Outbreak response forecasting for vector borne diseases: *Theileria orientalis* (Ikeda) in NZ cattle.

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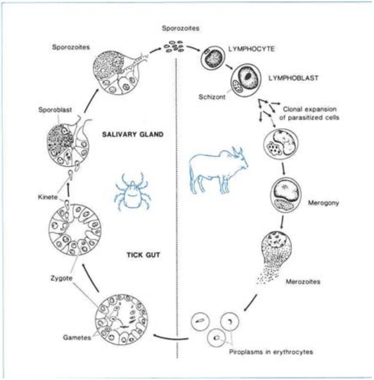
Theileria orientalis Ikeda

NZ Ministry for Primary Industries contract, Massey EpiCentre

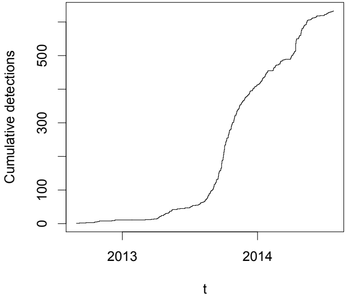
- Protozoal vector borne disease
  - Host: Cattle
  - Vector: Tick *H. longicornis*

- Endemic, but...
- August 2012 new virulent subspecies Ikeda

- Case morbidity $< 35\%$
- Mortality $\approx 1\%$
- Cost NZ$25k per farm



Theileria in NZ cattle



Epidemic at 1st Aug 2014

- 655 Case detections
- 136837 Farm locations
- Dairy/non-dairy
- NAIT cattle movement network frequencies

Databases: AgriBase, FarmsOnLine, NAIT

Theileria in NZ cattle

...video...

Theileria orientalis Ikeda

Mechanisms of spread

How does theileriosis spread?

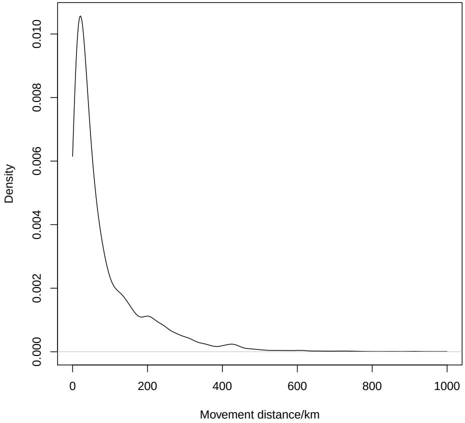
- Ticks don't walk very far
- Wildlife alternative hosts?
  - *Haemaphysalis* is a 3-host tick
  - "Leapfrog effect"? $\Longrightarrow$ proximity of farms important

- Animal movements farm-farm

- Prior: 2-months from infection to detection

National Animal Identification and Tracing (NAIT)

- Mandatory tracing of cattle and deer
- Began 2012
- 517328 recorded movements
- 0.0003% connectivity
- Represented as sparse matrix



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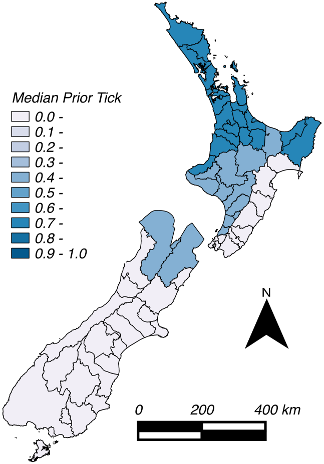
Tick habitat



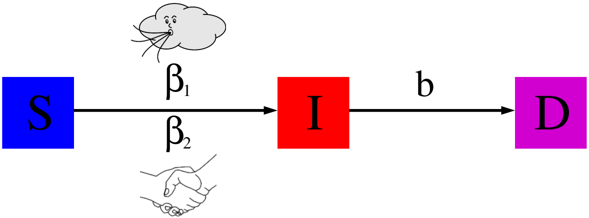
- Samples tested from BVD surveillance
- All *T. orientalis* spp.
- Aggregated at TLA level
- Prior risk: Alan Heath

Theileria in NZ cattle
Questions

- What are the main determinants of transmission?
  - Environmental (spatial) spread
  - Spread via NAIT network
  - Importance of tick presence
- Where might any undetected infections be?
- How fast will the epidemic spread?

