National Center for Emerging and Zoonotic Infectious Diseases

# Genomic Epidemiology

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Senior bioinformatician
Enteric Diseases Laboratory Branch

Computational Genomics course

Feb 11, 2020

# Acknowledgements up front

- Every single compgenomics class since 2008
- My branch at CDC
- Federal partners
- State partners

# Enteric Diseases Laboratory Branch (EDLB)

Food Safety Informatics Group,
Center for Food Safety,
University of Georgia

Enteric Diseases Bioinformatics Team (EDBiT)

April 16, 2008

http://www.compgenomics.biology.gatech.edu/index.php/Group_photos

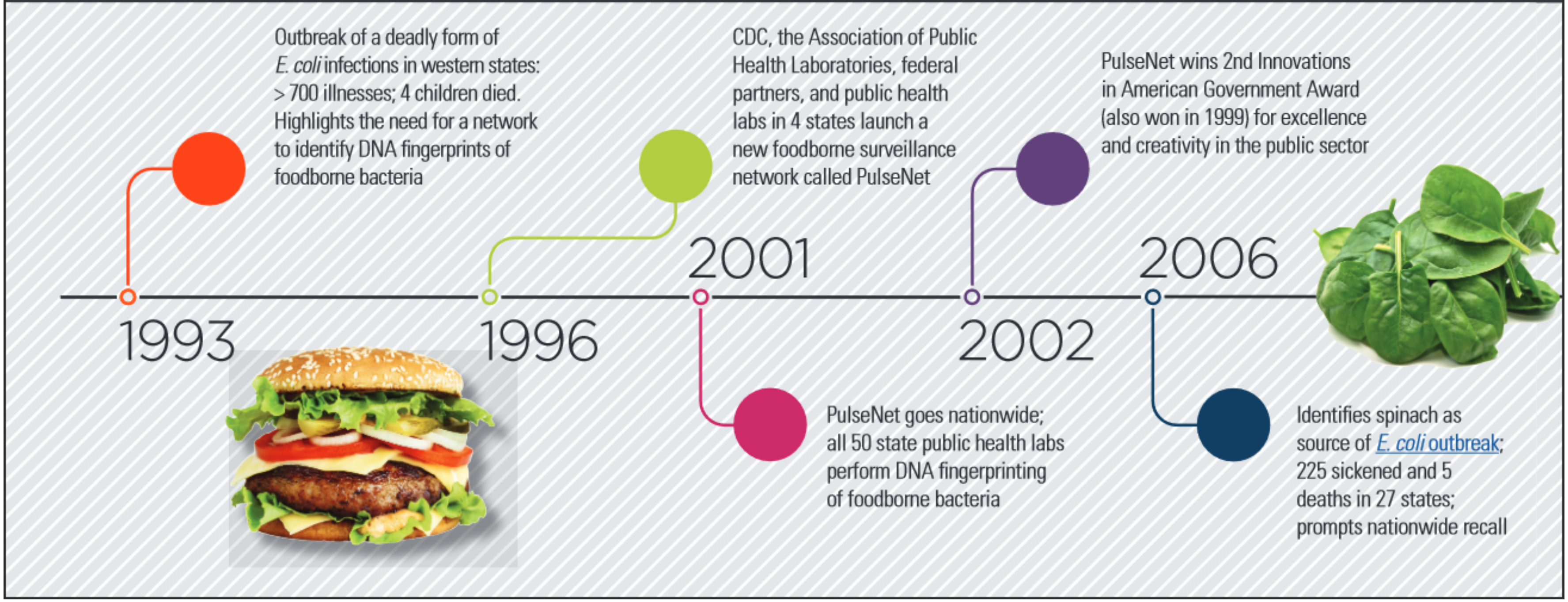
April 23, 2008

# Enteric Diseases Laboratory Branch

2011 to present

*Vibrio, Campylobacter, Escherichia, Shigella, Yersinia, Salmonella*

# PulseNet's 20-year history of making food safer to eat



1993

Outbreak of a deadly form of *E. coli* infections in western states: > 700 illnesses; 4 children died. Highlights the need for a network to identify DNA fingerprints of foodborne bacteria

1996

CDC, the Association of Public Health Laboratories, federal partners, and public health labs in 4 states launch a new foodborne surveillance network called PulseNet

2001

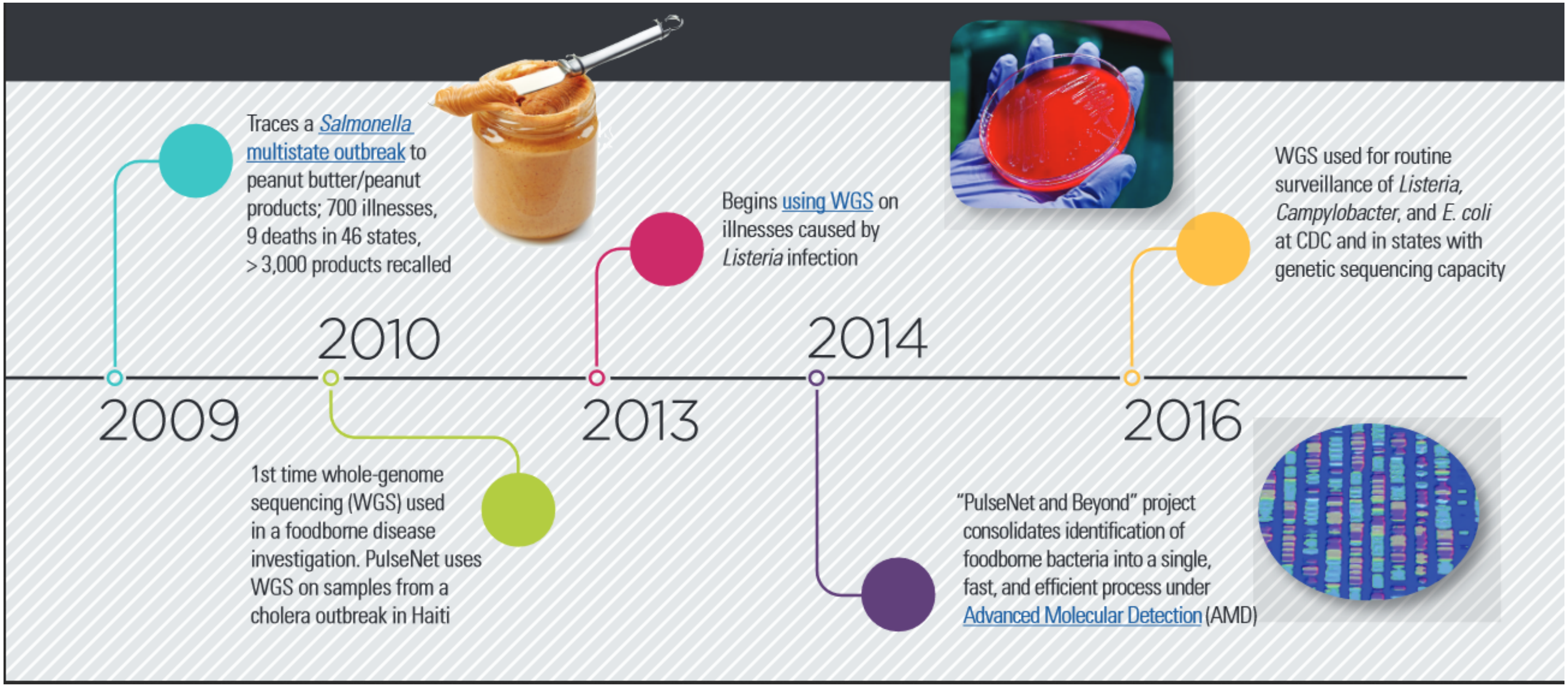
PulseNet goes nationwide; all 50 state public health labs perform DNA fingerprinting of foodborne bacteria

2002

PulseNet wins 2nd Innovations in American Government Award (also won in 1999) for excellence and creativity in the public sector

2006

Identifies spinach as source of *E. coli* outbreak; 225 sickened and 5 deaths in 27 states; prompts nationwide recall



2009

Traces a *Salmonella* multistate outbreak to peanut butter/peanut products; 700 illnesses, 9 deaths in 46 states, > 3,000 products recalled

2010

1st time whole-genome sequencing (WGS) used in a foodborne disease investigation. PulseNet uses WGS on samples from a cholera outbreak in Haiti

2013

Begins using WGS on illnesses caused by *Listeria* infection

2014

"PulseNet and Beyond" project consolidates identification of foodborne bacteria into a single, fast, and efficient process under Advanced Molecular Detection (AMD)

2016

WGS used for routine surveillance of *Listeria*, *Campylobacter*, and *E. coli* at CDC and in states with genetic sequencing capacity

# Outline

- Background
- Genomic Epidemiology
  - Algorithms
  - Software
- Example

**The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.**

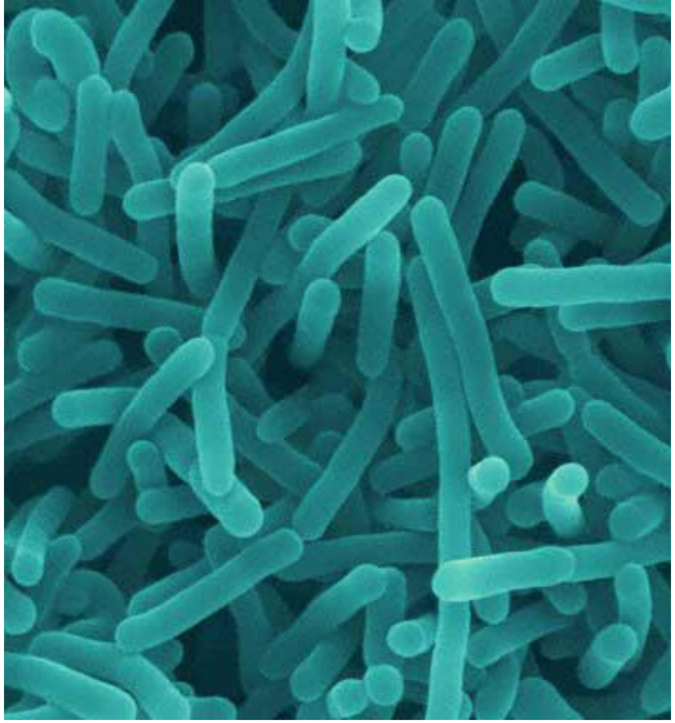
# Listeria pilot project

**As told from a bioinformatician's perspective**

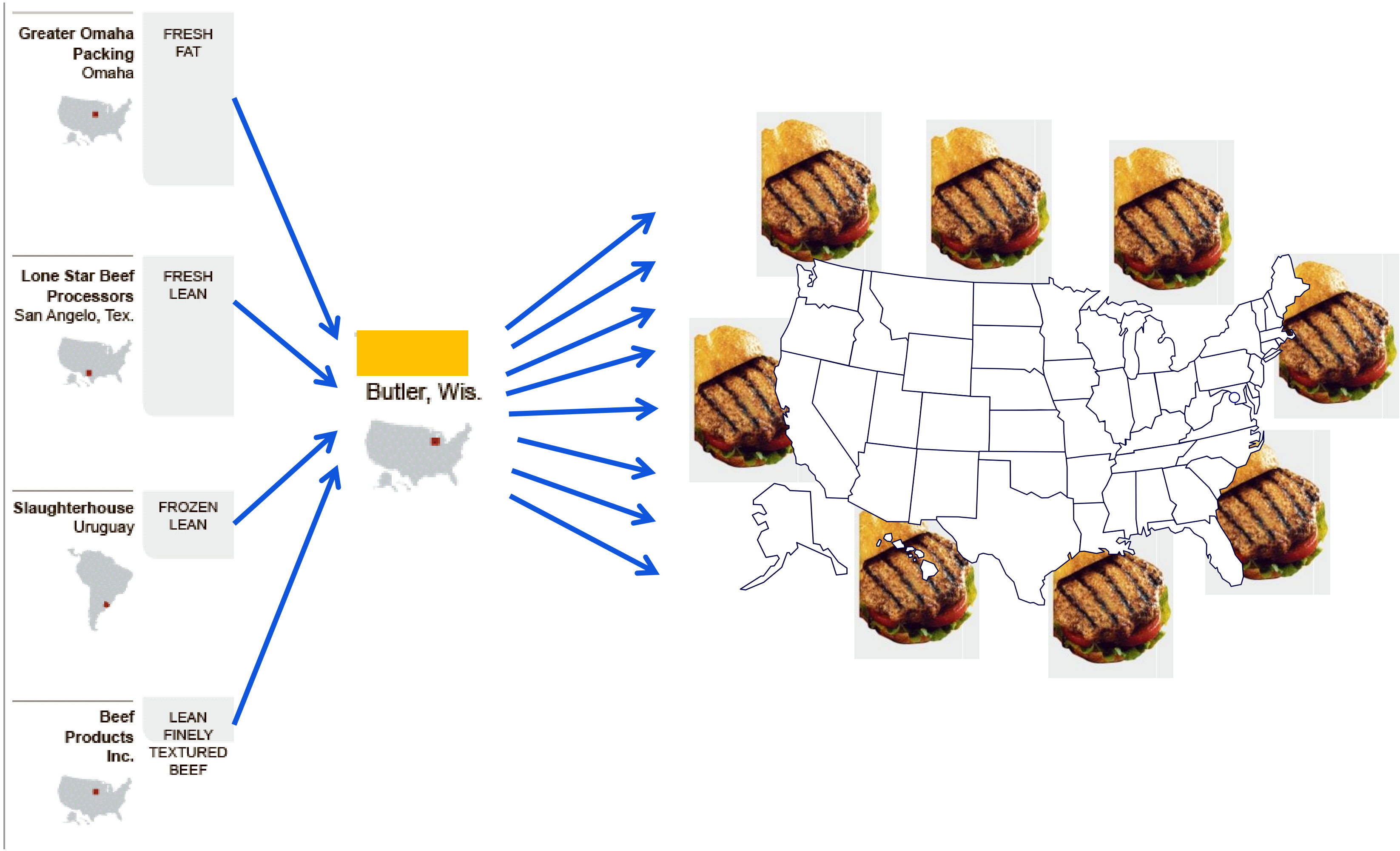
(It's an awesome perspective)

# Why *Listeria monocytogenes*?

- Illness is rare but serious, costly, and commonly outbreak associated
  - Estimated $2.8 billion in annual medical costs and lost productivity ($1.8 million/case)
- Current subtyping methods are not ideal
- Strong epidemiologic surveillance (Listeria Initiative)
- Strong regulatory component
- Listeria genome is fairly small, stable, and relatively easy to sequence and analyze. Most changes in the genome are due to point mutations and not phages.



