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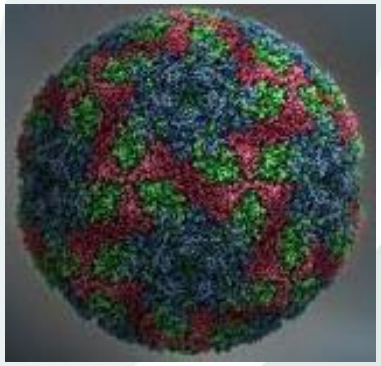
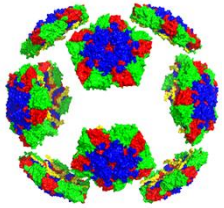


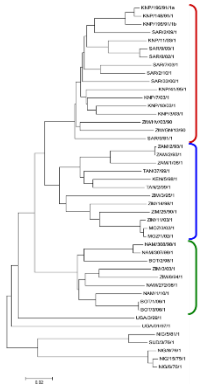
HOW ECOLOGY AND EPIDEMIOLOGY OF FMDV IN SUB-SAHARAN AFRICA GOVERNS CONTROL STRATEGIES

by Katherine Scott

Genetic relationship

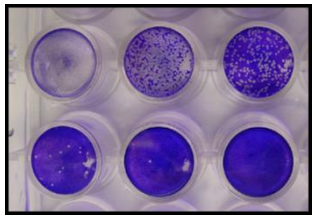


Stability
Virulence
Immune responses



Transmission:
Buffalo to buffalo
Wildlife/livestock interface

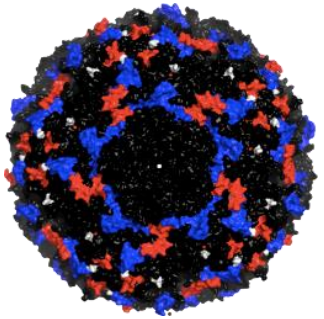
Risk models
Surveillance



Phenotype

Antigen matching

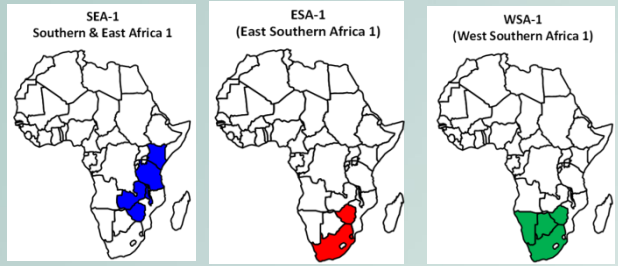
Fine epitopic structure

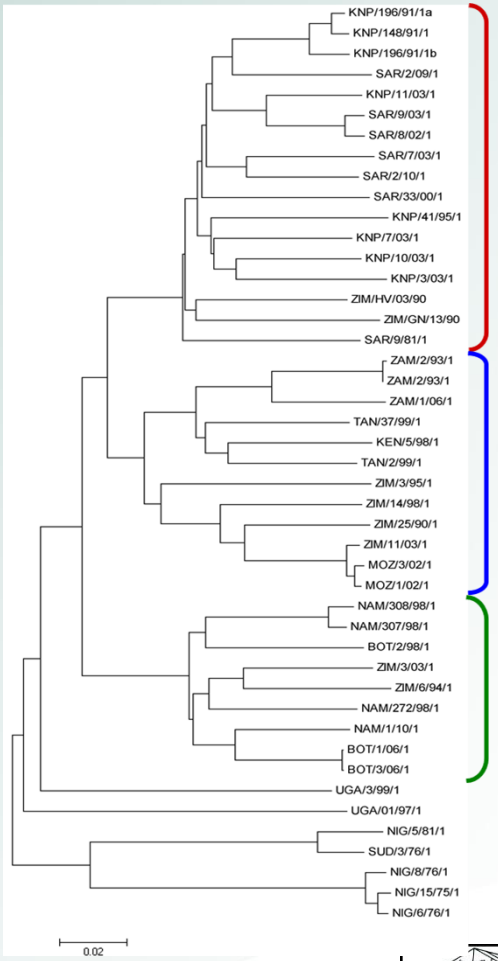


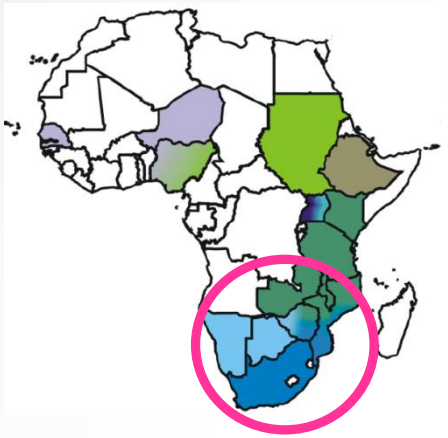
Vaccine strain selection & quality Control

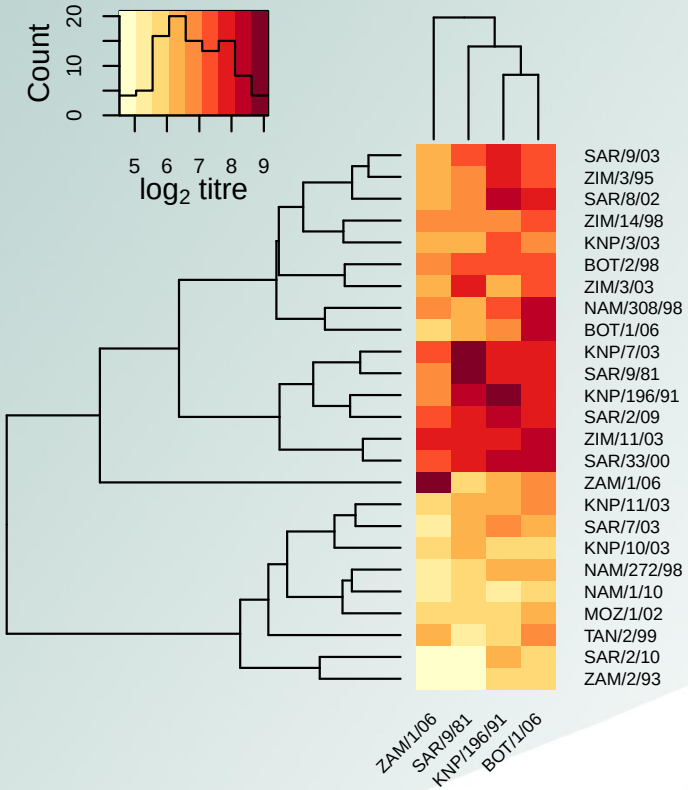
Sequence based prediction of the antigenic structure

