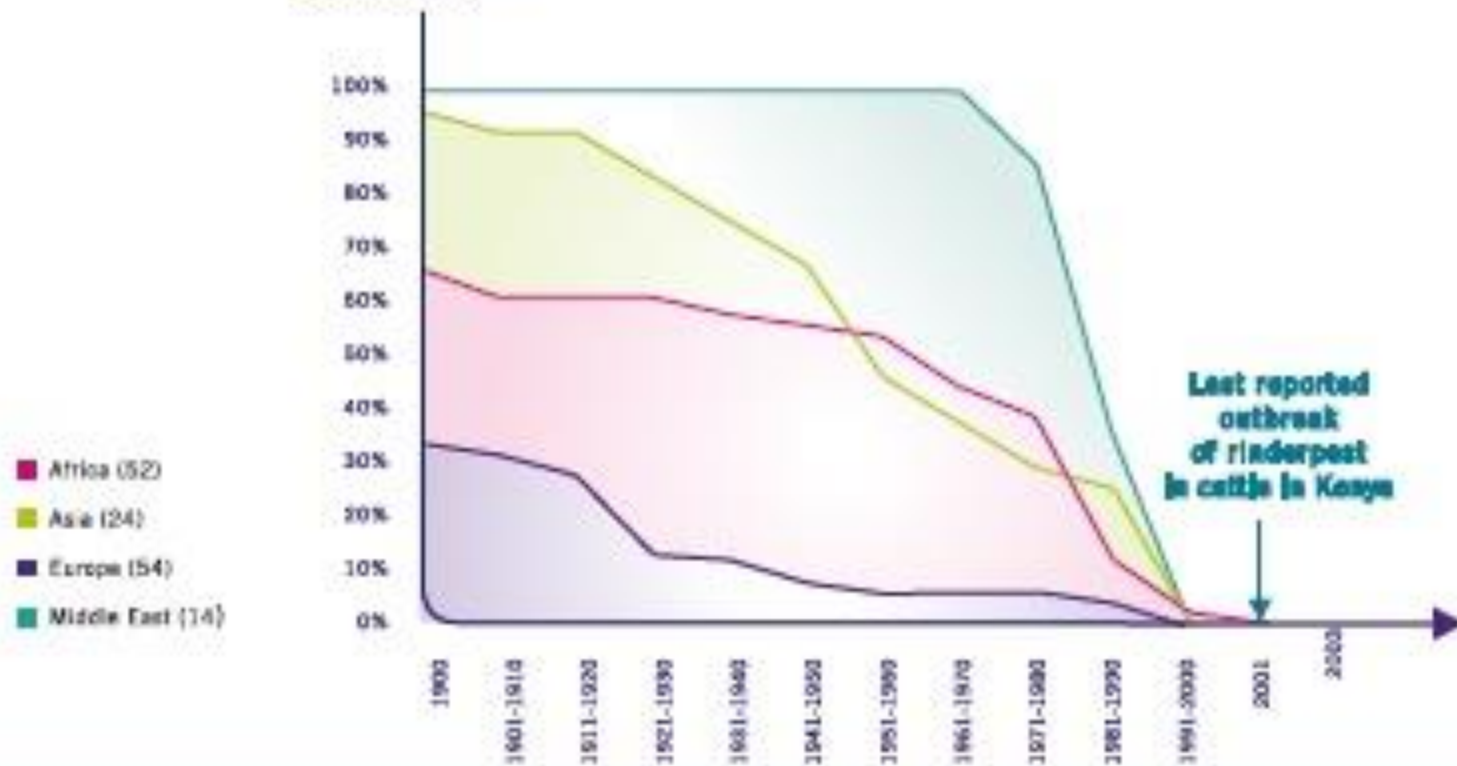




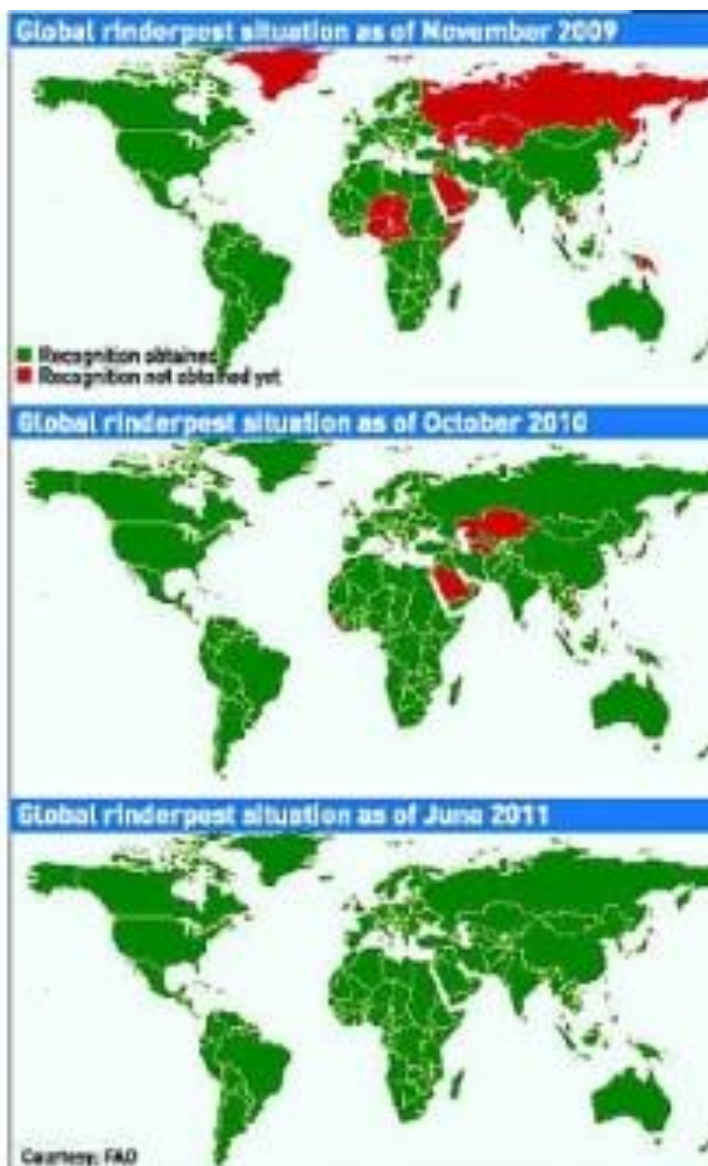
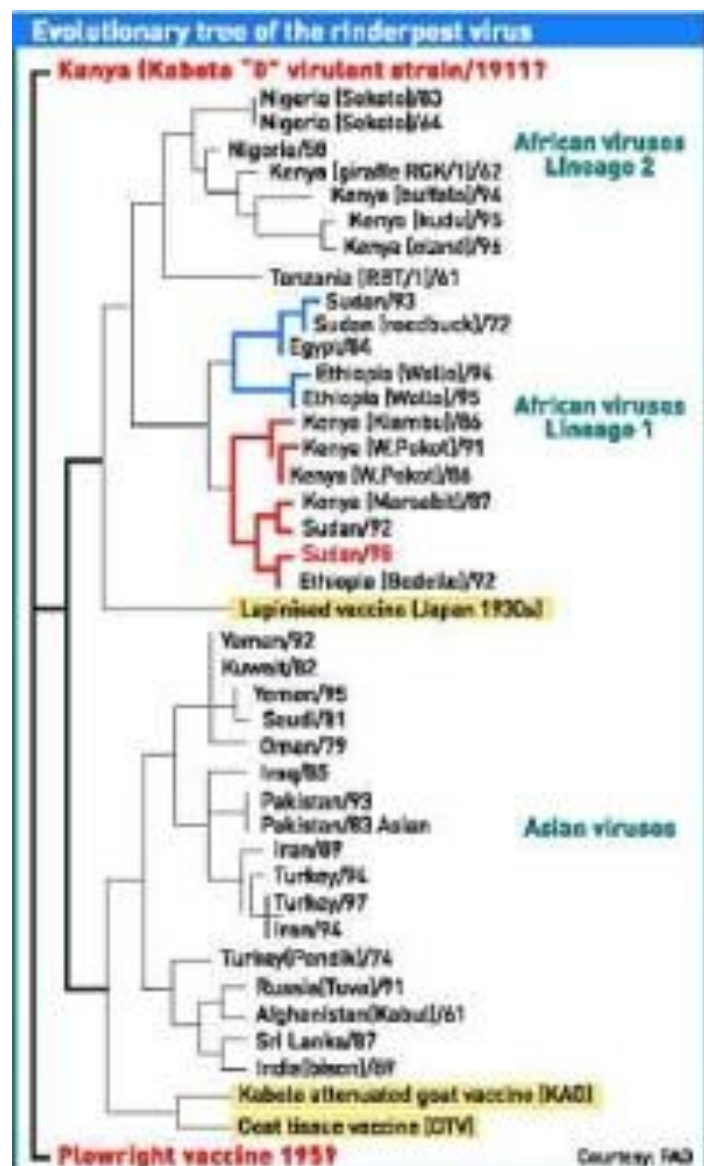
## ERADICATING RINDERPEST : moments in time

Reported outbreaks of rinderpest steadily declined over the last 100 years.

Share of countries affected  
with rinderpest in each of the  
regions of the world.

