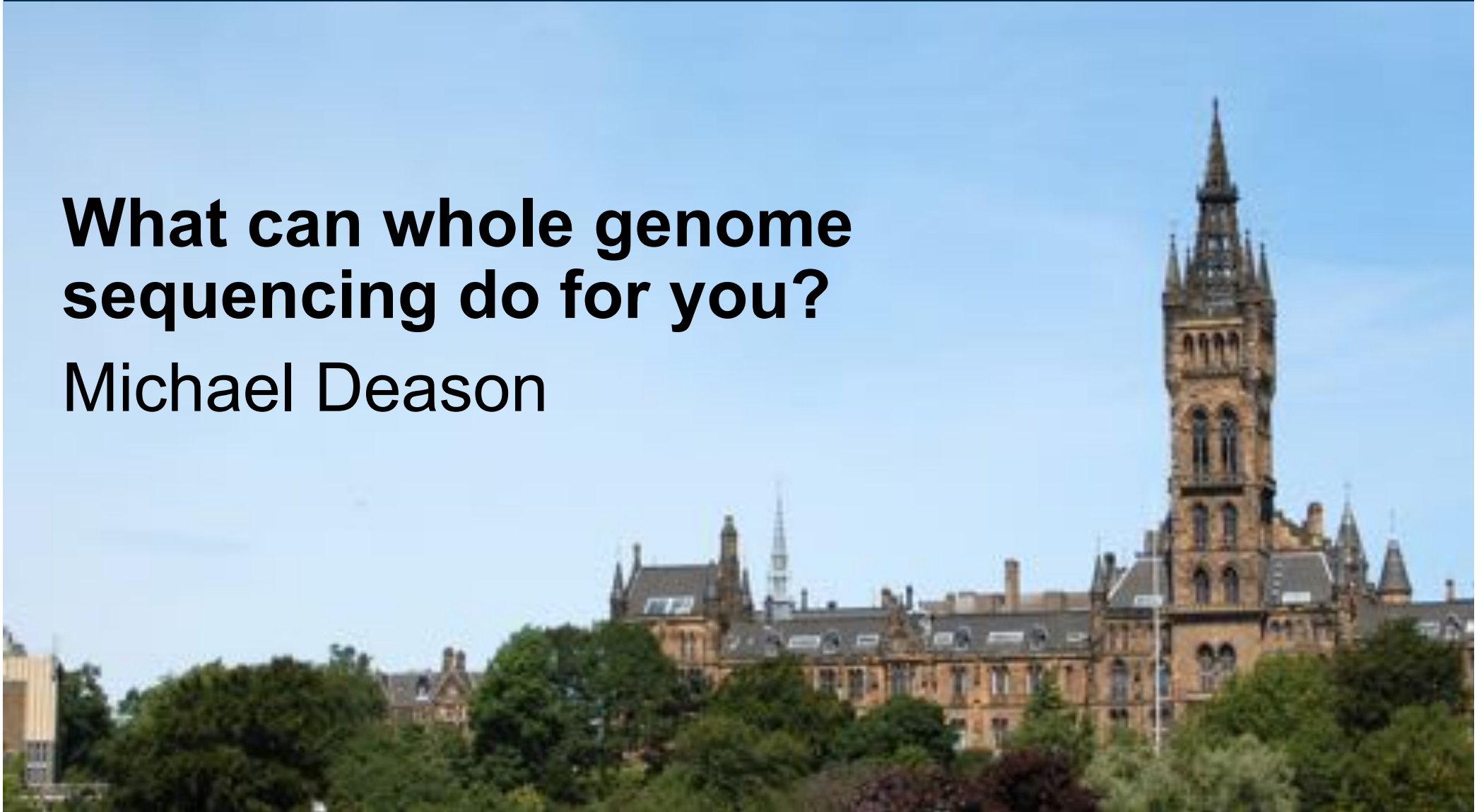# What can whole genome sequencing do for you?

Michael Deason

- **Entirely new technological approach**

- **Increasingly inexpensive**

- **Obvious uses retain challenges of interpretation**

- **Are there any 'un-obvious' uses?**

- **It isn't the solution**

- **What are the scientific questions that WGS can be used to address in different ways?**

  – And what are the limitations?

- **What can it do to change our understanding of the epidemiology**

- **What can it do to change our disease control paradigms?**

- **Brief Introduction**

- **Sequencing techniques**

- **"what we know about the resolution of this this technique "**
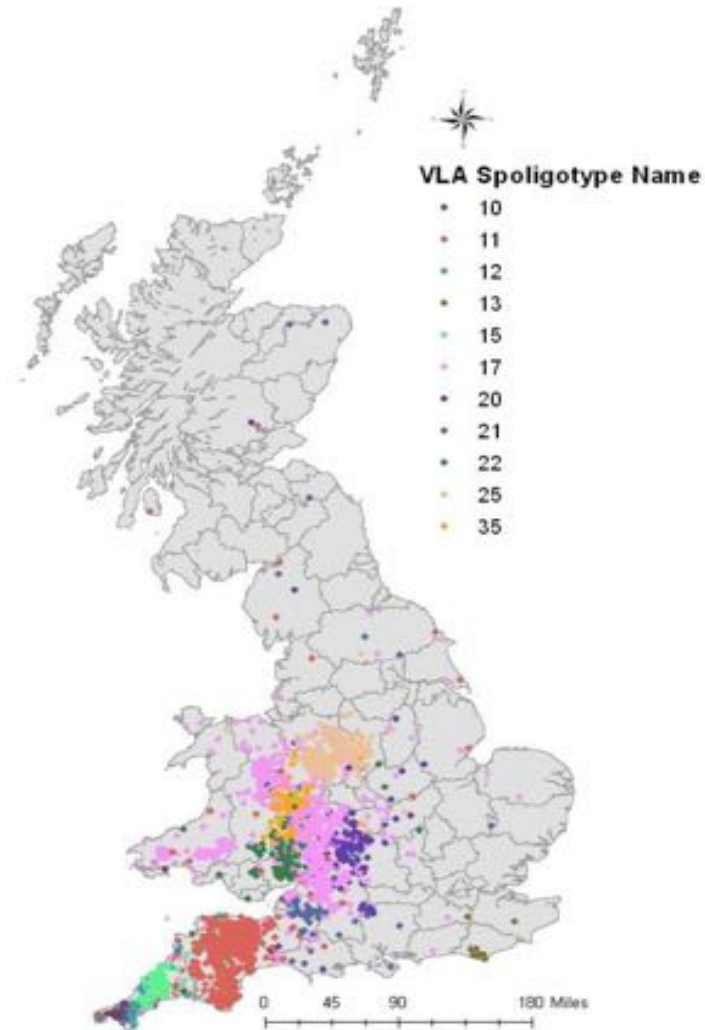
- **"how it can improve our research"**

