

Oligonucleotide fingerprint identification for microarray-based pathogen diagnostic assays

Mikk Eelmets

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DNA fingerprints

- Oligonucleotide sequences that uniquely identify a specific genome (specific strain, group of pathogenes, genus ...)
- Fingerprints have been used to develop diagnostic assays (medicine, enviromental monitoring, quality control of food products ...)

DNA fingerprints

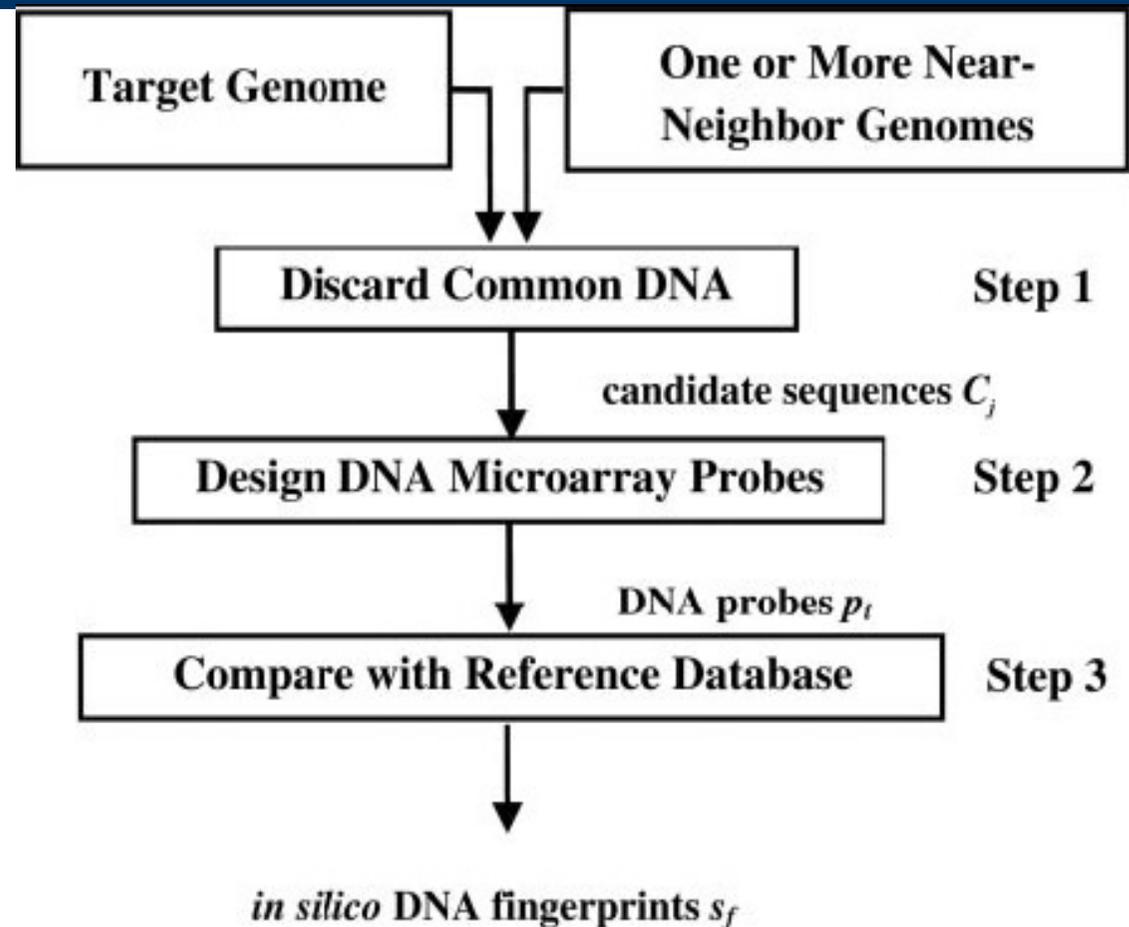
have to satisfy:

1. design constraints, so that they can be used as DNA probes on microarrays
2. specificity constraints, so that they can discriminate, in a microarray hybridization reaction, between target and non-target sequences

TOFI

- Tool for oligonucleotide fingerprint identification
- Implemented on a high-performance computing (HPC) platform

TOFI Algorithm



TOFI Step 1

- Input : target genome and one or more near-neighbour genomes
- Discard DNA sequences common to target and neighbour genomes
- Suffix-tree-based algorithm
- MUMer software