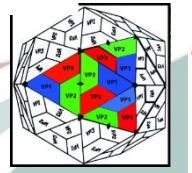
SAT1 Serotype

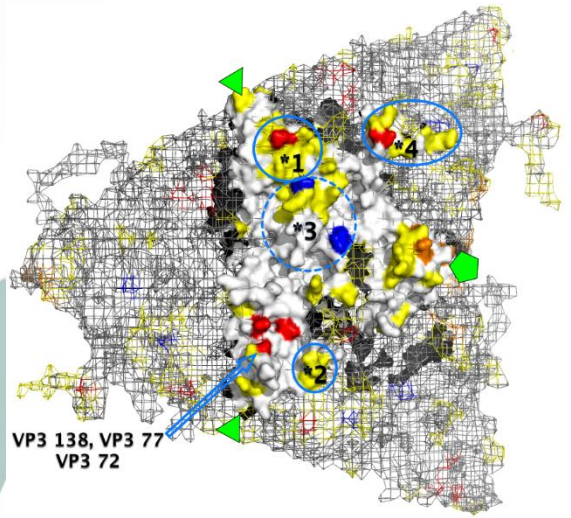






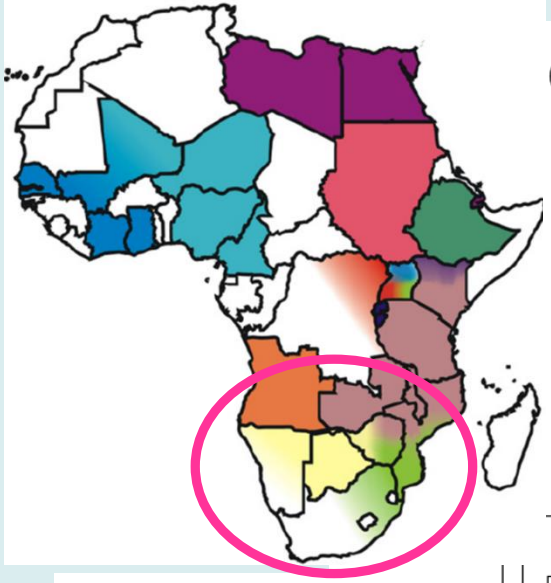


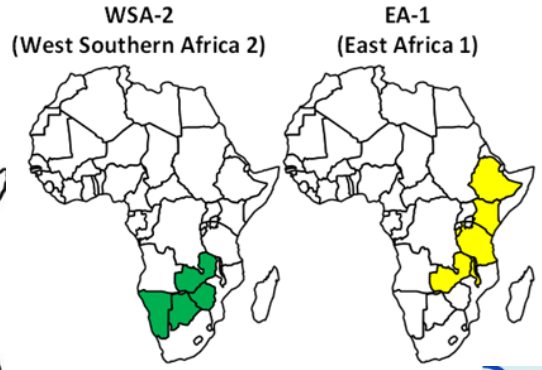


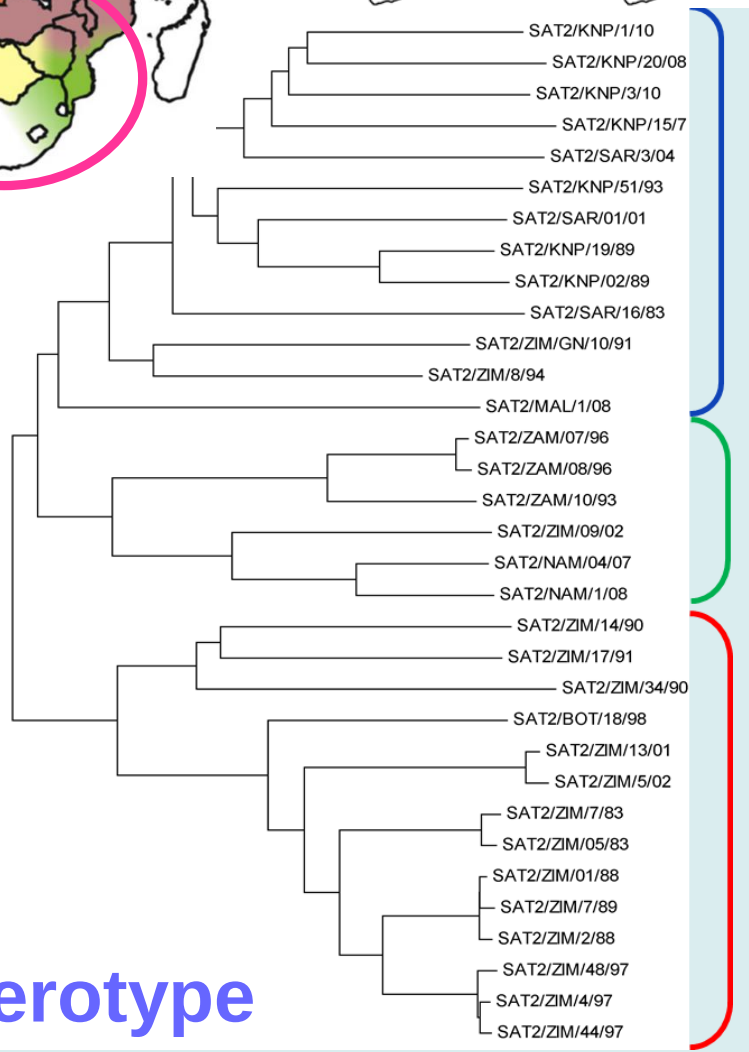


Reeve et al., 2016. **PLoSone.** 8, e61612

Virus	ZIm7/83	ZIM14/90	KNP19/89	SAR3/04 I	SAR3/04 2xV
KNP 1/10	*	*	*	*	*
KNP 20/08	*	*	*	*	*
KNP 3/10	*			*	
KNP 15/07	*		*		
SAR 3/04	*				
SAR 1/01	*	*	*	*	*
KNP 19/89	*				
MAL 1/03	*				
KNP11/07	*	*	*	*	*
MAL 1/08	*		*		*
MOZ 2/10	*	*	*		*
SAR 1/10	*		*		*
SAR 4/12	*	*	*	*	*
SAR 1/08					*
BOT 4/06	*	*	*	*	*
ZAM 10/93	*		*	*	*
ZAM 8/96	*		*	*	*
ZIM 8/94			*		
ZIM 9/02	*				*
NAM 1/08	*	*	*	*	*
NAM 1/07	*	*	*		*
ZIM 7/83			*		*
ZIM 4/97	*				*
ZIM 44/97					*
ZIM 48/97	*		*		*
BOT 18/98	*		*		*
ZIM 13/01	*				*
ZIM 14/90	*				