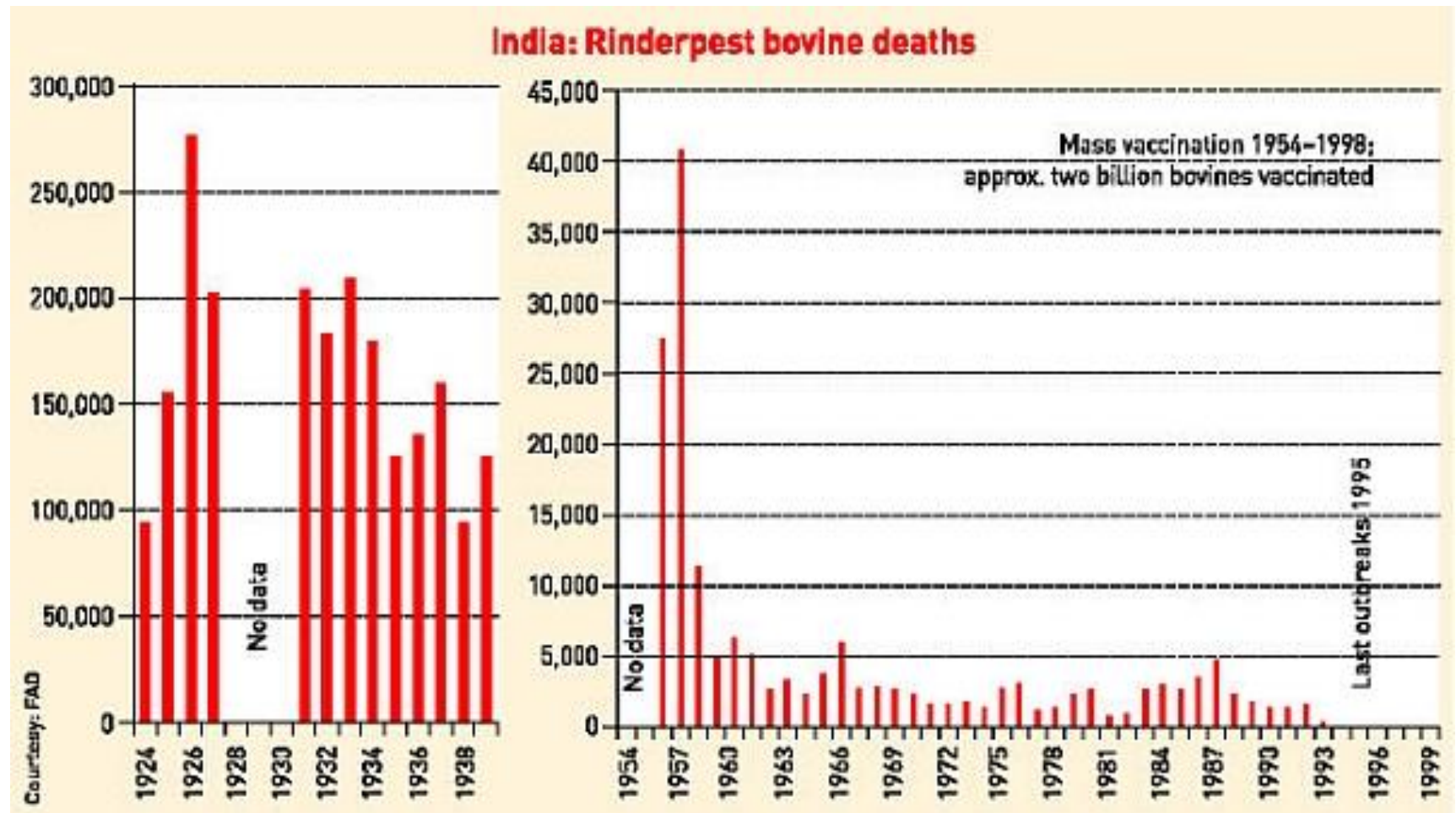




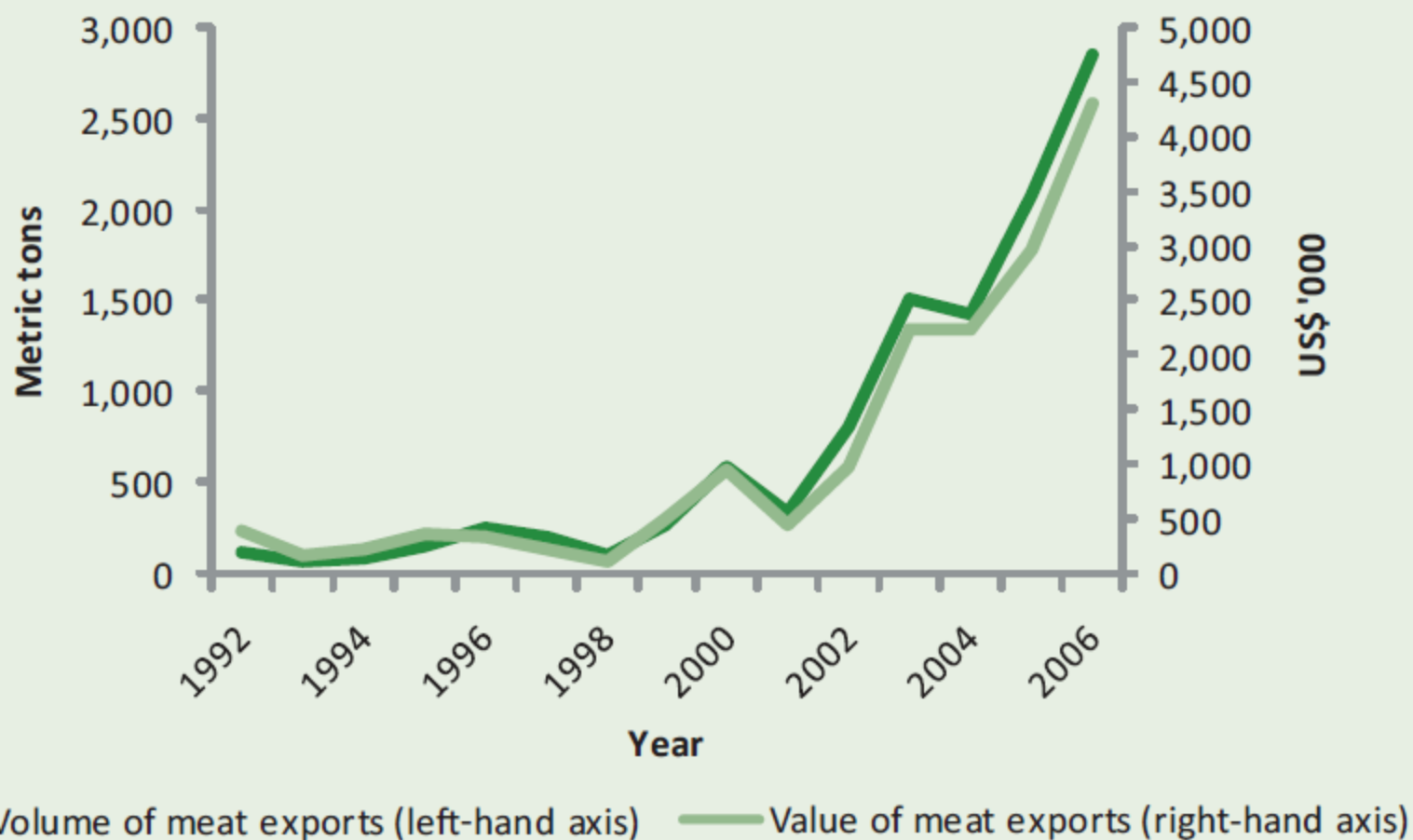




# Rinderpest eradication in India

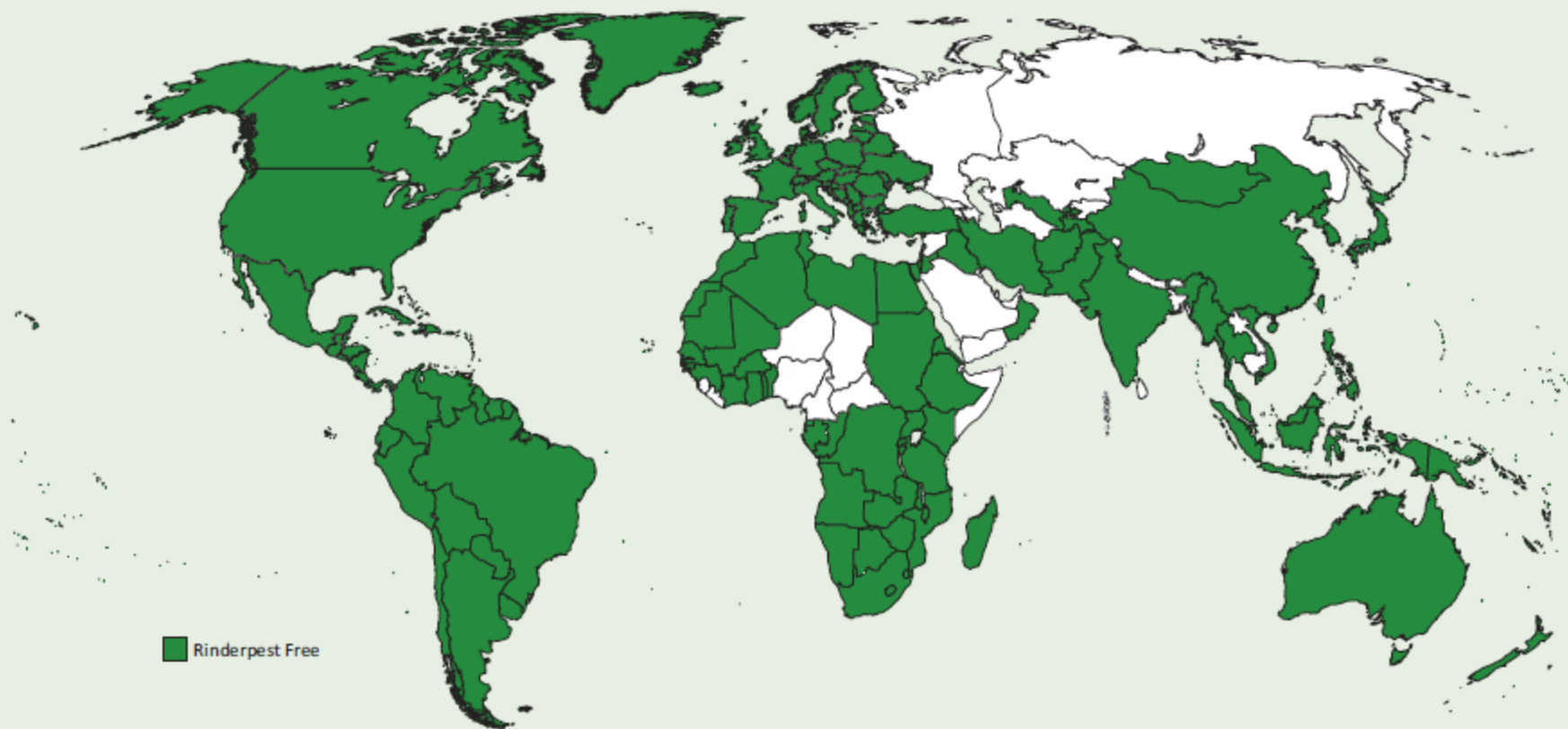


**Figure 16.1—Exports of beef products from Pakistan, 1992–2006**



Source: FAO (Food and Agriculture Organization of the United Nations). 2009. FAOSTAT statistical database. Rome.

**Figure 16.2— Status of accreditation of rinderpest freedom, 2009**



Source: World Organization for Animal Health. 2009. [www.oie.int/eng/status/Rinderpest/en\\_RP\\_free.htm](http://www.oie.int/eng/status/Rinderpest/en_RP_free.htm).

- Crucial importance of community-based animal health workers.

Community-based animal health workers were specifically used to combat rinderpest in South Sudan, the Afar region of Ethiopia, Karamoja in Uganda, and Turkana in Kenya, as part of the Pan African Rinderpest Campaign. The effort, directed by the Organization of African Unity/Interafrican Bureau for Animal Resources and implemented in partnership with various nongovernmental organizations working on the ground, quickly achieved dramatic results.

In South Sudan, where armed conflict had disrupted cold chains and brought vaccination efforts to a standstill by 1992, a community animal health worker program using the new vaccine succeeded in vaccinating over 4.3 million cattle between 1993 and 1995; as a result confirmed outbreaks of rinderpest decreased from 11 in 1993 to only one in 1998.<sup>b</sup> In Ethiopia's Afar region, where government teams had been unable to contain the disease through a 15-year campaign dating back to the late-1970s, community animal health workers succeeded in vaccinating 73,000 cattle in just one season in 1994. Because of this success there were no further cases of rinderpest after 1995; the reservoir of infection had been effectively removed.

*Prepared by: Andy Catley, Tim Leyland, and Peter Roeder*

- 
- a. Leyland, T. 1996. The case for a community-based approach with reference to southern Sudan. In *The world without rinderpest*, FAO (Food and Agricultural Organization of the United Nations) Animal Production and Health Paper 129. Rome: FAO.
  - b. Catley, A., T. Leyland, and S. Bishop. 2008. Policies, practice and participation in protracted crises: The case of livestock interventions in South Sudan. In *Beyond relief: Food security in protracted crises*, ed. L. Alinovi, G. Hemrich, and L. Russo. Rugby, England: Practical Action Publishing and Rome: FAO; Leyland 1996.



Walter Plowright receives World Food Prize for pioneering work on rinderpest vaccine