TOFI Step 2

- Microarray probe design
- Imposes a set of constraints (probe length, GC content, self-hybridization ...) to extract DNA microarray probes from the candidate sequence
- Commercial software OMP (oligonucleotide modeling platform)

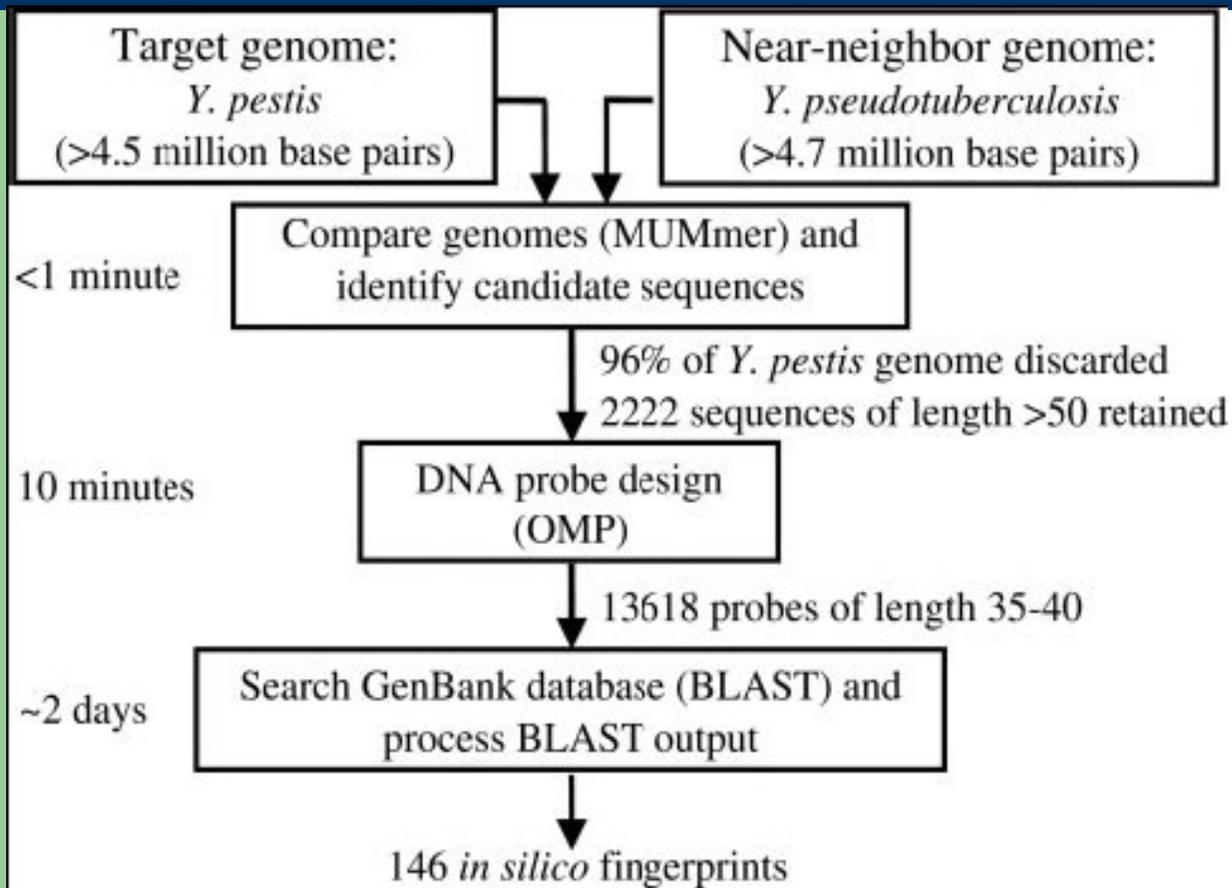
TOFI Step 3

- Specificity determination
- Every DNA probe is aligned with sequence in the reference nucleotide database.
- BLASTN

DNA fingerprints for *Y.pestis*

- Target genome: *Yersinia pestis* strain CO92
- Near-neighbour genome: *Yersinia pseudotuberculosis* strain IP 32953
- After Step 1 - 96% of target genome discarded, 2222 sequence of length > 50
- After Step 2 - 13618 probes of length 35-40
- After Step 3 - 146 *in silico* fingerprints