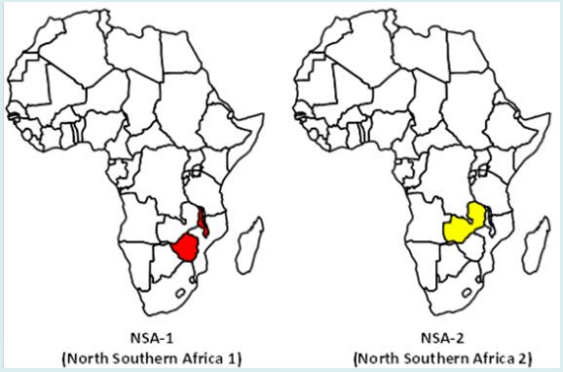


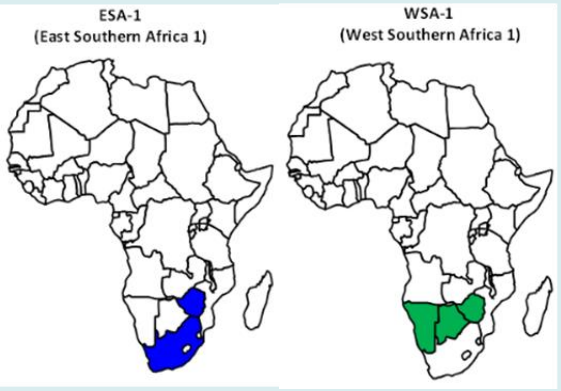


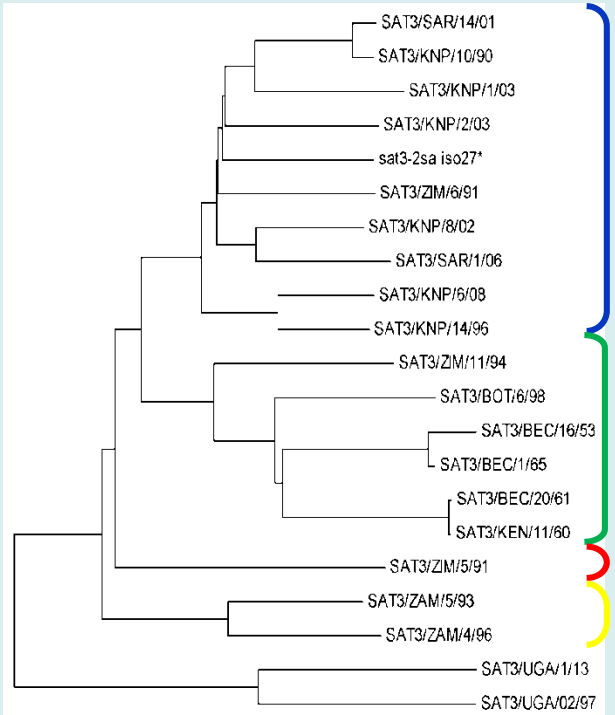


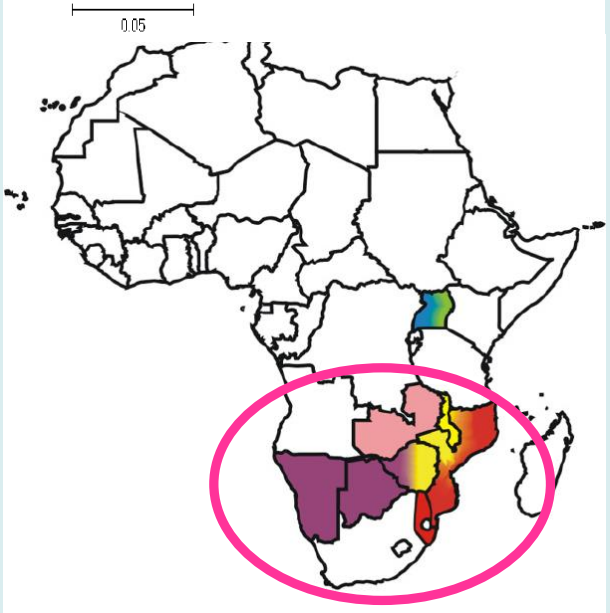
SAT2 Serotype

SAT3 Serotype



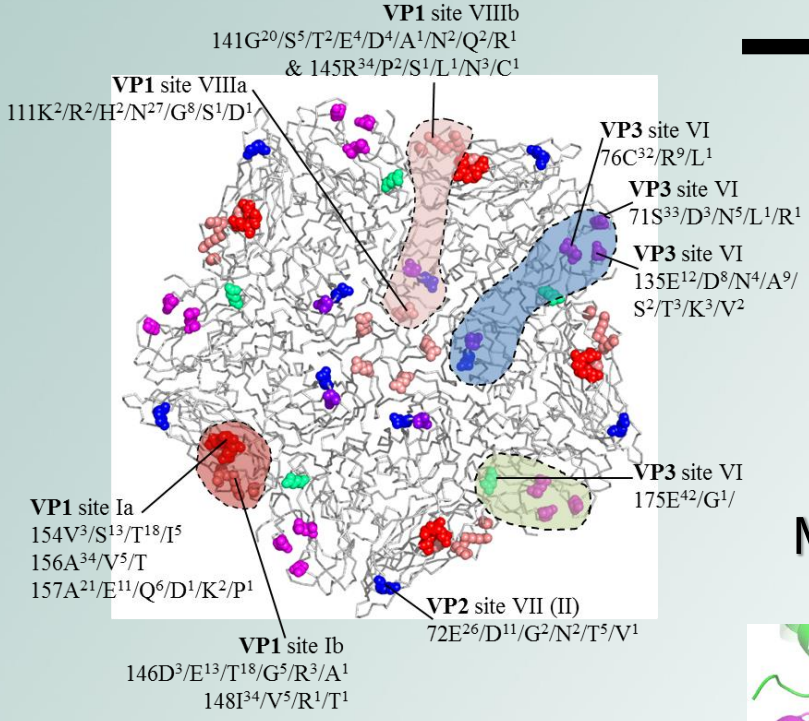


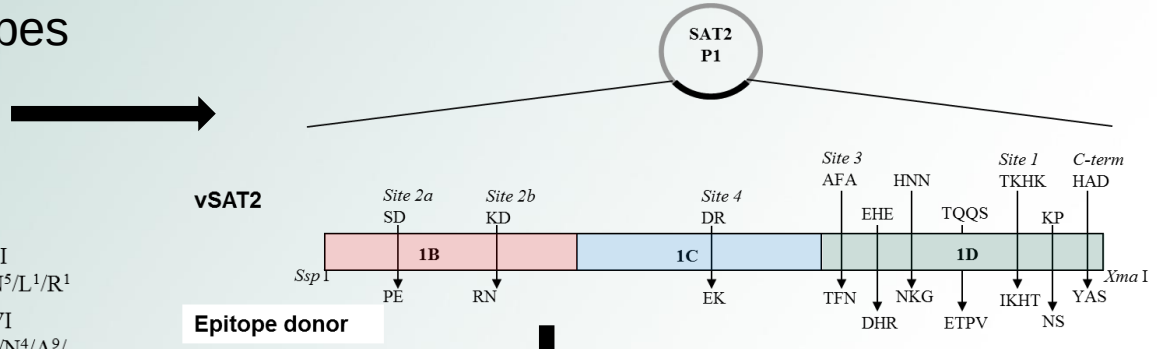




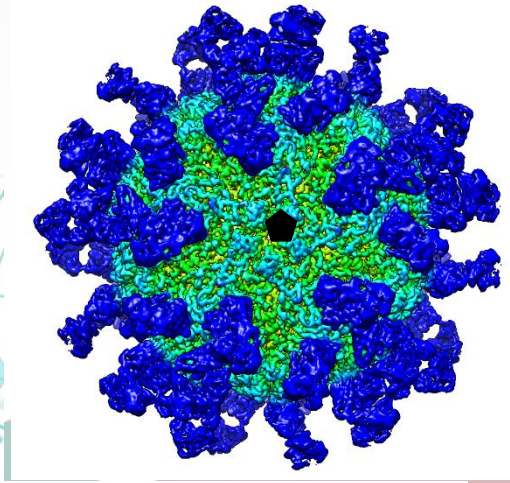
Antigenic structure of SAT viruses

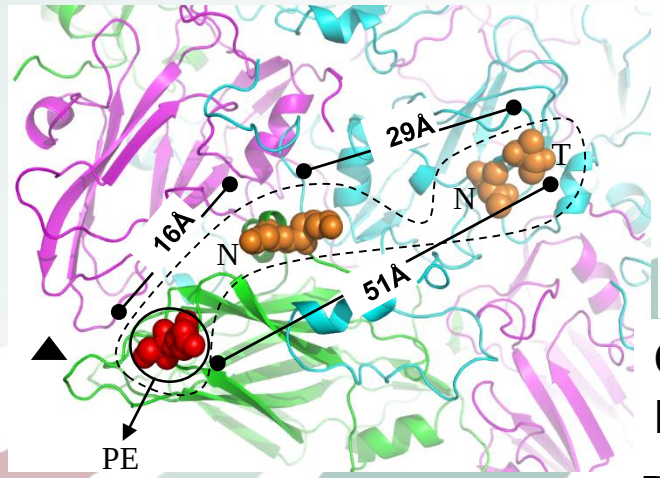
Discontinuous or multiple epitopes





Monoclonal Ab footprint





Courtesy of
Dr Kotecha, Oxford.

DA10 and GE11

Repetitive display of epitope
Sequence-based prediction

Opperman et al., 2014.

Inherent Stability

Serotype	topotype	virus isolate	1x PBS	6.1	6.7	7.2	7.6	8.2	9.1
SAT1	ESA	KNP/196/91	49	-13	-9	-4	-5	-2	4
	ESA	SAR/33/00	46	ds*	-11	-6	-4	-1	-2
	ESA	SAR/9/81	47	-14	-8	-5	-2	-1	-2
	WSA	BOT/1/06	51	-9	-8	-4	-4	-2	-3
	SEA	ZAM/1/06	52	-14	-9	-5	-4	-2	-3
	SEA	MOZ/1/02	46	-13	-6	-2	-1	2	-1
	SEA	TAN/2/99	43	ds*	-7	-6	-3	1	0