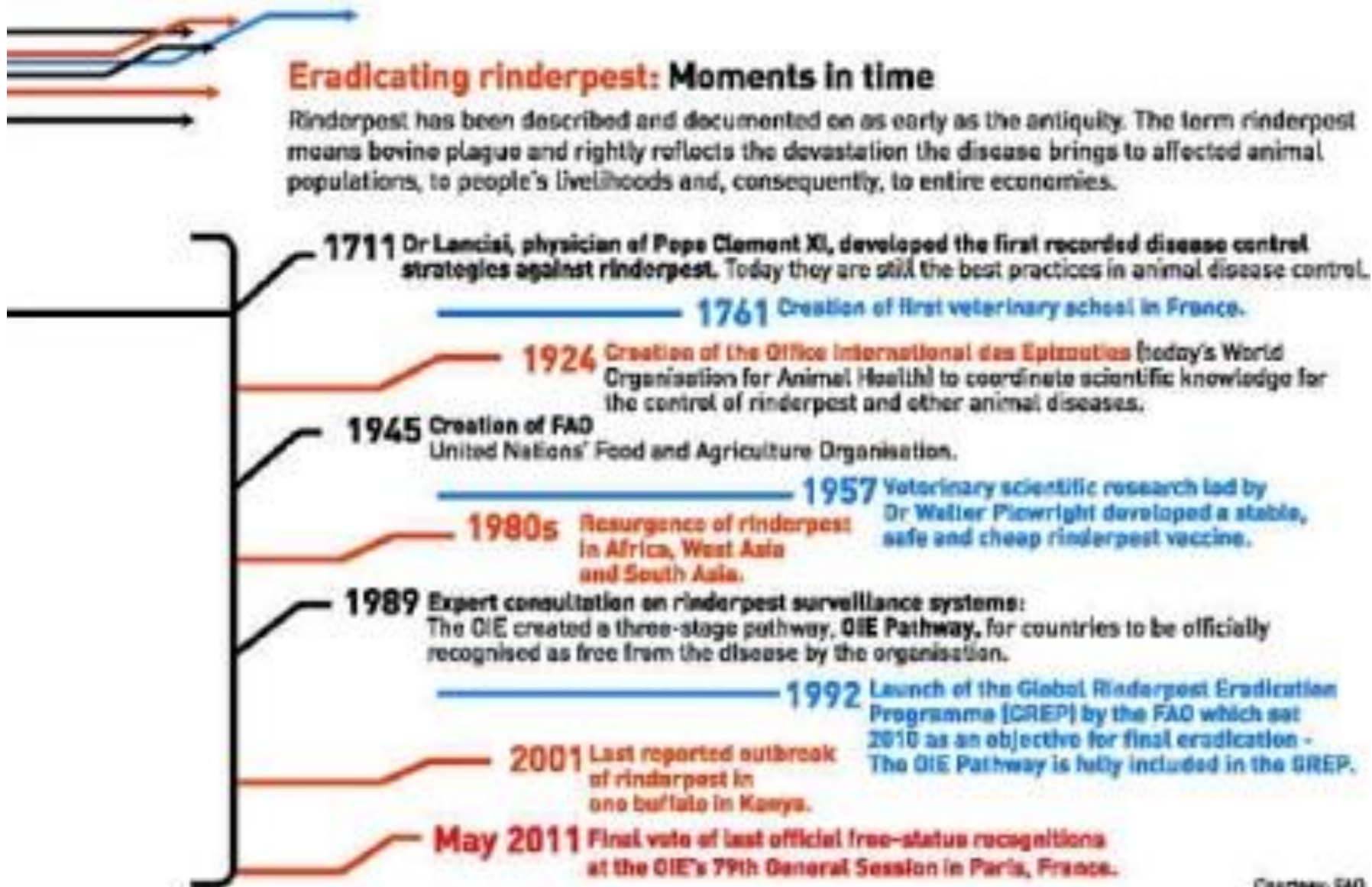


# More rinderpest heroes...!

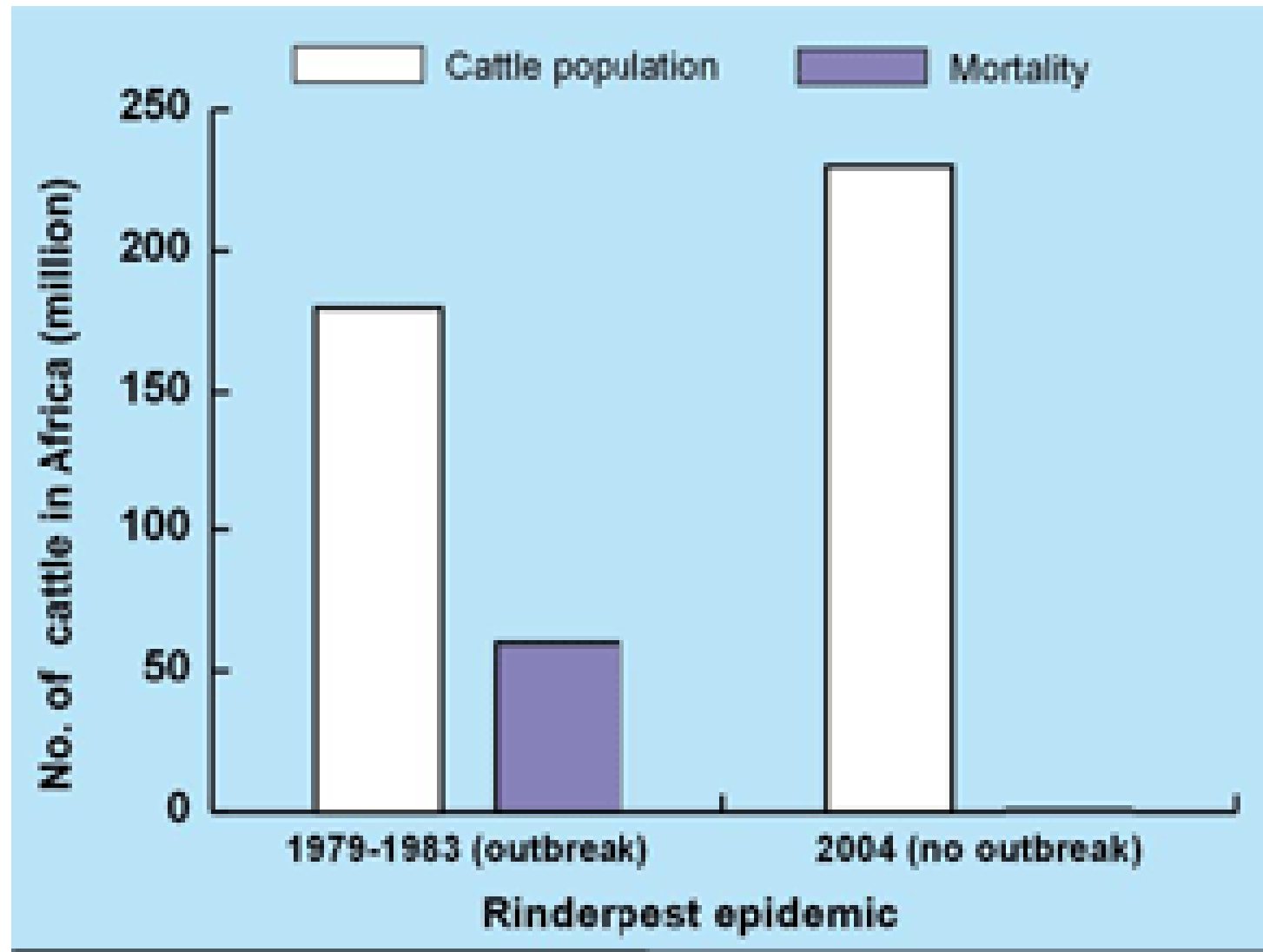


From left to right Michael Baron, Martyn Jeggo, Bill Taylor, Peter Roeder and John Anderson

# Time line for eradication of rinderpest



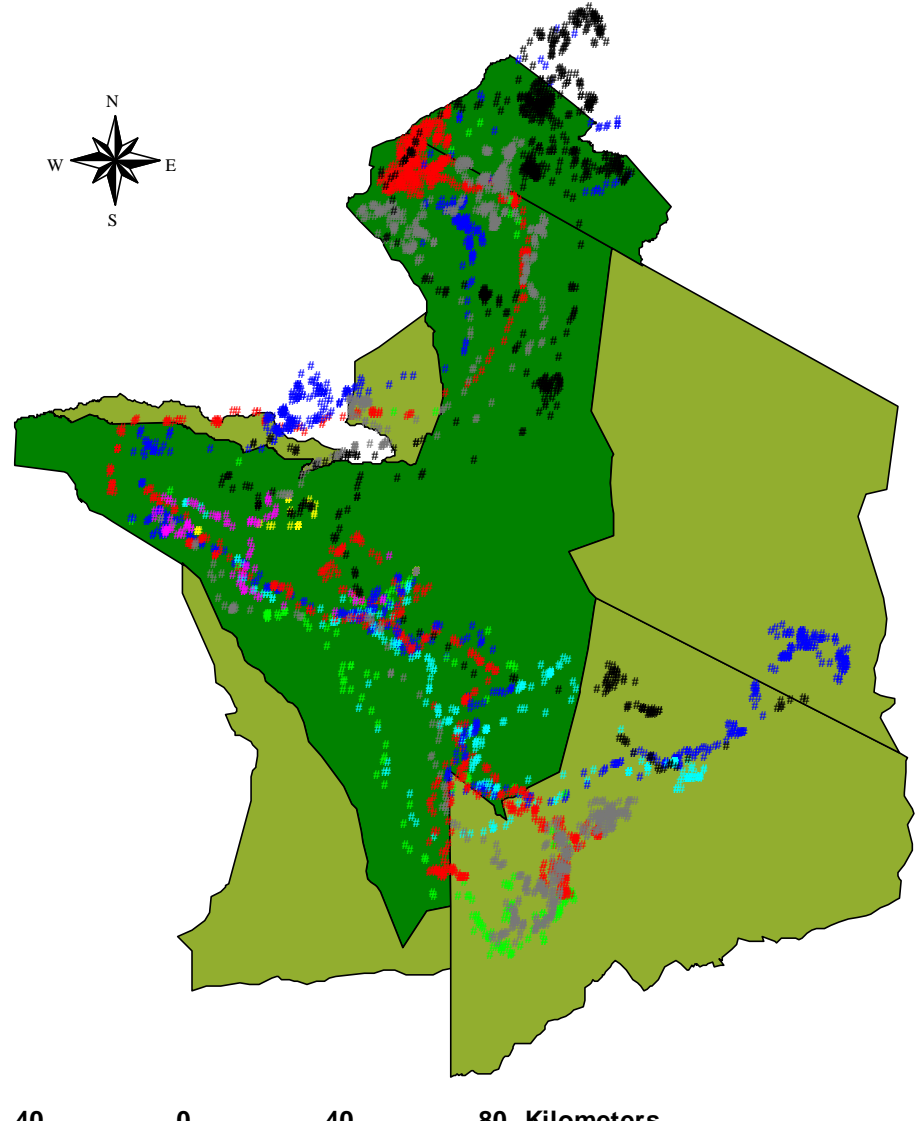
# Consequences of rinderpest control in Africa



Statistics showing numbers of animals and incidence of rinderpest outbreak

# Serengeti National Park

- Established as National Park in 1951, formally gazetted 1959
- Currently 14,763 km<sup>2</sup>
- Defined by the movements of migratory wildebeest
- Diversity of habitats – short-grass plains, woodlands and riverine forests