- **IS6110 RFLP typing**
- **Spoligotyping**
- **VNTR typing**
- **Whole Genome sequencing**
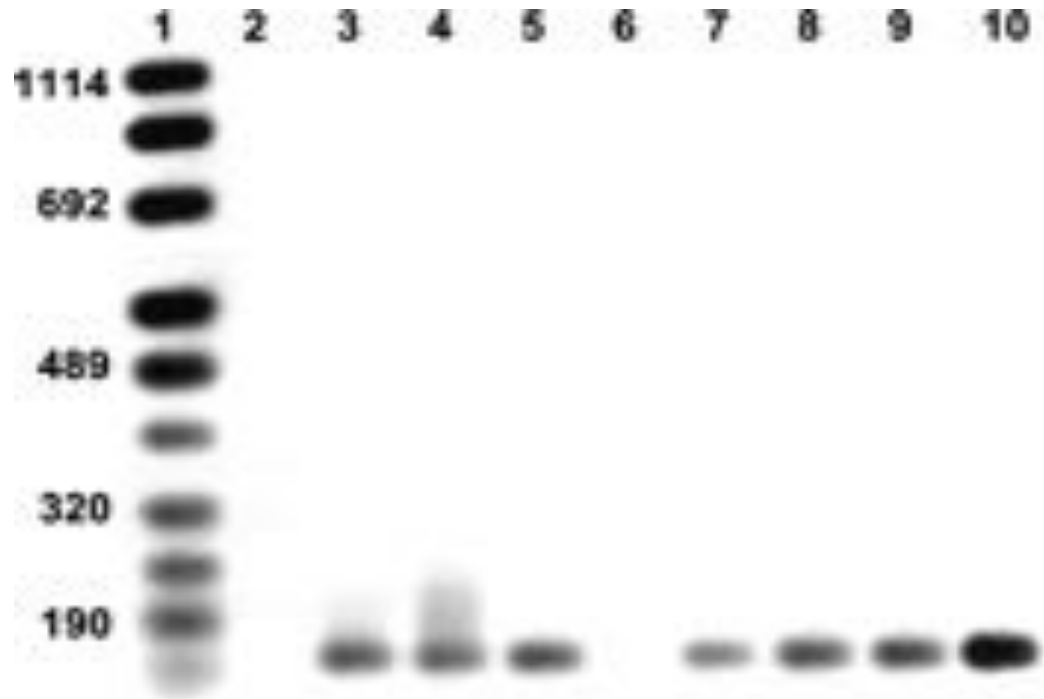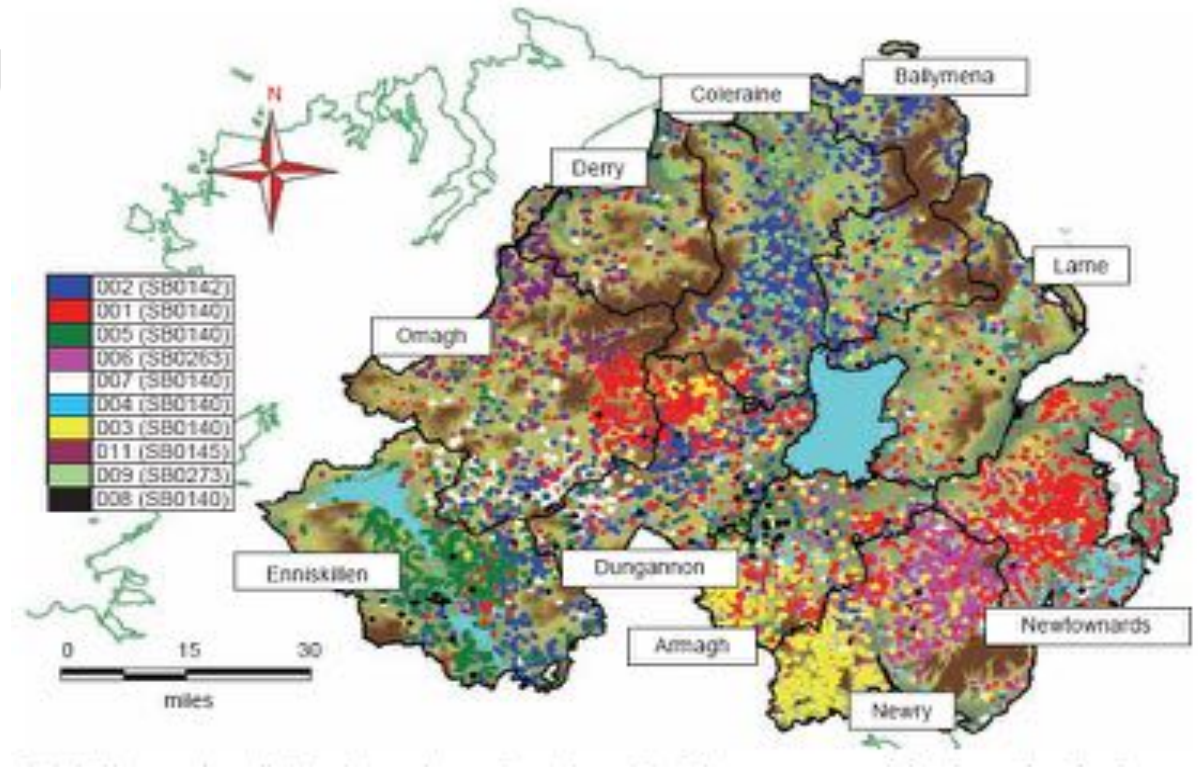