SAT2	ESA	MAL/1/08	56	-17	-8	-7	-5	-3	-8
	ESA	SAR/3/04	56	-12	-8	-7	-5	-3	-6
	ESA	ZIM/8/94	56	-18	-12	-9	-6	-3	-5
	WSA-1	ZIM/14/90	56	ds*	-13	-12	-9	-4	-12
	WSA-1	ZIM/4/97	52	ds*	-13	-10	-7	-4	-9
	WSA-1	ZIM/13/01	55	ds*	-12	-9	-7	-4	ds*
	WSA-1	BOT/18/98	54	ds*	-11	-8	-5	-2	-12
	WSA-1	ZIM/7/83	54	-17	-13	-9	-8	-6	-10
SAT3	ESA	KNP/10/90	48	ds*	-10	-5	0	4	5
	ESA	SAR/14/01	52	-20	-12	-5	-1	3	2
	ESA	SAR/1/06	50	-14	-13	-7	-3	1	0
	ESA	KNP/14/96	47	ds*	-12	-7	-3	2	1
	WSA	BOT/6/98	48	-16	-9	-5	-1	3	3
A	control	A24 control	58	-20	-15	-8	-8	-6	-9

- At pH 6.1: SAT1 viruses stable (9-14 °C) compared acid labile SAT2 (12-18 °C) & SAT3 (14-20 °C). Similarly pH 6.7-7.2
- SAT3 viruses most pH stable compared to SAT1 & SAT2 viruses at pH 7.6-9.1.
- Overall SAT2 viruses were the most pH unstable pH range 6.1-9.1.
- SAT1 MOZ/1/02 virus most pH stable pH 6.7-9.1.
- SAT2 WSA-1 topotype pH unstable pH 9.1 all other SAT viruses