# The Problem: Detecting Outbreaks in an Increasingly Globalized Food System



Greater Omaha Packing
Omaha

FRESH FAT

Lone Star Beef Processors
San Angelo, Tex.

FRESH LEAN

Slaughterhouse
Uruguay

FROZEN LEAN

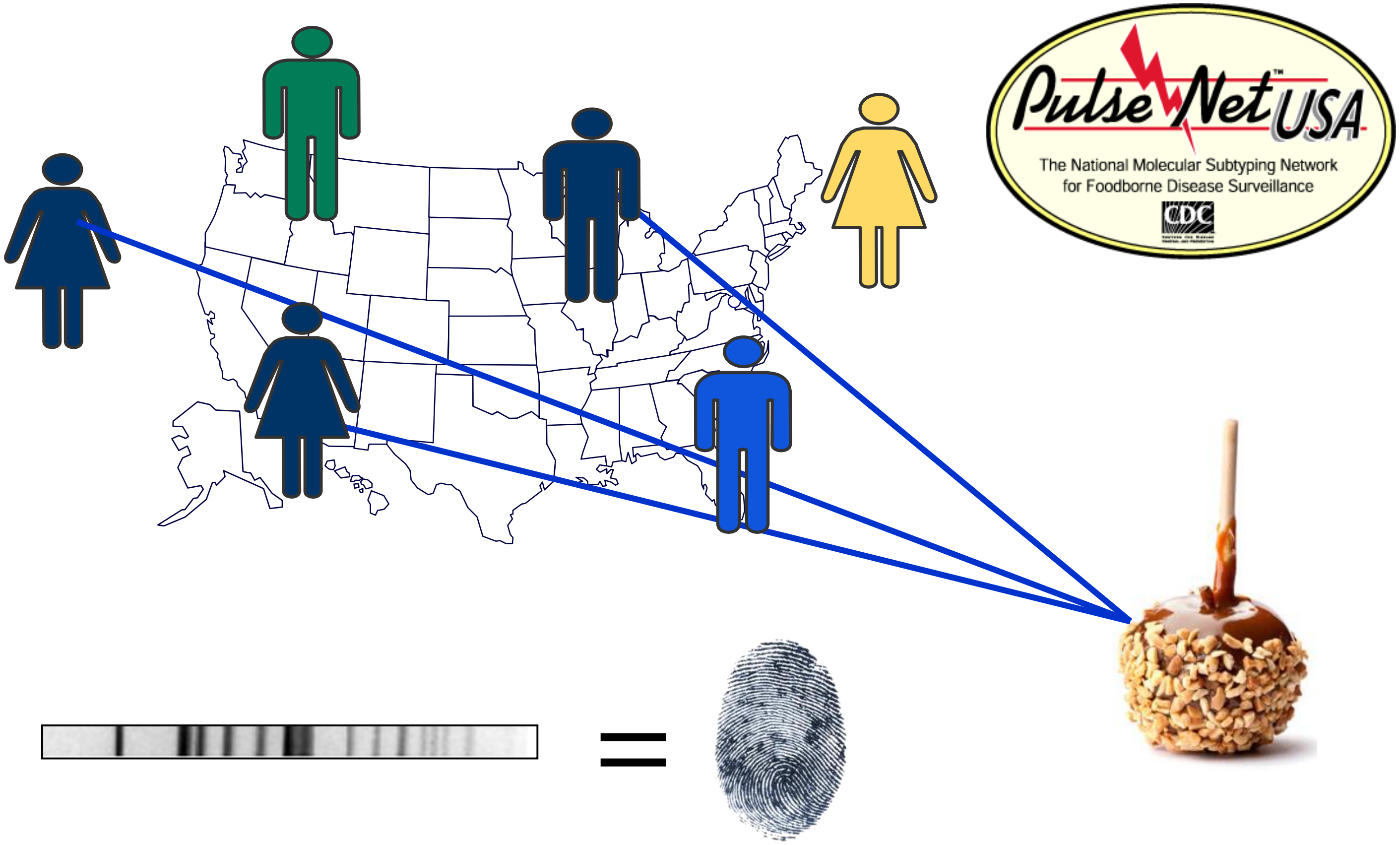
Beef Products Inc.

LEAN FINELY TEXTURED BEEF

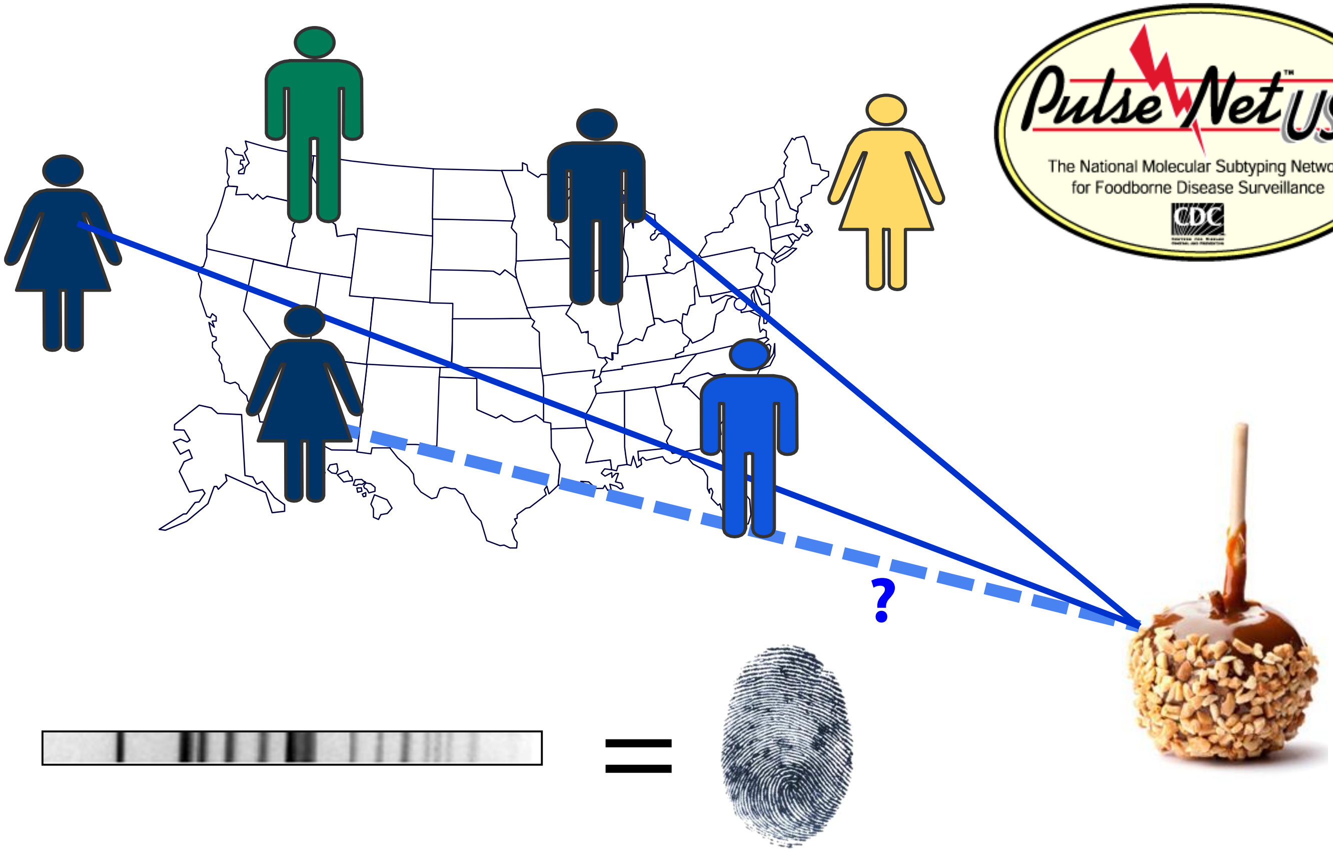
Butler, Wis.

Anatomy of a Burger. New York Times. October 4, 2009
Thanks to Brendan Jackson for letting me borrow this slide

# Limitations of
# Pulsed-Field Gel Electrophoresis (PFGE)


PulseNet USA
The National Molecular Subtyping Network
for Foodborne Disease Surveillance
CDC
=

# Limitation: Genetically Unrelated Isolate Might Appear Same by PFGE

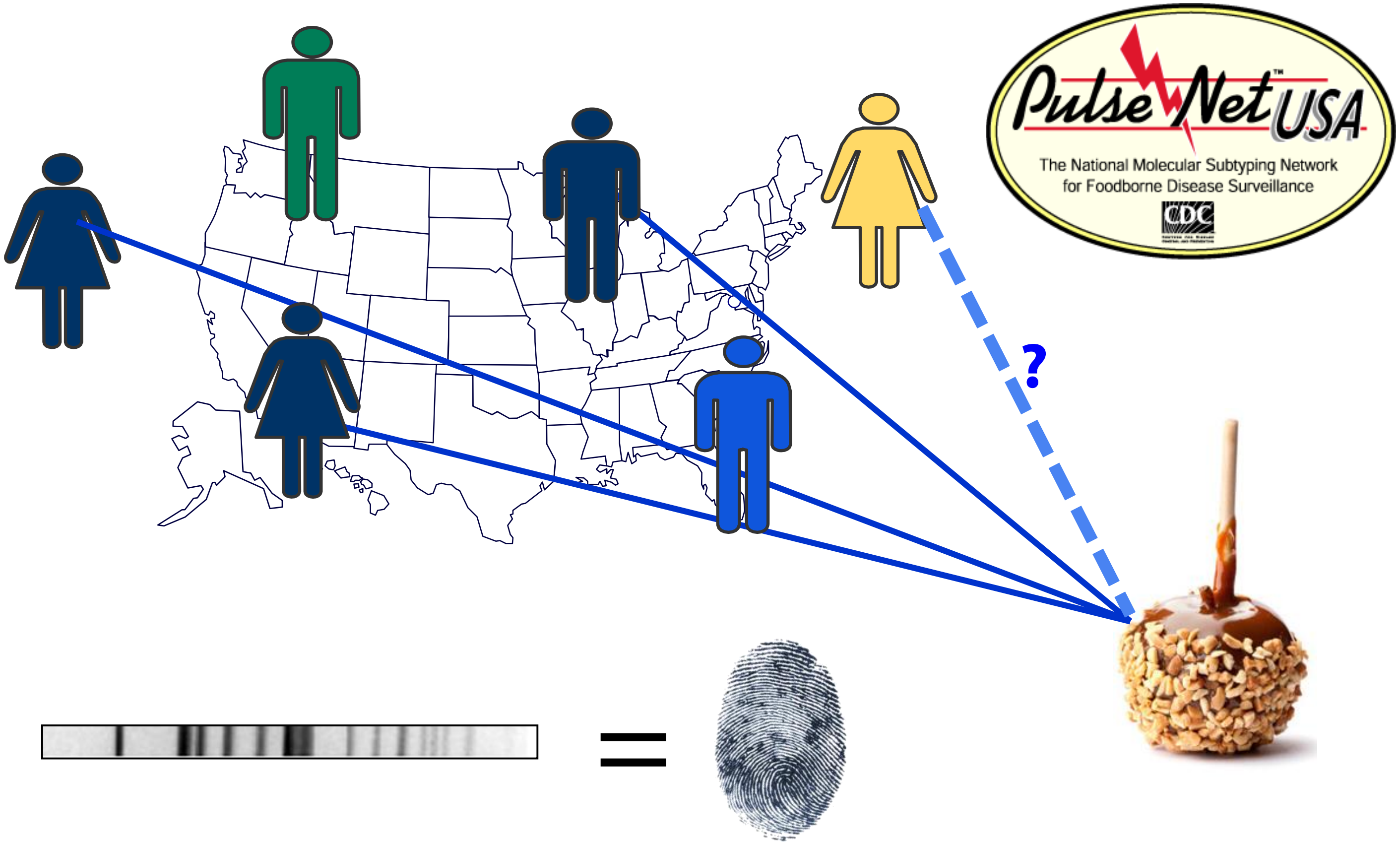


PulseNet USA

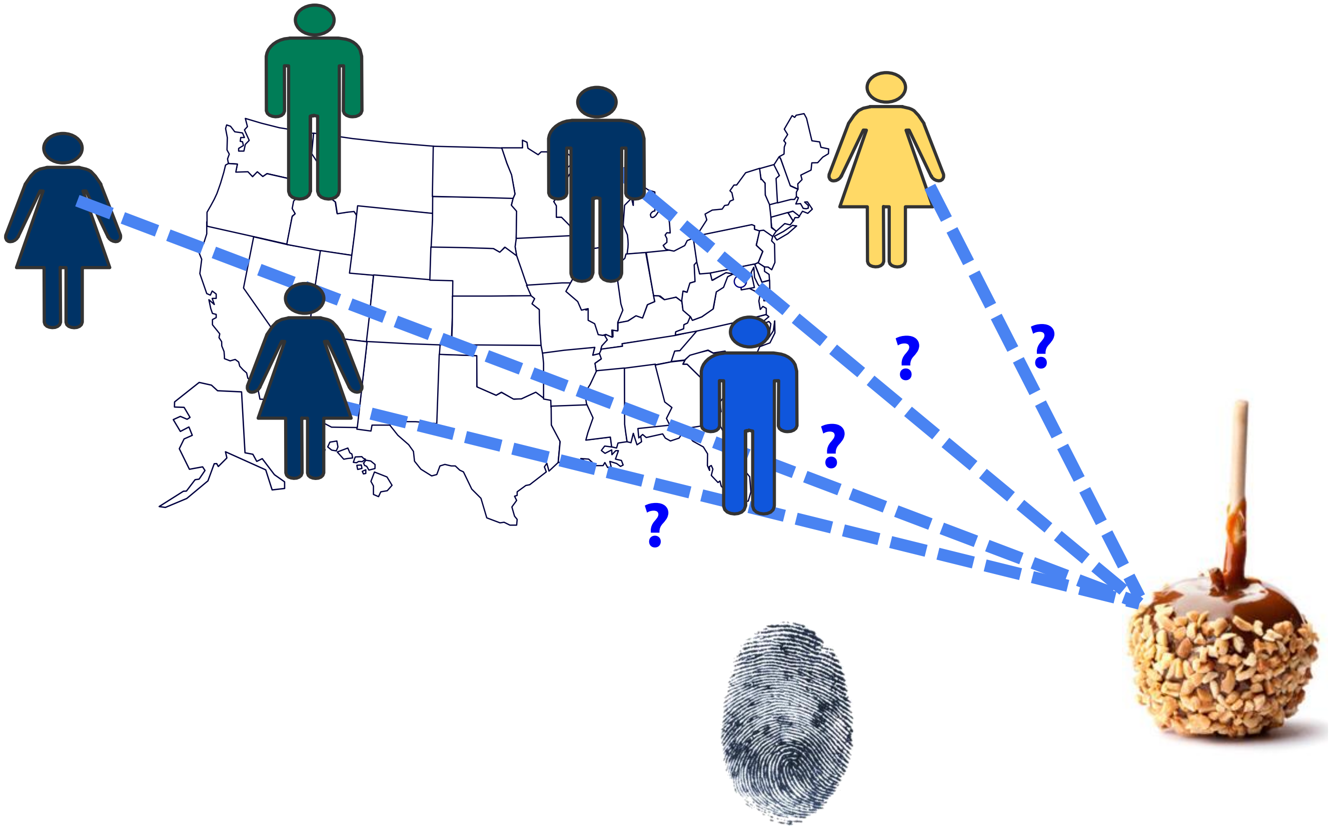
The National Molecular Subtyping Network for Foodborne Disease Surveillance

