

Phylogeographic Reconstruction of *Borrelia* *Burgdorferi*

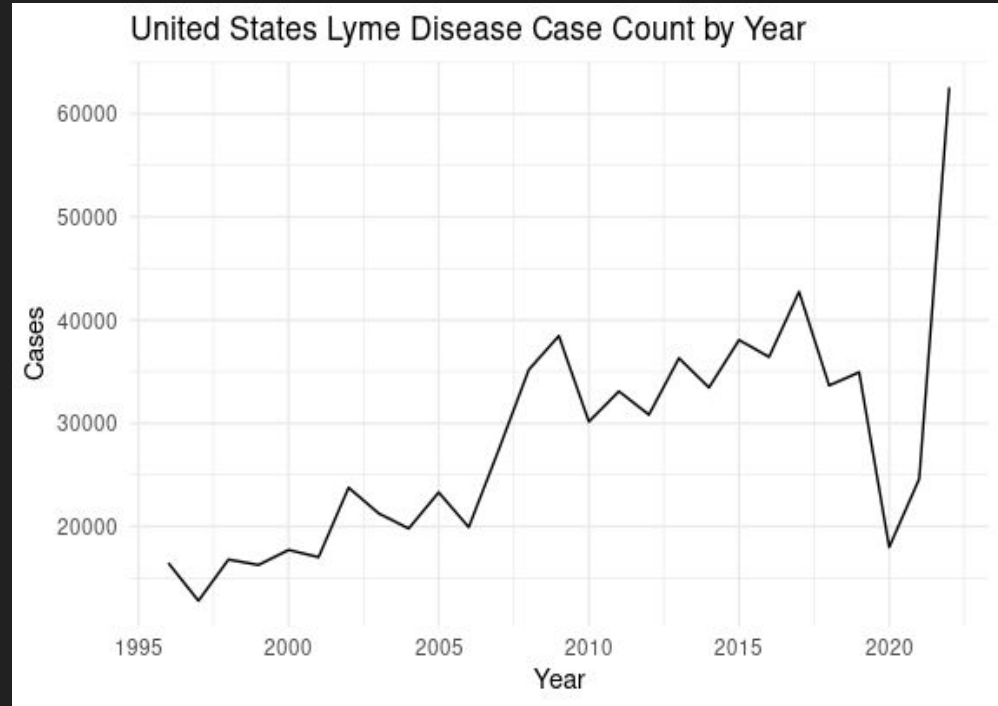
Frank Burkhart, Ethan Smith

Lyme Disease and *Borrelia Burgdorferi*

- Lyme disease is a vector borne illness caused by multiple different species of the spirochete *Borrelia Burgdorferi*
- The primary species found in North America and regions of Western Europe is *Borrelia Burgdorferi Sensu Stricto* [1]
- Commonly transmitted to humans via the *Ixodes scapularis* vector (also known as deer or black-legged ticks)
- Other host populations include white-legged mice, white-tailed deer, birds, and reptiles [2]
- The diverse migratory patterns of hosts make for a great phylogeographic reconstruct of *Borrelia Burgdorferi*

Recent Spike in Lyme Disease Case Count

- First case of Lyme disease clinically documented in Lyme, Connecticut in 1976 [1]
- Since then, it has become the most prevalent vector-borne disease in North America, with the CDC estimating 476,000 transmission per year [3]
- This estimate is far greater than the reported case counts



Who is ready for some trees?

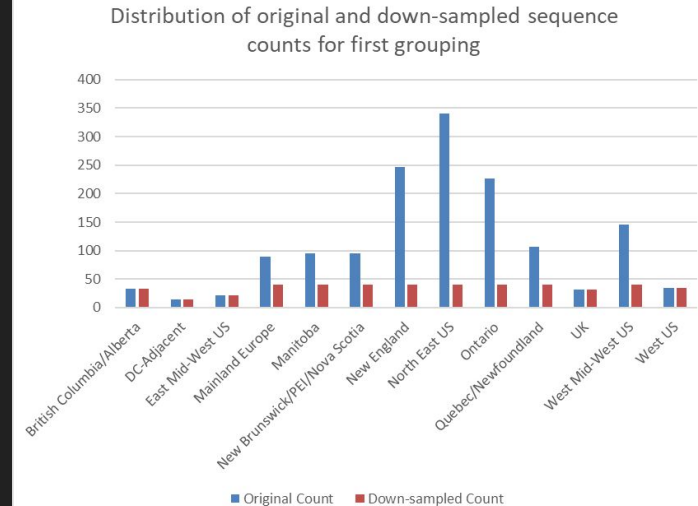
Given this pathogen's complex migratory system, working towards understanding its spatial spread can greatly aid in Lyme disease mitigation.

Our project seeks to reconstruct the phylogeography of *Borrelia Burgdorferi Sensu Stricto* across regions in North America and Western Europe using a discrete trait model.