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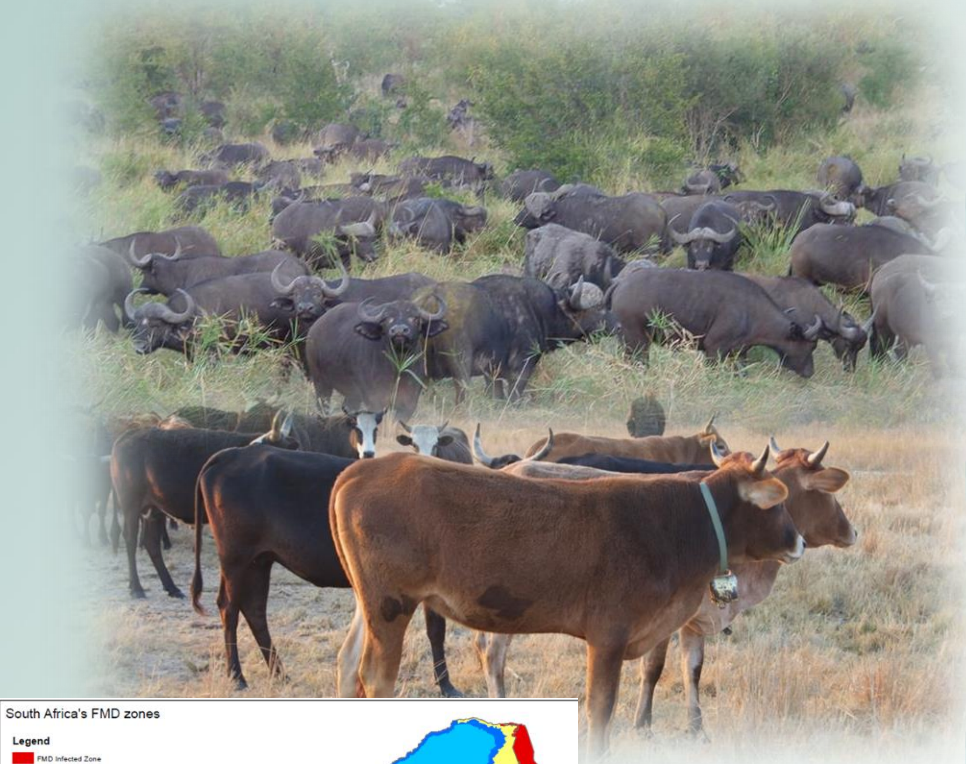
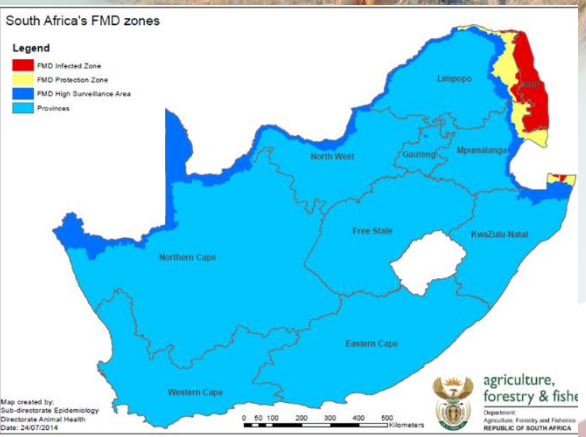
Serotype	topotype	virus isolate	NaCl 1M	KCl 1M	5% Glycine	30% sucrose	1xPBS	control
SAT1	ESA	KNP/196/91	6	1	-4	-3	49	46
	ESA	SAR/33/00	6	1	-9	-4	46	44
	ESA	SAR/9/81	5	0	-5	-3	47	46
	WSA	BOT/1/06	2	-3	-6	-2	51	51
	SEA	ZAM/1/06	5	0	-6	-5	52	51
	SEA	MOZ/1/02	4	3	-3	-3	46	46
	SEA	TAN/2/99	9	5	-6	-4	43	43
SAT2	ESA	MAL/1/08	3	-2	-15	-6	56	54
	ESA	SAR/3/04	2	0	-7	1	56	54
	ESA	ZIM/8/94	3	0	-11	-1	56	54
	WSA-1	ZIM/14/90	6	2	-14	-7	52	50
	WSA-1	ZIM/4/97	3	-1	-22	-9	56	52
	WSA-1	ZIM/13/01	3	0	-10	-1	55	52
	WSA-1	BOT/18/98	4	-2	-15	-5	54	52
	WSA-1	ZIM/7/83	2	-1	-1	-7	54	48
SAT3	ESA	KNP/10/90	-1	0	-6	-8	54	51
	ESA	SAR/14/01	1	1	-6	-5	58	53
	ESA	SAR/1/06	0	1	-4	-5	54	50
	ESA	KNP/14/96	3	2	-9	-10	55	51
	WSA	BOT/6/98	2	2	-6	-9	54	49
A	control	A24 control	2	0	-6	0	58	55

- **Thermostability**: SAT2 & SAT3 viruses range thermostability 48-54 °C.
- SAT1 viruses wider range thermostability (43-51 °C) many unstable at 43-46 °C.
- thermostable A-serotype A24 55 °C with some SAT2 and SAT3 similar.
- 12 °C difference between the most unstable SAT1/TAN/2/99.
- Confirms for the first time that more stable SAT field viruses are present in the Southern Africa region,
- **Ionic buffers capsid stability**: SAT1 (2-9 °C) and SAT2 (2-6 °C) viruses increased stability addition of 1 M NaCl. SAT3 viruses, no improved stabilisation - 1 M or 0.5 M NaCl buffers
- Divalent salts were poor stability
- Some buffers showed differing results dependent on the virus tested, highlighting the need to test SAT viruses with different solutions to establish the most stabilising option for storage.

Interaction between buffalo, FMDV and cattle

The epidemiology of FMD in Africa is influenced by two different patterns





African Buffalo herd

Endemic cycle

Persistently infected with SAT viruses

Buffalo calves

Escape

Infection of calves 6-18 months of age

Other cloven-hooved animals

Epidemic cycle

Livestock

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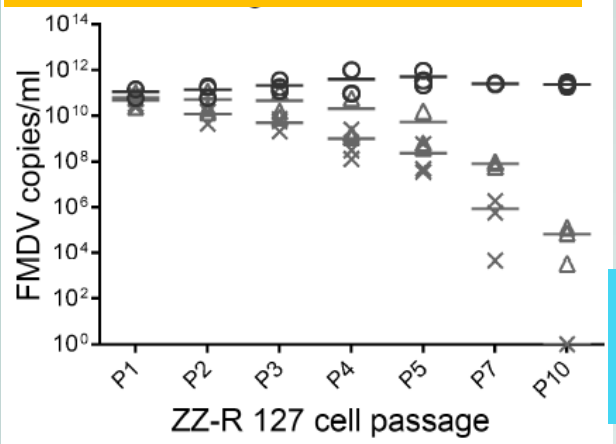
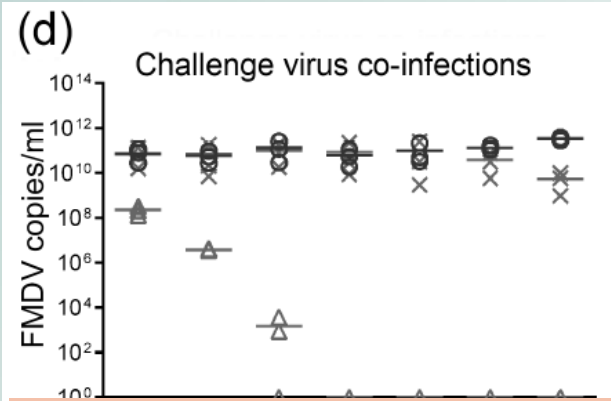
Cell culture co-infections