Miller et al. Vet Mic 2002

- IS6110 RFLP typing
- **Spoligotyping**
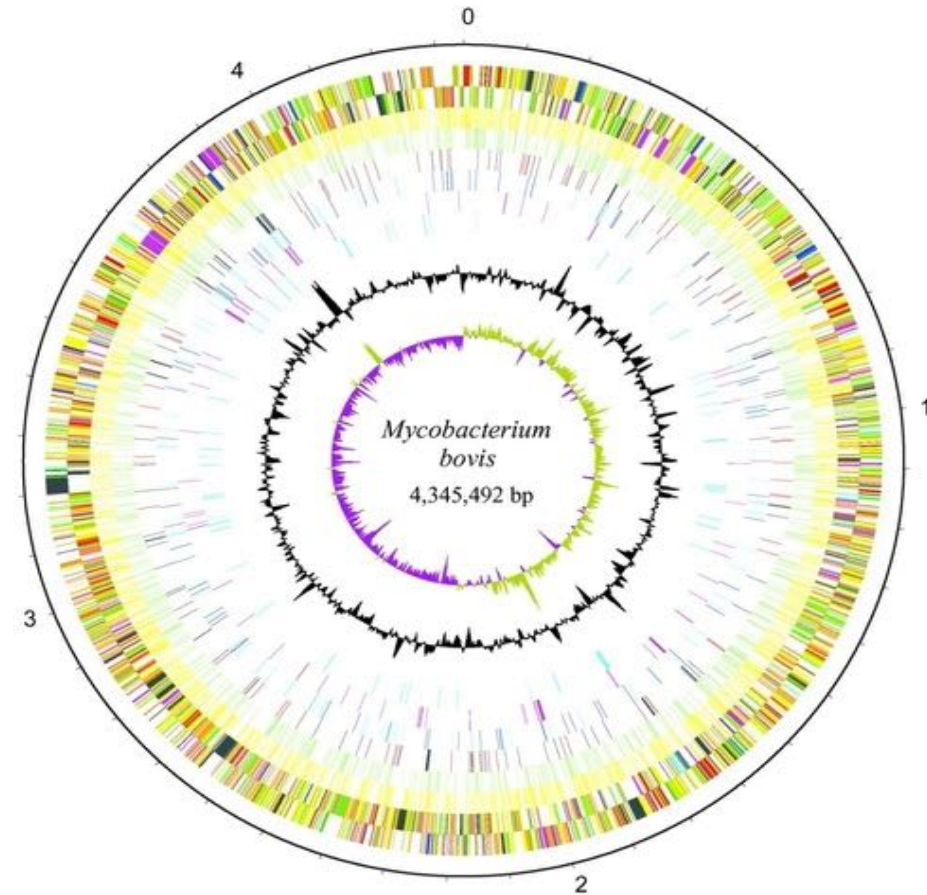- VNTR typing
- Whole Genome sequencing

O'Connor, unpub. thesis

- **IS6110 RFLP typing**
- **Spoligotyping**
- **VNTR typing**
- **Whole Genome sequencing**

Skuce et al. Vet Rec 2012

- IS6110 RFLP typing
- Spoligotyping
- VNTR typing
- **Whole Genome sequencing**

Mycobacterium bovis
4,345,492 bp

Garnier T et al. PNAS 2003

- **Isolates cultured and massively parallel- sequenced using Illumina technology**

- **5-8 Million paired-end reads (70bp) per isolate**

- **~100X coverage after data filtering**

- **Assembled to UK reference sequence**

- **Alignment of genome consensus sequences**

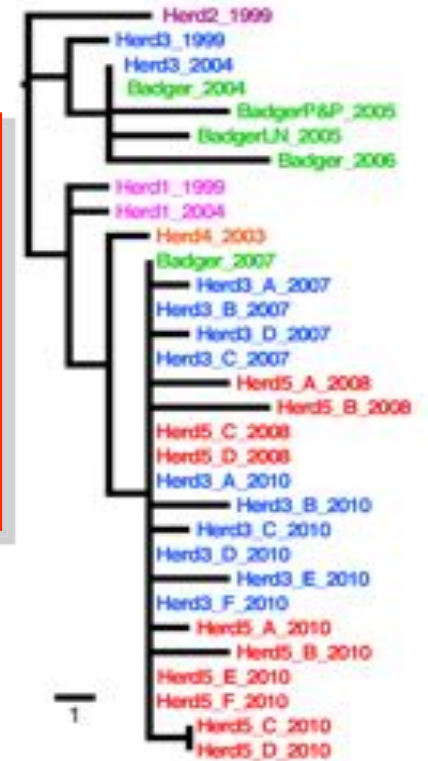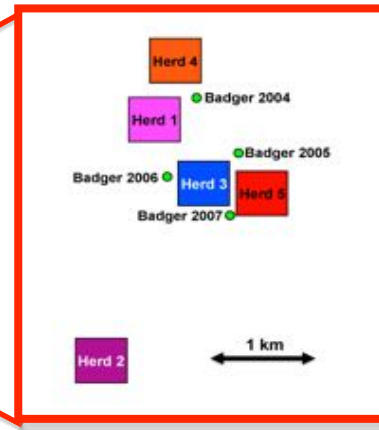 – (4.3 Mbp total, >99% of full genome)

- **Investigating one particular genotype**

- **31 field isolates from small area in NI (~10 km^2)**
- 26 from cattle (5 herds, multiple individuals/ outbreaks per herd)
- Circles: 5 samples from 4 road-killed badgers

- **Extract and sequence DNA from all isolates**

- **Analyse DNA to identify polymorphisms**

- **Construct parsimony tree to identify possible transmission chains:**
- Within Herd
- Between Herd
- Cattle -> Badger
- Badger -> Cattle
- Badger -> Badger