CDC

# Limitation: Genetically Related Isolate Might Appear Different By PFGE


PulseNet USA
The National Molecular Subtyping Network for Foodborne Disease Surveillance
CDC
?
=

# Can genomics clear up this picture?

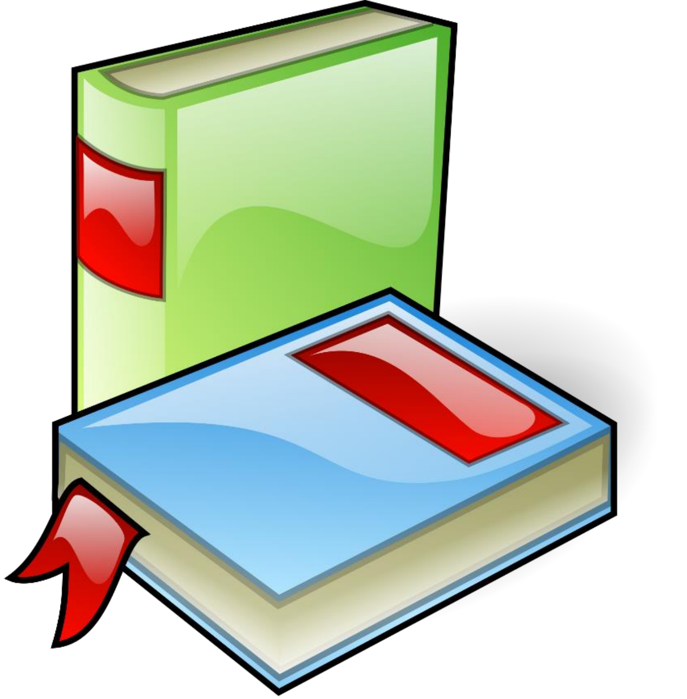


# How do we compare genomes?

# Three major methods we use

- Kmer-based: mile-high view (shredded paper)
- MLST-based: naked eye (book pages)
- SNP-based: microscope (book letters)

- The question in this analogy:
  how similar are these two books?



# kmers

- **Kmer:** a length of DNA *k* nucleotides long

1. Shred all reads in equal sizes *k*
2. How many kmers are in common?
3. Transform into a percentage **

** Known as the jaccard distance

Image credits:
"DEATH OF A SHREDDER"
https://digginginthedriftless.com/2011/01/04/death-of-a-shredder

# Kmers, jaccard distance

**CAAAAAAAAAAAAT** **CAAAAAAAAAAAAG**

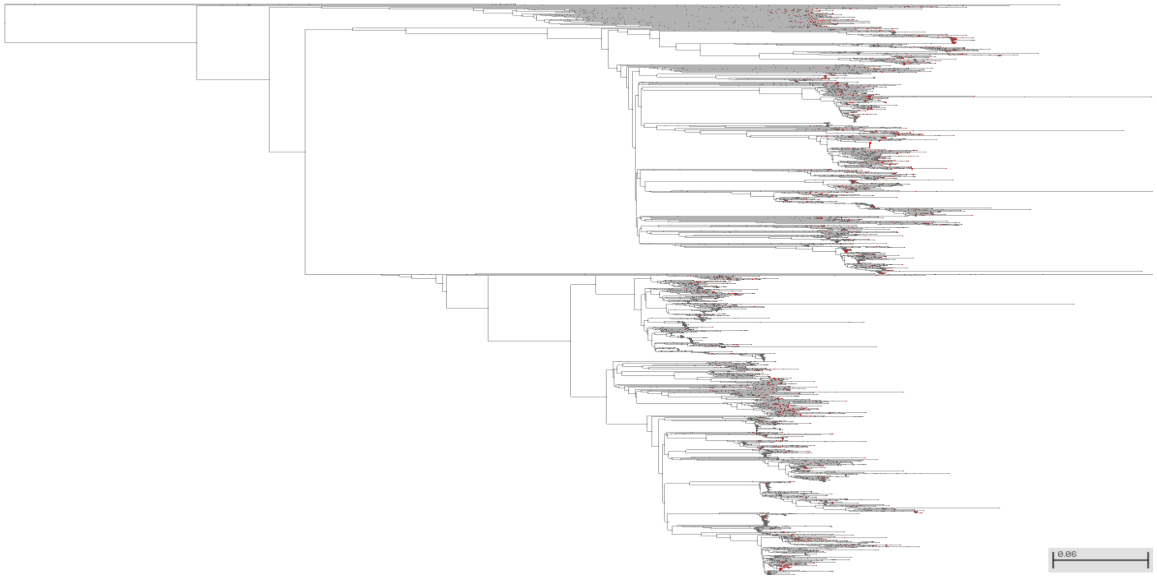
**Here, K=12**

| | | | |
|---|---|---|---|
| CAAAAAAAAAAA | 1 | 1 | CAAAAAAAAAAA |
| AAAAAAAAAAAA | 2 | 2 | AAAAAAAAAAAA |
| AAAAAAAAAAAG | 3 | 4 | AAAAAAAAAAAG |

Two out of four kmers different;
Jaccard distance = 2/4 = 0.5

# Example kmer tree

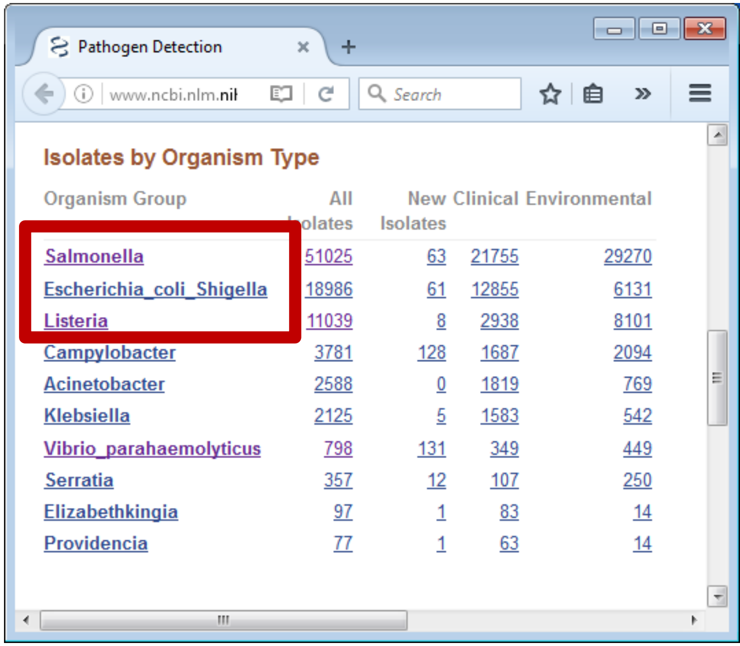
- http://www.ncbi.nlm.nih.gov/pathogens/
- Software: pathogen detection pipeline at NCBI



Mile-high view
7,800 *Listeria monocytogenes* genomes in this tree

# Kmer-based software

- NCBI Pathogen Detection Pipeline
  - Not available for individual use, but the results are comprehensive and public
- Mashtree
  - Based on min-hash, implemented in Mash
- SKA
  - Split Kmer Analysis



### Isolates by Organism Type

| Organism Group | All Isolates | New Isolates | Clinical | Environmental |
|---|---|---|---|---|
| Salmonella | 51025 | 63 | 21755 | 29270 |
| Escherichia_coli_Shigella | 18986 | 61 | 12855 | 6131 |
| Listeria | 11039 | 8 | 2938 | 8101 |
| Campylobacter | 3781 | 128 | 1687 | 2094 |
| Acinetobacter | 2588 | 0 | 1819 | 769 |
| Klebsiella | 2125 | 5 | 1583 | 542 |
| Vibrio_parahaemolyticus | 798 | 131 | 349 | 449 |
| Serratia | 357 | 12 | 107 | 250 |
| Elizabethkingia | 97 | 1 | 83 | 14 |
| Providencia | 77 | 1 | 63 | 14 |

NCBI kmer trees screen shot taken Sept 23, 2016

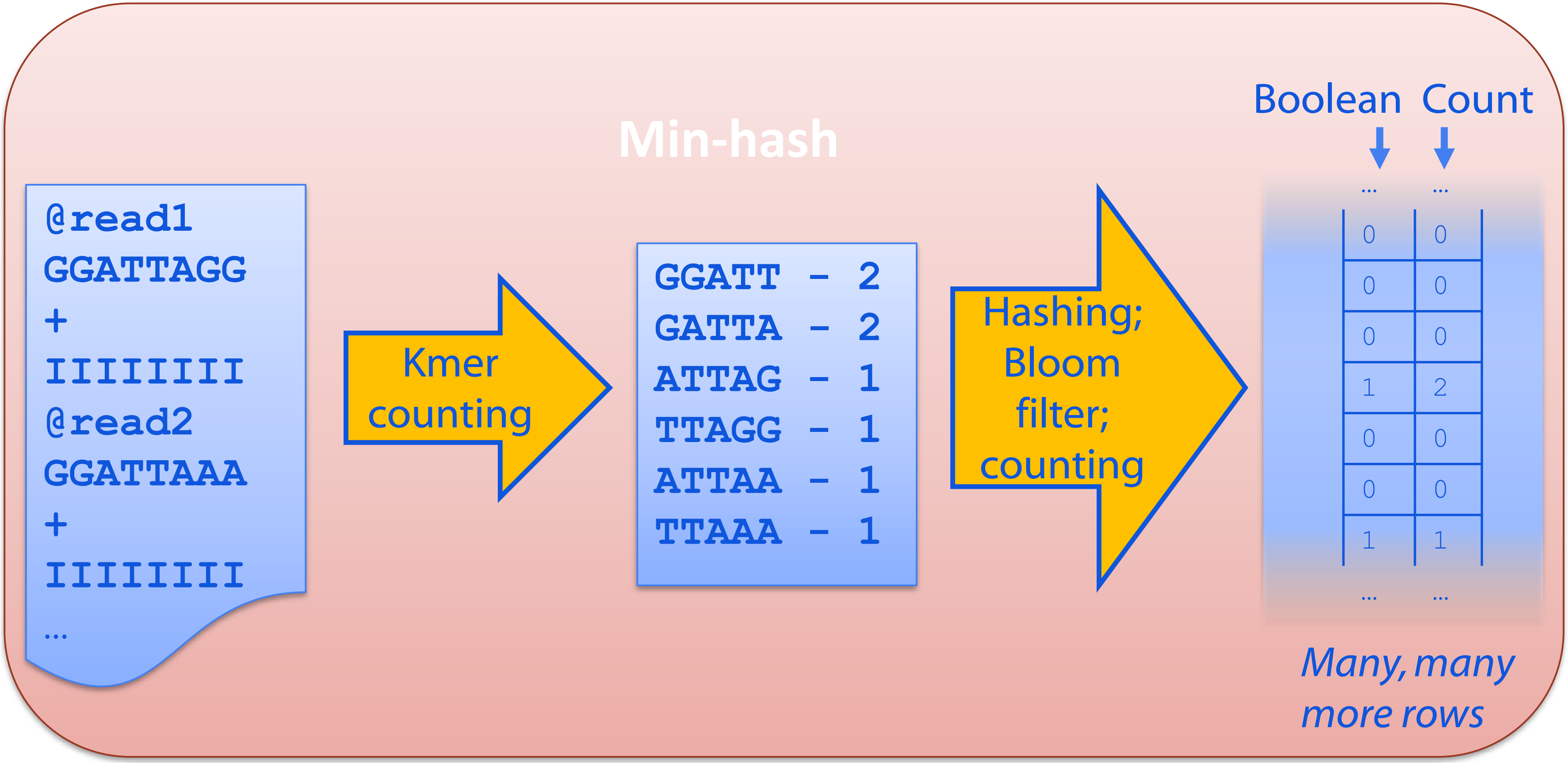
https://www.ncbi.nlm.nih.gov/pathogens

https://github.com/lskatz/mashtree (latest version: 1.0.4; Katz et al 2019, *JOSS*)

https://github.com/simonrharris/SKA/releases (latest version: 1.0)

# How does Mash work?

"Sketch"