# SERENGETI ECOSYSTEM





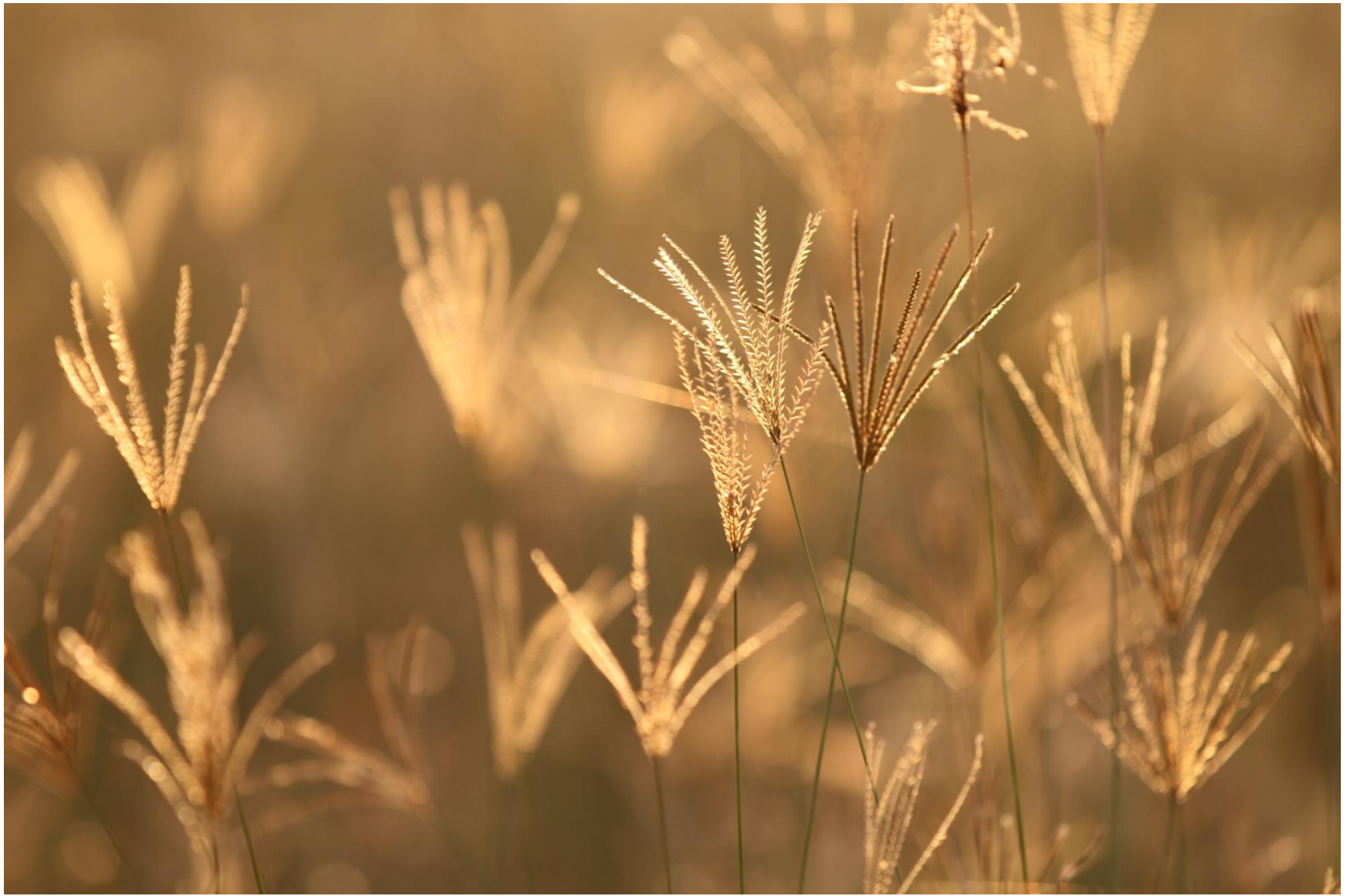






Photo from Felix Bonner, FZS

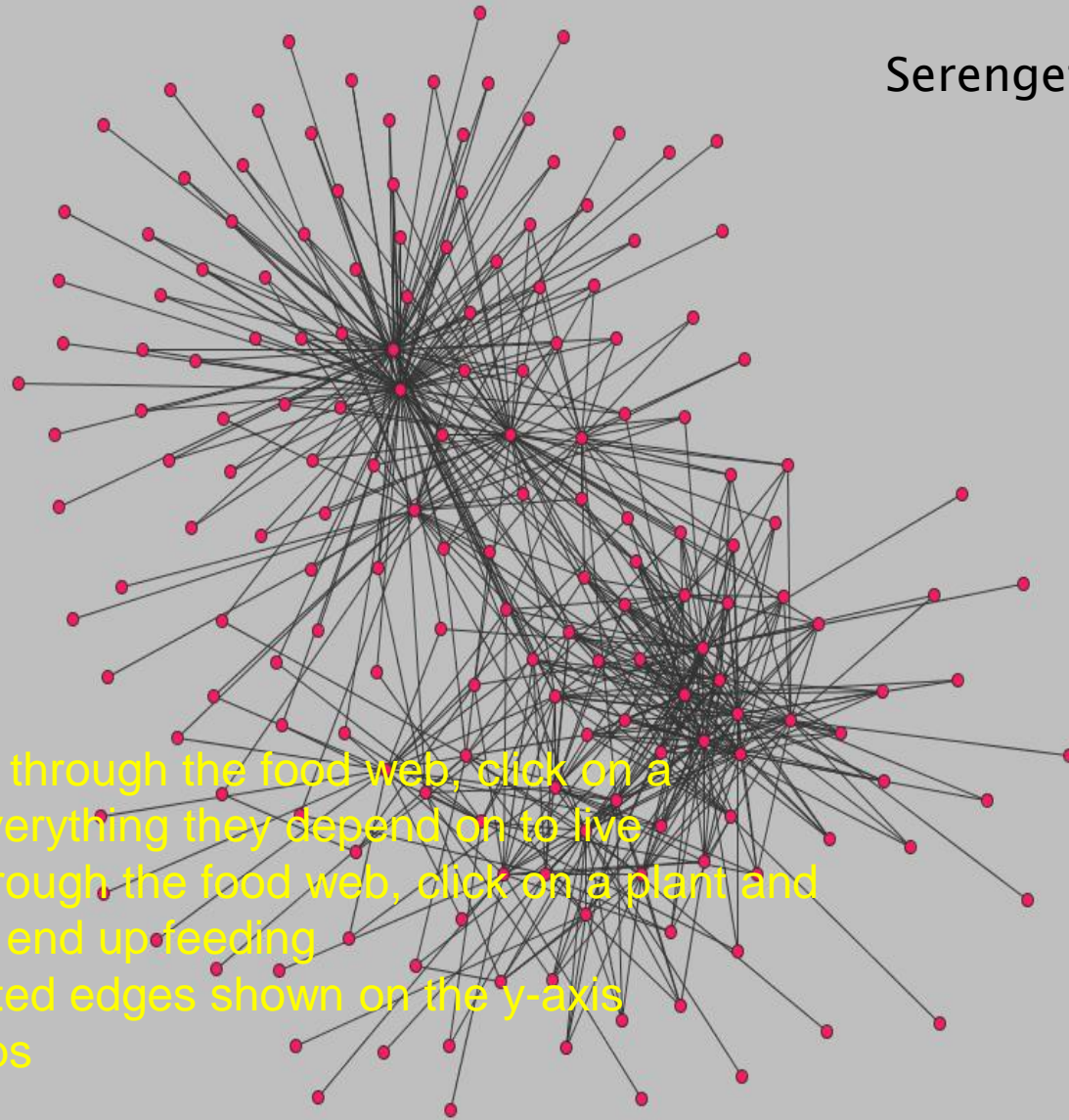






178 nodes  
0 selected  
1 group

## Serengeti foodweb

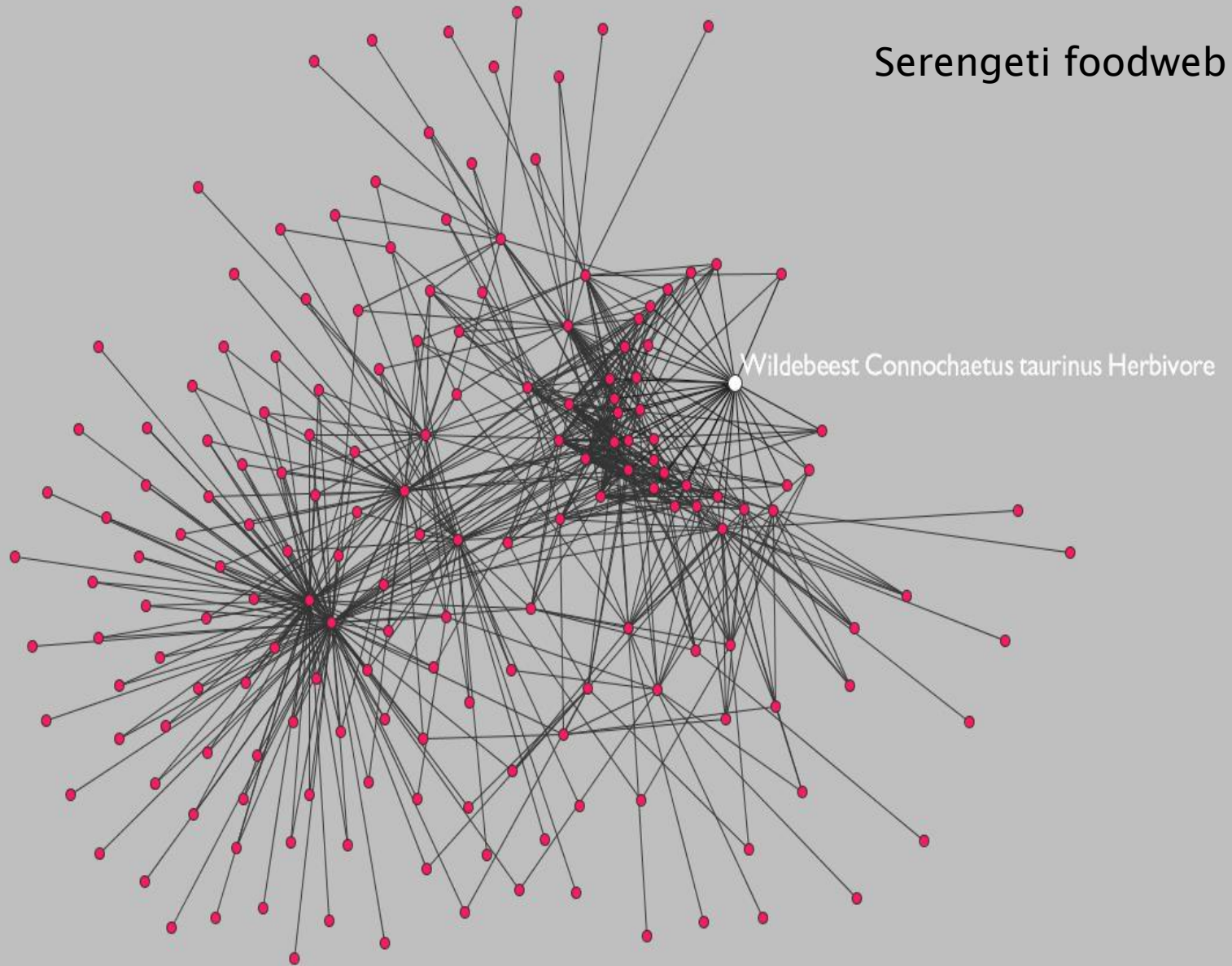


z = flow downwards through the food web, click on a predator and see everything they depend on to live  
x = flow upwards through the food web, click on a plant and see everything they end up feeding  
d = turn on/off directed edges shown on the y-axis  
g = turn on/off groups



178 nodes  
1 selected  
1 group

## Serengeti foodweb

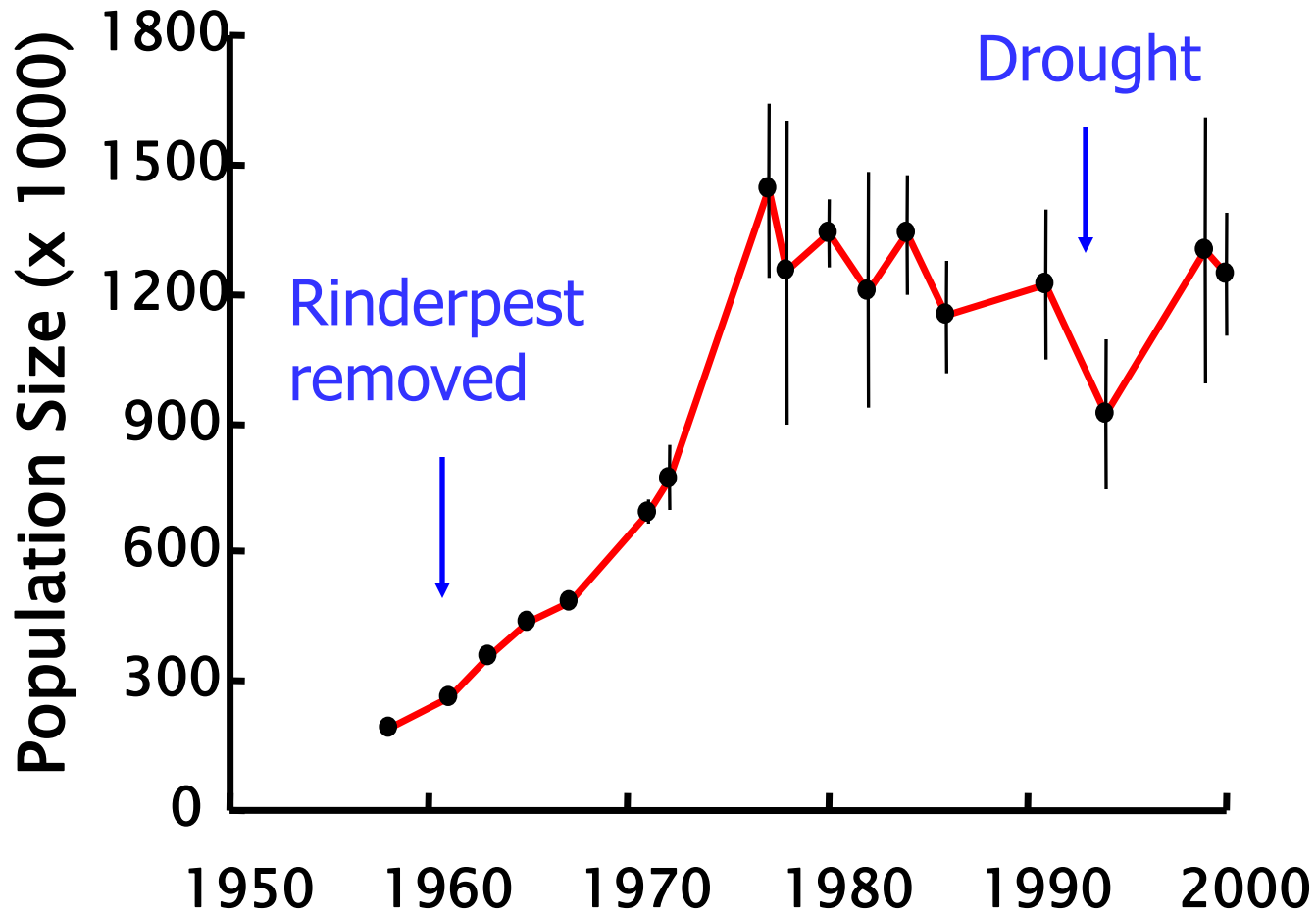


# The Great Rinderpest

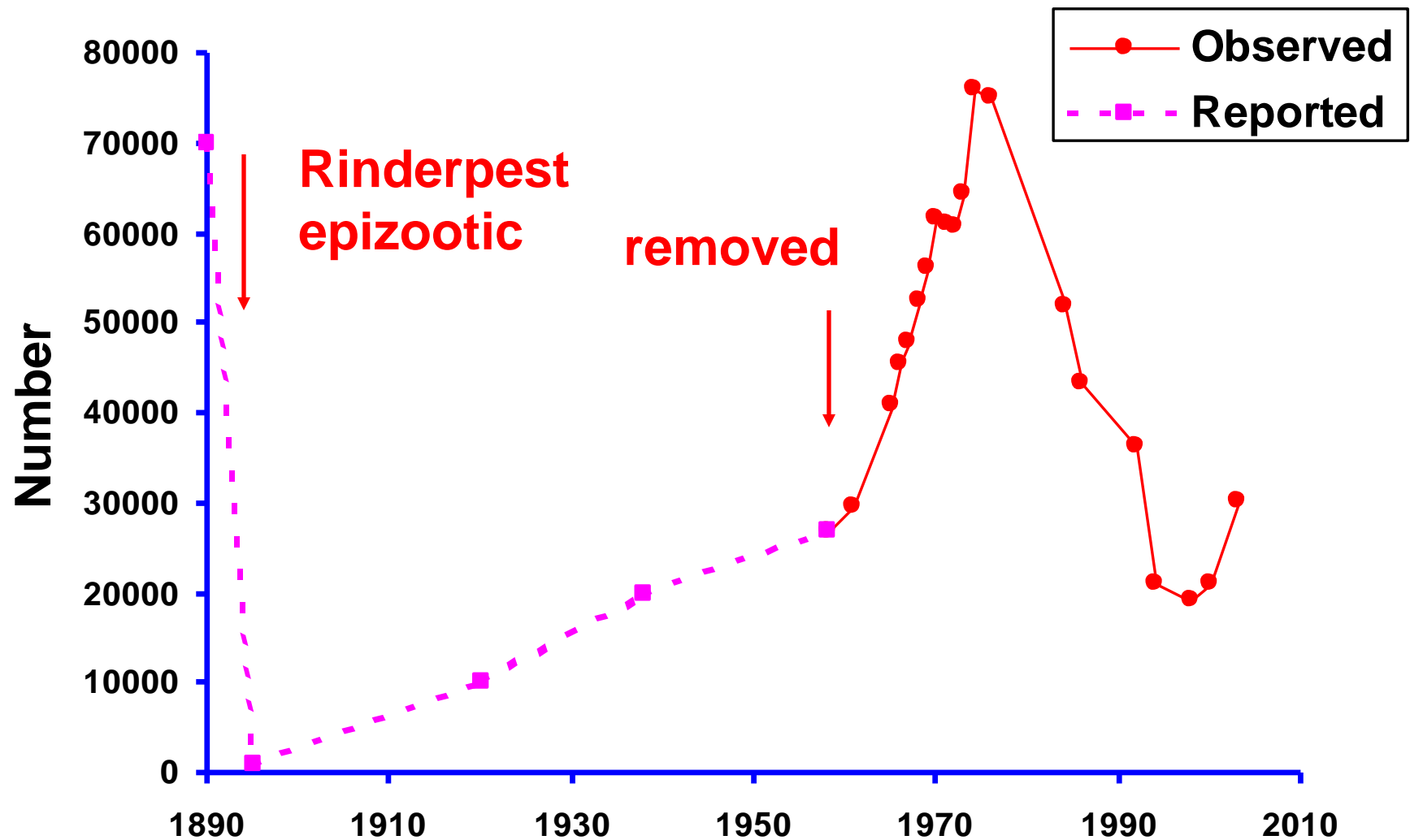
- The Epizootic of 1889
- Ethiopia to Cape by 1896
- Die-off of cattle and other ruminants 95%
- These include African buffalo
- Wildebeest yearling disease present up to 1963