Main holdings associated with herds and badger locations by year

Herd 4

2004

Herd 1

2005

2006 Herd 3 Herd 5

2007

Herd 2
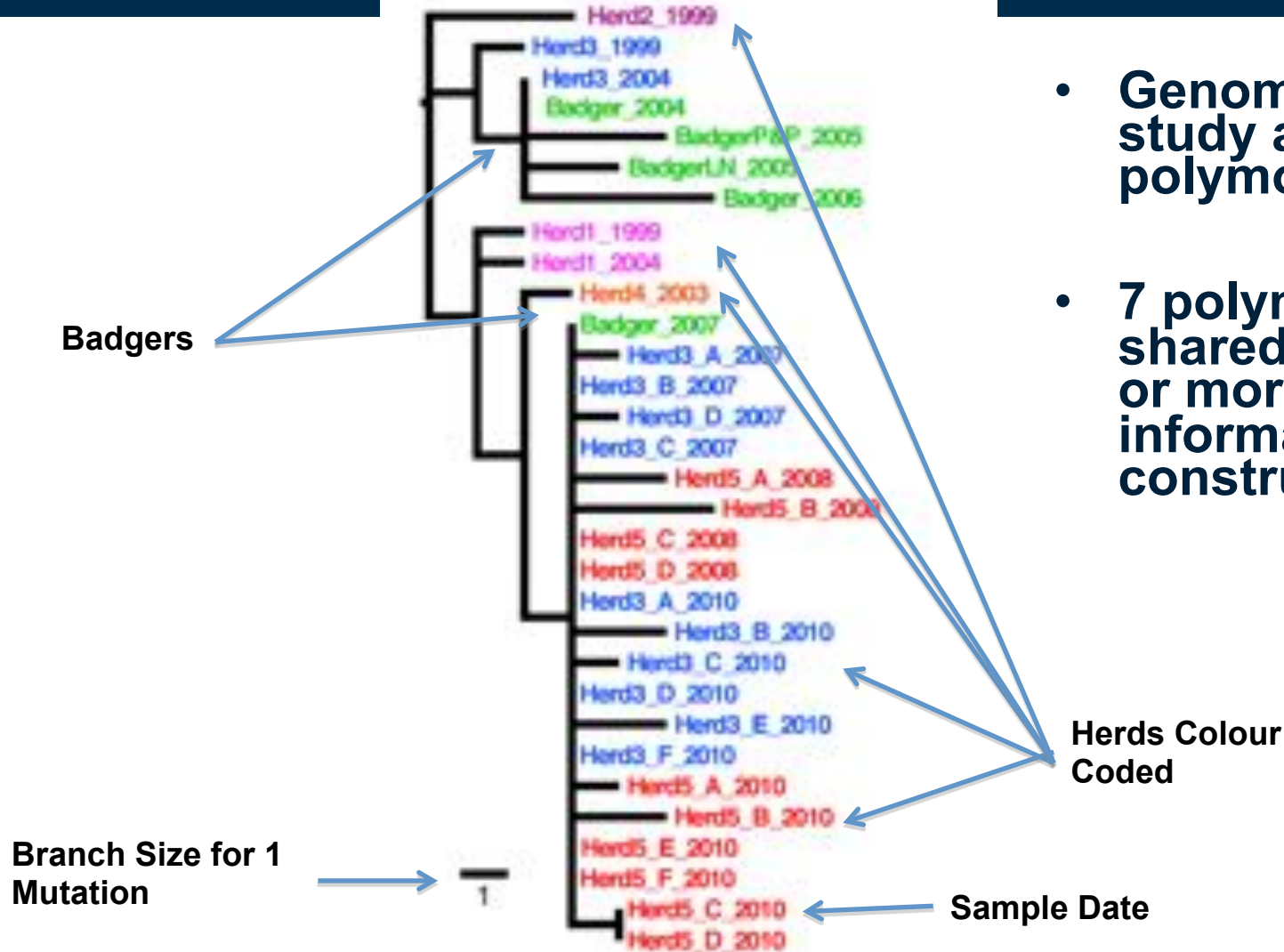
1 km

Unprecedented resolution
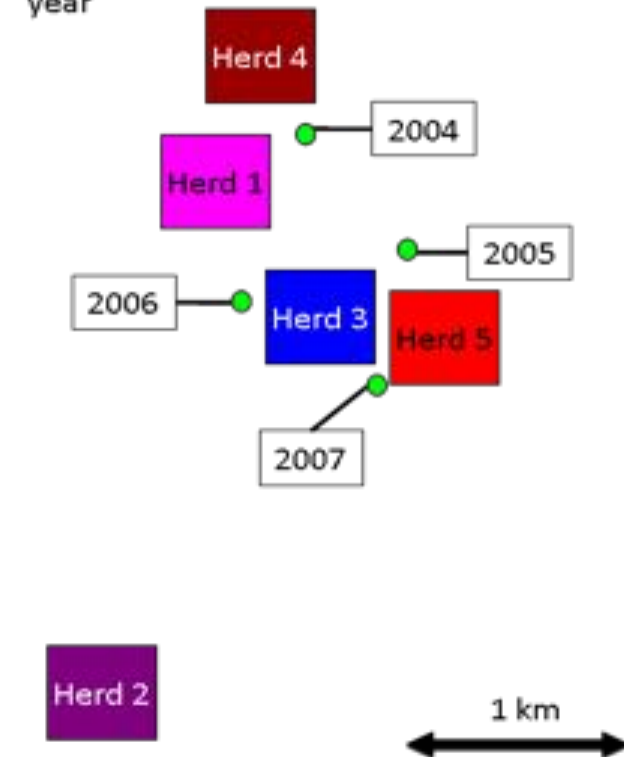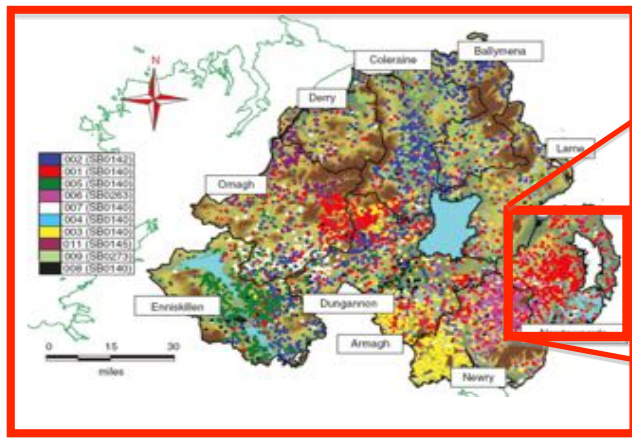
One colour = one VNTR type
Existing data coverage of entire country