Min-hash

```
@read1
GGATTAGG
+
IIIIIIII
@read2
GGATTAAA
+
IIIIIIII
…
```

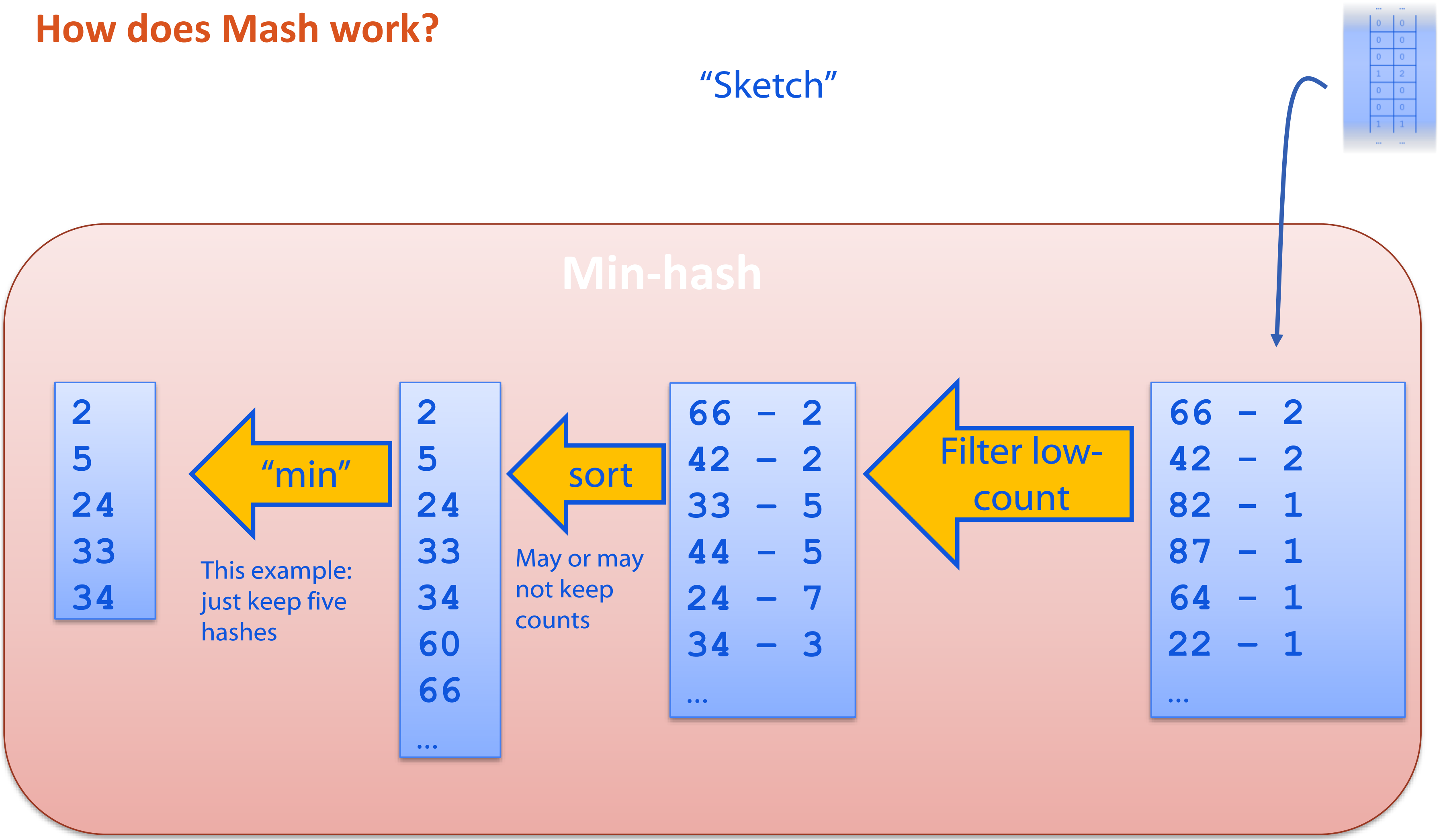
```
GGATT – 2
GATTA – 2
ATTAG – 1
TTAGG – 1
ATTAA – 1
TTAAA – 1
```

| Boolean | Count |
|---|---|
| … | … |
| 0 | 0 |
| 0 | 0 |
| 0 | 0 |
| 1 | 2 |
| 0 | 0 |
| 0 | 0 |
| 1 | 1 |
| … | … |

*Many, many more rows*

Ondov et al, "Mash", Genome Biology. http://genomebiology.biomedcentral.com/articles/10.1186/s13059-016-0997-x

# How does Mash work?



“Sketch”

Min-hash

2
5
24
33
34

“min”

This example: just keep five hashes

2
5
24
33
34
60
66
…

sort

May or may not keep counts

66 – 2
42 – 2
33 – 5
44 – 5
24 – 7
34 – 3
…

Filter low-count

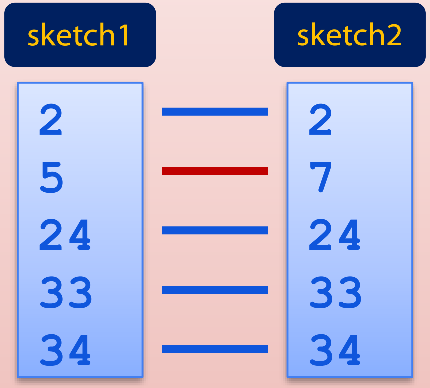
66 – 2
42 – 2
82 – 1
87 – 1
64 – 1
22 – 1
…

Ondov et al, “Mash”, Genome Biology. http://genomebiology.biomedcentral.com/articles/10.1186/s13059-016-0997-x

# How does Mash work?

“Distance” or “dist”

## Min-hash



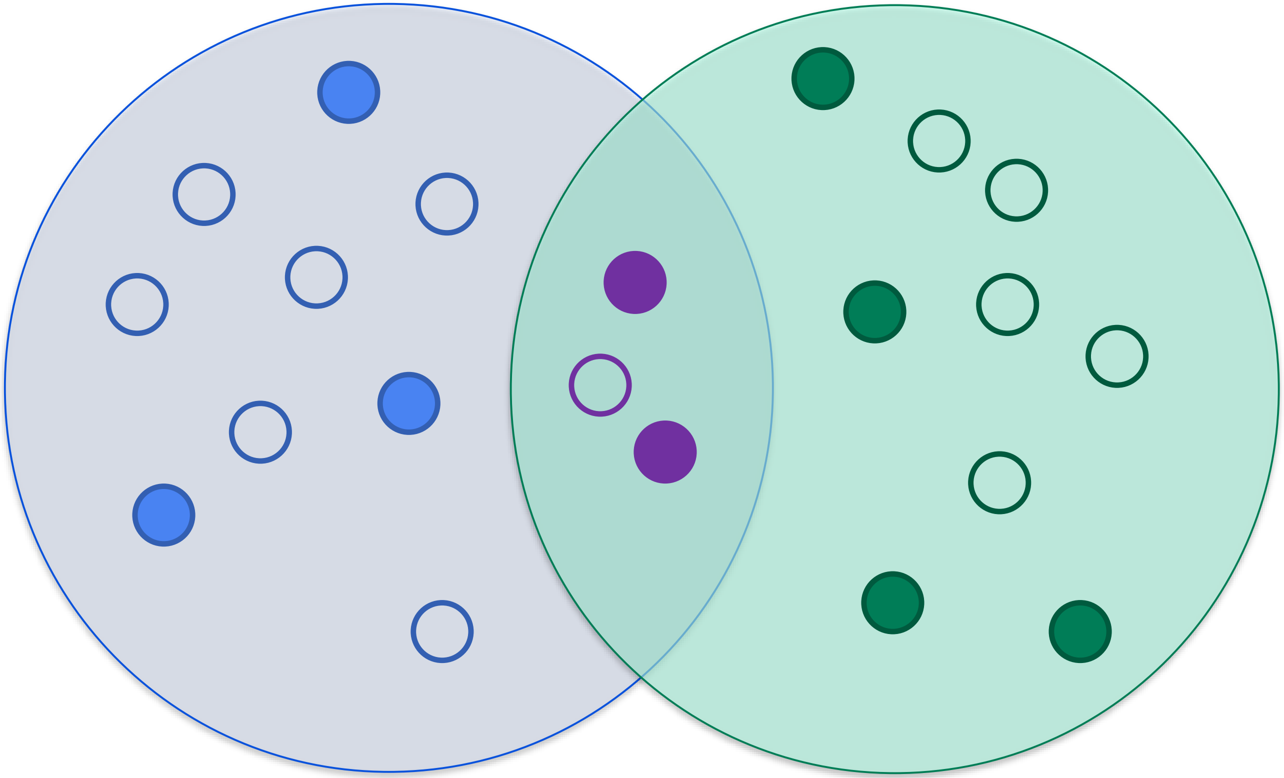
| sketch1 | sketch2 |
|---|---|
| 2 | 2 |
| 5 | 7 |
| 24 | 24 |
| 33 | 33 |
| 34 | 34 |

Six different hashes, two differences.
Jaccard distance = 2/6 = 0.33

The resolution gets better with more hashes.

Ondov et al, “Mash”, Genome Biology. http://genomebiology.biomedcentral.com/articles/10.1186/s13059-016-0997-x

# Min-hash visualization



A = ● + ○

S(A) = ●

B = ● + ○

S(B) = ●

# Mashtree

## What it is and what it isn’t

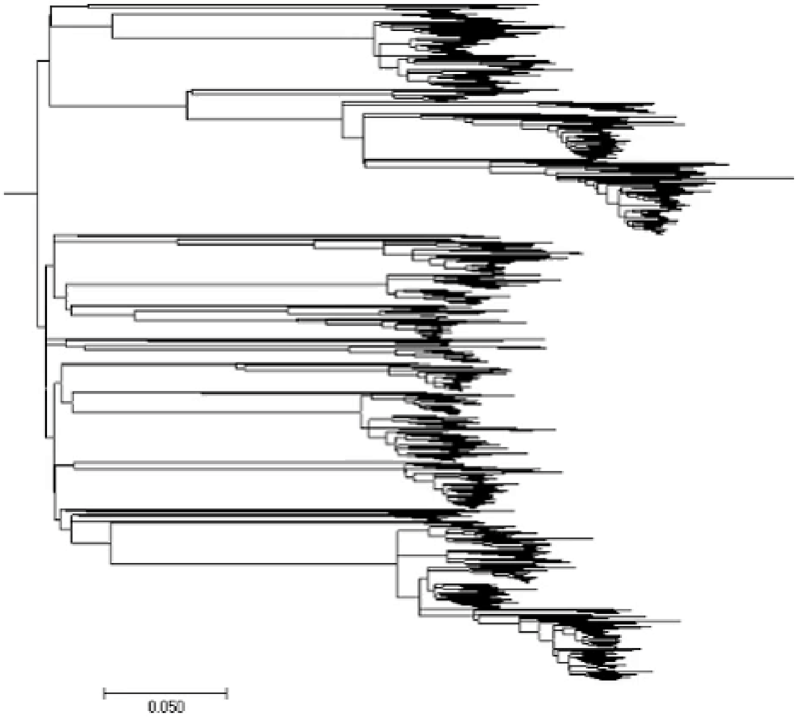
| Is | Isn’t |
|---|---|
| Builds trees | Infers phylogeny |
| Fast | Slow |

## When to use it

| Use it when | Don’t use it when |
|---|---|
| Need fast estimate | Need solid results |
| Need to know a good reference genome | Inferring phylogenetic relatedness |
| Large, diverse dataset | Not diverse or not large dataset |

# Mashtree is fast

- I had a tree of > 1500 genomes and ran Mashtree on the genomes of every clade with fewer than 101 taxa.
- The forward Illumina read of every genome was analyzed.
- Grey shading indicates the range of durations. (next slide)



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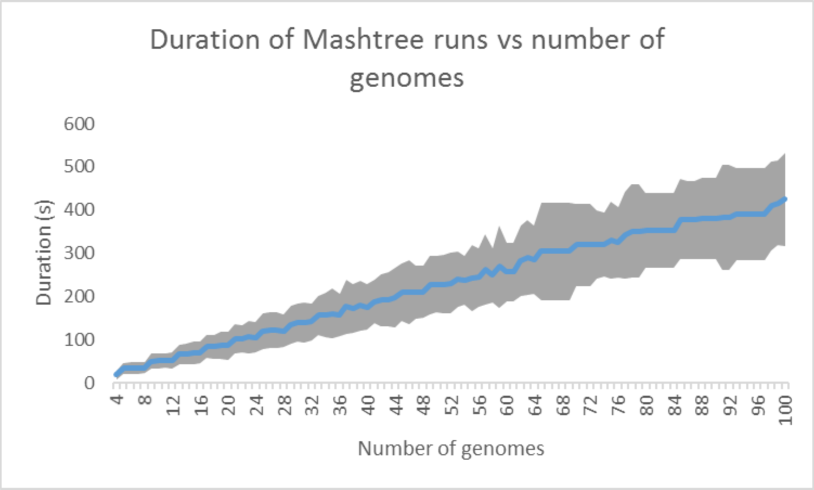
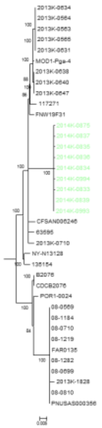
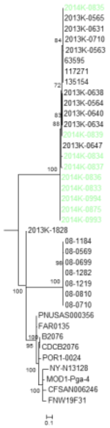


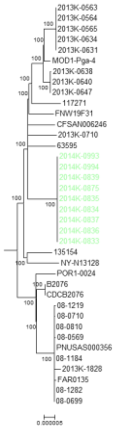
# The Mashtree v0.06 accuracy



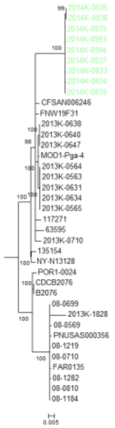
Lyve-SET
Sn = 100%
Sp = 100%



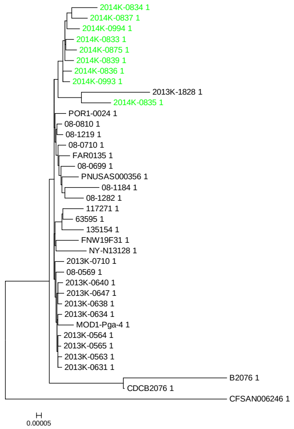
kSNP3
Sn = 100%
Sp = 58%



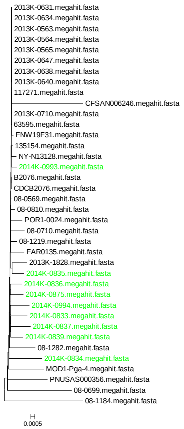
RealPhy
Sn = 100%
Sp = 100%



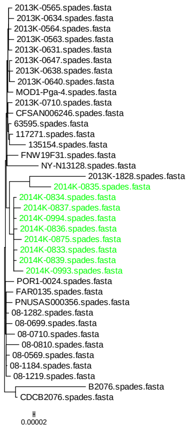
Snp-Pipeline
Sn = 100%
Sp = 100%



Mash v0.06
Raw reads
min_depth: 5x
Sn = 100%
Sp = 97%



Mash v0.06
Megahit asm
59-3141 contigs
Sn = 78%
Sp = 100%



Mash v0.06
SPAdes asm
23-46 contigs
Sn = 100%
Sp = 97%

1409MLJN6-1
$n_{pos} = 9$
$n_{neg} = 29$
Dataset from *Katz et al*, "Lyve-SET", 2017, MGEN