# Serengeti Wildebeest Population

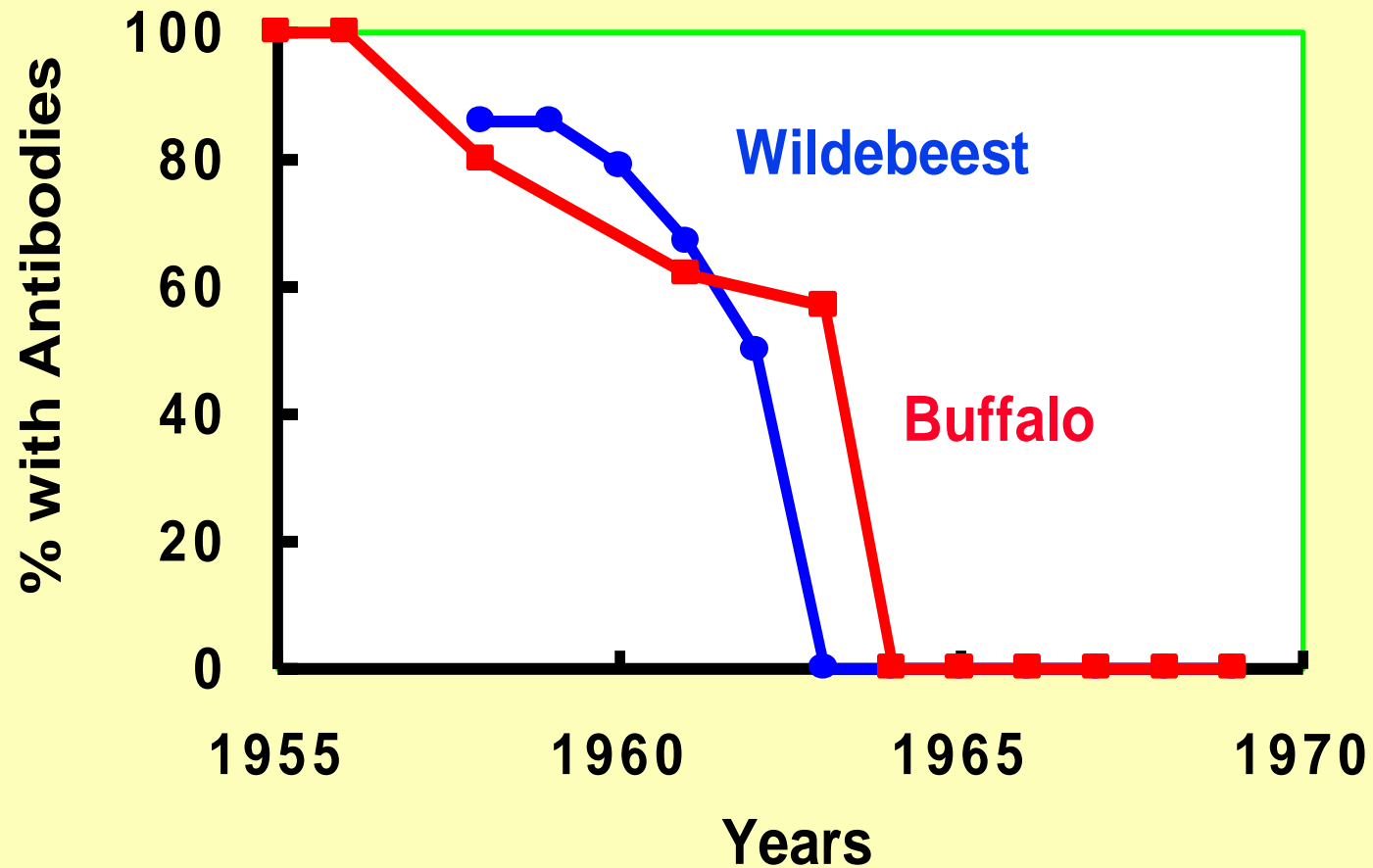


# Buffalo long-term change 1890-2003



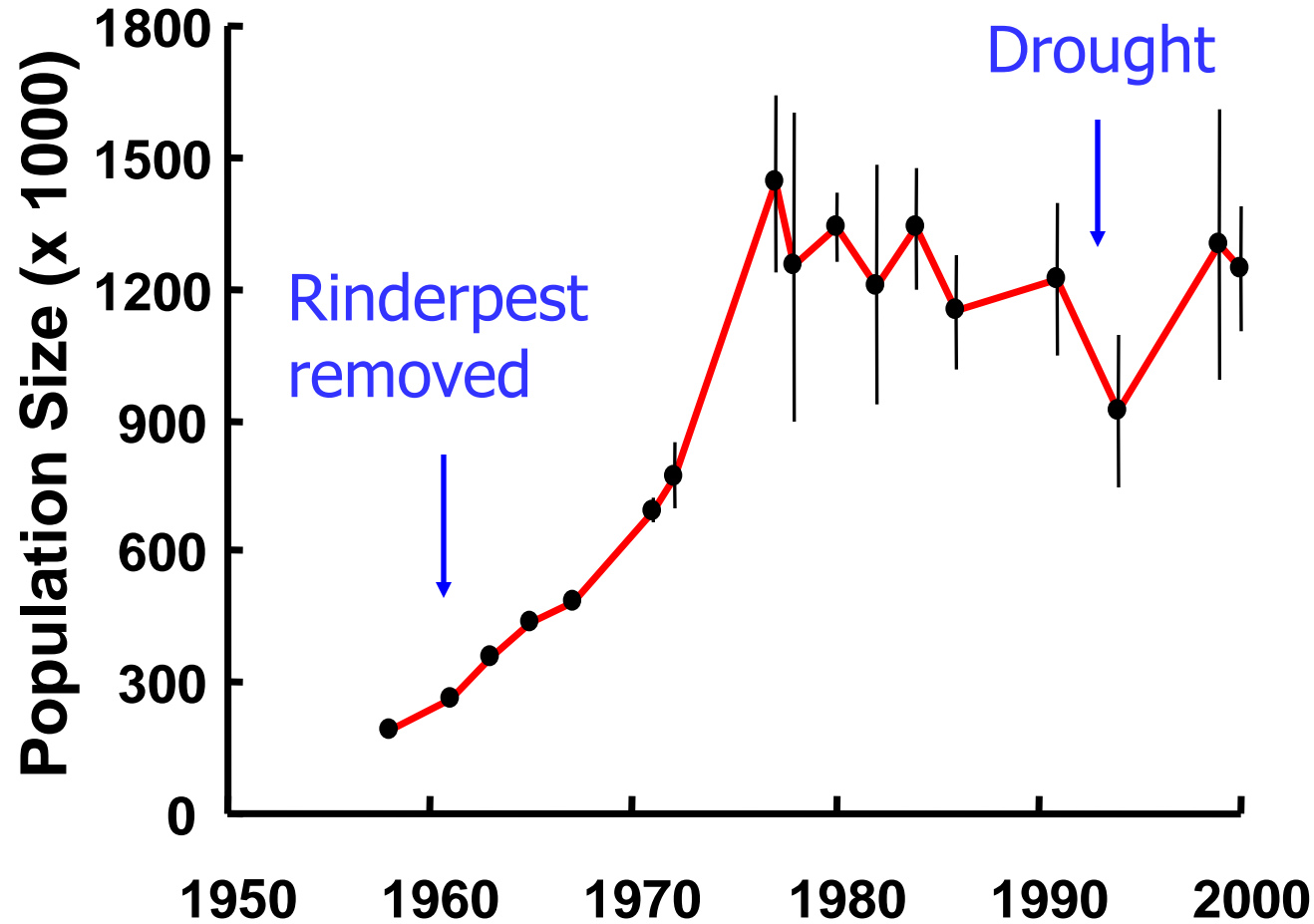


# Incidence of Rinderpest in Serengeti

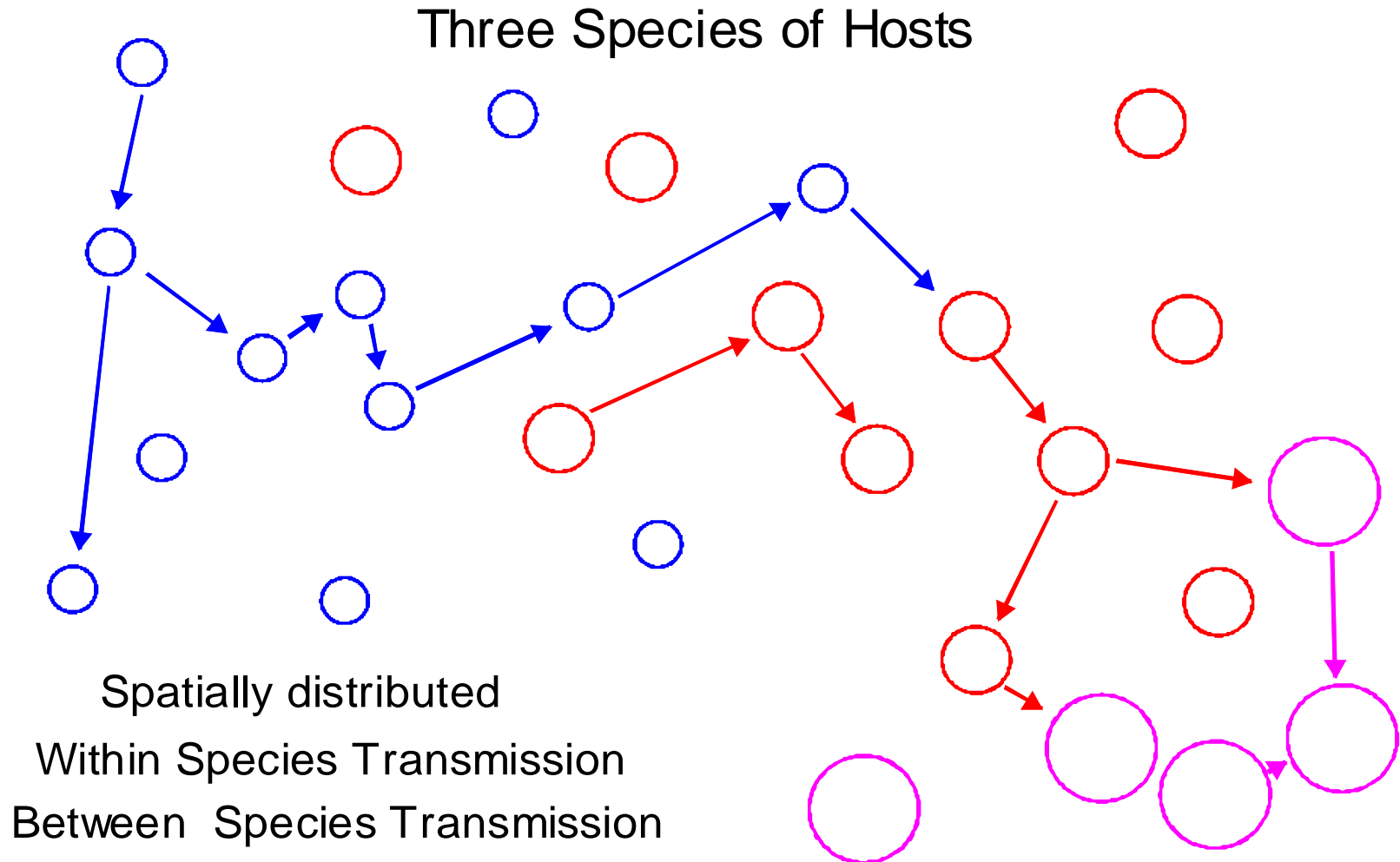




# Serengeti Wildebeest Population



# A cartoon of the talk.....





# Rinderpest - Serengeti





# Basic model structure..

Susceptibles

Allometric scaling of all birth and death rates

$$\frac{dS_i}{dt} = (b_i - d_i - \Delta_i(S_i + I_i))S_i - (\underbrace{\beta_{ii}I_i}_{\text{Within}} + \underbrace{\sum \beta_{ij}I_i}_{\text{Between}})S / (\sum_{j=1,n} N_n)^c$$

Infecteds

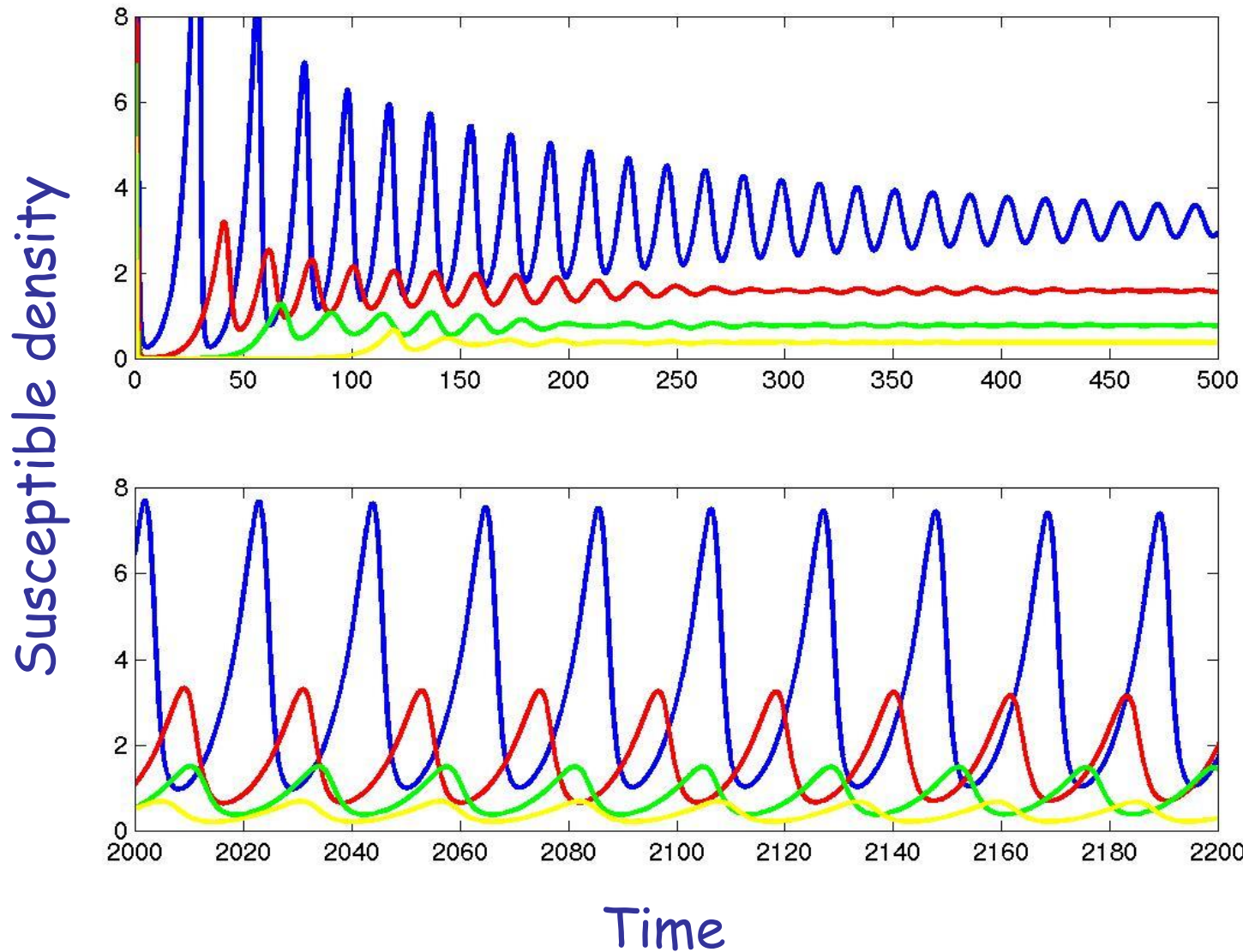
$$dI_i / dt = (\beta_{ii}I_i + \sum \beta_{ij}I_i)S / (\sum_{j=1,n} N_n)^c - d_i(1 + \alpha_i)I_i$$