SID models & population heterogeneity

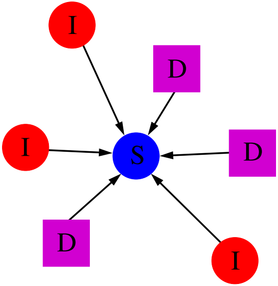
1. Individual herds infect each other
   - Spatial rate β_1
   - NAIT network β_2
2. Once infected, herds are infectious forever
   - Detected at rate b



$$\beta_1 = ?, \beta_2 = ?, b = ?$$

Infection process

- At any time t, susceptible j has infectious pressure exerted on it by
  - all infected or notified farms $i \in \mathcal{I}(t), \mathcal{D}(t)$
  - "Background" (not explicitly modelled)



In a small interval $\Delta t = (t, t+\delta]$:

$$P(j \text{ infected}) \approx \lambda_j(t) \cdot \Delta t$$

$$\lambda_j(t) = \epsilon + \sum_{i \in \mathcal{I}(t)} \lambda_{ij}(t) + \sum_{i \in \mathcal{N}(t)} \lambda^{\star}_{ij}$$

Transmission model

$S \rightarrow I$ model

$$\lambda_{ij}(t) = s(t;\boldsymbol{\alpha},\nu,p_{k(j)})\zeta^{\kappa_j}\left[\beta_1 K(i,j;\delta)+\beta_2 c_{ij}\right], \quad i \in \mathcal{I}, j \in \mathcal{S}$$
$$\lambda^{\star}_{ij}(t) = \beta_{ij}(t), \quad i \in \mathcal{N}, j \in \mathcal{S}$$

$$K(i,j;\delta) = \frac{\delta}{(\delta^2 + ||x_i - x_j||^2)^{1.2}}$$

$$D - I \sim Gamma(4, b)$$

ζ = effect of dairy cf. beef

$s(t;\boldsymbol{\alpha},\nu,p_{k(j)})$ = tick effect

$p_{k(j)}$ = tick occurence in TLA k

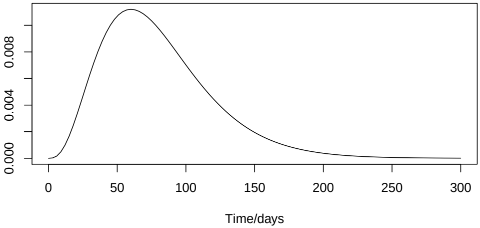
Unknowns
$\boldsymbol{\theta} = \{\beta_1, \beta_2, \delta, \boldsymbol{p}, \zeta, \boldsymbol{\alpha}, \nu, b\}$

Detection model

$I \rightarrow D$ model

$$D_i - I_i \sim \text{Gamma}(4, b)$$

- Suspect ≈ 40 days:
  - $b \sim Gamma(2.5, 50)$



Tick model – dynamics

IMA Journal of Mathematics Applied in Medicine and Biology (1999) **16**, 261–296

A mathematical model of the ecology of Lyme disease

TRAVIS C. PORCO

Community Health Epidemiology and Disease Control, 25 Van Ness Avenue, Suite 710, San Francisco Department of Public Health, San Francisco, California 94102, USA

[Received 14 February 1994 and in revised form 17 June 1998]

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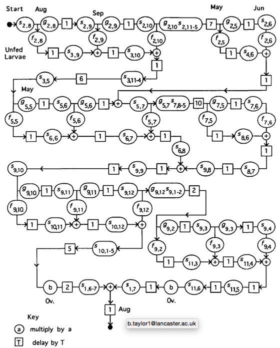


Life-History of *Ixodes scapularis*

CHICAS combining health information, computation and statistics

Tick model – proxy sampling

- BVD samples collected during 2013
- Tested for *Theileria orientalis* spp.