🟩 part of outbreak

# Mashtree is command line

```
# Installation
$ cpanm -L ~ Mashtree
$ export PERL5LIB=$PERL5LIB:$HOME/lib/perl5

# Usage
$ mashtree.pl --help

# Execution
$ mashtree.pl --numcpus 12 --genomesize 4700000 \
  *.fastq.gz \
  [*.fasta] [*.gbk] [*.fasta.gz] [*.gbk.gz] \
  > mashtree.dnd
```

https://github.com/lskatz/mashtree

# MLST

- **MLST:** multilocus sequence typing
- **Locus:** a place in a genome. Plural: **loci**

- Identify a set of loci (genes) in the genome
- Compare each locus in a genome against the set of loci
- Count differences and the number of loci compared

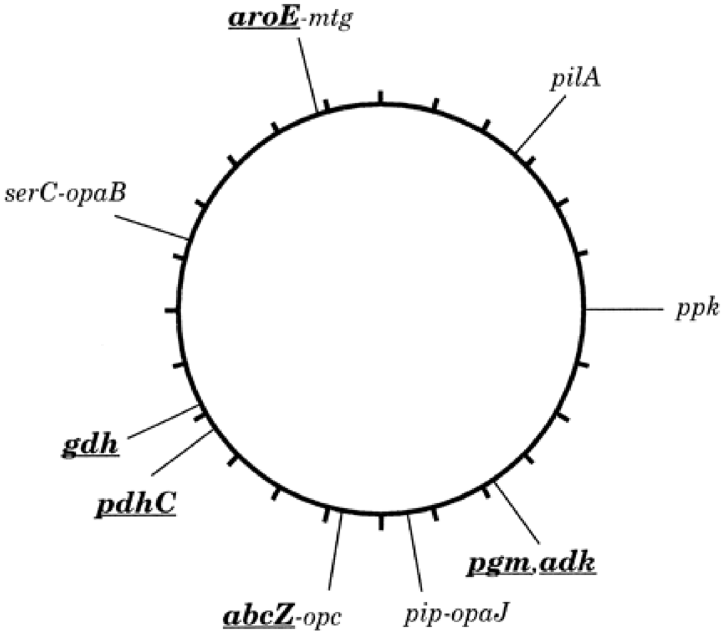
Different kinds

- 7-gene MLST
- wgMLST (whole genome MLST)
- cgMLST (core genome MLST)
- … and more

Image credit: Wikipedia.org
Software: BioNumerics

# 7-gene MLST

- Choose about seven loci in the genome
- Compare all genomes based on these seven loci
- This profile of alleles is called a **sequence type (ST)**

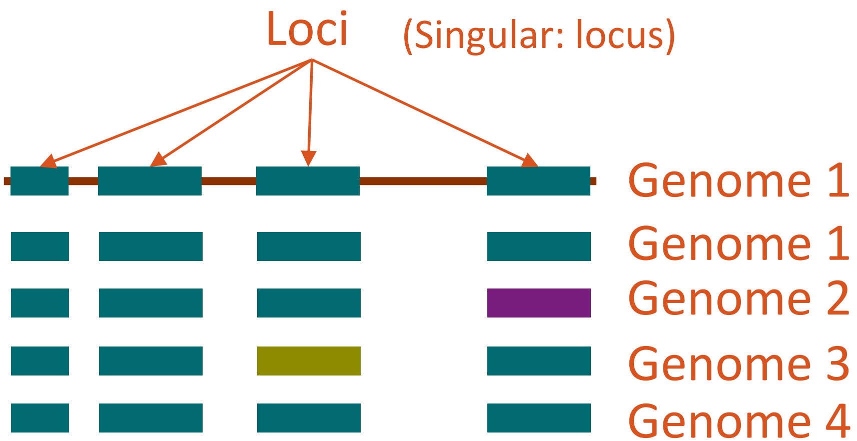


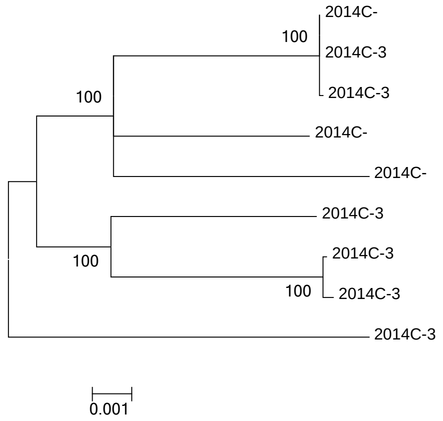
Maiden et al 1998 *PNAS*

# Animation of MLST

0. Assemble the genome
1. Identify the loci
2. Call alleles
3. Compare with other genomes and their alleles
4. Create a phylogeny

- Note: many methods do not require an assembly and these are called **assembly-free methods**.





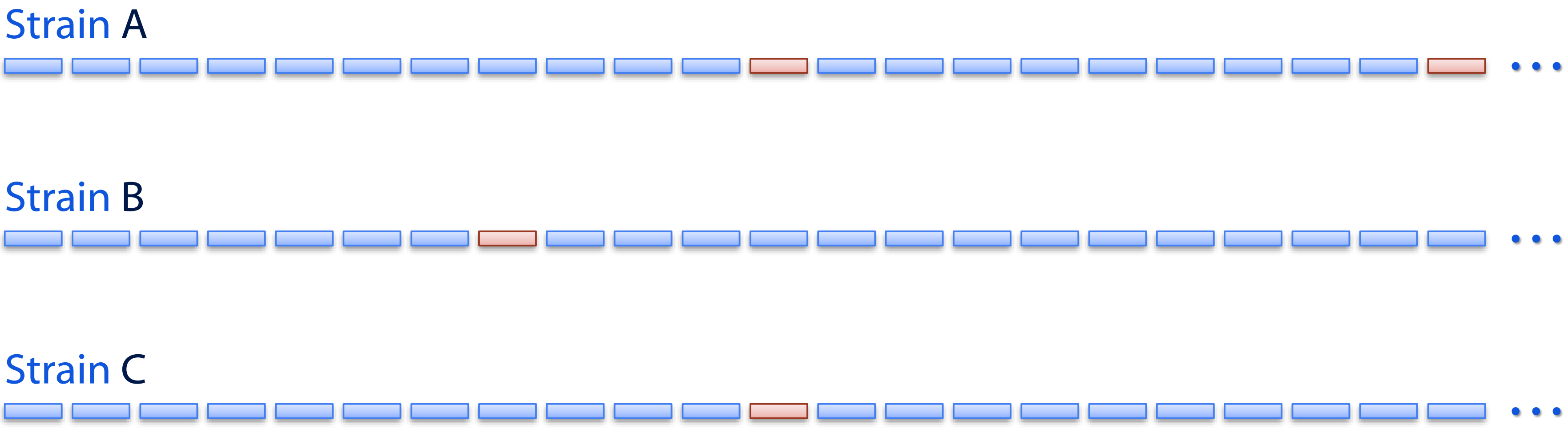
Phylogeny

# Whole-genome MLST

~one locus per 1,000 nucleotides (nt) in the genome.

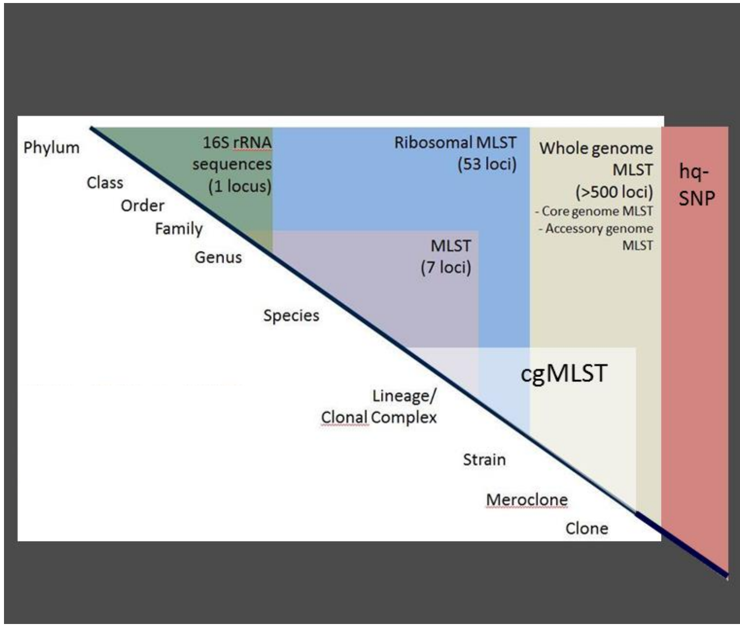
Different species have different sizes

e.g., *L. monocytogenes* has ~3,000,000 nt and ~3,000 loci



# Flavors of multilocus sequence type analysis

- Subsets of genes can be used to identify genus/species and lineage (rMLST/ MLST)
- Core genome MLST are the genes that are in common in vast majority of genomes belonging to a genus species (for Listeria – 1748 genes belong to core and are present in ~98% of isolates tested)

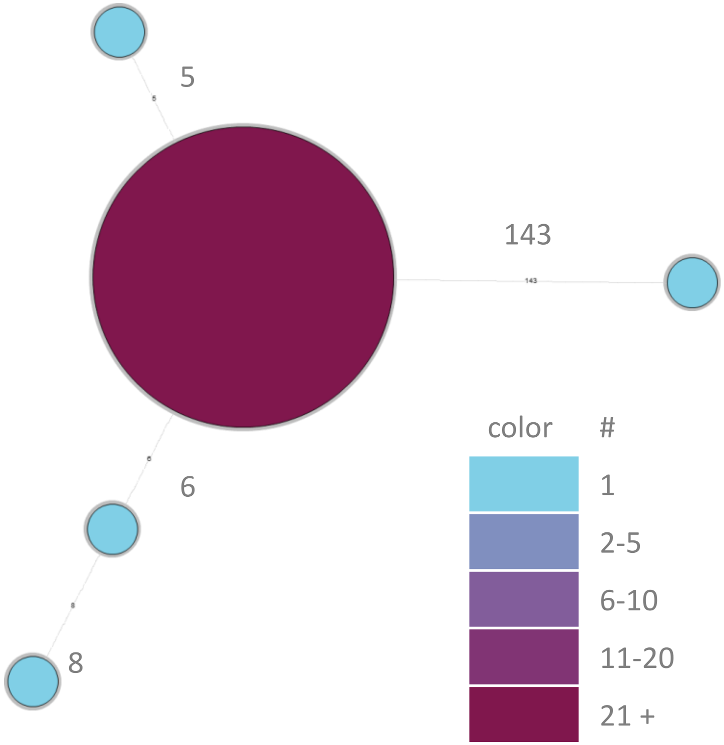


Maiden et al *Nat Rev Microbiol.* 2013 **11:**728-36

# Example wgMLST tree

- Larger circles represent more with the same sequence type (ST)
- 4800 loci represented
- Distances shown on the connecting lines

- The style of tree shown is called a **minimum spanning tree**
- wgMLST can also be displayed in a conventional tree



# MLST software

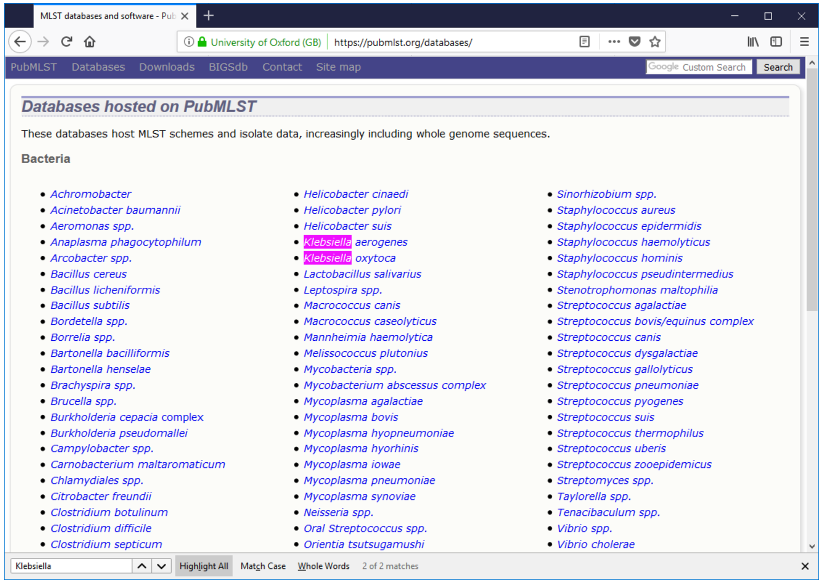
- StringMLST
  - Compare kmers of raw reads against a database
- BioNumerics
  - Graphical user interface
- SRST2, Ariba
  - Map raw reads onto database
- *mlst*
  - BLAST genome assembly against database
- Mentalist
  - Command line, meant for wgMLST schemes

Image taken from http://www.applied-maths.com/applications/wgmlst

For more information: Page et al 2017, “Comparison of Multi-locus Sequence Typing software for next generation sequencing data.”

# MLST Resources

- Main MLST site: https://pubmlst.org/
- BigsDB manual: [http://bigsdb.readthedocs.io/en/latest/concepts.html](http://bigsdb.readthedocs.io/en/latest/concepts.html)
- API: [https://pubmlst.org/rest/](https://pubmlst.org/rest/)
- Also see:
  - [https://enterobase.warwick.ac.uk/](https://enterobase.warwick.ac.uk/)
  - [http://bigsdb.web.pasteur.fr/listeria/](http://bigsdb.web.pasteur.fr/listeria/)

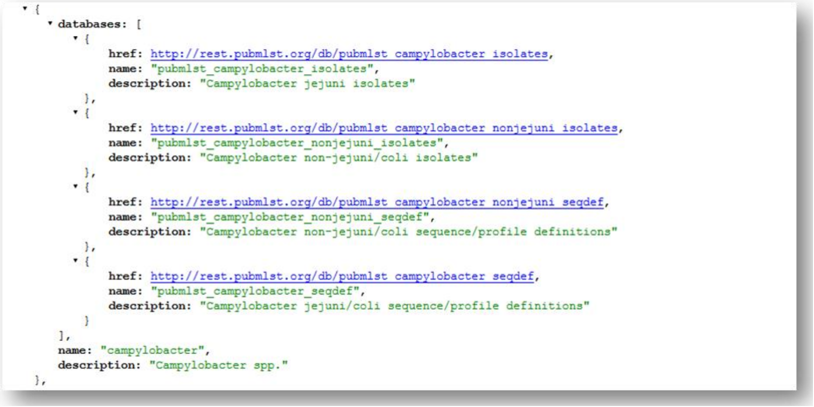


## Databases hosted on PubMLST

These databases host MLST schemes and isolate data, increasingly including whole genome sequences.