Data Collection and Preprocessing

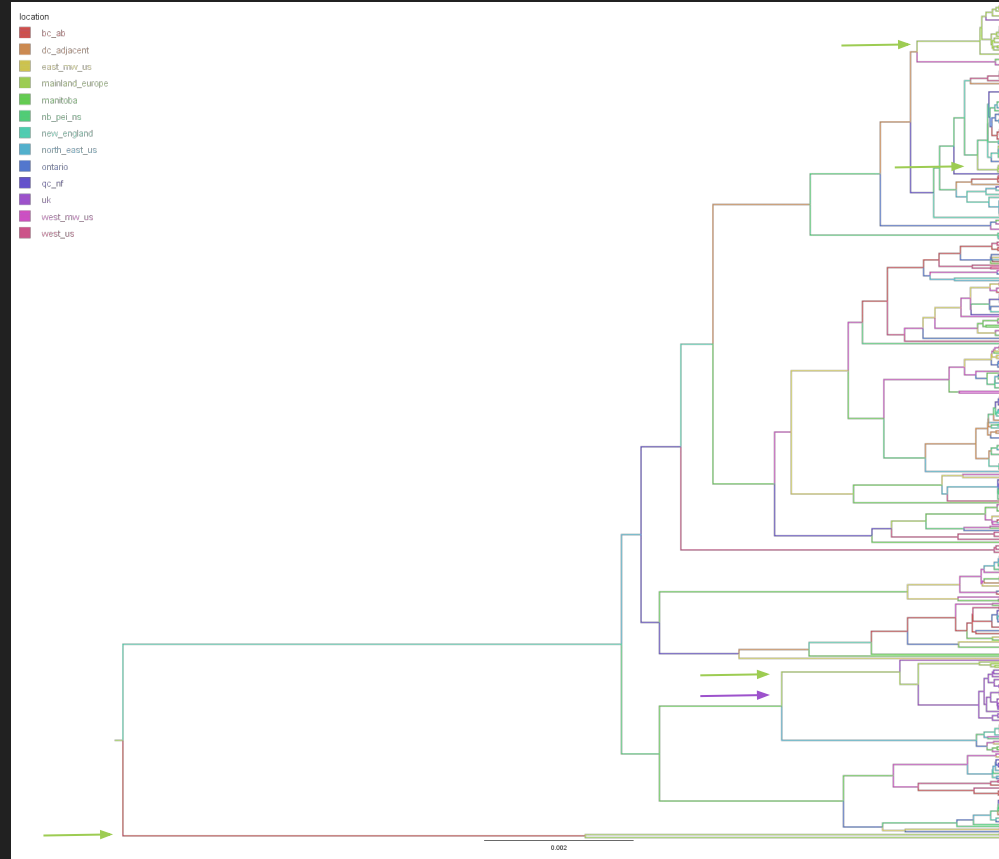
- Used MLST data instead of whole genome sequences
- Housekeeping genes: *clpA*, *clpX*, *nifS*, *pepX*, *pyrG*, *recG*, *rplB*, *uvrA*
- Downloaded over 1,500 sequences from the Public database for molecular typing and microbial genome diversity [4]
- Group samples into 13 location groups
- Down-sample groups to max of 40 samples
- Perform down-sampling multiple times to validate results

Group Name	Locations
Europe	
UK	UK
Mainland Europe	IT, DE, FR, CH
Canada	
Quebec/Newfoundland	QC, NL
New Brunswick/PEI/Nova Scotia	NB, PE, NS
Ontario	ON
Manitoba	MB
British Columbia/Alberta	BC, AB
USA	
New England	ME, VT, NH, MA, RI, CT
North-East US	NY, PA, NJ
DC-Adjacent	MD, VA
East Mid-West US	MI, IN, IL, MO
West Mid-West US	WI, MN, IA
West US	CA



First Grouping Results

- Group resolution too high, making tree less readable
- Migration between major North American regions and between NA and EU
- Some samples from EU are significantly diverged, indicating an early introduction of *Borrelia Burgdorferi* s.s. into EU from NA
- Distinct clade for majority of UK samples, suggesting independent introduction event of *Borrelia Burgdorferi* s.s. into the UK
- Key takeaways:
 - Gene transfer between North America and Western Europe
 - Multiple distinct European introduction events of *Borrelia Burgdorferi* s.s.