Between species transmission

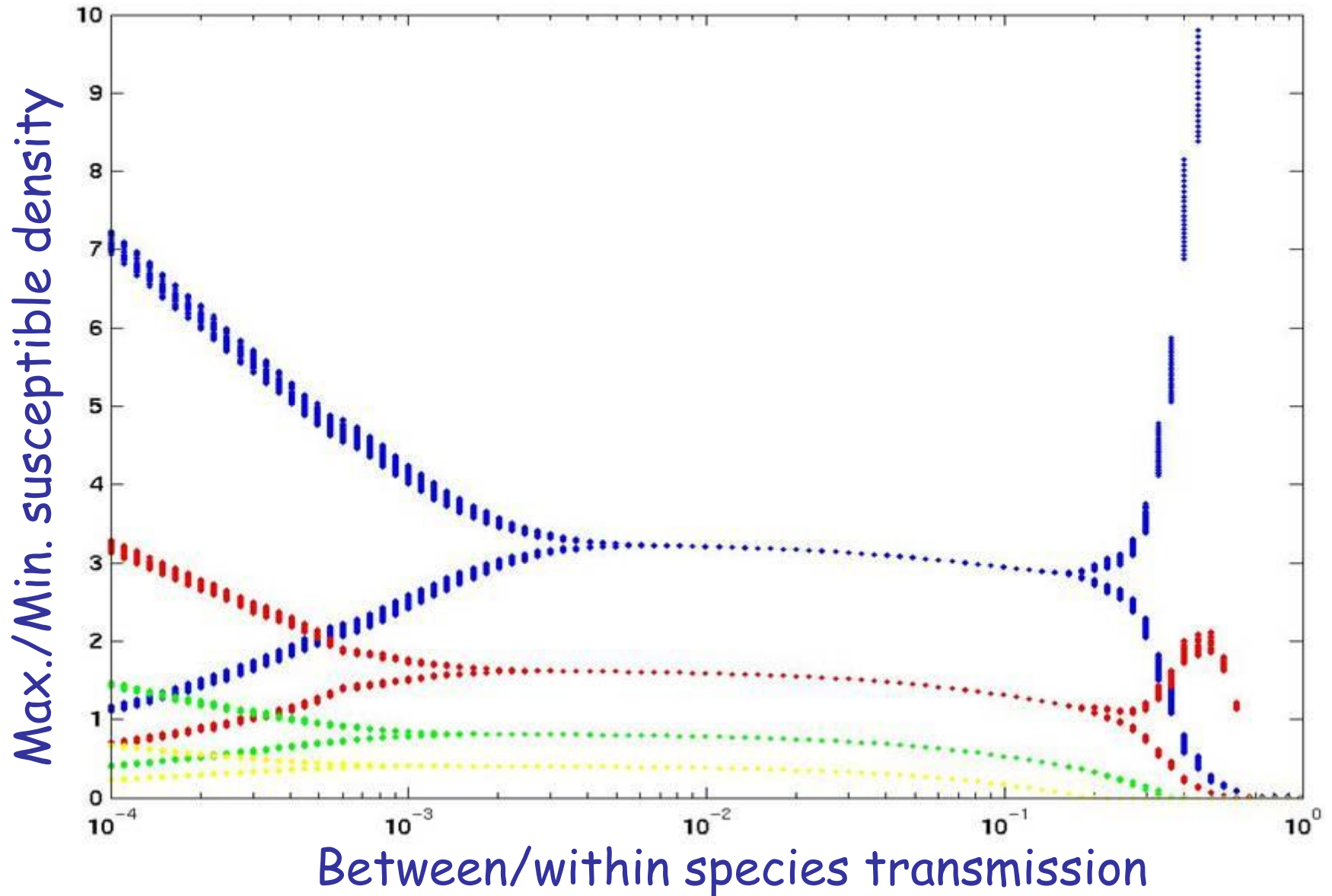
Scale virulence  
as a proportion  
of life expectancy

$$\beta_{ij} = c\sqrt{\beta_{ii}\beta_{jj}}$$

# Buffering: dynamics in DD case



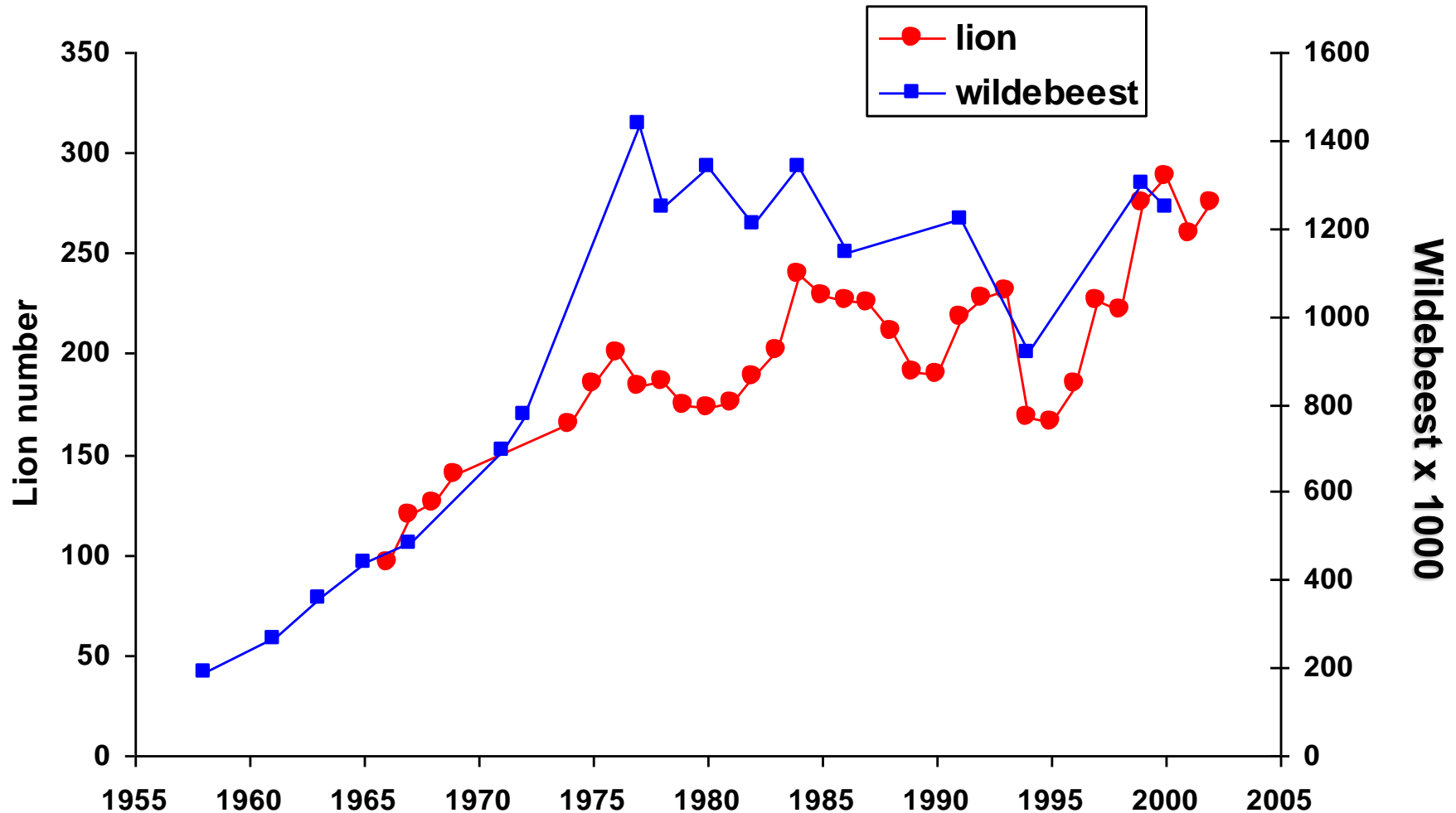
# Buffering: dynamics in DD case







# Serengeti woodland lion numbers



Lion data from C. Packer

Grass fires prevent regeneration below 2 m height



Repeated burning prevents regeneration and produces a distorted age structure of old trees