**Bacteria**

- *Achromobacter*
- *Acinetobacter baumannii*
- *Aeromonas spp.*
- *Anaplasma phagocytophilum*
- *Arcobacter spp.*
- *Bacillus cereus*
- *Bacillus licheniformis*
- *Bacillus subtilis*
- *Bordetella spp.*
- *Borrelia spp.*
- *Bartonella bacilliformis*
- *Bartonella henselae*
- *Brachyspira spp.*
- *Brucella spp.*
- *Burkholderia cepacia* complex
- *Burkholderia pseudomallei*
- *Campylobacter spp.*
- *Carnobacterium maltaromaticum*
- *Chlamydiales spp.*
- *Citrobacter freundii*
- *Clostridium botulinum*
- *Clostridium difficile*
- *Clostridium septicum*
- *Helicobacter cinaedi*
- *Helicobacter pylori*
- *Helicobacter suis*
- *Klebsiella aerogenes*
- *Klebsiella oxytoca*
- *Lactobacillus salivarius*
- *Leptospira spp.*
- *Macrococcus canis*
- *Macrococcus caseolyticus*
- *Mannheimia haemolytica*
- *Melissococcus plutonius*
- *Mycobacteria spp.*
- *Mycobacterium abscessus complex*
- *Mycoplasma agalactiae*
- *Mycoplasma bovis*
- *Mycoplasma hyopneumoniae*
- *Mycoplasma hyorhinis*
- *Mycoplasma iowae*
- *Mycoplasma pneumoniae*
- *Mycoplasma synoviae*
- *Neisseria spp.*
- *Oral Streptococcus spp.*
- *Orientia tsutsugamushi*
- *Sinorhizobium spp.*
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Staphylococcus haemolyticus*
- *Staphylococcus hominis*
- *Staphylococcus pseudintermedius*
- *Stenotrophomonas maltophilia*
- *Streptococcus agalactiae*
- *Streptococcus bovis/equinus complex*
- *Streptococcus canis*
- *Streptococcus dysgalactiae*
- *Streptococcus gallolyticus*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- *Streptococcus suis*
- *Streptococcus thermophilus*
- *Streptococcus uberis*
- *Streptococcus zooepidemicus*
- *Streptomyces spp.*
- *Taylorella spp.*
- *Tenacibaculum spp.*
- *Vibrio spp.*
- *Vibrio cholerae*



```
▾ {
   ▾ databases: [
      ▾ {
            href: http://rest.pubmlst.org/db/pubmlst_campylobacter_isolates,
            name: "pubmlst_campylobacter_isolates",
            description: "Campylobacter jejuni isolates"
         },
      ▾ {
            href: http://rest.pubmlst.org/db/pubmlst_campylobacter_nonjejuni_isolates,
            name: "pubmlst_campylobacter_nonjejuni_isolates",
            description: "Campylobacter non-jejuni/coli isolates"
         },
      ▾ {
            href: http://rest.pubmlst.org/db/pubmlst_campylobacter_nonjejuni_seqdef,
            name: "pubmlst_campylobacter_nonjejuni_seqdef",
            description: "Campylobacter non-jejuni/coli sequence/profile definitions"
         },
      ▾ {
            href: http://rest.pubmlst.org/db/pubmlst_campylobacter_seqdef,
            name: "pubmlst_campylobacter_seqdef",
            description: "Campylobacter jejuni/coli sequence/profile definitions"
         }
      ],
      name: "campylobacter",
      description: "Campylobacter spp."
   },
```

- Jolley & Maiden 2010, *BMC Bioinformatics* **11**:595
- Jolley *et al.* (2017) *Database* **2017:** bax060

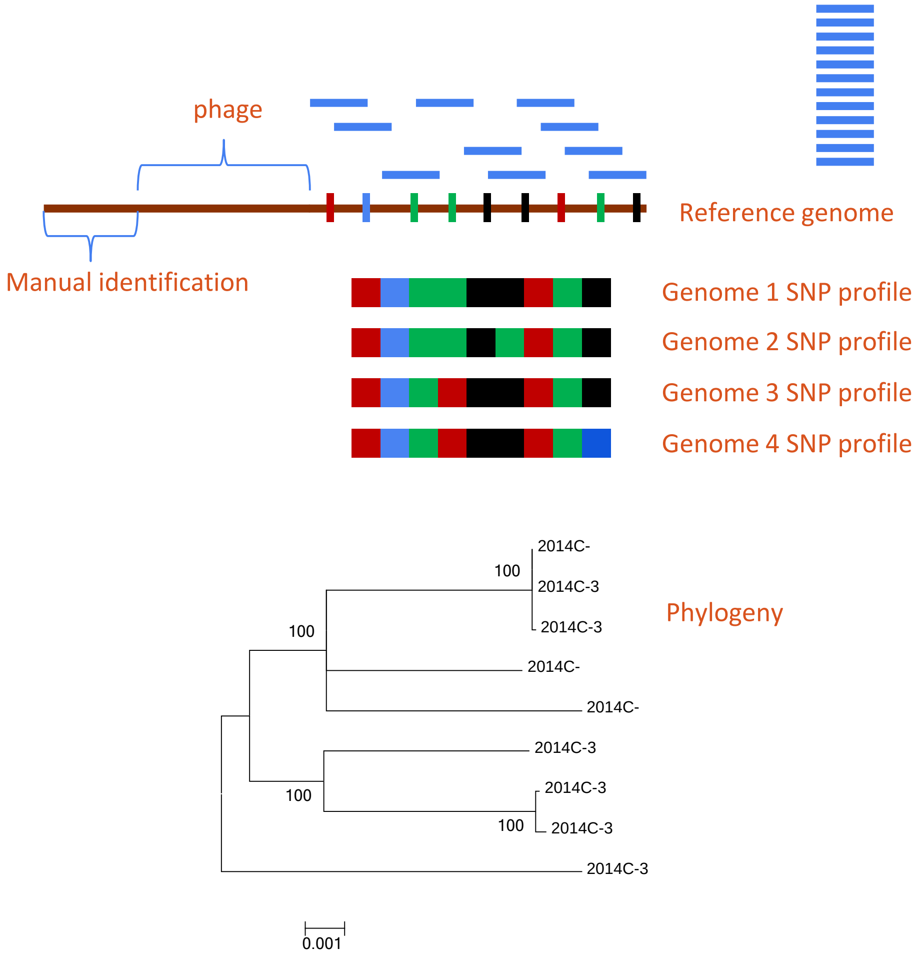
# SNPs

- Compare individual letters in a query genome against the reference genome
- hqSNP: high-quality SNP (ie, high confidence)
- hqSNP indicates some high threshold, e.g.,
- 10x coverage
- 75% consensus

Image taken from geneious.com

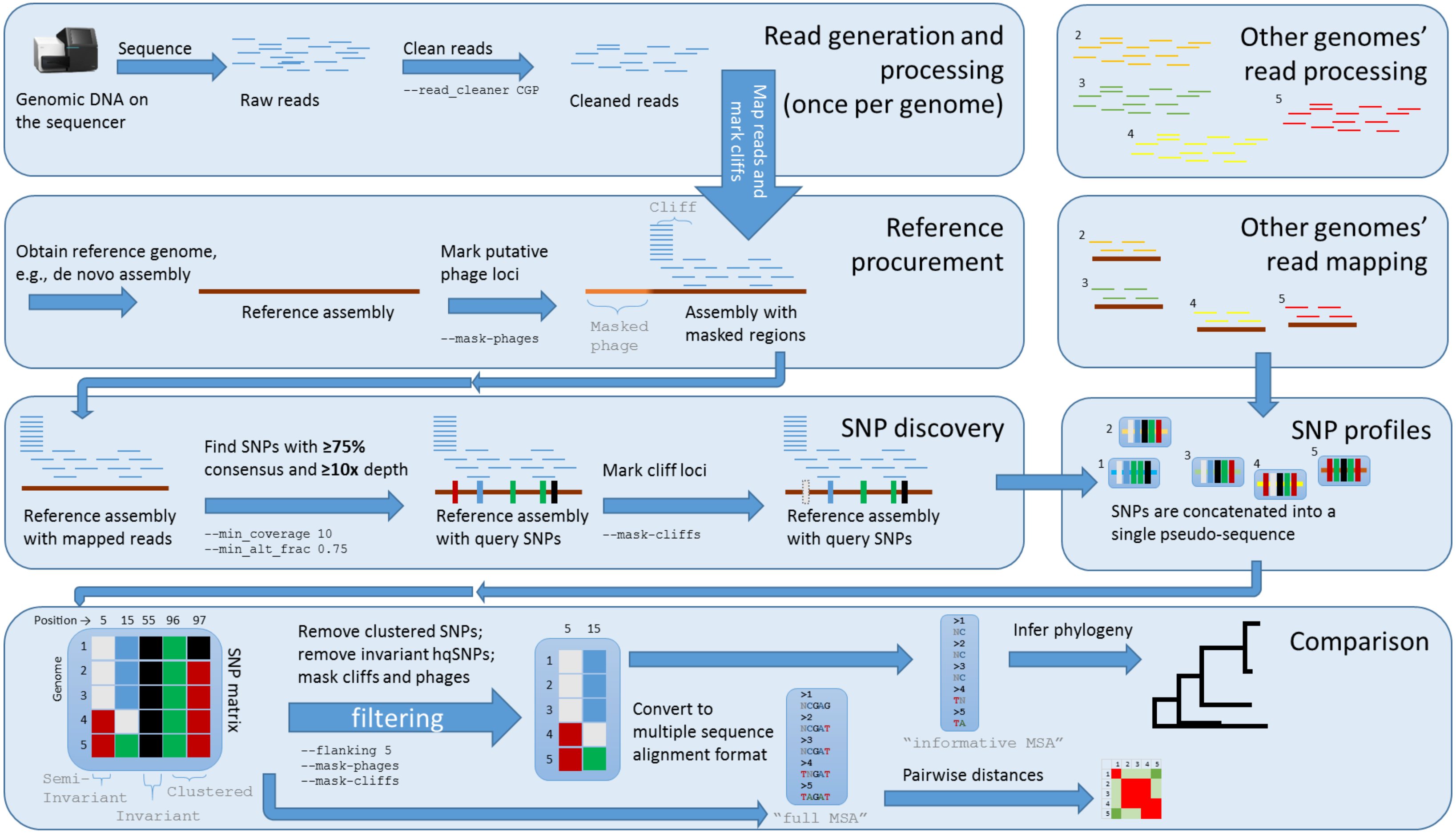
# SNP analysis

0. Pre-processing
   a) Identification of troublesome regions
   b) Read cleaning
1. Mapping
2. SNP calling
   a) % consensus
   b) x depth
   c) Other filters
3. Phylogeny inference



https://github.com/lskatz/lyve-SET
Katz et al. (2017) A comparative analysis of the Lyve-SET phylogenomics pipeline for genomic epidemiology for foodborne pathogens. Frontiers in Microbiology 8: 375.

# More details



Read generation and processing (once per genome)

Sequence

Genomic DNA on the sequencer

Raw reads

Clean reads

```
--read_cleaner CGP
```

Cleaned reads

Map reads and mark cliffs

Other genomes' read processing

Reference procurement

Obtain reference genome, e.g., de novo assembly

Reference assembly

Mark putative phage loci

```
--mask-phages
```

Cliff

Masked phage

Assembly with masked regions

Other genomes' read mapping

SNP discovery

Reference assembly with mapped reads

Find SNPs with **≥75%** consensus and **≥10x** depth

```
--min_coverage 10
--min_alt_frac 0.75
```

Reference assembly with query SNPs

Mark cliff loci

```
--mask-cliffs
```

Reference assembly with query SNPs

SNP profiles

SNPs are concatenated into a single pseudo-sequence

Comparison

Remove clustered SNPs; remove invariant hqSNPs; mask cliffs and phages

filtering

```
--flanking 5
--mask-phages
--mask-cliffs
```

Convert to multiple sequence alignment format

```
>1
NCGAG
>2
NCGAT
>3
NCGAT
>4
TNGAT
>5
TAGAT
```

"full MSA"

```
>1
NC
>2
NC
>3
NC
>4
TN
>5
TA
```

"informative MSA"

Infer phylogeny

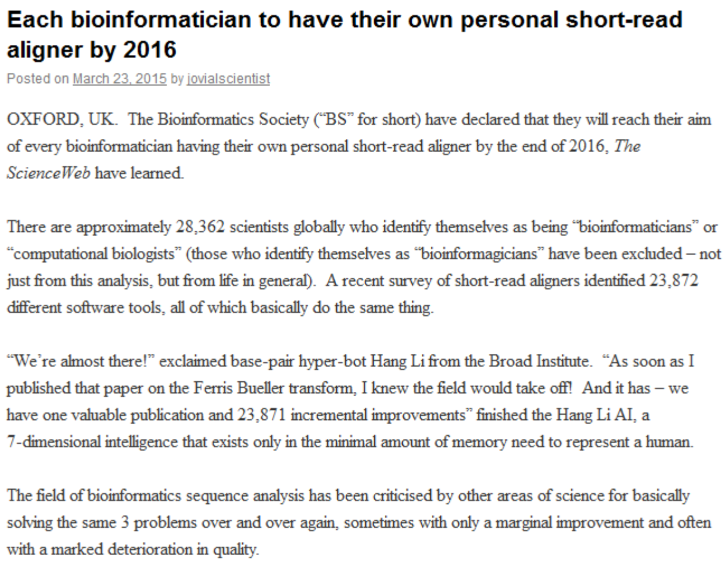
Pairwise distances

https://github.com/lskatz/lyve-SET

Katz et al. (2017) A comparative analysis of the Lyve-SET phylogenomics pipeline for genomic epidemiology for foodborne pathogens. Frontiers in Microbiology 8: 375.

# SNP software

- Lyve-SET
  - Optimized for outbreak surveillance.
- SNP-Pipeline
  - FDA SNP pipeline. Optimized for regulatory workflow. Optimized for speed and accuracy of SNPs.
- SNVPhyl
  - Public Health Agency of Canada. Graphical User Interface in Galaxy.