- Implies Binomial sampling model, TLAs $k = 1, \ldots, m$

$$x_k \sim \text{Binomial}(n_k, p_k)$$

n_k herds sampled, x_k *Theileria* +ve, $p_k \propto$ tick occurrence

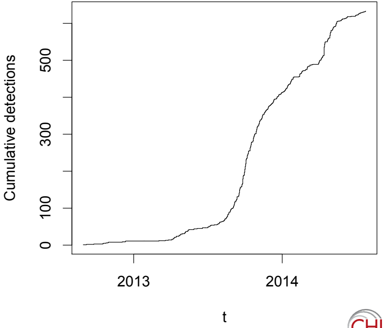
- Independent sampling $\rightarrow$ joint likelihood
- Robust to test Sensitivity and Specificity.

Seasonality

$s(t; \alpha, \nu, p_{k(j)})$

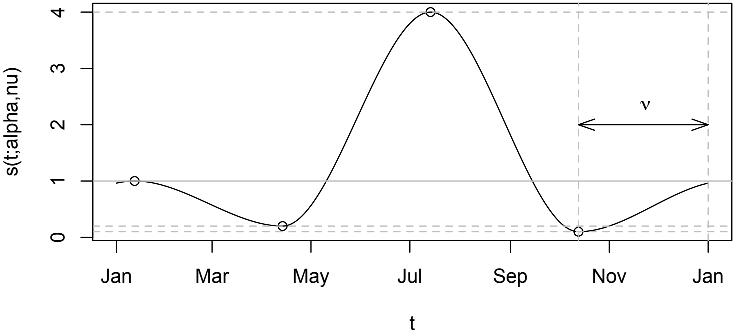
- Biannual peak incidence – autumn/spring
- Due to vector ecology

- Vector seasonality
  - Smooth? (common sense!)
  - On/off threshold? (literature*)
- Candidates:
  - Periodic piecewise cubic spline
  - Periodic square wave



*e.g. Stafford KC (1994), Ogden *et al.* (2004)

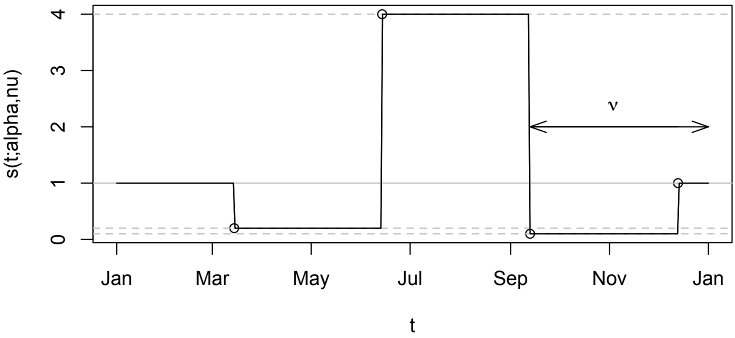
Seasonality
Piecewise cubic spline



- Heath (1998), but literature sparse!

Seasonality

Square wave



- Appears to fit better (see later)
- Heath (2014) suggests on/off effect.