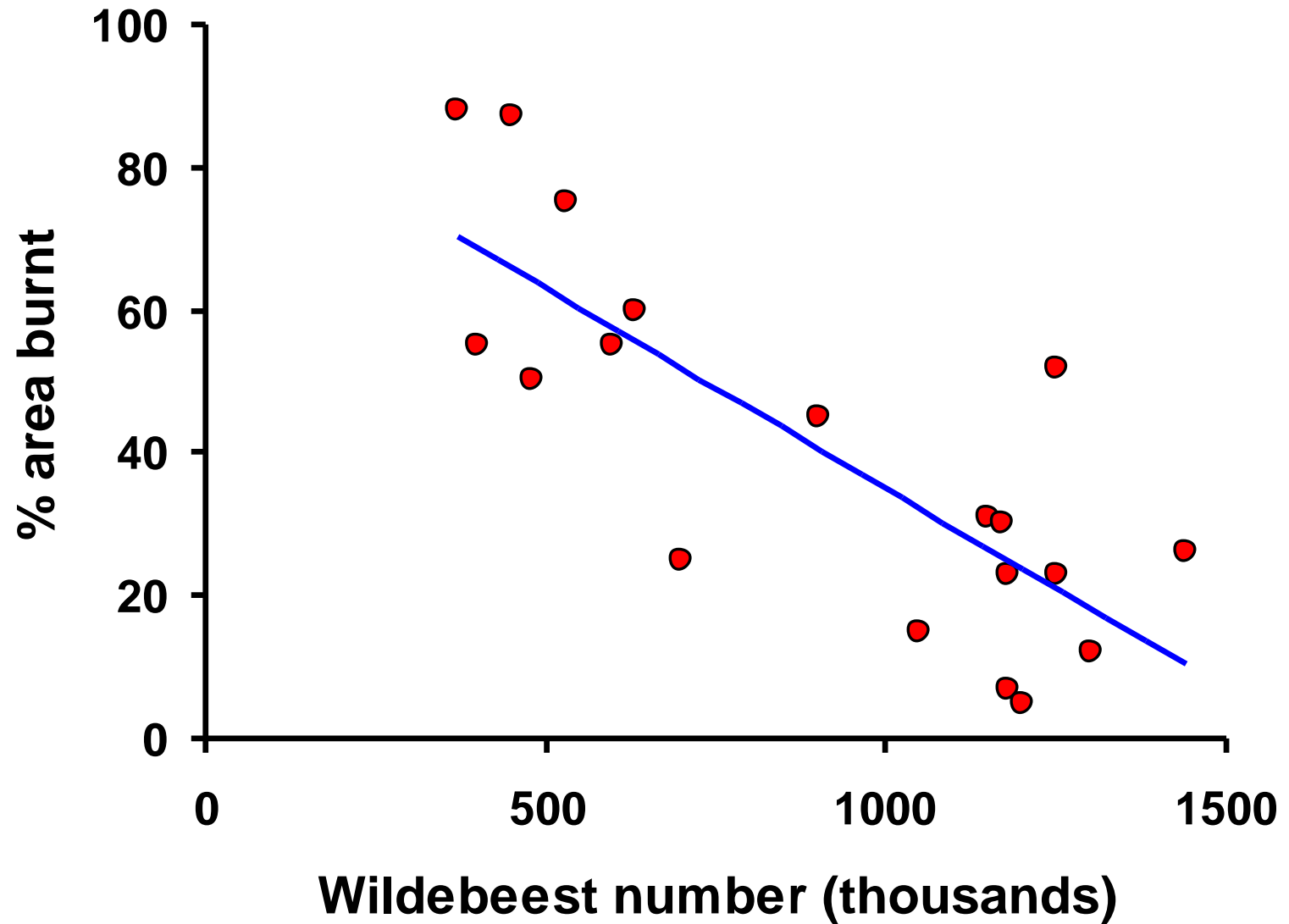




Wildebeest grazing reduces grass fuel and area burnt



**Increase in wildebeest causes decrease  
in burning**

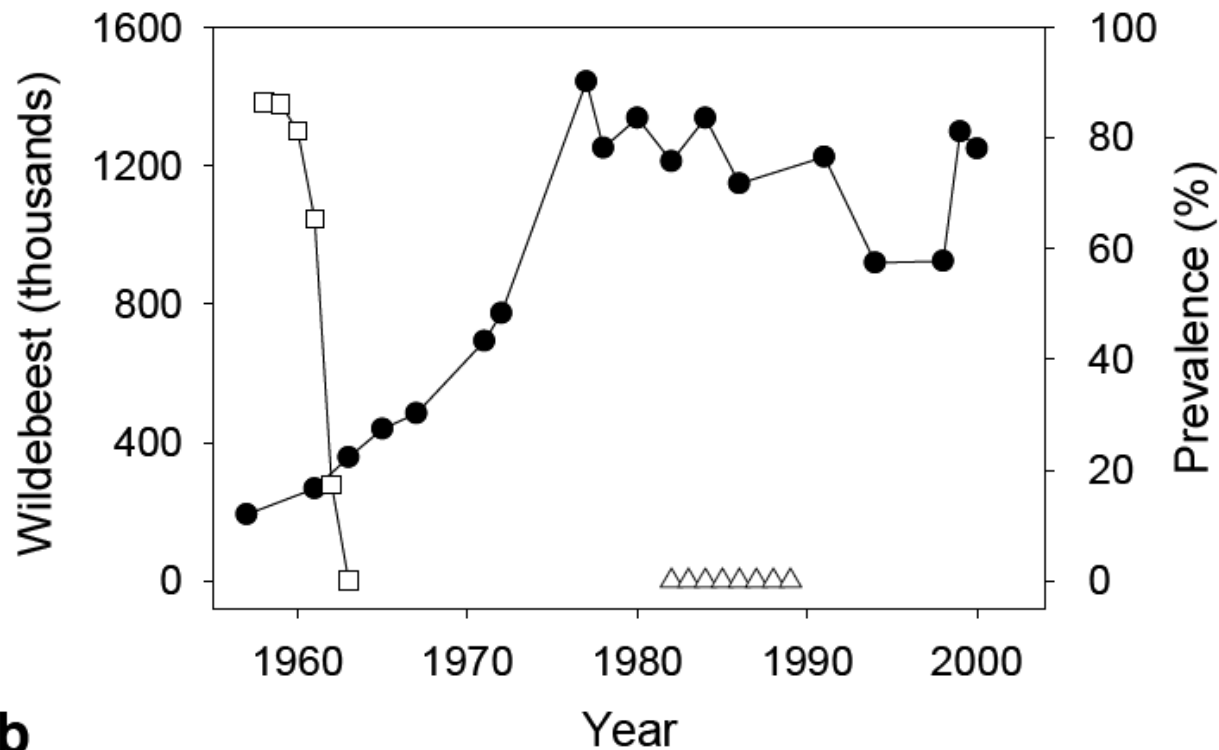


# Serengeti as Carbon sink...

- The 2.5 million wildebeest, zebra and gazelles remove at least 50% of the 100-200 g/m<sup>2</sup> of plant material each year.
- The poop and beetles return this to the soil
- Fire suppression allows woodland to recover, trees are carbon...
- How much C does this store 50?, 100?, 200? 500? Mg/km<sup>2</sup>/year??

# Rinderpest and wildebeest...

**a**



**b**

Plus – series of annual photographs of tree and grass cover since 1960's...



1980



1986



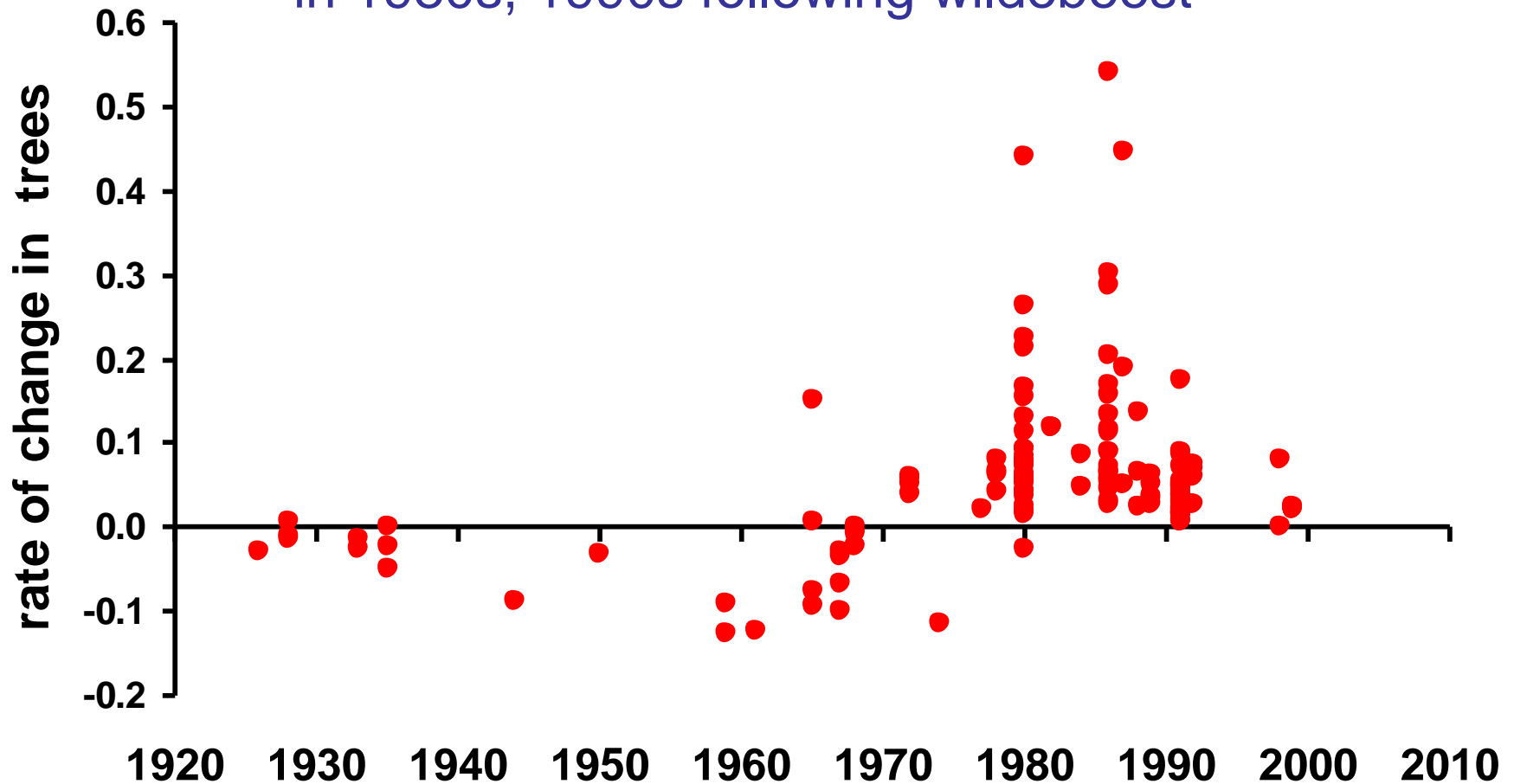
1991

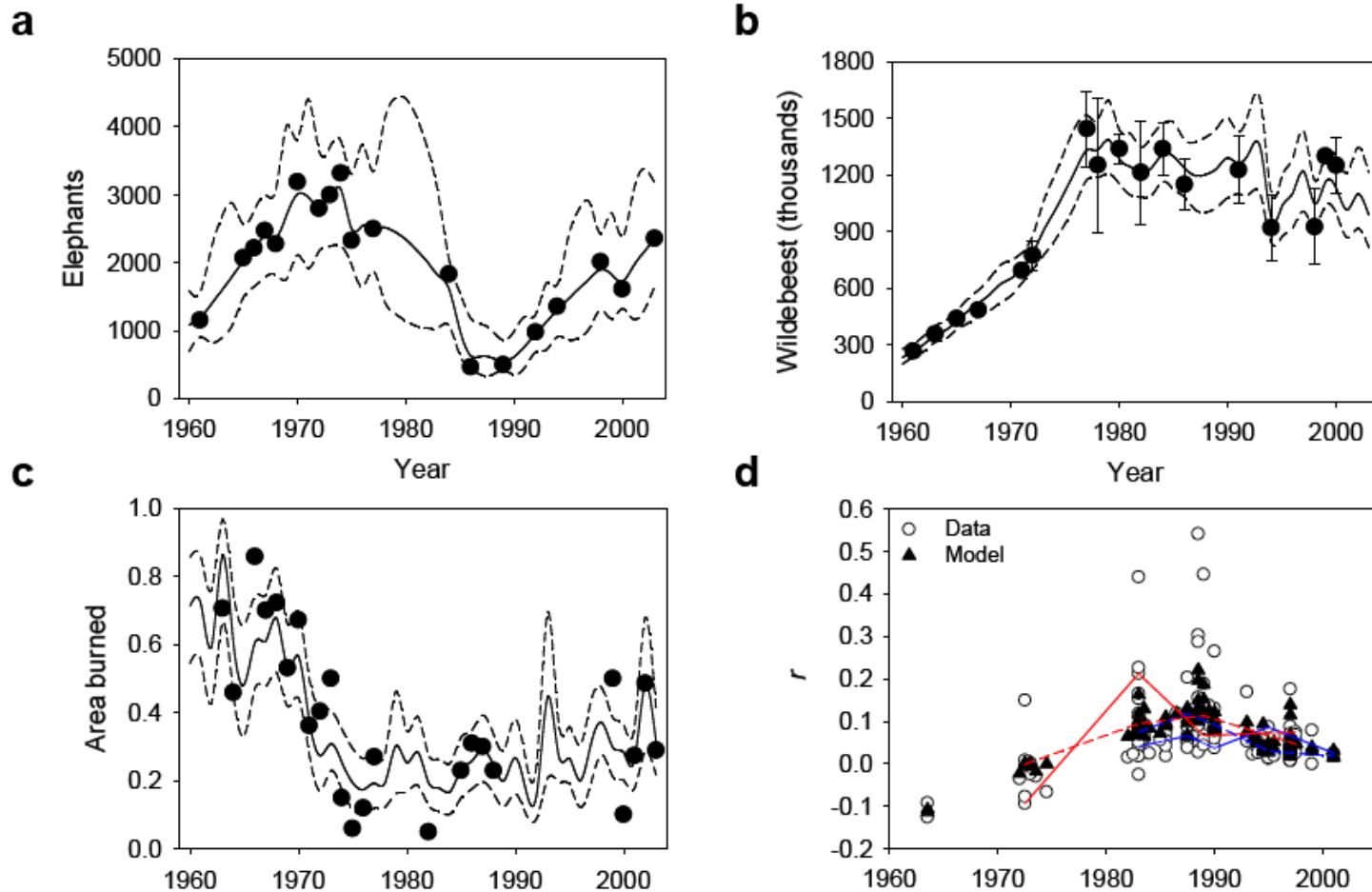




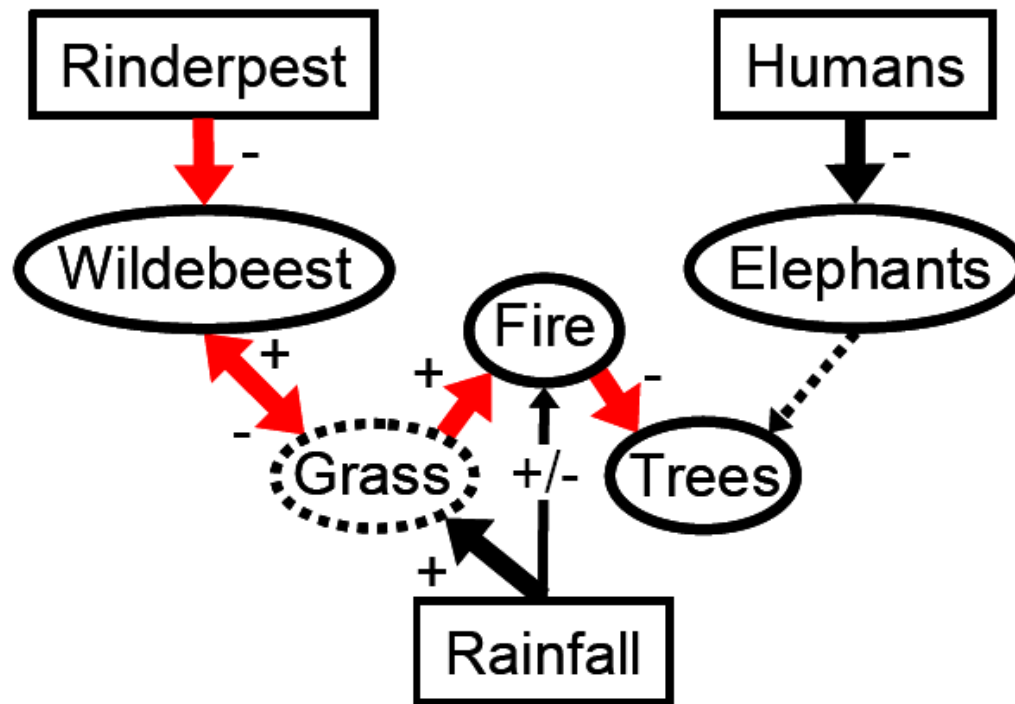
# SERENGETI TREE DENSITY

Instantaneous rate of change in tree density  
negative 1920s-1960s, then increases rapidly  
in 1980s, 1990s following wildebeest





**State-space model fits to the data for the best model.** **a**, Elephants, **b**, Wildebeest, and **c**, Proportion of SNP burned. Shown are observations ( $\bullet$ ), posterior means of estimated true values (solid line), and 95% credible intervals for the posterior distributions (shaded area). Standard errors for the observed values are shown for the wildebeest data. **d**, Annualized rates of tree cover change ( $r$ ), centred on the midpoints of each time span (e.g., a value of  $r$  based on photos taken in 1980 and 1990 is centred on 1985). Correlations among points (corresponding to photo sites) are not shown for legibility, except for two sites: (blue and red solid lines = data; dashed lines = model fit).