**Each bioinformatician to have their own personal short-read aligner by 2016**

Posted on March 23, 2015 by jovialscientist

OXFORD, UK. The Bioinformatics Society ("BS" for short) have declared that they will reach their aim of every bioinformatician having their own personal short-read aligner by the end of 2016, *The ScienceWeb* have learned.

There are approximately 28,362 scientists globally who identify themselves as being "bioinformaticians" or "computational biologists" (those who identify themselves as "bioinformagicians" have been excluded – not just from this analysis, but from life in general). A recent survey of short-read aligners identified 23,872 different software tools, all of which basically do the same thing.

"We're almost there!" exclaimed base-pair hyper-bot Hang Li from the Broad Institute. "As soon as I published that paper on the Ferris Bueller transform, I knew the field would take off! And it has – we have one valuable publication and 23,871 incremental improvements" finished the Hang Li AI, a 7-dimensional intelligence that exists only in the minimal amount of memory need to represent a human.

The field of bioinformatics sequence analysis has been criticised by other areas of science for basically solving the same 3 problems over and over again, sometimes with only a marginal improvement and often with a marked deterioration in quality.

https://thescienceweb.wordpress.com/2015/03/23/each-bioinformatician-to-have-their-own-personal-short-read-aligner-by-2016/

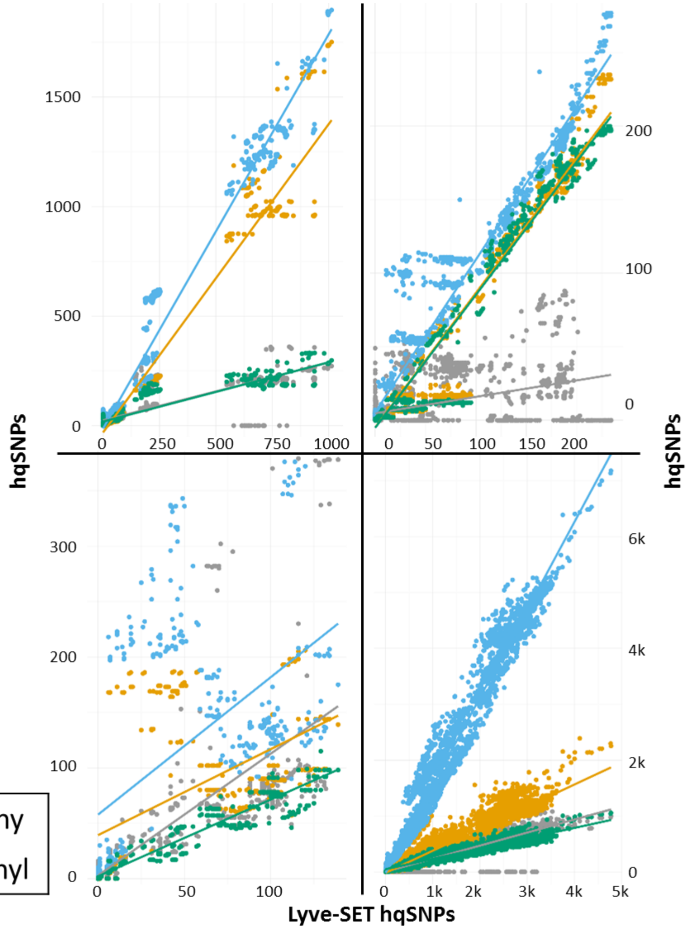
# Installation and sample run

```
$   cd ~/bin/
$   git clone https://github.com/lskatz/lyve-SET
$   cd Lyve-SET
$   git checkout v1.1.4f
$   make install
$   export PATH=$PATH:~/bin/lyve-SET/scripts
#  You may also add this to your bash profile
$   echo >> ~/.bash_profile "export PATH=$PATH:~/bin/lyve-SET/scripts"
$   which launch_set.pl
$   set_test.pl lambda lambda --numcpus 4
# Takes about two minutes
$   ls lambda/msa/tree.dnd
```

# Comparison of Lyve-SET with other SNP pipelines

| *L. monocytogenes* | | |
|---|---|---|
| **Pipeline** | **y=mx+b** | **$R^2$** |
| kSNP | y=0.26+24 | 0.69 |
| RealPhy | y=1.14+31 | 0.96 |
| SNP-Pipeline | y=1.8x-13 | 0.97 |
| SNVPhyl | y=0.27x+19 | 0.58 |

| *S. enterica* | | |
|---|---|---|
| **Pipeline** | **y=mx+b** | **$R^2$** |
| kSNP | y=0.11x+4.7 | 0.23 |
| RealPhy | y=0.92x-5 | 0.95 |
| SNP-Pipeline | y=1.0x+5.4 | 0.96 |
| SNVPhyl | y=0.91-5.1 | 0.94 |



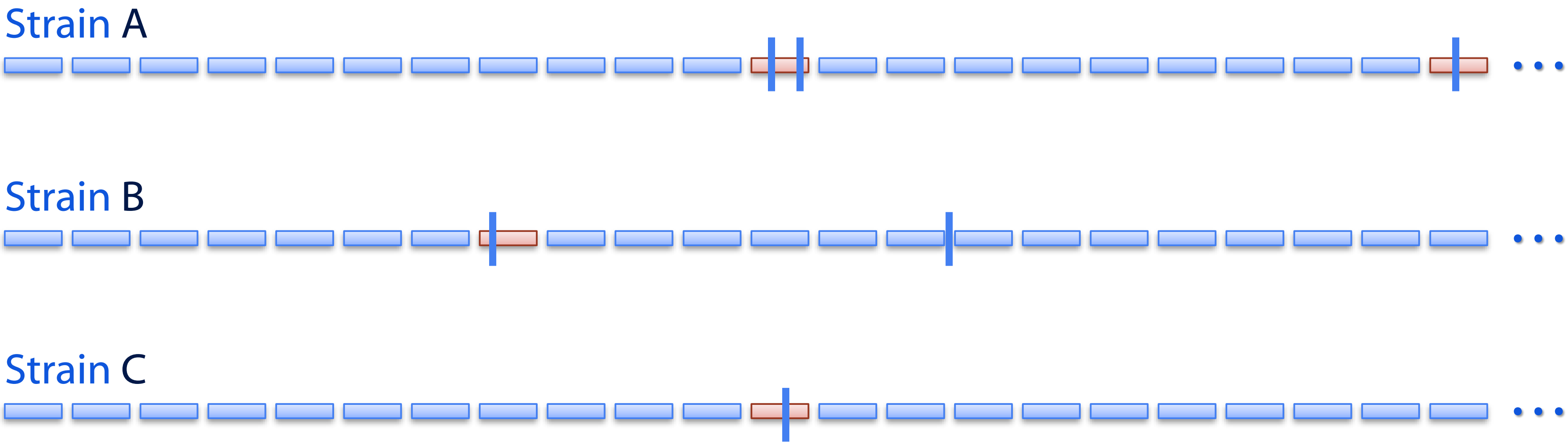
| *E. coli* | | |
|---|---|---|
| **Pipeline** | **y=mx+b** | **$R^2$** |
| kSNP | y=1.1x+2.9 | 0.43 |
| RealPhy | y=0.78+39 | 0.27 |
| SNP-Pipeline | y=1.2x+58 | 0.3 |
| SNVPhyl | y=0.69x+2.1 | 0.92 |

| *C. jejuni* | | |
|---|---|---|
| **Pipeline** | **y=mx+b** | **$R^2$** |
| kSNP | y=0.23x+4 | 0.89 |
| RealPhy | y=0.4x-15 | 0.88 |
| SNP-Pipeline | y=1.6x-17 | 0.97 |
| SNVPhyl | y=0.18+49 | 0.92 |

● kSNP ● RealPhy
● SNP-Pipeline ● SNVPhyl

Each data point is a SNP distance as determined by Lyve-SET (x-axis) and the distance of an alternative SNP pipeline (y-axis). The slope indicates the number of SNPs per Lyve-SET SNP.

# SNPs overlayed on MLST loci

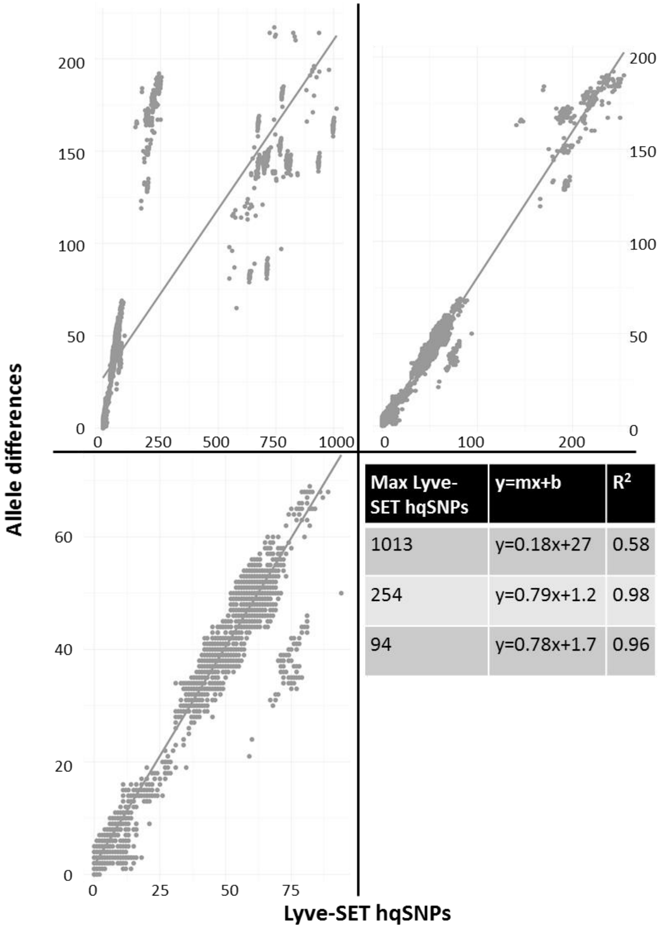


Strain A

Strain B

Strain C

# Comparison with whole-genome MLST (Listeria monocytogenes only)



| Max Lyve-SET hqSNPs | y=mx+b | $R^2$ |
|---|---|---|
| 1013 | y=0.18x+27 | 0.58 |
| 254 | y=0.79x+1.2 | 0.98 |
| 94 | y=0.78x+1.7 | 0.96 |

Katz et al 2017, *Lyve-SET*, Frontiers in Microbiology.

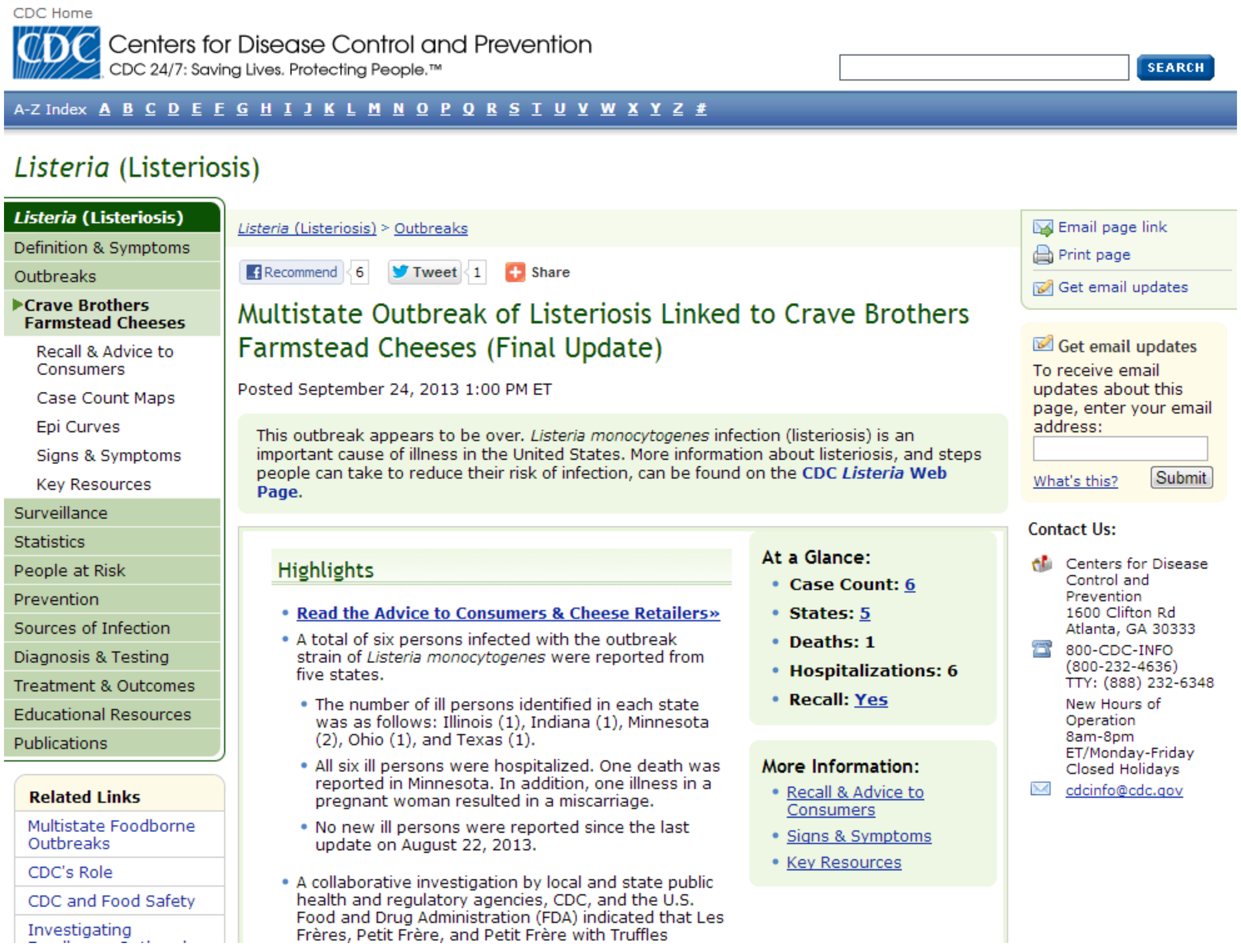
# Which algorithm should you use?

| | Kmer-based | wgMLST | hqSNP |
|---|---|---|---|
| Diversity | ✓✓ | ✓ | ✗✗ |
| Outbreak-level resolution | ✗ | ✓✓ | ✓✓ |
| Further genomic information | ✗ | ✓ | ✓ |
| Minimal upfront effort | ✓ | ✗✗ | ✓ |
| Fast | ✓✓ | ✓✓ | ✗ |
| Easy to use for anyone | ✗ | ✓ | ✗ |

# Fun examples

More information can be found in the virtual lab talk given on Jan 7, 2019: https://youtu.be/YPnU63Le53Y?t=1234

# Multistate outbreak of farmstead cheeses



## *Listeria* (Listeriosis)

### Multistate Outbreak of Listeriosis Linked to Crave Brothers Farmstead Cheeses (Final Update)

Posted September 24, 2013 1:00 PM ET

This outbreak appears to be over. *Listeria monocytogenes* infection (listeriosis) is an important cause of illness in the United States. More information about listeriosis, and steps people can take to reduce their risk of infection, can be found on the **CDC *Listeria* Web Page**.