Approach to inference

Bayesian approach for risk forecasting

$$P(\theta|X) = \frac{L(X|\theta)f(\theta)}{\int_{\Theta} L(X|\theta)f(\theta)d\theta}$$

- Coherent inclusion of Prior information
- Likelihood assimilates *all* data
- Posterior encodes uncertainty $\rightarrow$ Predictive distribution
- Complicated integral $\rightarrow$ MCMC
  - Unobserved infection times
  - Occult infections

Approach to inference

- Bayesian approach for risk forecasting

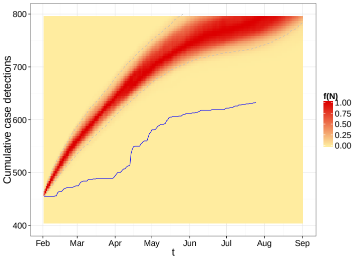
$$
\begin{aligned}
L(\boldsymbol{\theta}|\boldsymbol{I},\boldsymbol{D}) &= \sum_{j:I_\kappa<I_j<T_{obs}} \left(\lambda_j(I_j^-)\right) - \exp\left[\int_{I_\kappa}^{T_{obs}} \left(\sum_{j\in\mathcal{P},j\neq\kappa} \lambda_j(t)\right) \mathrm{d}t\right] \\
&\times \prod_{k=1}^{m} p_k^{x_k}(1-p_k)^{n_k-x_k} \\
&\times \sum_{j:D_j\leq T_{obs}} \left(f_D\left(D_j - I_j\right)\right) + \sum_{j:D_j>T_{obs}} \left(1 - F_D\left(T_{obs} - I_j\right)\right)
\end{aligned}
$$

- Jump algorithm integrates over dimension of $\boldsymbol{I}$
- GPU as a likelihood coprocessor
  - NVIDIA CUDA software libraries
  - Parallelise likelihood within MCMC.

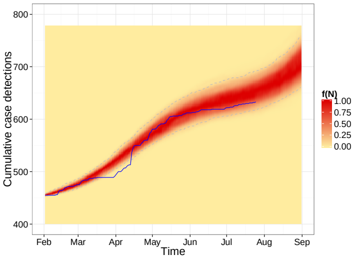
Theileria in NZ cattle

Prediction: in sample cumulative detections

Cubic Spline



Square Wave



Analysis at 1st Aug 2014, simulate from 1st Feb 2014

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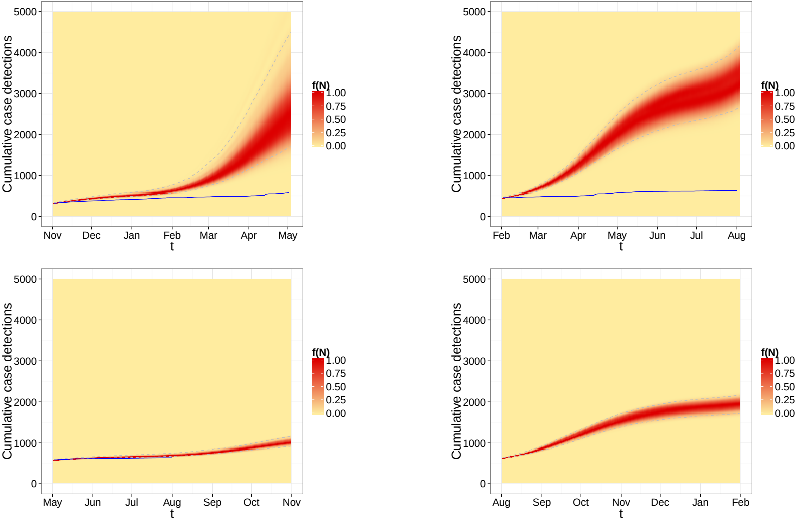
Prediction: out of sample cumulative detections – justification for square wave



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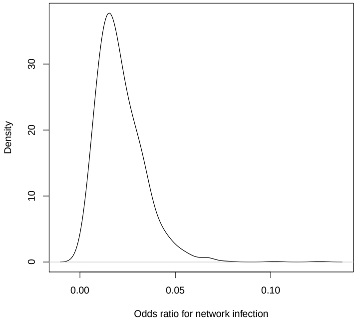
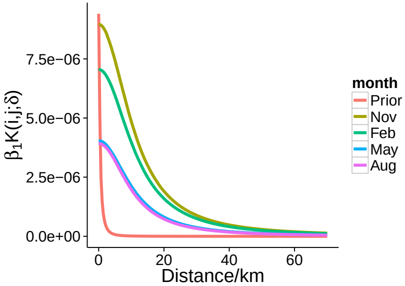
Parameter estimation