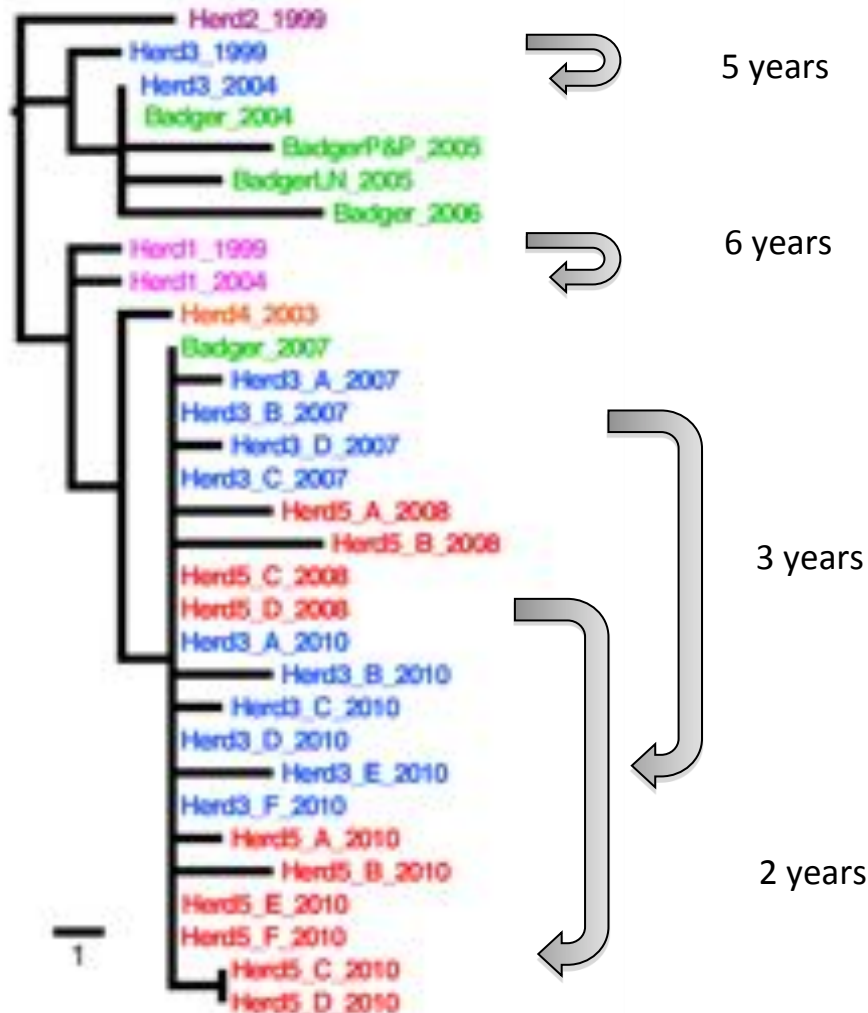First direct demonstration of a close spatio-temporal link between badger and cattle bTB

- **Genomes from study area had 39 polymorphic sites**

- **7 polymorphisms shared amongst 2 or more isolates => informative for tree construction**

Badgers

Herds Colour Coded

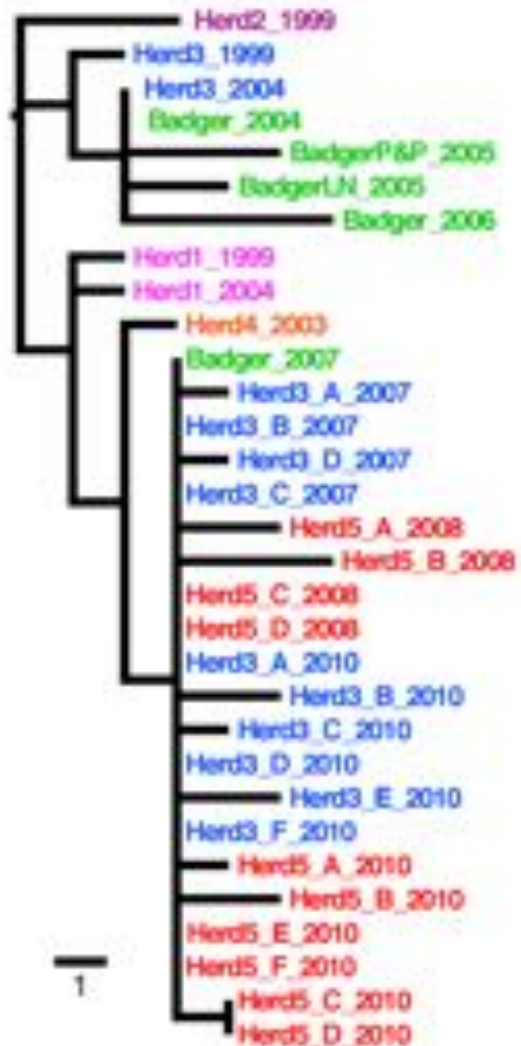**Branch Size for 1 Mutation**

Sample Date

Likelihood tree of *M. bovis* genomes

- **Subsequent outbreaks in the same herd usually caused by the same type**

- **Could suggest herds are continually exposed to the same genotype via local or environmental factors**

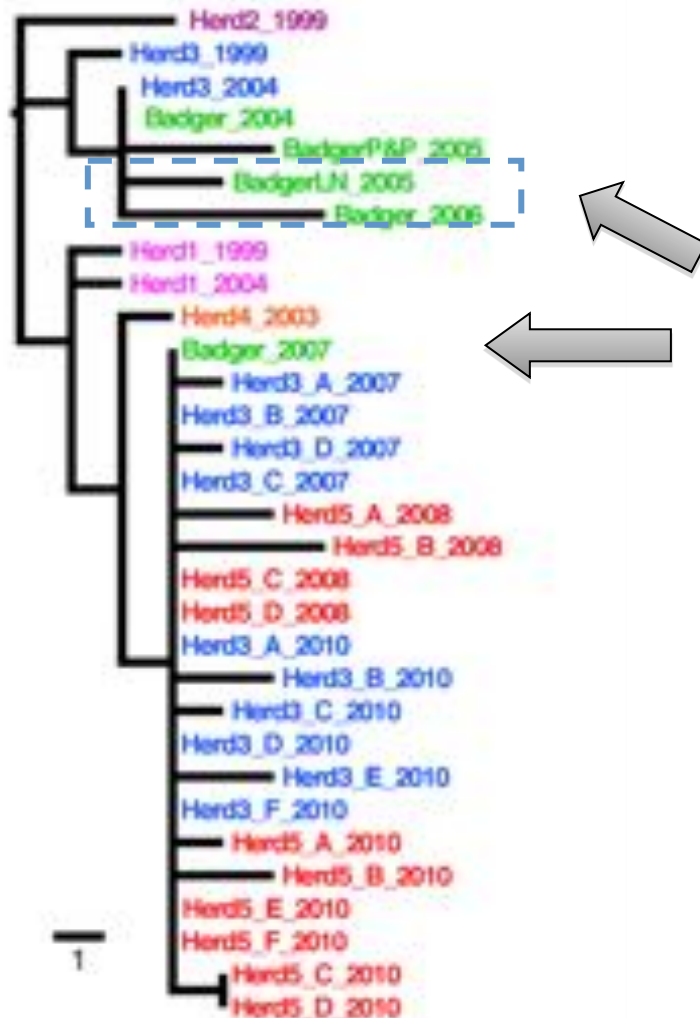- **But could also be latent or anergic infection in cattle herd**