#### Highlights

- **Read the Advice to Consumers & Cheese Retailers»**
- A total of six persons infected with the outbreak strain of *Listeria monocytogenes* were reported from five states.
  - The number of ill persons identified in each state was as follows: Illinois (1), Indiana (1), Minnesota (2), Ohio (1), and Texas (1).
  - All six ill persons were hospitalized. One death was reported in Minnesota. In addition, one illness in a pregnant woman resulted in a miscarriage.
  - No new ill persons were reported since the last update on August 22, 2013.
- A collaborative investigation by local and state public health and regulatory agencies, CDC, and the U.S. Food and Drug Administration (FDA) indicated that Les Frères, Petit Frère, and Petit Frère with Truffles

**At a Glance:**

- **Case Count: 6**
- **States: 5**
- **Deaths: 1**
- **Hospitalizations: 6**
- **Recall: Yes**

**More Information:**

- Recall & Advice to Consumers
- Signs & Symptoms
- Key Resources

Get email updates

To receive email updates about this page, enter your email address:

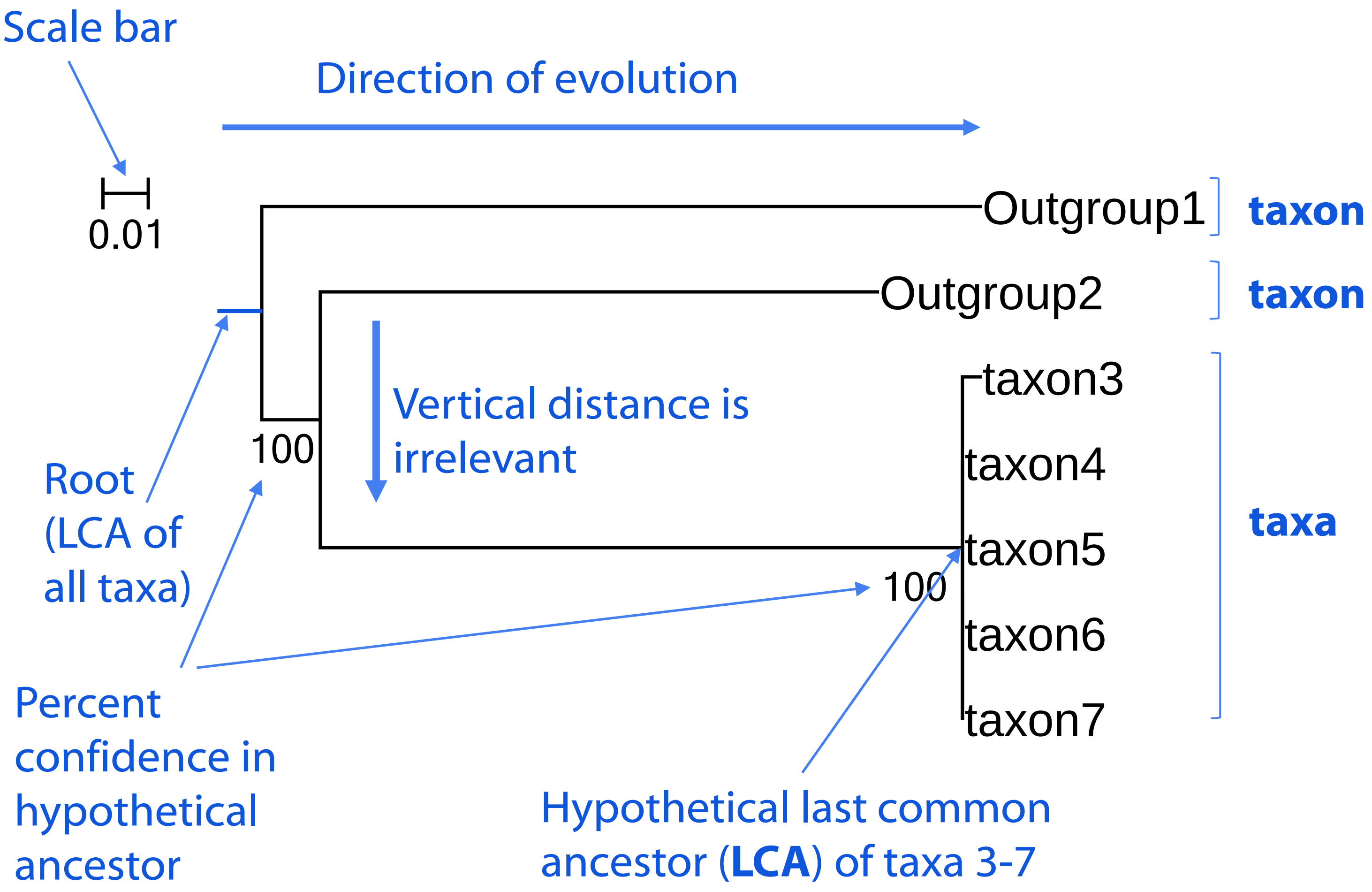
**Contact Us:**

Centers for Disease Control and Prevention
1600 Clifton Rd
Atlanta, GA 30333

800-CDC-INFO
(800-232-4636)
TTY: (888) 232-6348
New Hours of Operation
8am-8pm ET/Monday-Friday
Closed Holidays

cdcinfo@cdc.gov

# How to read a phylogeny


Scale bar
Direction of evolution
0.01
Outgroup1
taxon
Outgroup2
taxon
taxon3
Vertical distance is irrelevant
100
taxon4
taxa
Root (LCA of all taxa)
taxon5
100
taxon6
Percent confidence in hypothetical ancestor
taxon7
Hypothetical last common ancestor (**LCA**) of taxa 3-7

# 2013 outbreak linked to farmstead cheese

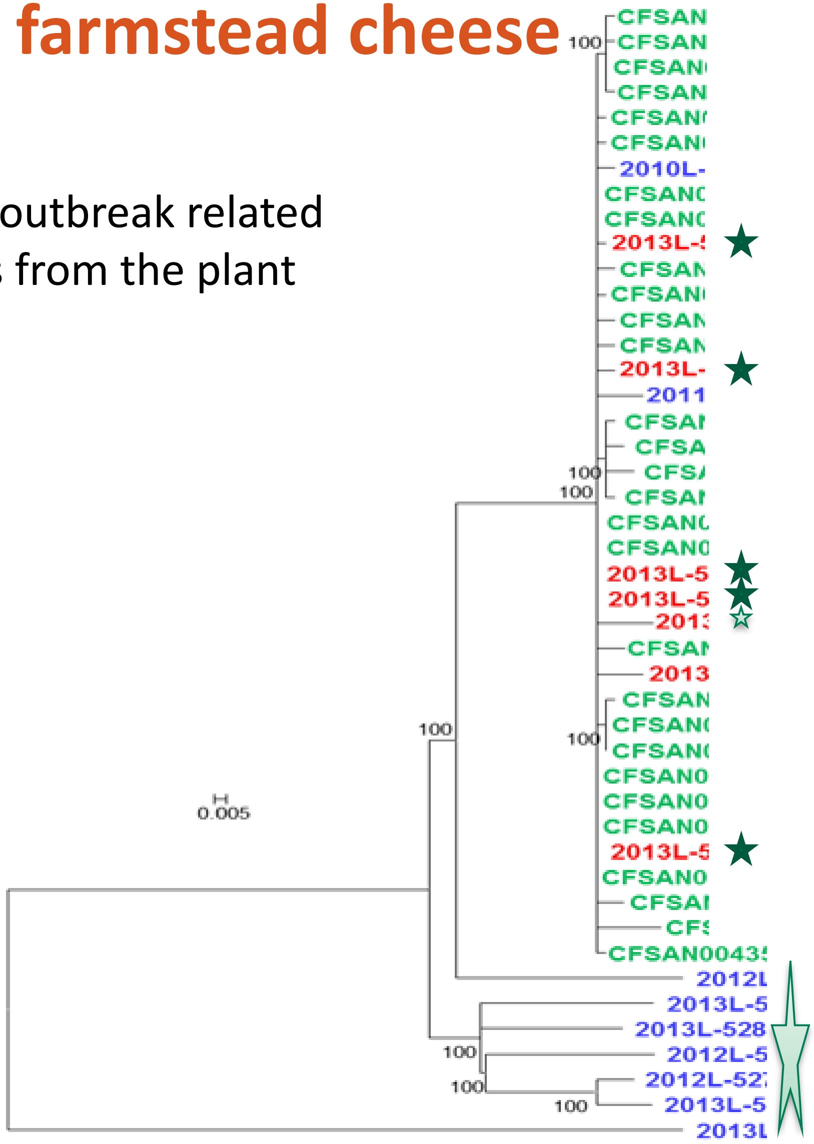
Red= epi-related clinical isolates

Blue= retrospective clinical cases or not outbreak related

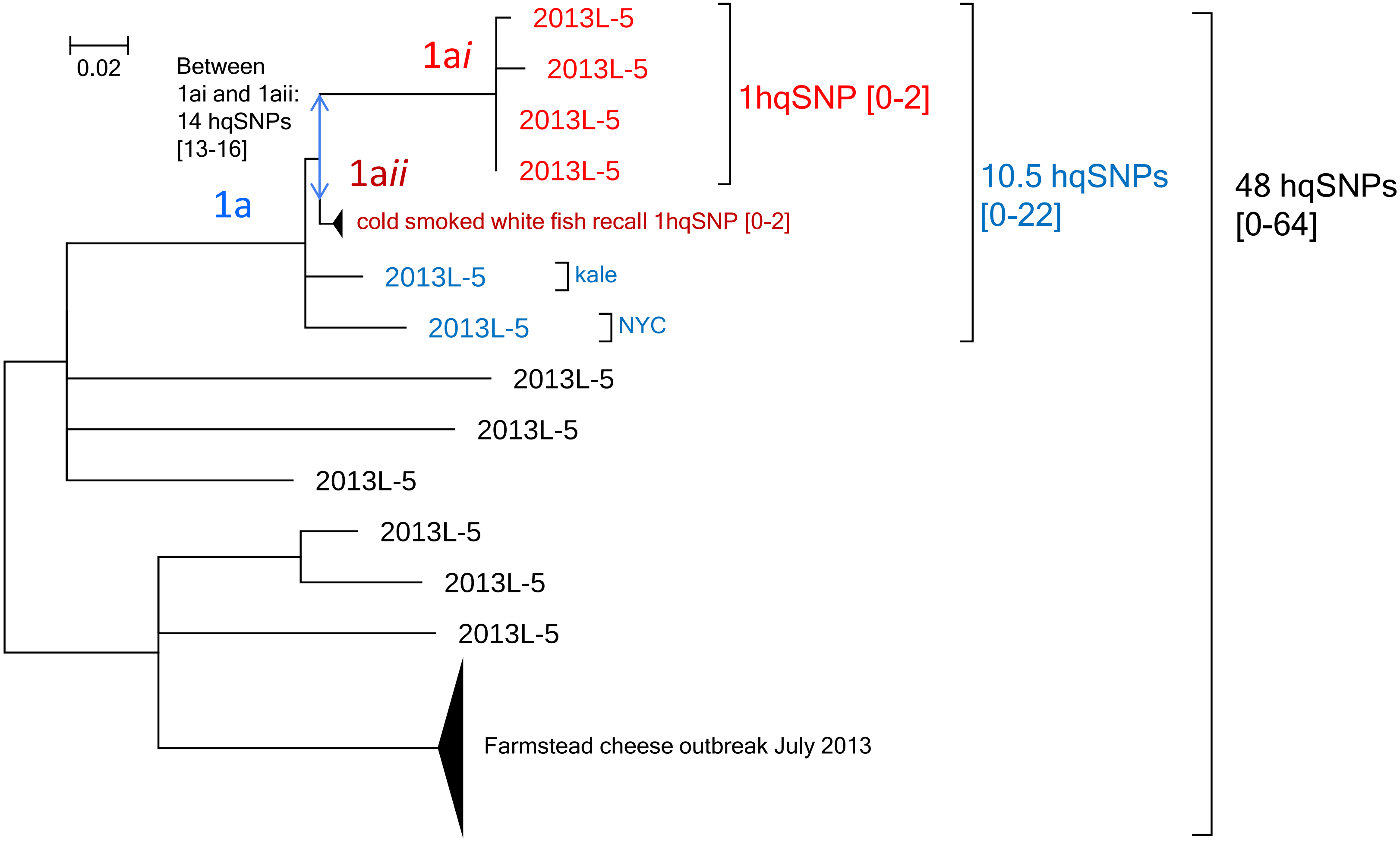
Green= historical environmental isolates from the plant

★ Exposure

☆ No Exposure



# Phylogenetically related outbreak of unknown etiology, December 2013



# In conclusion

- **WGS provides high resolution**
- **We have many tools for differing levels of resolution**
- **We can and have used it on outbreak investigations**

# Micro Binfie Podcast

**Your Hosts**

Lee Katz (CDC)
Andrew Page (QIB)
Nabil Alikhan (QIB)

Microbial Bioinformatics is a rapidly changing field marrying computer science and microbiology. Join us as we share some tips and tricks we've learnt over the years.

If you're getting to grips to the field, or someone who wants to keep tabs on the latest and greatest - this podcast is for you.

Most popular tracks

1. Writing good bioinformatics software with Torsten Seemann
2. Wham BAM, thank you SAM
3. History of Genotyping
4. History of File Formats
5. Nobel Prize or Contamination

**https://soundcloud.com/microbinfie**

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# Questions?

👤 Lee Katz

✉ gzu2@cdc.gov

🐦 lskatz

github.com/lskatz