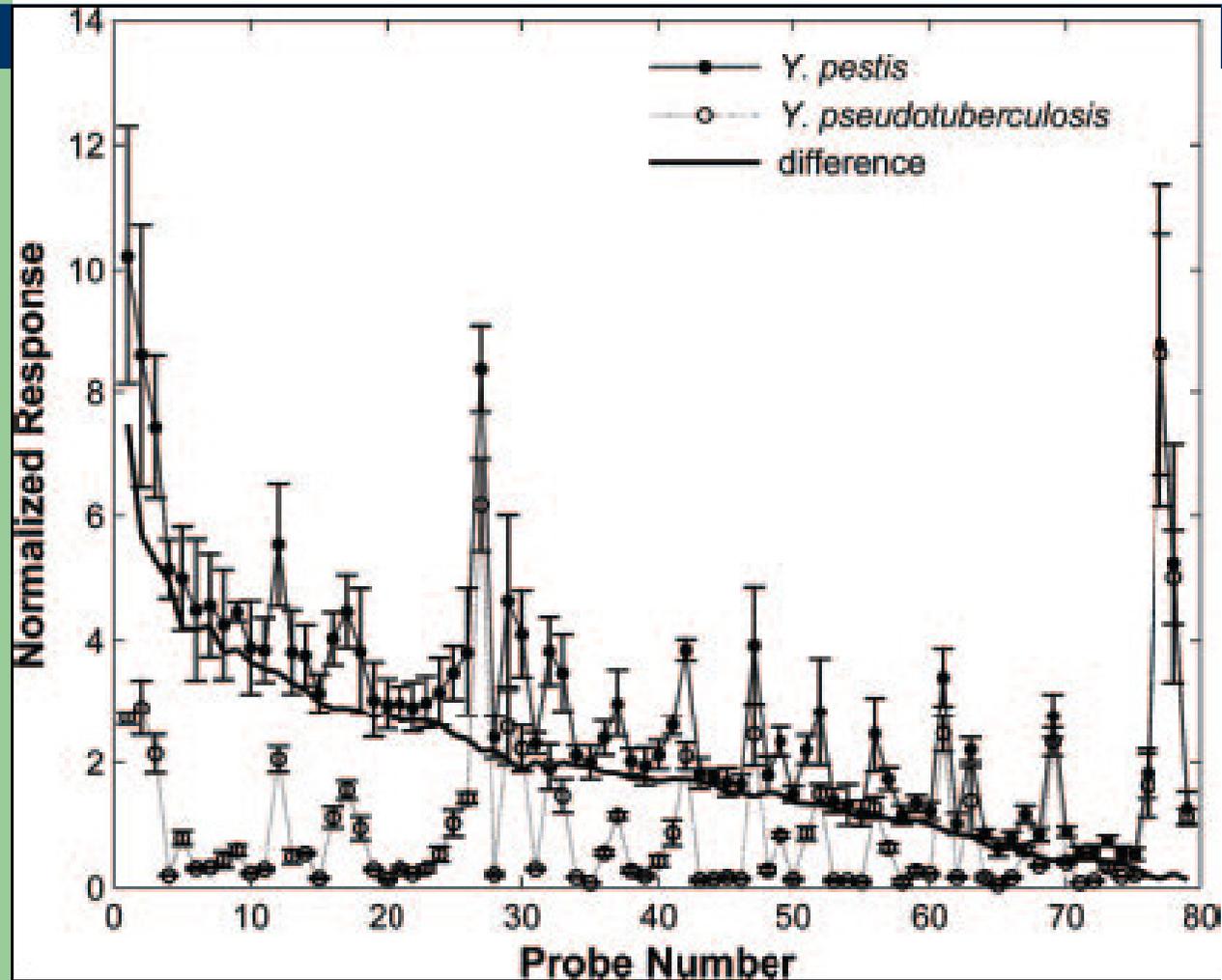
DNA fingerprints for *Y.pestis*



DNA fingerprints for *Y.pestis*

- Further screening leave 99 *in silico* fingerprints for testing
- 10 chips – 6 hybridized with the target genome, 4 with the near-neighbor
- 20 probes produced higher response for near-neighbor than target genome

DNA fingerprints for *Y.pestis*



DNA fingerprints for *F.tularensis*

- Target genome: *Francisella tularensis* strain SCHU S4
- No near-neighbor genome (TOFI first step was omitted)
- 121 *in silico* fingerprints
- 1 probe produced higher response for near-neighbor (*Francisella philomiragia*) than target genome

Reference

Tembe W, Zavaljevski N, Bode E, Chase C, Geyer J, Wasieloski L, Benson G, Reifman J.

Oligonucleotide fingerprint identification for microarray-based pathogen diagnostic assays.

Bioinformatics. 2007 Jan 1;23(1):5-13