- **One exception in herd 3 (blue): new type introduced between 2004 and 2007**
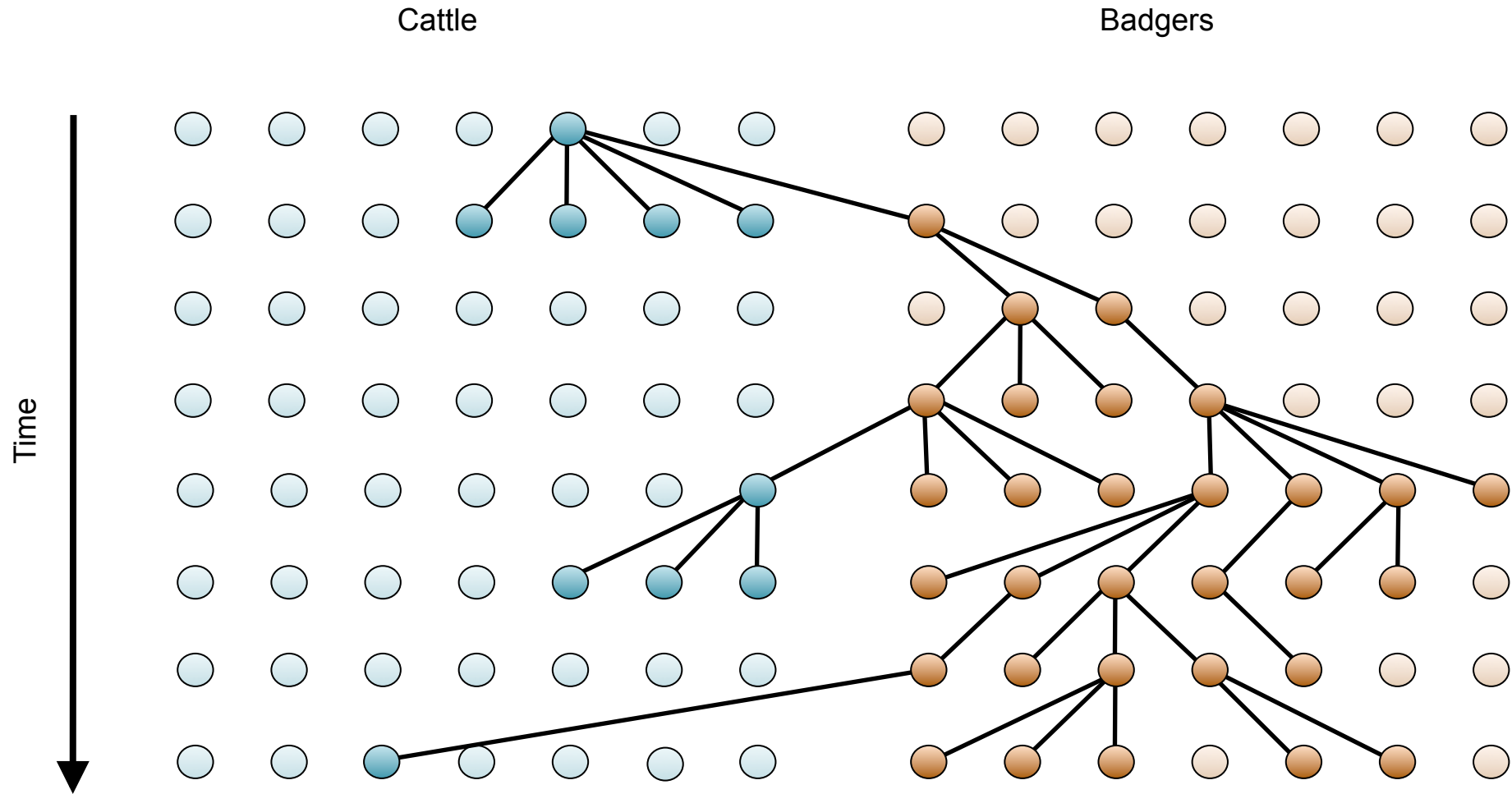
- **Why? Unsampled individuals?**

What about badgers?

- Jenkins et al. (2009) showed association between spoligotypes in cattle and badgers during Randomised Badger Culling Trial

- Here, finer scale resolution shows the same or directly derived types found in badgers (one exception)

- Could suggest that the disease is circulating within the badger population, but not possible to infer direction of transmission at this point