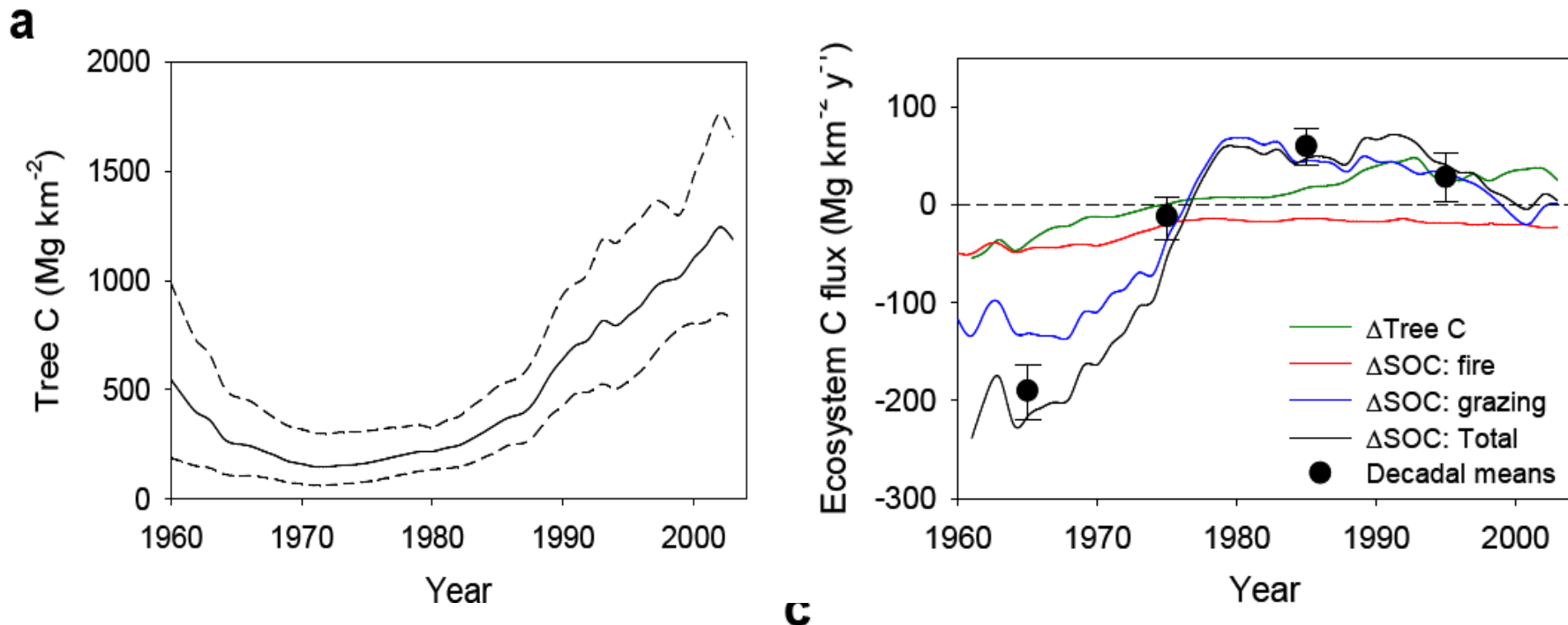
Inferred causal relationships driving tree dynamics in the Serengeti.

The dominant effects are shown with thick arrows.

Highlighted in red is a four-step pathway of causality linking rinderpest with tree population dynamics.

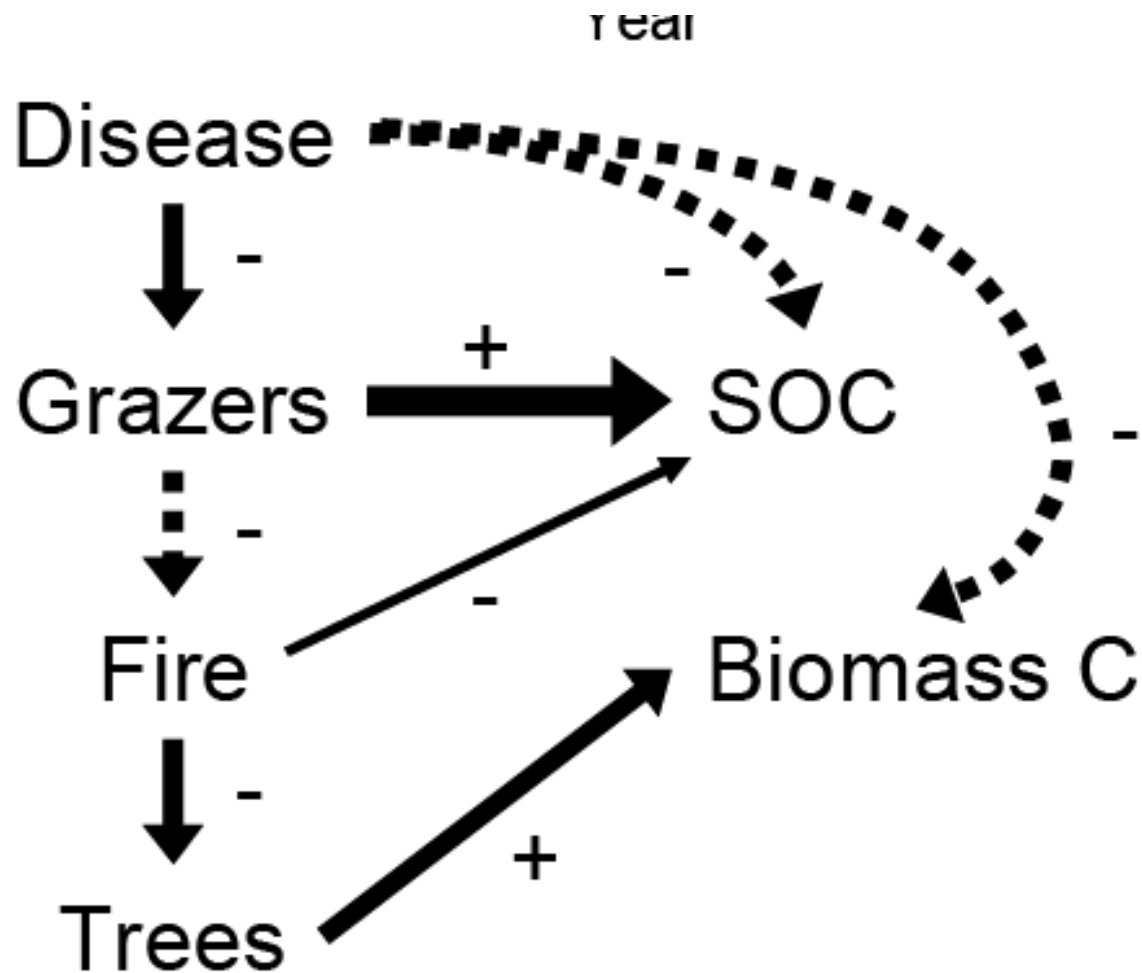
The grass compartment, as an unobserved variable, is shown in dotted outline.

# Carbon stored in Serengeti trees



**Simulated shifts in ecosystem C balance.** **a**, Simulated trajectory of woody biomass C in the Serengeti ecosystem between 1960-2003; **b**, Simulated changes (as 5-year moving averages) in ecosystem C balance (total, tree biomass C, and SOC changes driven by fire and grazing) and annualized decadal net changes in total ecosystem C balance (means  $\pm$  95 CIs); the temporary shift from net sink to source predicted by our simulation in 2000 was driven by drought and the resulting overgrazing.



**c**

Inferred causal pathways linking disease with ecosystem C flux as a result of a trophic cascade (solid line=direct effects and dashed line=indirect effects).  
(Holdo et al, in press)

# Carbon stored in Serengeti soils

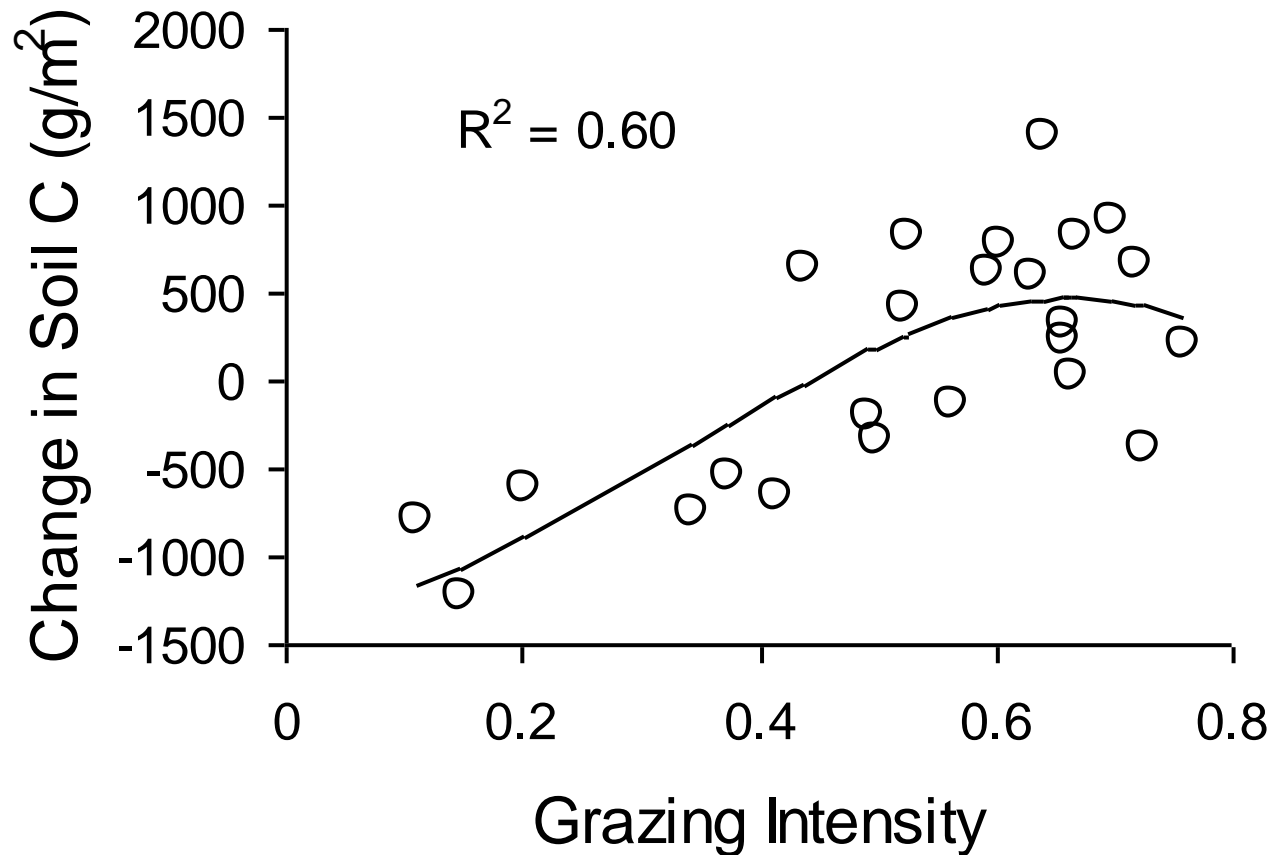


Fig. 1. Mean ( $\pm$ SE) difference in SOC estimated to a depth of 40 cm among paired fenced and unfenced plots across eight sites in Serengeti National Park as a function of the mean grazing intensity (proportion of production consumed) for each set of paired plots (Ritchie et al, in press).

# SOC in Serengeti Soil and Wood

- Our simulations of C fluxes suggest that the changes in wildebeest population density, fire prevalence, and tree cover that have occurred over the past half-century have had important effects on the stocks of both woody biomass and of soil C that determine the total C stocks in the Serengeti ecosystem (Fig. 3). At present, the Serengeti constitutes a net C sink, removing on the order of 40-70 Mg C km<sup>-2</sup> y<sup>-1</sup> from the atmosphere in woodland habitat (Fig. 3b). Across 25,000 km<sup>2</sup> of mostly protected woodland habitat across the entire ecosystem, this is equivalent to 10<sup>6</sup> Mg C y<sup>-1</sup> (Holdo et al, in press)
- **Expected greater methane production from higher herbivore densities was too low to cancel the potential CO<sub>2</sub> offset from increased grazing from wildlife conservation and a moderation of fire frequency, which in the Serengeti could offset the equivalent of 400-600 Mg.km<sup>-2</sup>.yr<sup>-1</sup> of CO<sub>2</sub>.**
- Mg – Megagrams – 10<sup>6</sup> – grams / square kilometer / year

# *Value of carbon stored*

- 200-400 Mg/km<sup>2</sup> is worth
- = \$2000-\$4000 / km<sup>2</sup> / year
- Serengeti NP + surrounding ecosystem =  
12,700 + 29,000 km<sup>2</sup> = 40,000km<sup>2</sup>
- Net annual value = \$80 to \$160 million!
- Need to set up deal with airlines to retrieve significant amount of this.



# Serengeti Multihost Pathogens and Ecosystem Consequences of Roads and Parasites

Based on Work in Collaboration with

*Tony Sinclair*, Simon Nduma,  
Craig Packer, Sarah Cleaveland,  
*Mark Ritchie*, *Han Olff*, Ray Hilborn,  
John Fryxell, Katie Hampson,  
Megan Craft, Peter Hawthorne,  
Ed Baskerville, Mercedes Pascual,  
Trevor Bedford, Grant Hopcraft,  
***Ben Bolker, Ricardo Holdo,***  
***Gerald Bigarube, Laura Hartstone***  
***Markus and Felix Borner***



## Walter Plowright

**Walter Plowright**, [CMG](#), [FRS](#)<sup>[1]</sup>, [FRCVS](#) (born 20 July 1923, [Holbeach](#), Lincolnshire – 19 February 2010 London<sup>[2]</sup>) was an English [veterinary scientist](#) who devoted his career to the [eradication](#) of the cattle plague [rinderpest](#). Dr Plowright received the 1999 [World Food Prize](#) for his development of tissue culture rinderpest vaccine (TCRV), the key element in the quest to eliminate rinderpest.<sup>[3]</sup> Rinderpest became the first animal disease to be eliminated worldwide



# Worries for the future..

**Pestes des petites ruminants, PdPRv**



**Disease of goats and gazelles**



Cross-immunity to Rinderpest (distemper) – increasingly significantly in Africa..





**Thank you!**