SAT-1 (MOI=0.5) outcompeted SAT-2 & SAT-3 (MOI=2)

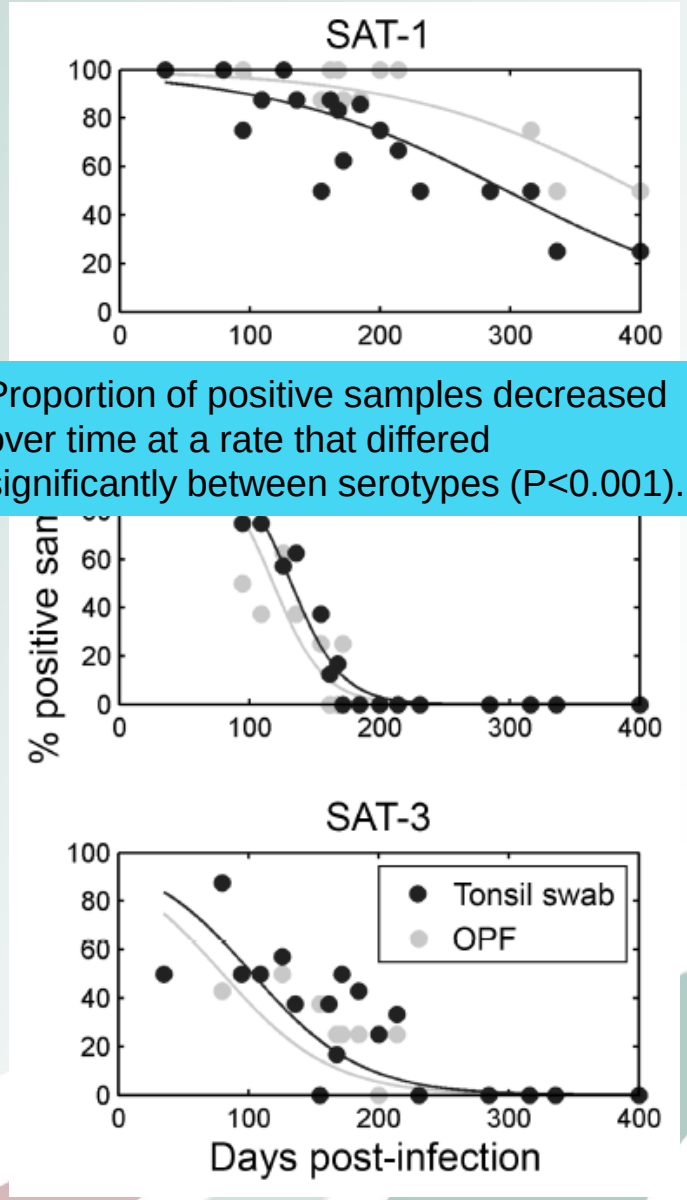




SAT-1 (MOI=0.5) & SAT-2 (MOI=2) outcompeted SAT-3 (MOI=2).

○ SAT-1 × SAT-2 △ SAT-3

Buffalo infections



Proportion of positive samples decreased over time at a rate that differed significantly between serotypes (P<0.001).

Maree et al., 2016. Journal of Virology

Buffalo to cattle transmission not observed

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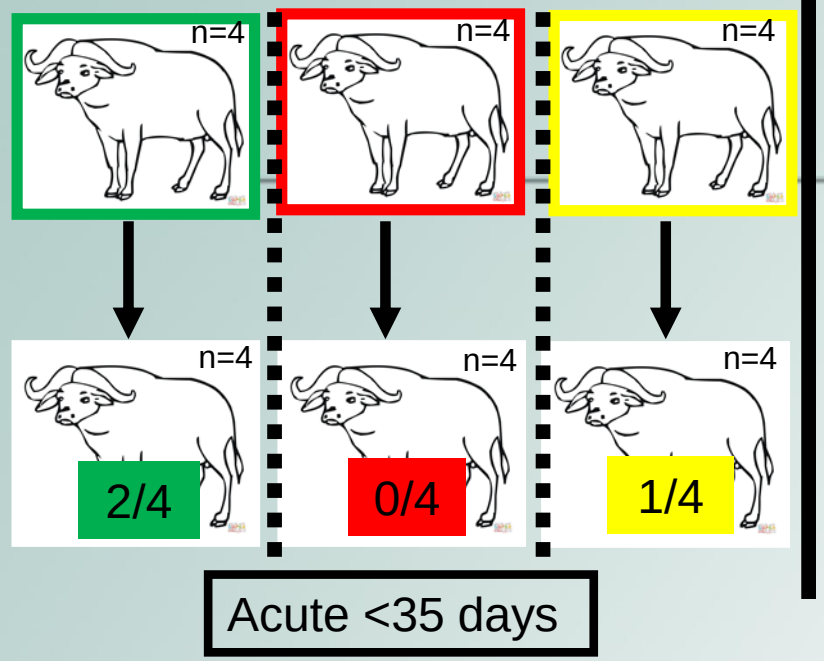