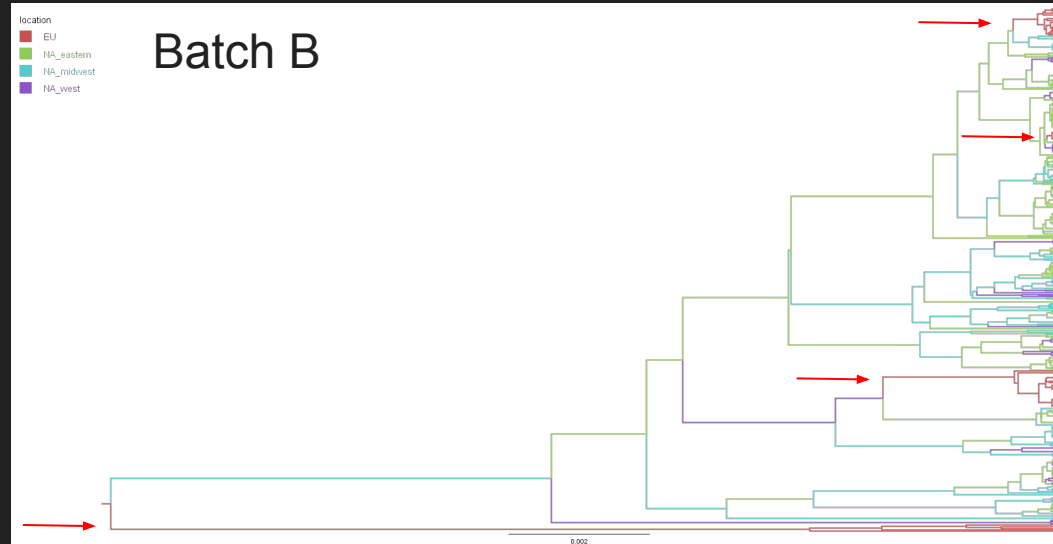
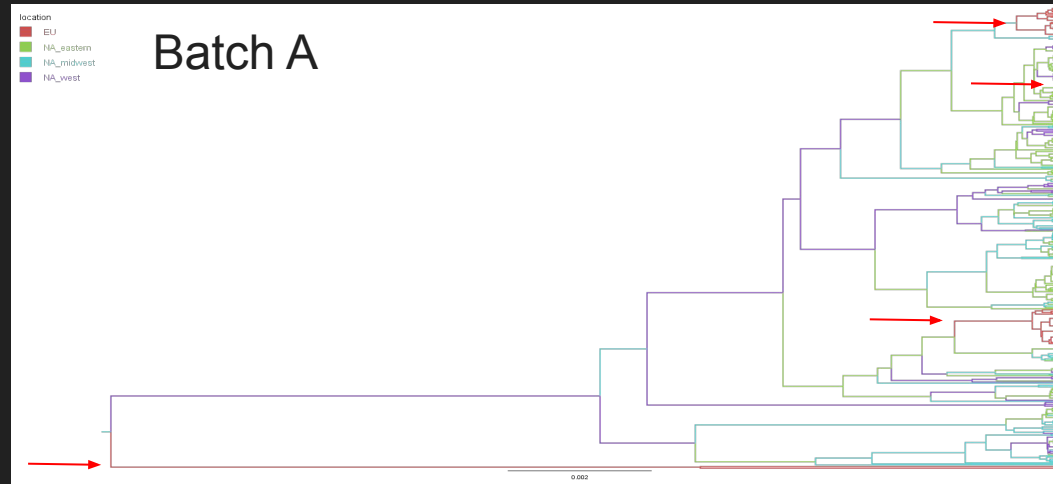
Re-grouping of samples

- Large number of groups can result in a messy, unreadable tree
- Samples were re-grouped into pooled groups based on their original location groupings
- While sample distribution is no longer uniform, it helps to produce a more readable tree

Pooled Group	Original Groups	Sequence Count
EU	UK, Mainland Europe	72
NA East	New England, North-East US, QC/NF, NB/PEI/NS, Ontario	214
NA Midwest	East Mid-West US, West Mid-West US, Manitoba	102
NA West	West US, BC/AB	68

Second Grouping Results

- Bi-directional gene transfer between regions in Eastern and Mid-Western NA
- Identifies at least four separate introduction events of *Borrelia Burgdorferi* s.s. from NA to EU
- Mixed evidence on origin point, with variability near tree roots
- Down-sampling did not impact the ability to infer migration between regions based on tree similarities



Conclusions

- Both location groupings suggests that the migration of *Borrelia Burgdorferi Ssensu Stricto* is occurring between each region of North America
- Our trees suggest that migration across continents also exists, with four sets of independent clades forming in Western Europe that originated in North America
- With conflicting consensus origins for each tree, it is unclear from our analysis where *Borrelia Burgdorferi Ssensu Stricto* originated

References

- [1]. Anna Szymanska, Anna E Platek, Mirosław Dłuzniewski, and Filip M Szymanski. History of lyme disease as a predictor of atrial fibrillation. The American Journal of Cardiology, 125(11):1651–1654, 2020
- [2]. Gerold Stanek, Gary P Wormser, Jeremy Gray, and Franc Strle. Lyme borreliosis. The Lancet, 379(9814):461–473, 2012
- [3] Centers for Disease Control and Prevention. How many people get lyme disease? Accessed on April 21, 2024
- [4] Keith A Jolley, James E Bray, and Martin CJ Maiden. Open-access bacterial population genomics: Bigsdb software, the pubmlst. org website and their applications. Wellcome open research, 3, 2018