- Badger population is under-sampled (road kills), cattle population very well sampled (but there will be some missed and latent infections)
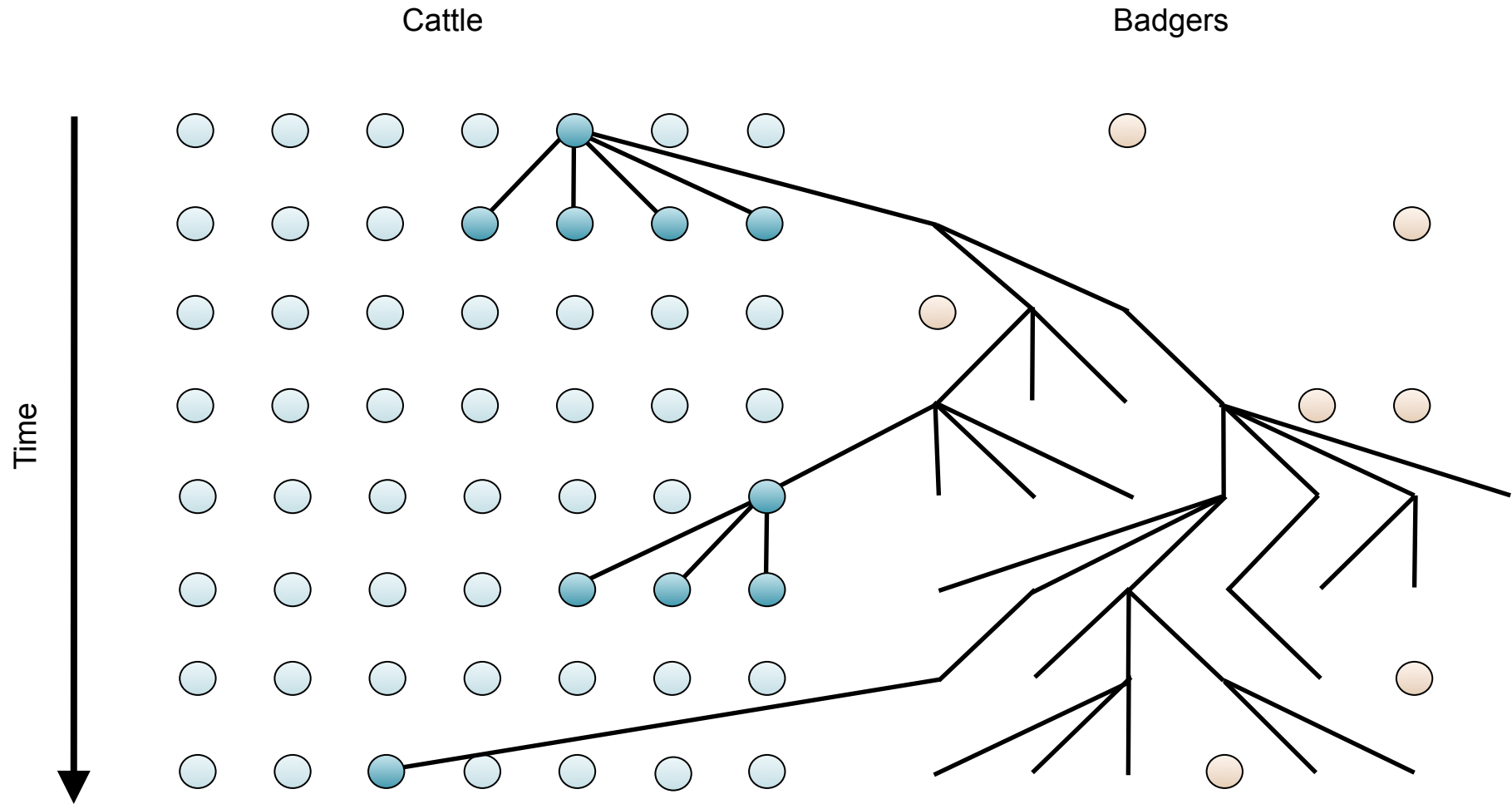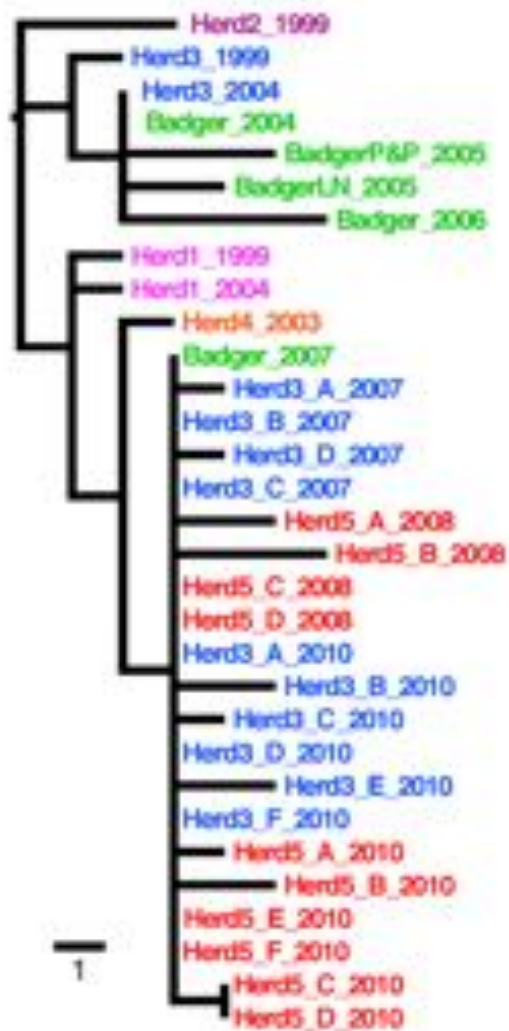
Cattle