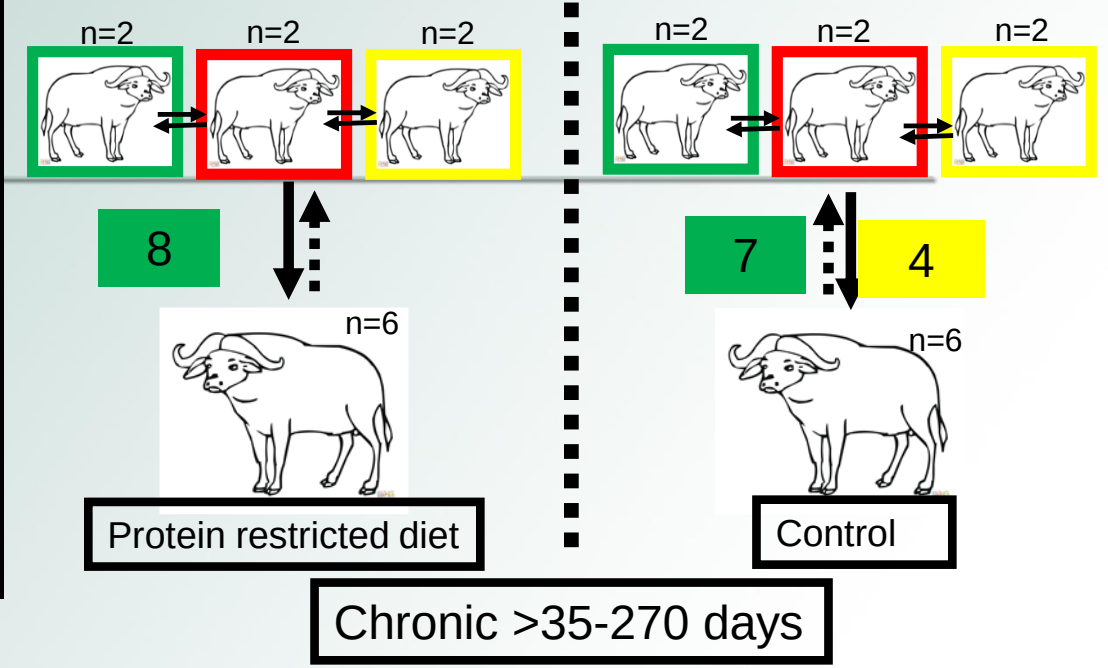

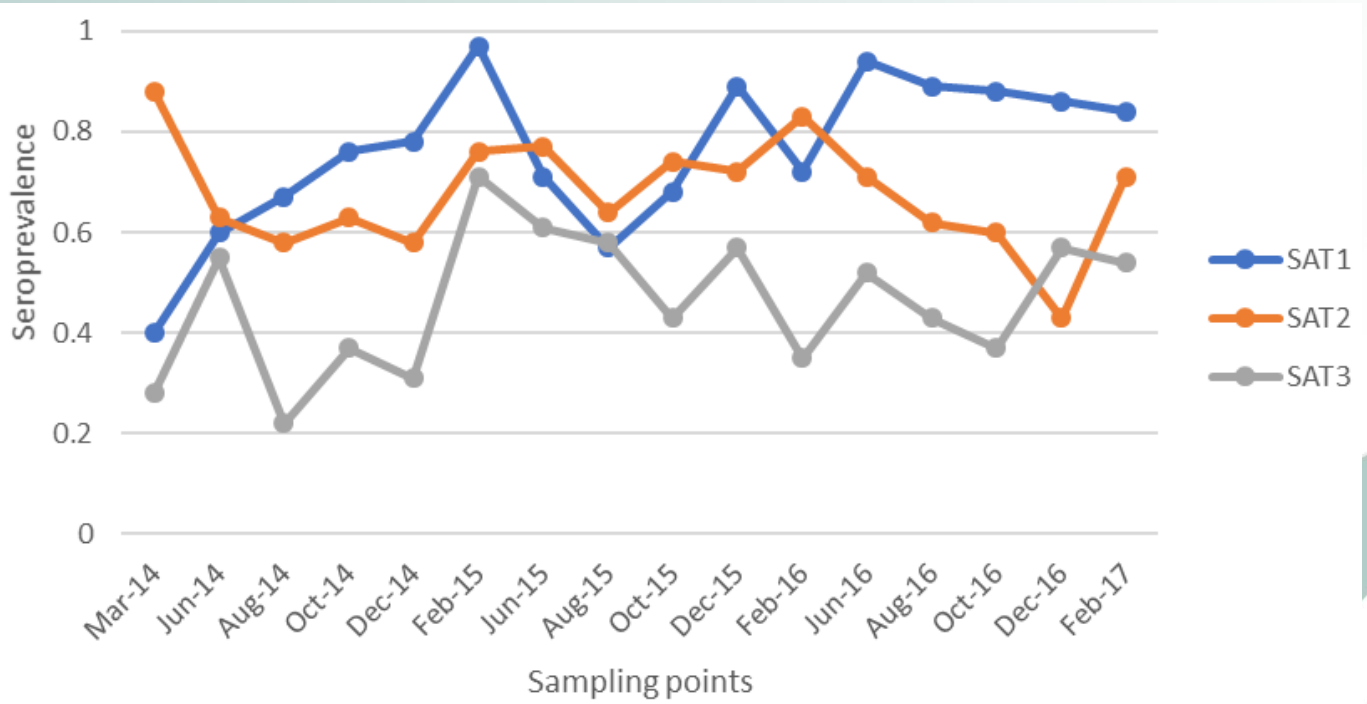

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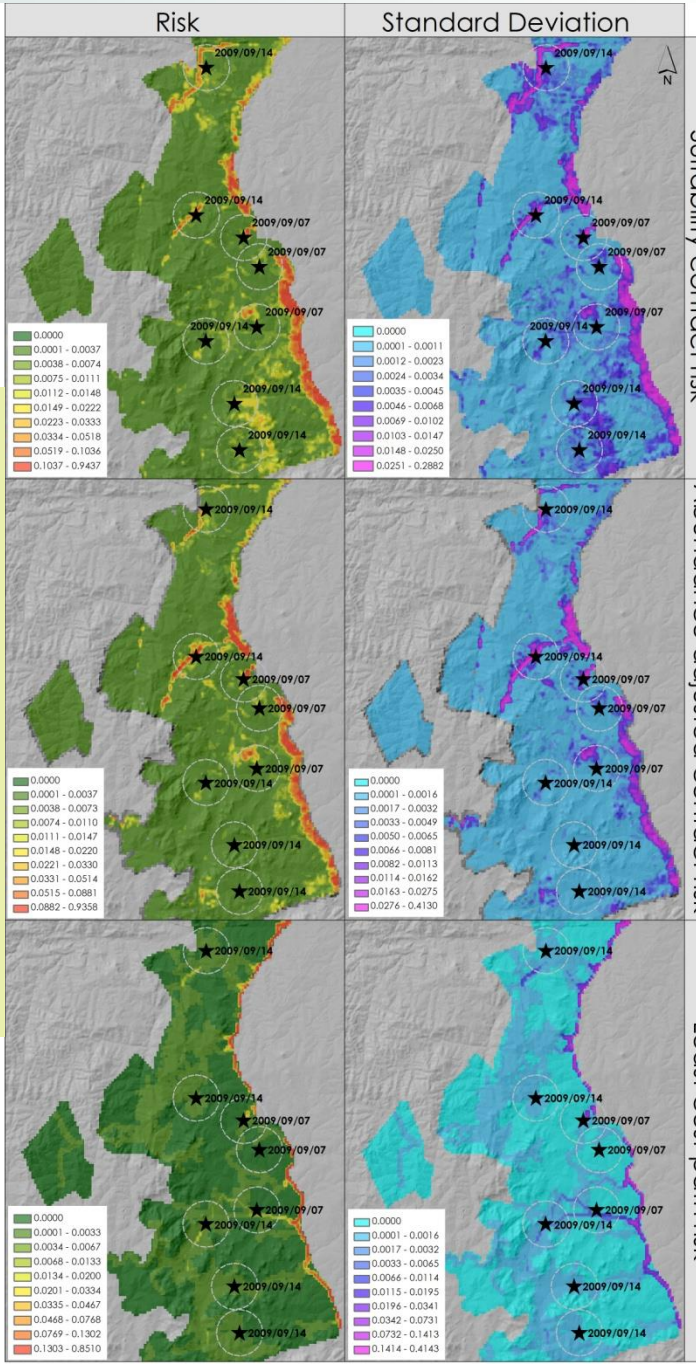
Contact risk modelling