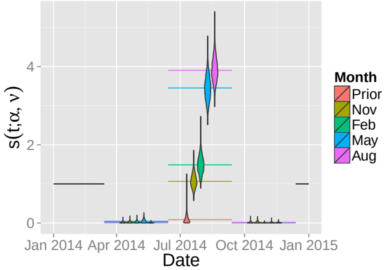
NAIT vs Environmental spread

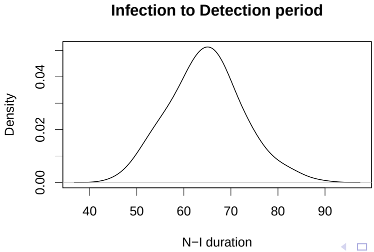


Distance Kernel



Seasonality and infectious period





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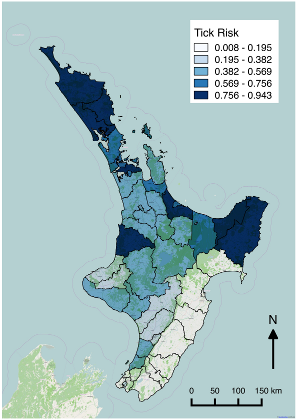
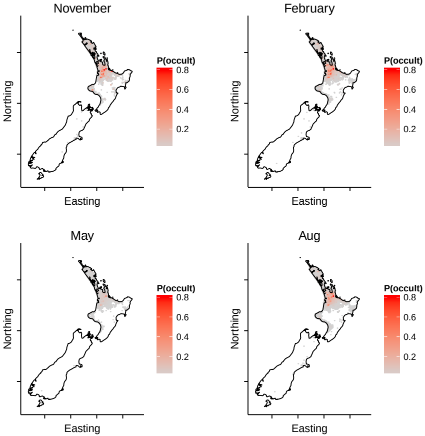
Tick occurrence probability and occults





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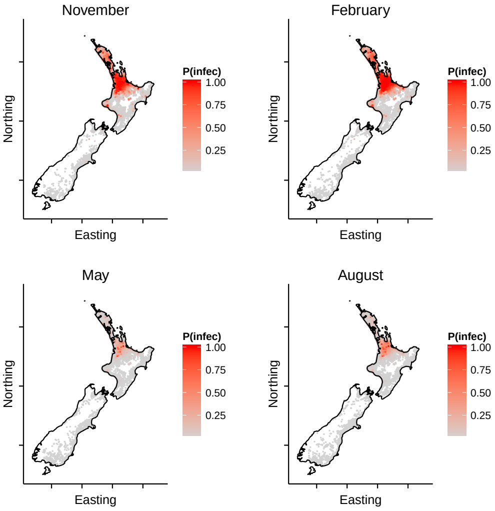
Prediction: 6 month infection risk



Theileria in NZ cattle
Conclusions

- Environmental spread main driver
  - NAIT spread limited (currently)
  - Caveat – AgriBase, FOL, NAIT joining issues
- Epidemic appears to be slowing
  - Complacency vs. effective pop size.
- Modelling issues
  - Ticks
    - Seasonality – tie in with climate data (resolve $Cor(b, \nu)$)
    - e.g. MAXLIK and MAXENT, etc.
  - Continuous space – spatial GP!
  - Priors – care required to not overpredict

Thanks to...

Thanks to...

- Massey
  - Richard Brown
- MPI
  - Daan Vink
  - Kevin Lawrence
  - Andy McFadden
  - Mary van Andel
- AsureQuality
  - Robert Sanson

Jewell and Brown (2015) *JRS Interface* **12**:20150367