Badgers

Time

Cattle

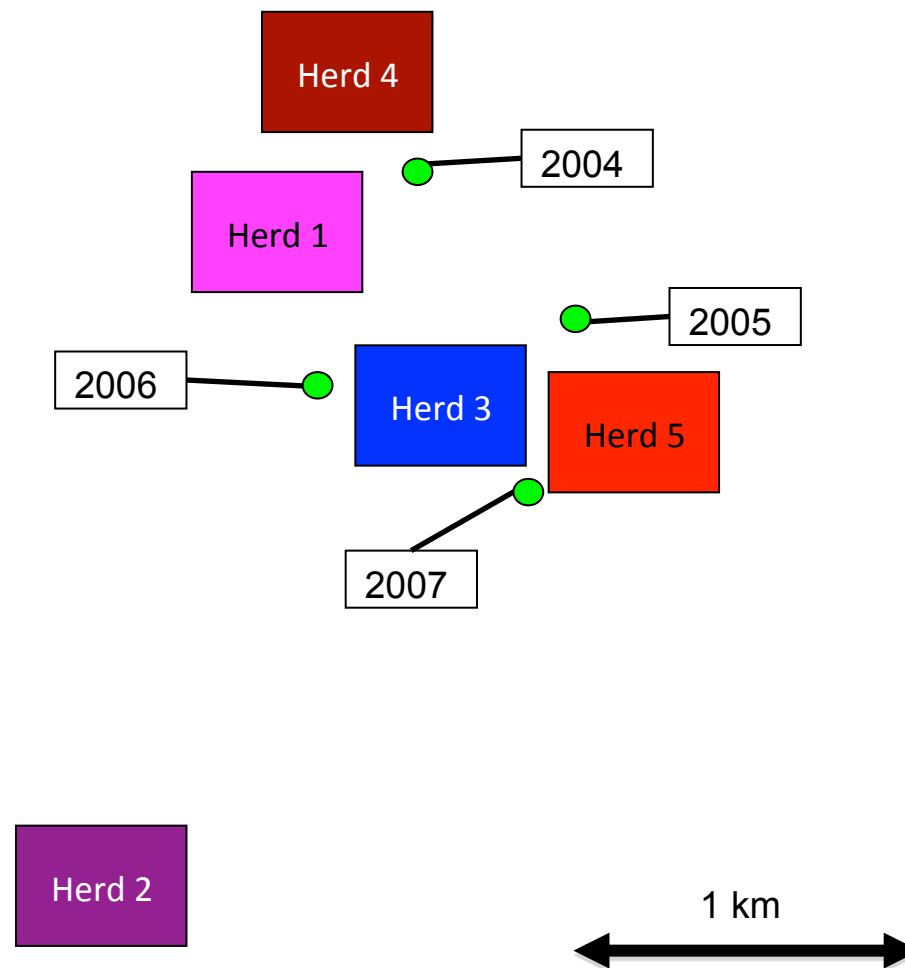Badgers

Time

Main holdings associated with herds and badger locations by year

Bayesian Clustering with network parameters

University of Glasgow
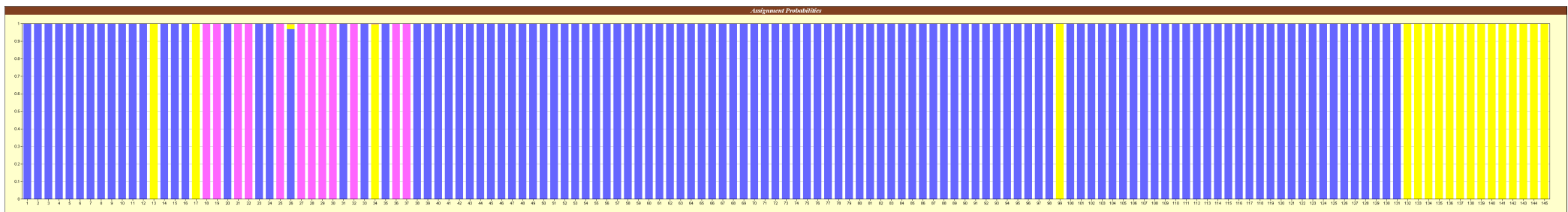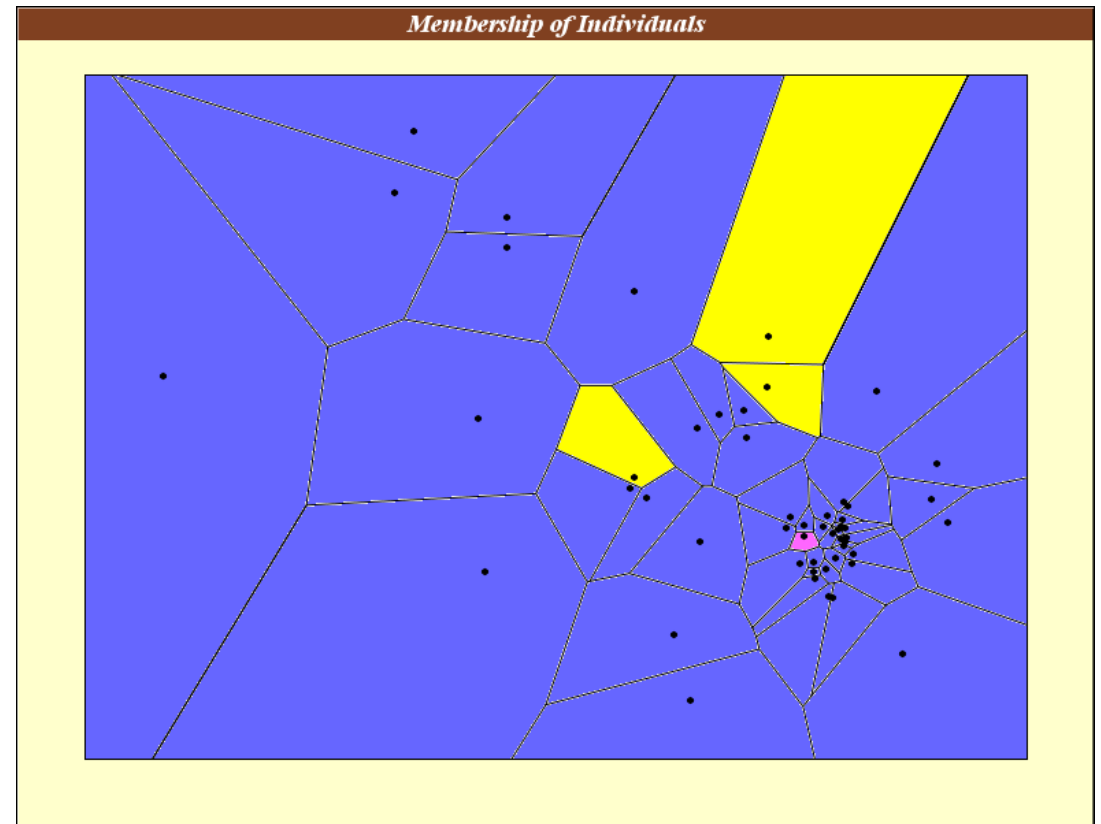
- **Whole genome sequencing an exciting pathway for investigating transmission dynamics of bacteria**

- **Enough resolution to investigate short-distance transmission of bTB**

  - Untangle the roles of different mechanisms involved

- **Insights into "unobserved" component of multi-host system**

- Bacterial sequences + mathematical models

University of Glasgow

wellcome trust

- Rowland Kao
- Hannah Trewby
- Roman Biek
- Anthony O'Hare
- Richard Orton
- Paul Bessell

Boyd Orr Centre for Population and Ecosystem Health

- Julie Galbraith, Pawel Herzyk – Sir Henry Wellcome Functional Genomics Facility

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defra Department for Environment Food and Rural Affairs

RADAR project
AHVLA

afbi Agri-Food and Biosciences Institute

Queen's University Belfast

Department of Agriculture and Rural Development
www.dardni.gov.uk

- Robin Skuce,
- Tom Mallon,
- Stanley McDowell,
- Carl McCormick

David Wright

(Data for WGS analysis including badger samples)