Mhala 2001	Vhembe 2003	Mopani 2004	Sibasa 2006	Nsikazi 2009
SAT-2	SAT-2	SAT-2	SAT-3	SAT-1
Warm wet season	Cool dry season	Cool dry season	Cool dry season	Warm wet season
★ IP with case	★ IP with case	★ IP with case	★ IP with case	★ IP with case
IP 2.5km buffer	IP 2.5km buffer	IP 2.5km buffer	IP 2.5km buffer	IP 2.5km buffer
Cattle exclusion area	Cattle exclusion area	Cattle exclusion area	Cattle exclusion area	Cattle exclusion area

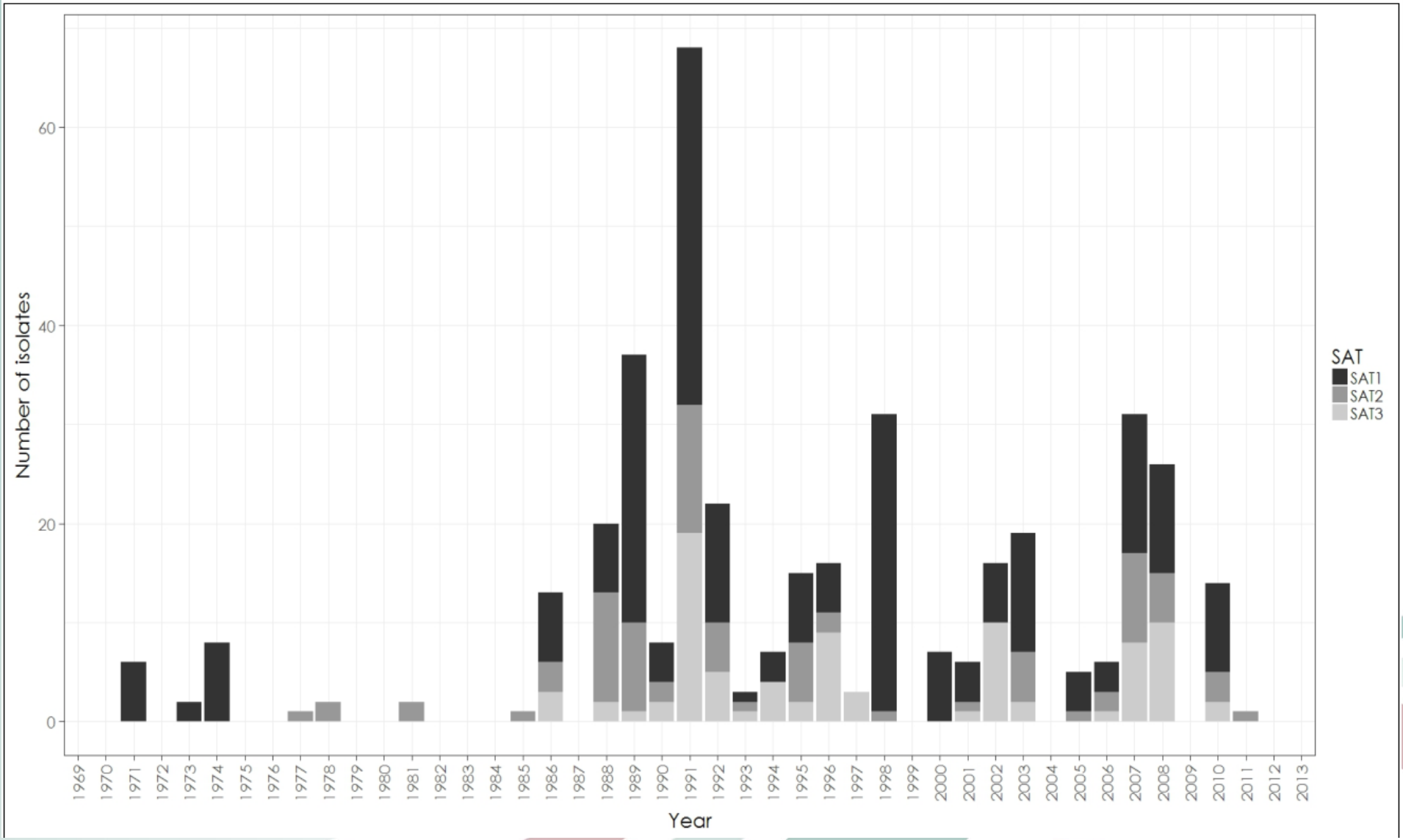
- Cattle suitability
  - Adjust for abundance (census data)
  - NB assumption: density~suitability
- Stray buffalo suitability
  - No abundance adjustment necessary
  - (Already incorporates some fence permeability)
- Least cost path
  - More explicitly incorporate the fence

Seasonal	Seasonal	Se		
-SCR: p<0.001	-SCR: p<0.001	-SCR: p<0.001	-SCR: p>0.1	-SCR: p<0.001
-ACR: p<0.001	-ACR: p<0.001	-ACR: p<0.001	-ACR: p>0.1	-ACR: p<0.001
-LCP$^{0.95}$: p<0.05	-LCP$^{0.95}$: p>0.1	-LCP$^{0.95}$: p<0.001	-LCP$^{0.95}$: p>0.1	-LCP$^{0.95}$: p>0.1
All year	**All year**	**All year**	**All year**	**All year**
-SCR: p<0.001	-SCR: p<0.001	-SCR: p<0.001	-SCR: p>0.1	-SCR: p<0.001
-ACR: p<0.001	-ACR: p<0.001	-ACR: p<0.001	-ACR: p>0.1	-ACR: p<0.001
-LCP$^{0.95}$: p>0.1	-LCP$^{0.95}$: p>0.1	-LCP$^{0.95}$: p<0.001	-LCP$^{0.95}$: p>0.1	-LCP$^{0.95}$: p<0.001

Kilometers 0 4.5 9 18 | Kilometers 0 3.25 6.5 13 | Kilometers 0 4.5 9 18 | Kilometers 0 3.25 6.5 13 | Kilometers 0 4.75 9.5 19



FMDV isolated from Game (KNP & surrounds)



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Maclaughlin Rathogwa
Lorens Maake
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TAD Diagnostic team